

**SCHOOL OF PUBLIC HEALTH, COLLEGE OF HEALTH
SCIENCES, UNIVERSITY OF GHANA, LEGON**

**MALARIA AND HIV INFECTIONS IN PREGNANCY:
MATERNAL, PERINATAL AND INFANT HEALTH ISSUES**

BY

AMOS KANKPONANG LAAR

**THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF
GHANA, LEGON IN PARTIAL FULFILMENT OF THE
REQUIREMENT FOR THE AWARD OF DOCTOR OF
PHILOSOPHY (Ph.D) PUBLIC HEALTH DEGREE**

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DECLARATION

This thesis is composed of my original work. It is the result of an independent investigation under the supervision of Professor Isabella A. Quakyi, Dr. William K. Ampofo, and Dr. Juliette M. Tuakli. Where my work is indebted to the works of others, I have made due acknowledgements.

I have clearly stated the contribution by others to jointly-authored works that I have included in this thesis. I have also clearly stated the contribution of others to my thesis as a whole, including study design, statistical analysis, and any other original research works used or reported in my thesis. The content of my thesis is the result of work I have carried out since my enrollment into the School of Public Health (SPH), College of Health Sciences, University of Ghana, as a higher degree candidate. I have clearly stated which portion of my research has been submitted to qualify for another award.

I declare, therefore that this work has not been accepted in substance for any other degree, nor is it concurrently being submitted in candidature for any other degree.

Statement of Contributions to Jointly-Authored Works Contained in this Thesis:

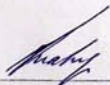
Four jointly-authored works presented at scientific conferences, and one manuscript accepted for publication: I was responsible for the conception, the statistical analyses, the drafting and revision of the papers. All authors read and approved the final documents.

Statement of Contributions by Others to the Thesis as a Whole:

No contributions by others to this thesis, except the tutelage from my supervisors and advisors who have been duly acknowledged.

Statement of Parts of the Thesis Submitted to Qualify for the Award of Another Degree:

Baseline data on 52 HIV-positive pregnant women of the 1,154 study participants enrolled into the study were used in the write up of a Master of Public Health Degree, awarded to me by the University of Ghana in 2005.



Prof. Isabella A. Quakyi

ACADEMIC SUPERVISOR



Dr. William K. Ampofo

ACADEMIC SUPERVISOR



Amos Kankponang Laar

PhD Candidate



Dr. Juliette M. Tuakli

ACADEMIC SUPERVISOR

DEDICATION

To the hundreds of HIV-positive pregnant women from the Manya Krobo District and Tema Municipality who participated in this study, to the several hundreds of HIV-positive women in Ghana, to the millions of HIV-positive women on earth, to the children of these women who have the constitutional and God given right to a better life and future;

&

To Professor Ebenezer Laing, an Emeritus Professor of Botany, University of Ghana, Legon, and to my Son. Amos Ethan Naanbuak Laar, I dedicate this work.

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ABSTRACT

In sub-Saharan Africa, several hundreds of pregnancies are exposed to both malaria and HIV infections annually. Consequences of these infections include maternal anemia, immunosuppression, preterm delivery, low birth weight, low Apgar score, and cord malaria. Unfortunately, these infections in relation to these adverse outcomes are not well characterized in Ghana. This study determined whether maternal malaria and HIV infections during pregnancy are associated with increased risk of these outcomes. The study enrolled 1154 (443 HIV-positive and 711 HIV-negative) women at their first antenatal visit, and prospectively collected data at delivery on 761 mother-infant pairs. Maternal and cord blood malaria parasitemia status were determined using a Rapid Immunochromatographic Test Kit. Hemoglobin concentrations were determined using an automated hematologic analyzer, and CD4+ count determined using the Becton Dickinson FACScount system. This study demonstrates a significantly increased risk of LBW among HIV-positive women who had malaria at recruitment; odds ratio (OR) = 4.4, 95% Confidence Interval [CI] (2.3 – 8.4), at delivery; OR = 2.5, 95% CI (1.1 – 3.7), and at both time points; OR = 11.3, 95% CI (4.6 – 27.4). Women dually-infected with HIV and malaria at both time points had a 4-fold risk of delivering preterm; OR = 3.96, 95% CI (1.8 – 8.5). Neonates with cord malaria were more likely to be born to women dually-infected with HIV and malaria at recruitment and at delivery; OR = 10.5, 95% CI (4.5 – 24.0). Maternal anemia and immunosuppression (as measured by reduced CD4+ count) were significantly associated with maternal infection with malaria and HIV ($p < 0.05$) in each case. These findings suggest that maternal infection with HIV and/or malaria is associated with increased risk of adverse maternal and perinatal outcomes. Routine screening of pregnant women for both malaria and HIV at antenatal visits, and successful treatment of malaria may reduce these adverse outcomes.

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ABU

ACI

ADP

ADP-

AI

AKP

AKP/

AKP/AM

AKP

AKP

AKP/A

AKP

AKP

AKP/

AKP/

AKP

AKP

AKP/

AKP

AKP

AKP

AKP

AKP+AM/1-1

AKP+AM/1-1

AKP+AM/1-1

AKP+AM/1-1

LIST OF ABBREVIATIONS

AFASS	Acceptable, feasible, affordable, sustainable, safe
AGH	Atua Government Hospital
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal clinic
ANOVA	Analysis of Variance
AOR	Adjusted Odds Ratio
ART	Antiretroviral therapy
ARV	Antiretroviral
BMI	Body Mass Index
BWT	Birth weight
CD4+	CD4+ T cell count
CI	Confidence Interval
CMP	Umbilical cord malaria parasitemia
DHMT	District Health Management Team
DITRAME	Diminution de la Transmission Mère-Enfant du VIH (study)
dl	Deciliter
EBF	Exclusive breast feeding
EDTA	Ethylenediaminetetraacetic acid
ERF	Exclusive replacement feeding
FA	Fetal anemia
FPRO	Food Processor Plus
FU	Follow-up
GHS	Ghana Health Services
GLM	Generalized Linear Model
HAART	Highly Active Antiretroviral Therapy
Hb	Hemoglobin
HIV	Human Immunodeficiency Virus
HIV+	Human Immunodeficiency positive
HIV-	Human Immunodeficiency negative
HIV-&M[r-d-]	women with no HIV, & also no malaria both at recruitment and at delivery
HIV-&M[r+d-]	women with no HIV, but malaria positive at recruitment & not at delivery,
HIV+&M[r-d+]	women with HIV, no malaria at recruitment but malaria positive at delivery,
HIV+&M[r+d+]	HIV-positive women with malaria positive both at recruitment and at delivery

IFN- β	Interferon beta
IPTp	Intermittent preventive treatment of malaria in pregnancy
IRB	Internal Review Board
IUGR	Intra Uterine Growth Retardation
LAS	Low Apgar score
LBW	Low birth weight
LIF	Leukocyte inhibitory <i>factor</i>
ml	milliliter
MOH	Ministry of Health
MTCT	Mother-to-Child Transmission of HIV
MUAC	Mid-upper arm circumference
NACP	National AIDS Control Program for Ghana
NMIMR	Noguchi Memorial Institute for Medical Research
OIs	Opportunistic infections
OPD	Outpatient Department
OR(s)	Odds ratio(s)
PFRH	Population, Family, and Reproductive Health
PMTCT	Prevention of Mother-to-Child Transmission of HIV
PTD	Preterm delivery
SB	Stillbirth
SE	Socio-economic
SES	Socio-economic status
SP	Sulfadoxine–Pyrimethamine
SPH	School of Public Health
SPSS	Statistical Package for Social Scientists
STI	Sexually Transmitted Infections
TALIF	Teaching and Learning Innovation Fund
TB	Tuberculosis
TDC	Tema Development Council
TGH	Tema General Hospital
TMA	Tema Municipal Assembly
TNF- α	Tumor necrosis factor alpha
TSF	Triceps skinfold thickness
UN	United Nations

UNAIDS	Joint United Nations Program on HIV and AIDS
UNICEF	United Nations International Children's Educational Fund
VCT	Voluntary Counseling and Testing
WHO	World Health Organization
ZEBS	Zimbabwe Exclusive Breastfeeding Study
ZVITAMBO	In local Shona language, means "precious" or "very valuable"

DEFINITIONS

Adverse perinatal outcome: incidence of any of the four events (preterm delivery, low birth weight, umbilical cord blood malaria parasitemia, low Apgar score)

Exclusive breastfeeding (EBF): giving the infant no other food or drink, not even water, apart from breastmilk (including expressed breastmilk), with the exception of drops or syrups consisting of vitamins, mineral supplements or prescribed medicines

High morbidity profile: presentation with four or more symptoms of morbidity conditions at recruitment.

Low Apgar score: average Apgar score < 7

Low birth weight: birth weight < 2500g

Malaria infection at one time point: *P. falciparum* malaria parasitemia either at first antenatal visit or at delivery

Malaria infection at two time points: *P. falciparum* malaria parasitemia both at first antenatal visit and at delivery.

Maternal anemia: hemoglobin concentration < 11 g/dl

Maternal immunosuppression: maternal CD4+ T cell count < 350 cell/mm³

Maternal moderately severe anemia: hemoglobin concentration < 9 g/dl

Mixed feeding: giving a baby some breastmilk and also any other fluid or feeds, even a teaspoon of water

Preterm delivery: birth before 37 completed weeks of gestation

Recent fever: axillary temperature of >37.5 degrees centigrade at the time of enrollment or a history of fever with the previous two weeks

Replacement feeding : the process of feeding a child who is not receiving breastmilk with a diet that provides all the nutrients the child needs, until the child is fully fed on family foods

Umbilical cord malaria parasitemia: the presence of *P. falciparum* in cord blood at delivery

Very low birth weight: birth weight < 1500g

APPENDICES

Appendix 1. Sample informed consent form

Appendix 2. Two-phased structured questionnaire

Appendix 3. Semi-structure questionnaire on infant feeding choices/behavior

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Appendix 11a. Infant feeding behavior by level of education

Appendix 11b Infant feeding behavior by place of residence

Appendix 11c Infant feeding behavior by marital status

Appendix 11d Infant feeding behavior by disclosure of HIV-sero status to husband/cohabitant

Appendix 11e Infant feeding behavior by marital status

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Appendix 12. Disseminations and utility of preliminary findings of study

Appendix 12a A paper presented at the 1st Annual College of Health Sciences Scientific Conference, Accra International Conference Center, September 26-28, 2007

Appendix 12b. A paper presented at the 2nd National HIV/AIDS Research Conference (NHARCON), 3-5 March 2008, La Palm Royal Beach Hotel, Accra, Ghana.

Appendix 12c. A paper presented at the 2nd Annual College of Health Sciences Scientific Conference, Accra International Conference Center, September 24-26, 2008

Appendix 12d. A conference paper to be presented at the 19th International Congress of Nutrition scheduled to take place in Bangkok from 4th – 9th October 2009

Appendix 12e A manuscript accepted for publication: Journal of AIDS and HIV Research

CHAPTER ONE

1.0 INTRODUCTION

This chapter gives the background to the study, presents a summary of the epidemiology of HIV and malaria, and the evidence regarding HIV-malaria interactions in pregnant women for whom the likely overall public health impact is manifold. Following this is the study's conceptual framework, the statement of the problem/justification for the study, the research questions, the research hypotheses, and objectives.

1.1 Background

Malaria in pregnancy has long been shown to be one of the most important preventable causes of adverse perinatal outcomes worldwide. It is also a major cause of poor maternal health contributing to maternal mortality. It is estimated that 40% of the world's pregnant women are exposed to malaria infection during pregnancy (Shulman and Dorman, 2003). Other estimates show that over 500 million people globally suffer from severe malaria-related illnesses annually (Na-Bangchang and Congpuong, 2007). Most of these cases and the deaths associated with them are in sub-Saharan Africa, where pregnant women and children under five years of age bear most of the brunt. In such settings, where repeated exposures to the parasite confer semi-immunity, malaria infection during pregnancy may show no symptoms in the mother but can result in adverse perinatal outcomes for the unborn baby, including low birth weight (LBW), preterm delivery (PTD), still birth (SB), cord blood malaria parasitemia (CMP), fetal anemia (FA), and low Apgar score (LAS).

Some of these complications have been shown by various studies (Ayisi et al., 2003; Ticconi et al., 2003; ter Kuile et al., 2004; Kublin et al., 2005; Noble et al., 2005; Slutsker and Marston, 2007) to be compounded if the malaria parasitized pregnant woman is infected with

the Human Immunodeficiency Virus (HIV) as well. For these reasons, HIV-infected pregnant women living in malaria endemic areas form a special group that needs special attention. HIV for example has serious implications on infant feeding given that the virus can be transmitted through breastfeeding (Adejuyigbe et al., 2008; Akue et al., 2000; Aleem et al., 2001; Avila et al., 2000; Balsekar, 1996; Becquet and Leroy, 2005; Bertolli et al., 1996; Bezner Kerr et al., 2008; Biddulph, 1989; Brierley et al., 1988; Colebunders et al., 1988).

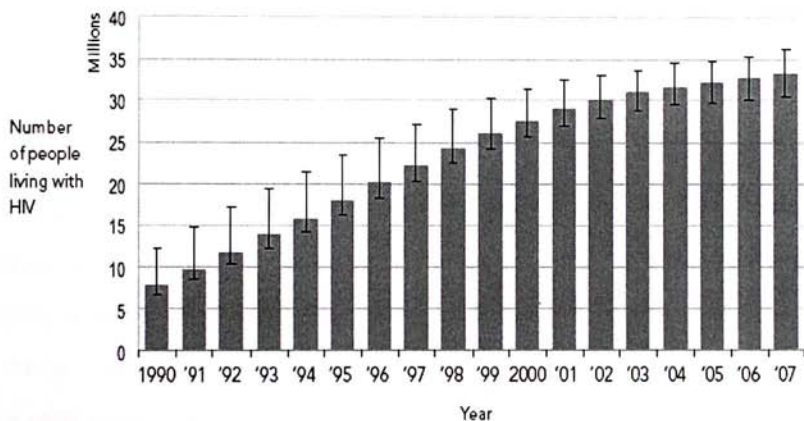
1.1.1 The epidemiology of malaria and HIV: a global overview

Global health experts have long recognized that malaria and HIV represent significant health risks to all mankind. Malaria, is said to cause approximately 500 million clinical cases and one million deaths each year, 90% of them in sub-Saharan Africa (Snow, 2005). A considerable proportion of these deaths occur amongst African pregnant women and children under five years of age (Na-Bangchang and Congpuong, 2007).

Even though, advances in the methodology of estimations of HIV epidemics applied to an expanded range of country data in 2007 resulted in substantial reductions in estimates of numbers of persons living with HIV worldwide, the numbers to that date were still high. The estimated number of persons living with HIV worldwide in 2007 according to the Joint United Nations Program on HIV/AIDS (UNAIDS) was 33.2 million, a reduction of 16% compared with the estimate published in 2006 (UNAIDS, 2007). Even though the 2007 report showed that, global HIV prevalence appeared to have leveled off; the number of people living with HIV had risen to 33.2 million in 2007 from 29.0 million in 2001 (Figs 1.1 and 1.2). This seemingly paradoxical phenomenon is explained by the very nature of this epidemiologic measure – prevalence. The measure takes into consideration both the existing and the new

HIV infections. With the increasingly high uptake of life-saving antiretroviral treatment, the numbers of HIV-positive persons dying as a result of AIDS is declining. Sub-Saharan Africa remains the most affected region throughout the world according to this report. The trajectory of the epidemic from 1990 to 2007 is presented in Fig 1.1 below.

Fig 1.1 Estimated number of people living with HIV globally 1990-2007¹



┌ This bar indicates the range around the estimate.

Source: UNAIDS/WHO, 2007

1.1.2 The epidemiology of malaria and HIV: regional overview

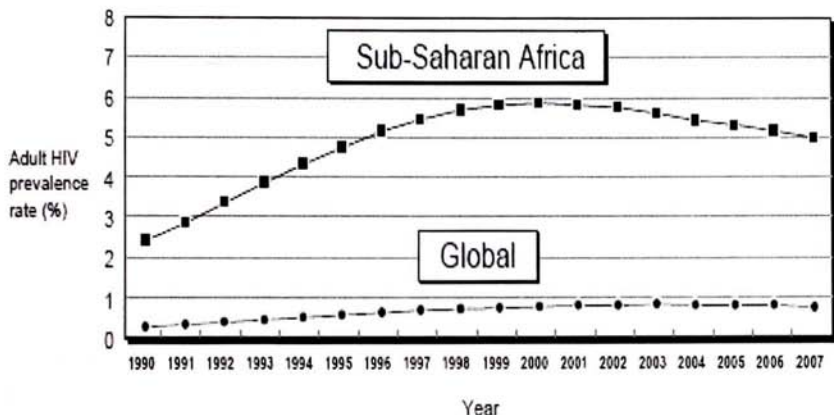
In sub-Saharan Africa, malaria during pregnancy has for several decades been a major public health problem. Currently an estimated 24 million pregnant women in Africa are said to be at risk of *P. falciparum* malaria (Desai *et al.*, 2007). For over two decades now, HIV has also emerged as a major problem in many of these malaria endemic areas of sub-Saharan Africa, where close to 23 million adults and children are living with HIV. This accounts for over two-

¹ These are the adjusted estimates derived from the introduction of the new and advanced methodologies in 2007.

third of the world's 33.2 million HIV-infected persons (UNAIDS, 2007). The region is also home to close to 90% of the 2.5 million children living with HIV globally. Almost all nations in this region have generalized HIV epidemics. In other words, the epidemic in most of these nations has beyond the high-risk behavior population groups such as commercial sex workers, men who have sex with men, long distance commercial car drivers. It also means the prevalence of HIV among pregnant women is above one per cent. Unlike other regions, the majority of people (61%) living with HIV in this region are women (UNAIDS, 2007).

The continent's epidemic, however, vary significantly in scale, with national adult (15–49 years) HIV prevalence, ranging from less than 2% in some countries of the Sahel to above 15% in most of southern Africa. Even though in sub-Saharan Africa, adult HIV prevalence declined from 5.8% in 2001 to 5.0% in 2007, AIDS continues to be the single largest cause of mortality in the region (UNAIDS, 2007). Of the global total of 2.1 million adult and child deaths due to AIDS in 2007, 1.6 million occurred in sub-Saharan Africa. Such high mortality rates could be attributed to the very low access to life-saving antiretroviral agents in this region. Presented in Fig 1.2 is a comparison of the global adult HIV prevalence to that of sub-Saharan Africa from 1990 to 2007.

Fig 1.2. Estimated adult HIV prevalence rate (%) globally and in sub-Saharan Africa, 1990-2007

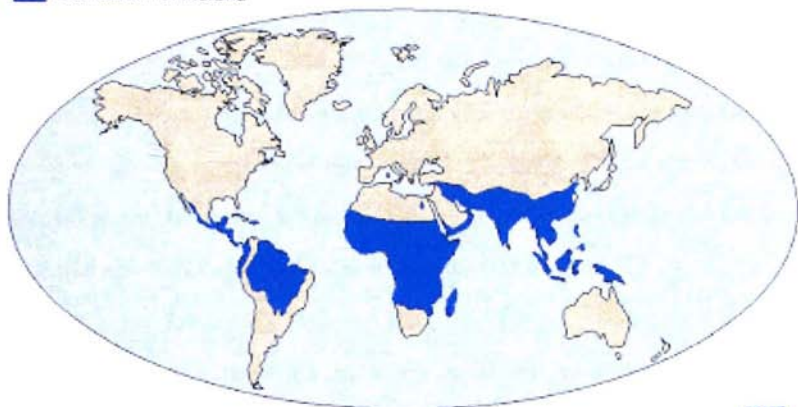


Source: UNAIDS, 2007

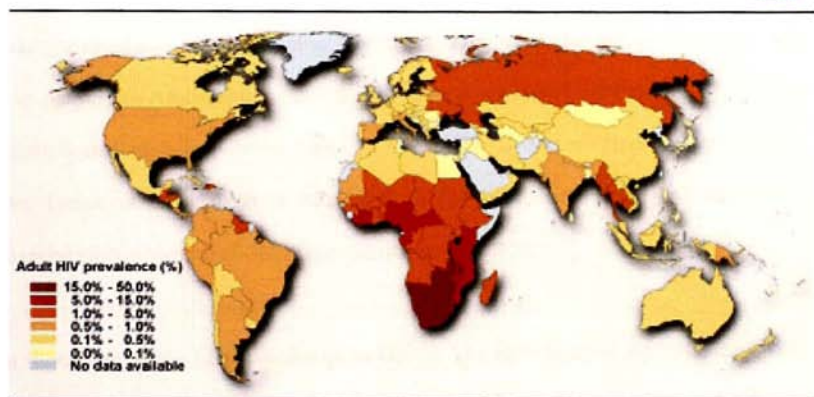
Figure 1.2 above presents the magnitude of HIV and malaria infections in the sub-Saharan Africa. Fig 1.3 updated from the Centers for Disease Control and Prevention (CDC) reveals that most of the sub-Saharan countries which have malaria as a public health problem also have HIV as a serious public health challenge (CDC, 2004; UNAIDS, 2007). This is sometimes described in technical terms, as a “the geographic overlap between HIV and malaria”

Fig 1.3 Geographic overlap between HIV and malaria in the African continent²

■ Distribution of Malaria



CDC



Source: Centers for Disease Control and Prevention, UNAIDS/WHO

1.1.3 The epidemiology of malaria and HIV: local overview

In Ghana, malaria is a major public health problem especially among pregnant women and children under five years of age. The disease is estimated to cause 80% of all deaths certified by medical professionals, 44% of all out-patient attendances, and 22% of all deaths in children

² Malaria and HIV are leading causes of morbidity and mortality in sub Saharan Africa. Both diseases are highly endemic and have a wide geographic overlap.

younger than five years of age (MOH, 2006). This, however, does not escape my speculation that the statistics may be underestimating the problem since the majority of infections are treated at home and go thus unreported (Owusu-Agyei *et al.*, 2007). Over one third of all inpatient admissions are due to severe malaria. This on the other hand could also be an overestimation of the problem due to possible misdiagnosis of the condition.

The Malaria Control Program of the Ghana Health Service, is however very active in reducing the burden of malaria in the population. In response to research demonstrating high levels of malaria parasite resistance to Chloroquine, the national drug policy for malaria treatment was changed to Artesunate-Amodiaquine (an effective artemisinin-based combination therapy) to treat uncomplicated malaria (Owusu-Agyei *et al.*, 2007). Ghana adopted the Intermittent Preventive Treatment for malaria in pregnancy (IPTp) with three doses of Sulfadoxine-Pyrimethamine (SP) at the end of 2004 (Hommerich *et al.*, 2007).

HIV is a significant public health challenge in Ghana. The HIV Sentinel Surveillance by the National AIDS Control Program (NACP) reported annual HIV sero-prevalence of 4.0% in 1992, 2.3% in 2000, 3.2% in 2006 and 2.6% in 2007 (NACP, 2008)³.

In the two districts that this study was conducted, both malaria and HIV are recognized public health problems. The Manya Krobo District is one of the highest HIV affected districts in Ghana according to HIV Sentinel Surveillance data. HIV prevalence rates in the district ranged from 18% in 1992 to 8.9% in 2007 (NACP, 2008)⁴. Available data from the District Health Management Team (DHMT) show that malaria has since the year 2000 been a major

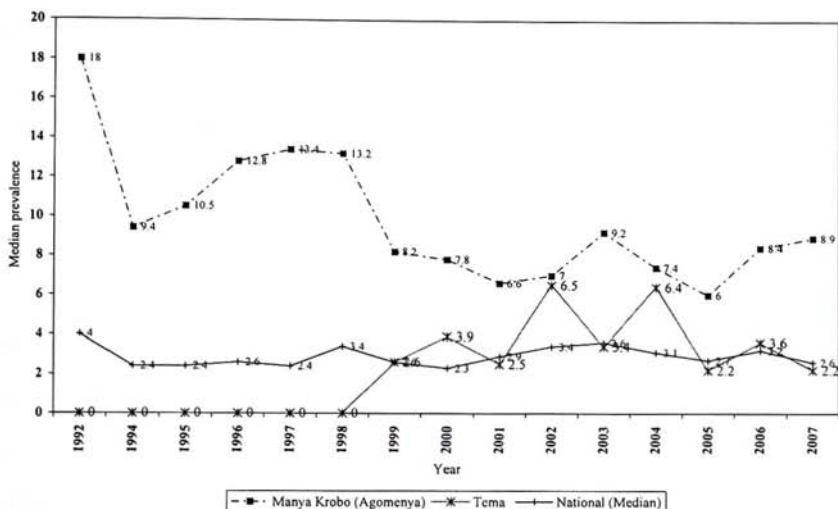
³ Details of trend of HIV prevalence can be seen in Fig 1.4.

⁴ Details of trend of HIV prevalence can be seen in Fig 1.4.

public health problem in this district. It has consistently been one of the top ten cases presenting at the out-patient department (OPD) and also number one of the top ten causes of admission and the second top cause of death after HIV disease (District-Health-Directorate-Many-Krobo, 2000 - 2006).

The Tema Municipality is part of the Greater Accra Region. Malaria and HIV have consistently been among the top causes of admissions and death respectively from 2002-2006 in this Municipality (Tema-Municipal-Health-Administration, 2002-2006). Available data on the HIV prevalence rates in the Municipality show a range from 2.6% in 1999, 6.5% in 2002, 3.6% in 2006, and 2.2% in 2007 (NACP, 2008). Fig 1.4 shows the trends of HIV prevalence in the Tema Municipality, and the Manya Krobo District against the national median. A review of various annual reports of the Tema Municipal Health Directorate also found malaria at the top of cases presented at OPDs, or admission, and in 2006 was in position six of the top ten causes of death (Tema-Municipal-Health-Administration, 2002-2006). Clearly, these two diseases are major public health problems in the Manya Krobo District, and the Tema Municipality.

Fig 1.4 HIV prevalence trends in Tema⁵ and Manya Krobo against the National median



1.2 The conceptual background to the study

This subsection examines how malaria and HIV infections during pregnancy can individually or jointly mediate their effects on maternal and perinatal health outcomes. Fig 1.5 summarizes how adverse maternal and perinatal outcomes are mediated in women with HIV, and malaria infections and predicts events that probably take place in HIV-positive immunosuppressed hosts that result in these outcomes.

HIV-uninfected or HIV-infected women who are relatively immunocompetent have normal levels of CD4+ T cells (>500 cells/ml of blood). These women can mount protective immune responses when exposed to malaria infection, and this can limit malaria and other infections. Malaria infection (at low density) can induce and sustain the production of the protective cytokine Interferon gamma (IFN- γ). At the same time, protective immune factors such as

⁵ HIV Sentinel Surveillance did not start in Tema until 1999; explaining the no records/zero prevalence from 1992 to 1998

Leukocyte inhibitory factor (LIF) that can reduce HIV-1 replication is also produced. Thus, relative levels of protective immune factors that can suppress viral replication are at high concentrations. Consequently, the adverse event may be much lower in these women (Ned *et al.*, 2005).

However, women who are relatively immunosuppressed, including those with low levels of CD4+ T cells, have a reduced ability to mount a protective immune response to limit either malaria or other infections. Consequently, these women might experience severe clinical malaria and other opportunistic illnesses, which can favor overproduction of cytokines such as Tumor necrosis factor alpha (TNF- α). This will, in turn, further enhance HIV-1 replication. Additionally, the low level of protective immune factors (IFN- γ , and, possibly, LIF) is not adequate to control HIV-1 viral replication, leading to higher viral load. All these can culminate in adverse outcomes both in the woman and her unborn baby (Ned *et al.*, 2005).

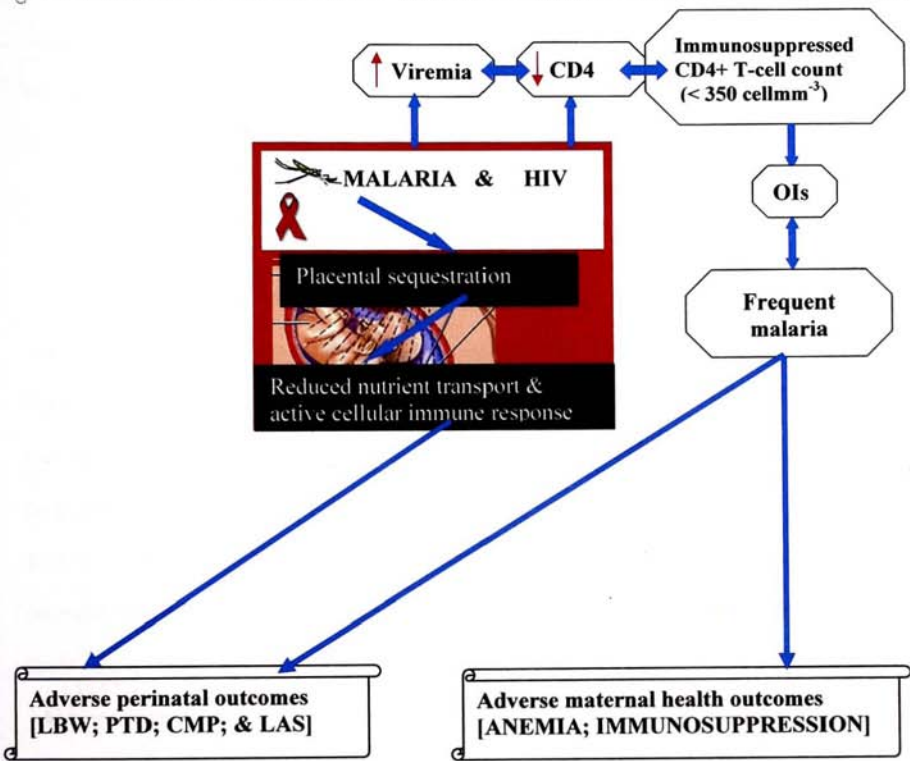
According to De Silva and colleagues cord blood may become infected with malarial parasites through maternal transfusion into fetal circulation either at the time of delivery or during pregnancy, direct penetration through the chorionic villi, and penetration through premature separation of the placenta (De Silva *et al.*, 1982). However, the effectiveness of the placenta to restrain malaria parasite passage to the fetus and the remarkable capacity of the fetus to resist infection has been demonstrated (Miller and Telford, 1996). The resistance may reflect among other things a) the physical barrier of the placenta to infected red cells, b) the passive transfer of maternal antibodies, c) the poor environment afforded by the fetal red cells for plasmodial replication (De Silva *et al.*, 1982; Miller and Telford, 1996). A free passage

therefore probably means that placental barriers are no more very effective when infected with malaria, and/ or HIV.

With respect to LBW, malaria is thought to reduce birth weight through a combination of systemic and local effects (Menendez *et al.*, 2000). These include malaria-induced anemia, and or, the effects of placental infection (Ibhanesebhor and Okolo, 1992; Okoko *et al.*, 2002; Kassam *et al.*, 2006). There is still no agreement as to the main mechanisms mediating reduction in birth weight in placental malaria (Menendez *et al.*, 2000). But a high density parasitemia, chronic infection in the placental blood, and the associated cellular immune response may result in the consumption of glucose and oxygen that would have gone to the fetus. Histopathologic studies of infected placentas have also found thickening of the cytotrophoblastic membranes which may interfere with nutrient transport to the fetus, subsequently leading to LBW (Ismail *et al.*, 2000; Guyatt and Snow, 2004).

Although the precise effect of malaria-parasitized placenta on PTD is uncertain, malaria-infected placentas according to some authorities have been shown to frequently carry antibodies, cytokines and macrophages which are indicative of active immune-response, and this response may stimulate early labor (Ismail *et al.*, 2000; Guyatt and Snow, 2004).

Fig 1.5 Conceptual Frame work: The known & probable mechanisms mediating the influence of malaria and HIV infections on maternal and perinatal outcomes



OIs = Opportunistic infections/illnesses

Source: The Investigator.

1.3 Statement of the problem, and justification for the study

This study addressed two main issues. First, there is a dearth of data on the influence of malaria and HIV infections on maternal anemia, immunosuppression, preterm delivery, low birth weight, low Apgar score and cord malaria in Ghana. Also addressed is the issue of paucity of local data on the choices, experiences, and challenges HIV-positive mothers face in implementing their infant feeding intentions.

Elsewhere studies have shown that HIV infection has the potential to impair both cellular (Moore et al., 2003; Ned et al., 2005) and humoral (Ayisi et al., 2003; Mount et al., 2004) immune responses to malaria. In consequence, co-infection with HIV and malaria during pregnancy results in increased parasitemia (Steketee *et al.*, 1996b), high incidence of clinical malaria (Whitworth *et al.*, 2000) maternal anemia (ter Kuile *et al.*, 2004), and adverse perinatal outcomes (Ticconi et al., 2003; Knight and Plugge, 2005; Villamor et al., 2005; Szyld et al., 2006). At present, there is no data regarding the influence of HIV and malaria infections in pregnancy on maternal, perinatal, and infant health in the Ghanaian setting.

Before the advent of HIV, infancy was acknowledged as the stage of life when initial contact with and orientation to foods typical of one's culture were established (Phillips, 2007). Today, infant feeding in the context of HIV is a subject of serious worry in settings like Ghana where breastfeeding is normative. Nurse-counselors are expected to counsel HIV+ women on safer infant feeding methods as defined in national and international guidelines. The international guidelines informing infant feeding counseling suggest that where it is acceptable, feasible, affordable, sustainable and safe (AFASS), replacement feeding should be adopted and breastfeeding avoided (WHO *et al.*, 2003). Acknowledging the fact that infant feeding choices

may not just be based on knowledge of medical risks of MTCT of HIV, but may be informed by the cultural usages and nuances of the community, this study explored HIV-positive women's choices, experiences and practices as it relates to infant feeding in the social and cultural context of the Manya Krobo and Tema areas. Documentation of this information will contribute to our understanding of the relevance of the various infant feeding options available to HIV-positive mothers in Ghana.

1.4 Research questions

This study thus investigated the following research questions:

- i. Are *P. falciparum* malaria and HIV infections among Ghanaian pregnant women associated with increased risk of low birth weight, preterm delivery, low Apgar score, and cord malaria parasitemia?
- ii. Are *P. falciparum* malaria and HIV infections among Ghanaian pregnant women associated with increased risk of maternal anemia, and immunosuppression?
- iii. What choices do HIV-positive women in the Manya Krobo and Tema areas make regarding infant feeding?
- iv. What challenges do they face in implementing their feeding options?
- v. What experiences can they share regarding HIV and infant feeding?

1.5 Study hypotheses⁶

The research addressed two key issues with regard to the influence of malaria and HIV infections on maternal and perinatal health. The central matter of these issues in the form of research hypotheses are stated as follows:

- (i) Newborns of mothers infected with malaria and HIV during pregnancy are at increased risk of low birth weight, preterm delivery, low Apgar score, and cord malaria parasitemia;
- (ii) Women infected with malaria and HIV during pregnancy are at increased risk of anemia, and immunosuppression.

1.6 Study objectives

1.6.1 Primary objectives

The study specifically determined:

- i. The associations between malaria-HIV co-infection during pregnancy and low birth weight, preterm delivery, low Apgar score, and cord malaria parasitemia ;
- ii. The associations between malaria and HIV infections during pregnancy and anemia, immunosuppression.

1.6.2 Secondary objective

The study also investigated:

- iii. The infant feeding choices, experiences, and infant feeding-related challenges faced by HIV-positive mothers in the Manya Krobo District and Tema Municipality.

⁶ Considering the goal of the "infant feeding choices/experiences of mothers, an a priori statement of testable hypothesis was unnecessary. This phase of the study sought to document the infant feeding choices and experiences of HIV-positive mothers so as to guide other HIV-positive women in choosing and implementing their infant feeding aspirations within their cultural milieu.

CHAPTER TWO

2.0 LITERATURE REVIEW

This chapter presents pertinent literature taking into consideration, the objectives of the study. It covers the following thematic areas: mounting evidence on the interactions between HIV and malaria in pregnancy, maternal morbidity and mortality in relation to malaria and HIV infections, and adverse perinatal outcomes among HIV-positive women in relation to malaria. The chapter concludes with a look at the current recommendations on infant feeding in the context of HIV, and the challenges faced by HIV-positive mothers in feeding their infants.

2.1.0 Malaria in pregnancy in the era of HIV: over two decades of mounting evidence

Malaria and HIV infections unarguably are the two most devastating health problems in sub-Saharan Africa. Malaria is estimated to be responsible for more than a million deaths per year globally, with 90% of these deaths in sub-Saharan Africa (Snow, 2005). In 2007, HIV/AIDS was estimated to have caused the deaths of over two million people worldwide, of whom 1.6 million lived in Africa (UNAIDS, 2007). Both diseases are endemic and have been shown to have a wide geographic overlap in the sub-Saharan region of Africa (Fig 1.3).

Acknowledging this geographic overlap between malaria and HIV infections in the African setting, concerns about the potential interactions between these two infections and the public health implications thereof were raised over two decades ago (Nguyen-Dinh et al., 1987; Allen et al., 1991; Greenberg et al., 1991). However, these early studies did not indicate any direct interactions between these two infections. For instance, the study by Nguyen-Dinh *et al.* (1997) and that of Greenberg and colleagues (1991) demonstrated that malaria parasitemia and clinical outcomes were independent of HIV status. Allen et al. (1991) in their study with

childbearing women in Rwanda also reported similar finding where malaria parasitemia in women was independent of HIV status. In a related study in Malawi, the prevalence of parasitemia appeared to be raised in only HIV-infected multigravids whereas parasite density was parity independent (Steketee *et al.*, 1996a). The authors in explaining this, speculated that HIV might be affecting the immune memory mechanism responsible for the parity-dependent acquisition of antimalarial immunity in pregnancy. This was later confirmed by Parise *et al.* (1998).

In 1998, Chandramohan and Greenwood reviewed several clinical studies on the interactions between HIV and malaria published to that date (Chandramohan and Greenwood, 1998). Their review showed a failure to demonstrate any convincing and consistent link between HIV and malaria, with the exception of an increased rate of placental malaria in HIV-infected pregnant women as reported by Steketee *et al.* (1996a).

Following this, Whitworth and colleagues in 2000, illuminated the effect of HIV on malaria parasitemia among rural Ugandan adults. They reported that clinical malaria was significantly more common among HIV+ adults and the odds of having clinical malaria increased with falling CD4+ cell count and advancing clinical stage. HIV infection they concluded was associated with an increased frequency of clinical malaria and parasitemia (Whitworth *et al.*, 2000).

Since these initial investigations, other potential ways in which malaria and HIV infection could interact have been suggested. Pieces of evidence have emerged such as more peripheral and placental parasitemia, higher parasite densities, more clinical malaria, more anemia, and increased risks of adverse birth outcomes (Grimwade *et al.*, 2004; Mwapasa *et al.*, 2004).

Data from a study by Mwapasa and colleagues (2004) in Malawi showed that placental HIV viral load was increased in women with placental malaria, especially those with high parasite densities. Other research findings have also shown that co-infection with malaria and HIV makes malaria in pregnancy more severe by impairing the ability of women to control the illness, resulting in increased frequency of clinical symptoms. These reports point accusing fingers at Malaria and HIV as culprits of the increased risk of adverse health outcomes found in co-infected pregnant women (Mount et al., 2004; Mwapasa et al., 2004; Hewitt et al., 2006).

Research on the interactions between malaria and HIV have continued to date. Currently, there is a plethora of scholarship on the influence of HIV or malaria infections on maternal and perinatal health. These studies reveal that these infections independently or collectively adversely affect maternal and perinatal health (Brocklehurst and French, 1998; Ellis et al., 2002; Ayisi et al., 2003; Ticconi et al., 2003; Abrams et al., 2004; Ayisi et al., 2004; Mount et al., 2004; ter Kuile et al., 2004; Noble et al., 2005; Villamor et al., 2005; Uneke, 2007b, 2007a). This apparent departure of findings of recent studies from those of the initial investigations may be attributed to increasing refinement in the research designs and also the advancement in the techniques employed in detecting both malaria and HIV.

The above findings were echoed by a recent systematic review which summarized the accumulating evidence on the interactions between HIV and malaria (Slutsker and Marston, 2007). The summary was that, adults with advanced HIV infection may be at risk for failure of malaria treatment, especially with sulfa-based therapies. This particular review may have some programmatic or policy implication especially in Ghana where sulfa-based preparations, for instance SP is currently being deployed as an IPTp irrespective of HIV status (Hommerich et al., 2007).

A related review mostly on studies from sub-Saharan Africa showed that LBW was associated with malaria in pregnancy and is estimated to result in 100,000 infant deaths in Africa each year (Desai *et al.*, 2007). It was postulated that successful prevention of these infections (malaria and HIV) could reduce the risk of low birth weight by 43% and perinatal mortality by 27% among paucigravidae.

2.2 .0 Malaria and HIV infections and maternal morbidity and mortality

More than half of the 33 million people who were living with HIV in 2007 were women (UNAIDS, 2007) while about 40% of the world's pregnant women were exposed to malaria infection during pregnancy (Shulman and Dorman, 2003). However, the extent of the contribution of these infections particularly HIV to maternal morbidity and mortality is difficult to quantify, as the HIV status of pregnant women is not always known.

Even though there is no indisputable evidence on the specific contributions of each of these infections on maternal mortality, various researchers have hypothesized that these infections may influence maternal mortality in several ways. For example, women living with HIV and AIDS according one recent publication may be more susceptible to direct or obstetric causes of maternal mortality, such as post-partum hemorrhage, puerperal sepsis and complications of caesarean section (Bansil *et al.*, 2007). In the past, direct obstetric causes have been responsible for most of the deaths of mothers, with the majority attributed to hemorrhage, hypertension, obstructed labor and abortion complications (WHO and UNICEF, 1996). This pattern is changing in many places, as AIDS-related complications now account for a high proportion of maternal deaths (McIntyre, 2005). Currently, AIDS and malaria have become

more important as causes of maternal morbidity and mortality particularly in developing countries (McIntyre, 2005; Desai et al., 2007; Walson et al., 2007).

Several studies in Africa have demonstrated the increasing role of AIDS and related illnesses as causes of maternal mortality. Some of these studies linked maternal mortality to infections such as malaria (Ampofo, 1969) whilst others linked it to HIV (Tannenbaum, 1992; Taha et al., 1996; Ahmed et al., 1999). In particular a Zambian study reported an eight-fold increased risk of maternal death over a period of two decades, despite better obstetric services (Ahmed et al., 1999). Indirect causes of maternal mortality were responsible for 58% of deaths, with malaria and AIDS-related tuberculosis the most common. In another study in the Rakai district of Uganda that looked at the impact of HIV on maternal mortality reported that, maternal mortality was five times higher in HIV-positive women than in HIV- women (Sewankambo et al., 2000). In Malawi and Zimbabwe, pregnancy-related mortality was doubled, in parallel with the increasing AIDS epidemic (Bicego et al., 2002). AIDS-related deaths were the primary cause of death in mothers in Brazzaville in 1993 (Iloki et al., 1997). According to some UN agencies, Ghana's maternal mortality rate was estimated to be 740 per 100,000 live births while the Ministry of Health calculates this to be 214 per 1,000 live births (WHO and UNICEF, 1996). This huge difference in the rate could be due to a number of factors including lack of standardization in the methods used for data collection, and also differences in the level of sophistication in the methods. As in many other African countries, there is the lack of data in Ghana regarding the specific contributions of malaria, HIV and AIDS to maternal mortality. As a result of the above problems, the data available currently are not only outdated, they are uncontrolled, and possibly biased.

With respect to maternal morbidity, an interaction between HIV-1 and malaria in pregnancy, causes more peripheral and placental parasitemia, higher parasite densities, more clinical malaria, more anemia, and increased risks of adverse birth outcomes (ter Kuile *et al.*, 2004). Even though HIV-infected women are susceptible to the effects of malaria, pregnant women are particularly vulnerable. Co-infection according to Mwapasa *et al.* leads to greater levels of anemia, and placental malaria (Mwapasa *et al.*, 2004). Usually in women who are not HIV positive, primigravidae are more likely to develop severe or complicated malaria. In HIV positive pregnant women, studies have shown that women of all gravidae are at risk of severe malaria (ter Kuile *et al.*, 2004). This HIV-associated risk of malaria is, however, greater in multigravidae suggesting that HIV affects the immune memory mechanism responsible for the parity-dependent acquisition of antimalarial immunity in pregnancy (Mount *et al.*, 2004). van Eijk *et al.* (2003), alternatively explain that, multigravid women without a doubt have longer sexual experience and may be more immunosuppressed because they have been infected with HIV longer than younger primigravid women. Thus, HIV alters the typical gravidity specific pattern of malaria risk by shifting the burden from primarily primigravidae and secundigravidae to all pregnant women.

HIV-infected persons are at increased risk of clinical malaria; the risk is greatest when immune suppression is advanced (Kublin *et al.*, 2005). Whitworth and Hewitt also suggest an increased risk of symptomatic malaria among people with AIDS (Whitworth and Hewitt, 2005). In a study by Ticconi *et al.* (2003), to investigate the effect of isolated or concomitant infection with malaria and HIV on pregnancy and neonatal outcome, HIV-infected women were found to be more likely to develop malaria attacks during pregnancy than seronegative women.

A related study by Ayisi et al. in a prospective study to determine the effect of dual infection with HIV and malaria on pregnancy outcome in western Kenya, both HIV and malaria were significant risk factors for postpartum maternal anemia, and HIV-seropositive women with malaria were twice as likely to have anemia as HIV-seronegative women with or without malaria (Ayisi et al., 2003).

In 2004, Mount and colleagues reported impairment of humoral immunity to *Plasmodium falciparum* malaria in pregnancy by HIV infection. The impairment, they concluded was greatest in the most immunosuppressed women thus explaining the increased susceptibility to malaria seen in pregnant women with HIV infection (Mount et al., 2004).

Following this study, a review by ter Kuile et al. on the burden of co-infection with HIV and malaria in pregnant women in sub-Saharan Africa reported that HIV-infected women experienced consistently more peripheral and placental malaria, higher parasite densities, more febrile illnesses, severe anemia, and adverse birth outcomes than HIV-uninfected women, particularly in multigravidae. This, the authors interpreted as, HIV altering the typical gravidity-specific pattern of malaria risk by shifting the burden from primarily primigravidae and secundigravidae to all pregnant women (ter Kuile et al., 2004).

In their study to assess the influence of HIV and malaria infections on the pregnant women's nutritional status in the Manya Krobo and Tema Districts, Ghana, a group of researchers from the School of Public Health, Legon also reported adverse findings in terms of maternal anemia. Very high prevalence of maternal anemia (over 80%), with the group of women co-

infected with both HIV and malaria having a greater relative odds (OR = 1.52; 95% CI: 1.12-2.40) of being anemic (Laar *et al.*, 2005).

2.2.1 Malaria and HIV infections and maternal anemia and immune status

This subsection elaborates on two of the adverse maternal health outcomes resulting from infection with either HIV or malaria during pregnancy. These adverse outcomes are maternal anemia and immunosuppression.

2.2.1.1 Malaria-HIV co-infection and maternal anemia

Anemia according to Massawe *et al.* (2002) has been and continues to be among the greatest health problems in women of reproductive age, particularly in developing countries. This condition more often than not is of infectious cause; particularly malaria and HIV. Verhoeff *et al.* (1999a) in their study of a cohort of mothers and their babies living in southern Malawi, found malaria and iron deficiency to be independently associated with moderately severe anemia in primigravidae. In a review on the burden of malaria in pregnancy in malaria-endemic areas, it was reported that HIV was associated with anemia with population attributable risk of between 12 and 14% (Steketee *et al.*, 2001). Another independent study by Ayisi and colleagues to determine the effect of dual infection with HIV and malaria on birth outcomes and maternal anemia among women delivering at a large public hospital in Kisumu, western Kenya, found that both HIV and malaria were significant risk factors for postpartum maternal anemia. HIV-seropositive women with malaria were twice as likely to have anemia than HIV-seronegative women with or without malaria (Ayisi *et al.*, 2003). The review by ter Kuile *et al.* (2004) cited earlier, also reported on the burden of co-infection HIV and malaria in pregnant women in sub-Saharan Africa. It showed that HIV-infected women experienced

consistently more severe anemia than HIV-uninfected women. Dairo *et al.* (2005) in their study to determine risk factors for anemia in pregnancy among women at primary care level, found that malaria parasitemia and HIV seropositivity significantly increased the risk of anemia.

2.2.1.2 Malaria-HIV co-infection and maternal and immunosuppression

A review by Chandramohan and Greenwood in 1998 revealed that infection with HIV-1 causes progressive cellular immunosuppression, and any resulting impairment in the immune response to malaria might be associated with failure to prevent infection or to suppress parasitemia and clinical disease (Chandramohan and Greenwood, 1998). However, laboratory-based studies close to a decade ago found that although some components of the human immune response to *Plasmodium falciparum* are modified by HIV-1, others were unaffected (Wabwire-Mangen *et al.*, 1999; Wabwire-Mangen *et al.*, 2001). A more recent study in Malawi showed that HIV plasma viral loads were significantly higher in patients with malaria infection than in those without, and these levels remained higher for up to 10 weeks after treatment (Kublin *et al.*, 2005). The increases in viral load were greatest in those with clinical malaria, high levels of parasitemia, and relatively low CD4 counts. This study suggests that malaria may speed the progression of HIV disease. This was supported by a related study from Uganda showing an association between CD4 cell decline and episodes of malaria despite prompt treatment (Mermin *et al.*, 2006). However, the true clinical impact of malaria on immune status of HIV-positive persons as well as HIV disease progression, according to Whitworth and Hewitt, remains unclear (Whitworth and Hewitt, 2005).

In an earlier investigation, some researchers showed that HIV disease was associated with loss of CD4+ T cells, chronic immune activation, and progressive immune dysfunction (Kinter et al., 2004). These investigators observed that HIV-specific responses, particularly those of CD4+ T cells, become impaired early after infection, before the loss of responses directed against other antigens. The basis for this diminution, they indicated, needs further elucidation. The role of malaria was not examined in that study. At present, the modulation of immune responses during co-infection and the immunological basis for the severe pregnancy-related outcomes is still unclear.

Some limited studies have identified that specific alterations in both the humoral and the cellular arms of the immune system provide some explanation of how HIV-1 infection might impair protective immune responses to malaria (Whitworth et al., 2000; Steketee et al., 2001; Okoko et al., 2002; Ayisi et al., 2003; Ayisi et al., 2004). However, many of the studies that have investigated the immunological and epidemiological interactions between placental malaria and HIV-1, according to Ned *et al.* (2005) have been limited by a variety of factors, including the use of different malaria diagnostic techniques, small sample sizes, and inadequate adjustment for the stage of HIV disease, the density of parasitemia and the duration of malaria exposure in the data analysis.

2.3.0 Adverse perinatal outcomes in relation to malaria and HIV infections

Neonates of women in malaria endemic areas may experience a variety of adverse consequences from malaria and HIV infections including LBW, and PTD. Other adverse outcomes that neonates of women co-infected with malaria and HIV may be at increased risk for include fetal malaria parasite exposure or cord blood malaria parasitemia (CMP), low

Apgar score (LAS) and consequently, infant mortality. Subsection 2.3 presents reports on PTD, LBW, CMP, and LAS in relation to malaria and HIV infections. These are of particular relevance to this current study.

2.3.1 LBW and PTD among HIV+ women in relation to malaria parasitemia

Malaria in pregnancy according to Shulman and Dorman is one of the most important preventable causes of LBW and PTD worldwide (Shulman and Dorman, 2003). In addition to malaria, maternal HIV infection has also been shown to be associated with the above outcomes (Whitworth *et al.*, 2000; Steketee *et al.*, 2001; Okoko *et al.*, 2002; Ayisi *et al.*, 2003; Ayouba *et al.*, 2003; Brahmhatt *et al.*, 2003; Ticconi *et al.*, 2003; Abrams *et al.*, 2004; Ayisi *et al.*, 2004; Mount *et al.*, 2004; Noble *et al.*, 2005; Brahmhatt *et al.*, 2006; Marti *et al.*, 2007; Onah *et al.*, 2007; Uneke *et al.*, 2007).

A systematic review and meta-analysis by Brocklehurst and French on the association between maternal HIV infection and perinatal outcome showed that adverse perinatal outcomes related to maternal HIV infection included intrauterine growth retardation, low birth weight, and preterm delivery (Brocklehurst and French, 1998). In a related review by *ter Kuile et al.* (2004), several studies were identified that examined the effect of dual infection with malaria and HIV on birth outcomes (Steketee *et al.*, 1996b; Leroy *et al.*, 1998; Weng *et al.*, 1998; Verhoeff *et al.*, 1999b; Ayisi *et al.*, 2003; Ticconi *et al.*, 2003). Although differences in study design limited direct comparisons between the studies, the studies showed an increased risk of poor birth outcome in terms of low birth weight, preterm birth, and IUGR with both HIV and malaria, with the greatest risk in women with dual infection (*ter Kuile et al.*, 2004). Studies that reported on gestational age, suggested that the effect on birth weight reflected a

combined effect of shortened gestational age and IUGR (Steketee *et al.*, 1996b; Leroy *et al.*, 1998; Weng *et al.*, 1998; Verhoeff *et al.*, 1999b; Ayisi *et al.*, 2003; Ticconi *et al.*, 2003).

Verhoeff *et al.* (1999b) in their study of a cohort of mothers and their babies living in southern Malawi showed that LBW was significantly associated with primigravidae with placental malaria, and in multigravidae with short stature. Dreyfuss *et al.* (2001) in their study to document the determinants of low birth weight among HIV-infected pregnant women in Tanzania corroborated the above finding with a recommendation that “better management of malaria and intestinal parasitic infections could reduce the incidence of LBW among HIV+ pregnant women in Tanzania”.

Ticconi *et al.* (2003) in their prospectively designed study to investigate the effect of isolated or concomitant infection with malaria and HIV on pregnancy and neonatal outcome concluded that women with either HIV or malaria infection have a significantly increased risk of adverse outcomes of pregnancy. In women dually-infected with HIV and malaria, this risk was more than doubled.

In a paper by Ayisi *et al.* (2003), maternal HIV, in the absence of malaria, was associated with a reduction in mean birth weight of 99g among all gravidae, while malaria was associated with both IUGR and PTD, resulting in a reduction in mean birth weight of 145g among HIV-seronegative and 206g among HIV-seropositive primigravidae, but not among multigravidae.

In a separate but related study in Malawi, Abrams *et al.* (2004) after examining risk factors and mechanisms of PTD in malaria-exposed pregnant women reported that HIV was associated with PTD, while malaria was not, contrary to the findings by Noble *et al.* (2005)

where both maternal HIV infection, and malaria history, among Zimbabwean women were associated with preterm delivery.

Other researchers who examined the risk of adverse perinatal outcomes in relation to maternal or umbilical cord *Plasmodium falciparum* parasitemia among HIV-infected women from Tanzania also suggested that malaria and HIV infections are associated with LBW and PTD (Villamor *et al.*, 2005).

A more recent review by Desai and colleagues on evidence of the clinical implications and burden of malaria in pregnancy suggest that successful prevention of these infections reduces the risk of low birth weight by 43% and perinatal mortality by 27% among paucigravidae (Desai *et al.*, 2007).

2.3.2 Cord malaria, and low Apgar score in relation to malaria and HIV infections

Infection with either HIV or malaria during pregnancy often results in adverse outcomes for mother and newborn. Such adverse outcomes may include placental exposure to malaria parasites, fetal malaria, and low Apgar score.

2.3.2.1 Umbilical cord malaria parasitemia

There is the biologic plausibility that malaria during pregnancy may result in fetal exposure to the parasite. For example if parasites are transmitted across the placenta, this could result in cord blood malaria or congenital malaria. De Silva *et al.* (1982) have long indicated three possible ways that cord blood may become infected with malarial parasites. These are through maternal transfusion into fetal circulation either at the time of delivery or during pregnancy,

direct penetration through the chorionic villi, and penetration through premature separation of the placenta. However, the effectiveness of the placenta to restrain malaria parasite passage to the fetus and the remarkable capacity of the fetus to resist infection has been demonstrated (Miller and Telford, 1996). The resistance may reflect among other things a) the physical barrier of the placenta to infected red cells, b) the passive transfer of maternal antibodies, c) the poor environment afforded by the fetal red cells for plasmodial replication (De Silva et al., 1982; Miller and Telford, 1996). A free passage therefore probably means that placental barriers are no more effective when infected with malaria, and or HIV.

Congenital malaria may be defined as the presence of asexual stages of *P. falciparum* in cord blood smear at delivery or in peripheral blood smear of the infant in the first seven days of life, irrespective of clinical symptoms (Uneke, 2007c). Though studies from other African countries (Seteketee et al., 1996b; Villamor et al., 2005) have shown the relationship between cord parasitemia and other adverse perinatal events, there is lack of data on this in Ghana. In 1996, Steketee and colleagues in their search for an effective strategy for malaria prevention programs for pregnant African women estimated that maximum benefits of an antimalarial intervention that clears placental and umbilical cord parasitemia are a 5-12% reduction of low birth weight, and a 3-5% reduction in the rate of infant mortality (Steketee et al., 1996b). Acknowledging the reality that the role of umbilical cord parasitemia has not been well characterized, Villamor et al. (2005) examined the risk of adverse perinatal outcomes in relation to maternal or umbilical cord *Plasmodium falciparum* parasitemia among HIV-infected women from Tanzania. The study reported that cord parasitemia was a serious problem among neonates. Factors that were found to be associated with cord parasitemia included maternal parasitemia at the first antenatal visit as well as at delivery but not CD4 cell counts, parity, or zinc supplementation. Based on these findings, the investigators

recommended treatment of malaria and avoidance of re-infection during the course of pregnancy.

Though previously thought to be a one-off event in sub-Saharan Africa, a recent review has indicated that cord malaria is more common than previously thought (Uneke, 2007c). Related reports from both malaria-endemic and non-endemic areas show higher prevalence of cord malaria ranging from 8% to 33% (Jelliffe, 1966; Akindele et al., 1993; Tobian et al., 2000). The condition in some cases has been shown to be strongly associated with placental malaria (Uneke, 2007c), increasing drug resistance, increasing virulence of the parasite, or HIV (Desai et al., 2007). Cord blood parasitemia, in relation to maternal infection with malaria and HIV are still subjects of investigations. A recent review reported that these infections particularly HIV, do not have a consistent effect on fetal malaria or on the relationship between maternal and infant malaria (Slutsker and Marston, 2007).

2.3.2.2 *Apgar score*

The Apgar score was devised in 1953 as a simple system for classifying neonatal condition at 1 minute and was later modified to include status at 5 minutes after birth (Apgar, 1953). The score is determined at birth by monitoring five characteristic features of the neonate. These are: a) heart rate and beat b) respiratory activity c) muscle tone d) reflexes; and e) color. Scores are given to each of these depending on the degree. The sum of the scores at one minute and at 5 minutes gives the Apgar scores at these respective times.

Although, the Apgar score has been in use for over 50 years, the prevalence of a low Apgar score and attendant risk factors and outcome have not been adequately documented in many sub-Saharan countries (Ondoa-Onama and Tumwine, 2003). In a study therefore to determine

the prevalence of low Apgar score and establish immediate outcome and possible risk factors for poor outcome in newborns with low Apgar score, Ondoa-Onama and Tumwine (2003) reported the prevalence of low Apgar score at one and five minutes to be 8.4% and 2.8% respectively. Maternal factors these investigators found to be significantly associated with low Apgar scores included primiparity, abnormal delivery, age and medical diseases during pregnancy, while birth injuries and cord accidents were the infant factors. The investigators reiterated the need to carefully evaluate and monitor babies with low Apgar scores immediately after birth. A study to establish the use of the Apgar score as a simple and clear classification of newborn infants concluded that "the Apgar score had survived the test of time and should continue to be used (Finster and Wood, 2005). The investigators were of the view that the prognosis of an infant is excellent if it receives one of the upper three scores, and poor if one of the lowest three scores.

The influence of infections such as malaria and HIV during pregnancy on low Apgar score has been the subject of investigation. Two studies have reported on low Apgar score and its associated factors among women infected with HIV (Tuomala et al., 2002; Ticconi et al., 2003). One of the studies reported that rates of low Apgar scores (<7) was independent of maternal receipt of ART during pregnancy (Tuomala *et al.*, 2002). The role of malaria was not considered. In a study designed to investigate the effect of isolated or concomitant infection with malaria and HIV on neonatal outcome among pregnant Zimbabwean women reported that malaria and HIV infections were independently associated with increased risk of low Apgar score (Ticconi *et al.*, 2003).

2.4.0 HIV and infant feeding

Before the advent of HIV, infancy was acknowledged as the stage of life when initial contact with and orientation to foods typical of one's culture are established (Phillips, 2007). Today, infant feeding in the context of HIV is challenging in settings where breastfeeding is routinely practiced.

In guiding health workers, a series of international guidelines have been developed over time depending on prevailing knowledge. The first generation guidelines informing infant feeding indicated that where it is acceptable, feasible, affordable, sustainable and safe (AFASS), replacement feeding should be adopted and breastfeeding avoided (WHO et al., 2003). However, upon reviewing accumulating evidence, a technical consultation convened by WHO on behalf of the Inter-Agency Task Team (IATT) in October 2006 updated these guidelines (WHO et al., 2006).

The review of substantial body of new evidence and experience regarding HIV and infant feeding since the previous technical consultation in October 2003 (WHO et. al., 2003), and since the Glion⁷ and Abuja⁸ calls to action on the prevention of mother-to-child transmission (PMTCT) of HIV gave birth to the 14-point second generation guidelines. This includes the following:

- 1. The most appropriate infant feeding option for an HIV-infected mother depends on her individual circumstances, including her health status and the local situation, but should take consideration of the health services available and the counselling and support she is likely to receive;*

⁷UNFPA and WHO. The Glion Call to Action on Family Planning and HIV/AIDS in Women and Children, 3-5 May 2004.

⁸Call to Action: Towards an HIV-free and AIDS-free Generation. Prevention of mother-to-child transmission. High-level global partners forum, Abuja, Nigeria, December 3, 2005.

2. *Exclusive breastfeeding is recommended for HIV-infected mothers for the first six months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time;*
3. *When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended;*
4. *At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed. All breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided.*

The principal factor considered in the evolution of the guidelines was the risk of perinatal transmission of HIV. The general range of HIV transmission through breastfeeding of any kind without any interventions is 5-20% (WHO et al., 2004). The consultation was also aware of the possible benefits of exclusive breastfeeding in relation to HIV transmission suggested by the work of Coutoudis and colleagues (Coutoudis et al., 1999b). Since then, other studies have shown that exclusive breastfeeding carries a lower risk of HIV transmission than mixed breastfeeding. A risk of about 4% was reported in South Africa (Coovadia et al., 2007) and 1.3% (HIV transmission rate between six weeks and six months) in Zimbabwe (Iliff et al., 2005). Against this background and in the midst of the confusion regarding what HIV-positive mothers should feed their infants, health workers are reminded that exclusive breastfeeding for the first six months is preferred to mixed feeding. Mixed feeding carries a higher risk of HIV transmission than exclusive breastfeeding (Coovadia et al., 2007).

Before and after the evolution of the first generation recommendations, some authorities contend that no single guideline can be universally applicable, and that every guideline ought to be implemented taking into consideration individual circumstances (Bobat, 2000;

Coutsoudis, 2005b; Leshabari et al., 2006; Bland et al., 2007; Leshabari et al., 2007a; Leshabari et al., 2007b).

A study that sought to determine the socio-economic and cultural factors influencing the choice of infant feeding methods in urban Zimbabwean women in the context of HIV transmission, reported that husbands had a greater influence on feeding practices than nurses (Gara *et al.*, 2005). It can therefore be inferred from this that, in the Zimbabwean setting, social factors may have higher influence than the advice of medical personnel when choosing a method of feeding. Also, the level of education and employment status as well as the opinions of other family members and health care personnel were identified by the study to be other factors influencing the choice of method of infant feeding. These multiplicity of factors the authors conclude, complicate the decision making process on infant feeding.

In Kwa-Zulu Natal, South Africa, Thairu and others highlighted the role of cultural, social, economic and psychological factors that affect HIV positive women's infant feeding decisions and behavior (Thairu *et al.*, 2005). Infant feeding decisions were influenced by social stigma of HIV infection; maternal age and family influences on feeding practices; economic circumstances; beliefs about HIV transmission through breastmilk; and beliefs about the quality of breastmilk compared to formula.

A study in Abidjan, Cote d'Ivoire, examined the acceptability of EBF with early cessation to prevent HIV transmission through breast milk among HIV+ women. The summary of the findings were that, the factors associated with failure to initiate early cessation of breast-

feeding were mainly socio-cultural; the main one being living with a partner's family (Becquet *et al.*, 2005a).

Another study among HIV-positive mothers in Ile-Ife, south-west Nigeria confirmed the difficulty of replacement feeding for HIV-infected mothers in sub-Saharan Africa (Abiona *et al.*, 2006). After exploring the AFASS of replacement feeding options for HIV-infected mothers, they investigators identified high costs of replacement foods, fuel for cooking; an unreliable supply of electrical power; poor access to safe water; and poor access to storage facilities as barriers to replacement feeding.

Against this background, Doherty and others in their bid to identify whether the WHO/UNICEF guidelines on infant feeding for HIV-positive women were being implemented effectively in South Africa, revealed that within operational settings, the guidelines were not being implemented effectively in South Africa, leading to inappropriate infant-feeding choices and consequent lower infant HIV-free survival (Doherty *et al.*, 2007).

2.4.1 Infant feeding in the context of HIV: challenges of exclusive breastfeeding (EBF) and exclusive formula feeding (EFF)

Mothers infected with HIV face a myriad of challenges and sometimes have to make desperate decisions regarding the choice of a particular infant feeding option as well as sustaining this choice. Reviewed below are specific challenges HIV-positive mothers face in their bid to exclusively breastfeed or to formula feed.

2.4.1.1 Challenges of exclusive breastfeeding

Earlier documentation that exclusive breastfeeding involves a lower risk of MTCT of HIV than mixed feeding (Coutsoudis et al., 1999a; Iliff et al., 2005) had raised hopes that MTCT can be reduced where breastfeeding is culturally normative. Unfortunately, the prime obstacle to this strategy has been the fact that mixed feeding patterns and not exclusive breastfeeding are practised throughout Africa (de Paoli et al., 2001; Bland et al., 2002; Piwoz et al., 2006). Exclusive breastfeeding has been noted to be an alien concept in most African cultures (Magoni *et al.*, 2005); the prevailing form of breastfeeding worldwide being mixed breastfeeding (WHO, 2001b). Studies from various countries in sub-Saharan Africa document very high breastfeeding initiation rates among rural women of unknown HIV status (de Paoli et al., 2001; Bland et al., 2003). Exclusive breastfeeding is, however rare, while early mixed feeding is common (Becquet et al., 2005b; Becquet and Leroy, 2005; Coutoudis, 2005a).

A study from South Africa found that women of unknown HIV status, who started out exclusively breastfeeding, introduced formula and/or solid foods from one to three months after birth (Chopra *et al.*, 2002). Other studies from South Africa reported that fluids were commonly introduced within the first 48 hours of life, and infant formula from six to eight weeks after birth. One of these studies implemented in rural South Africa reported that grandmothers tended to view formula as beneficial to the baby and when mothers were absent from home, formula was given (Bland *et al.*, 2002).

In summary, the various factors militating against the practice of exclusive breastfeeding include ineffective counseling information by health workers, effects of the mass media sometimes leading to confusion regarding the choice of infant feeding type, social pressure to

mix-feed and local norms such as water supplementation, belief about the quality of breast milk, fear of transmitting the virus to baby, and in certain settings, provision of free infant formula (Thairu et al., 2005; Abiona et al., 2006; Leshabari et al., 2007a; Leshabari et al., 2007b; Rollins, 2007; Sadoh et al., 2008).

2.4.1.2 Challenges of exclusive replacement feeding

In countries where breastfeeding is the norm, formula feeding has been noted to alert a woman's family or community that she is HIV+, and may result in stigma or other negative repercussions (Nduati et al., 2000; de Paoli et al., 2002; Rollins, 2007). In Botswana, where formula feeding in HIV+ women is strongly encouraged and offered free of charge in PMTCT programmes, Shapiro and colleagues observed that adherence to exclusive formula feeding was suboptimal and potentially over reported (Shapiro *et al.*, 2003). However, the Mashi sub-study in the same setting reported very high levels (91%) of adherence to formula feeding compared to only 18% adherence to exclusive breastfeeding (Thior *et al.*, 2006).

A study in Zambia similarly reported that HIV+ women changed to mixed feeding very early, whether they started out with replacement feeding or exclusive breastfeeding (Omari *et al.*, 2003). A Cote d'Ivoire study, by contrast, found that 69% of HIV-positive mothers who selected replacement feeding reported still doing so successfully at three months (Leroy *et al.*, 2002). Most studies on choice of infant feeding method show that while HIV+ women commonly make a distinct choice to exclusively breastfeed or exclusively replacement feed during pregnancy, they often end up practicing mixed feeding early in the baby's life. The multiplicity of factors leading to this behavior have been noted by various authorities to include social stigma, scorn and suspicion, harsh economic circumstances, technological

barriers (electricity and refrigeration requirements), and more importantly the cultural usages and nuances of any given community (Thairu et al., 2005; Abiona et al., 2006; Leshabari et al., 2007a; Leshabari et al., 2007b; Rollins, 2007; Sadoh et al., 2008).

CHAPTER THREE

3.0 METHODOLOGY

This chapter presents the methodology of the study, detailing the following: The study sites, study design and field procedures, study population and participants, sample size and sampling procedure, follow-up procedures, ethical issues, data collection techniques and instruments, outcome measures, maternal and infant covariates, data management, analysis and quality assurance.

3.1.0 The study sites

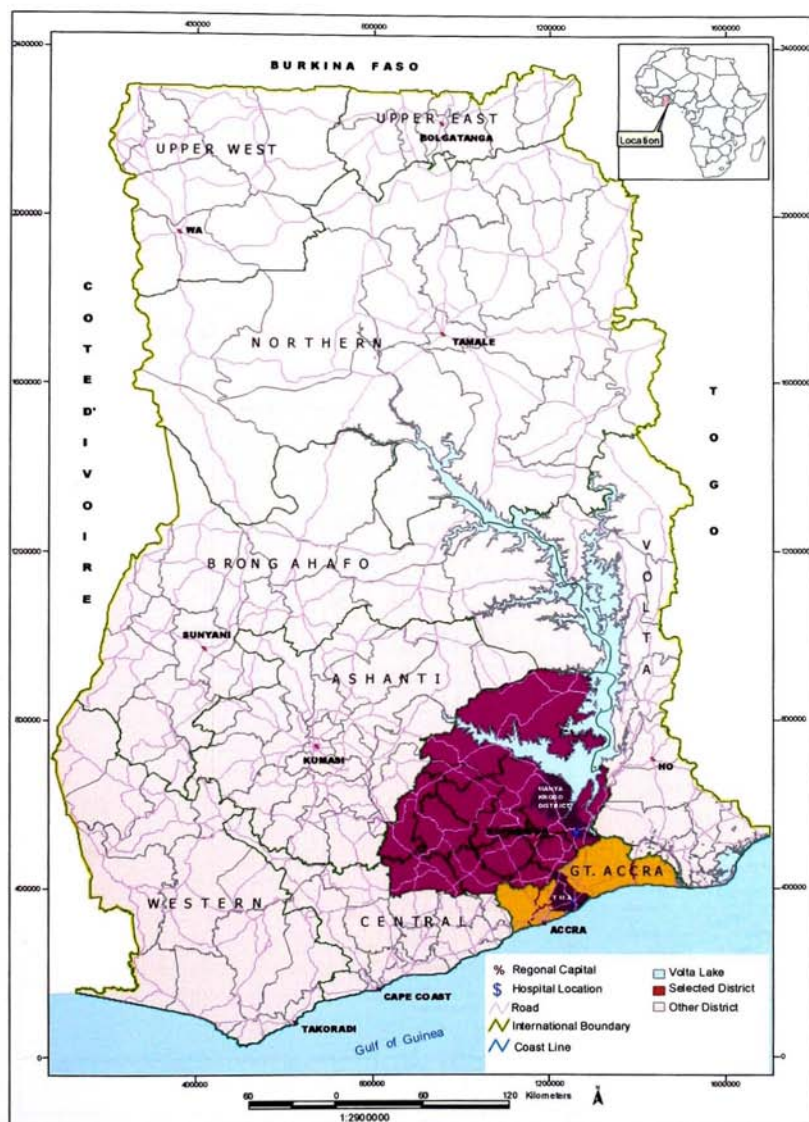
This research was conducted at three hospitals in the Eastern and Greater Accra regions of Ghana. These were:

1. The Tema General Hospital in the Tema Municipality, Greater Accra region;
2. The Atua Government Hospital in the Manya Krobo District, Eastern region;
3. The St Martins *de Porres* Hospital in the Manya Krobo District, Eastern region (Fig 3.1).

The two districts are illustrated in Fig 3.1, and the hospitals in Figs 3.2 – 3.4.

The following information on the geography, socio-economic, demography, culture and health facilities (subsections 3.1.1 to 3.2.3) are taken from the District Profiles of the Manya Krobo District (District-Health-Directorate-Manya-Krobo, 2000 - 2006) and the Tema Municipality (Tema-Municipal-Health-Administration, 2002-2006).

Fig 3.1. The Map Ghana showing the study districts – Manya Krobo district and Tema Municipal Assembly (TMA)

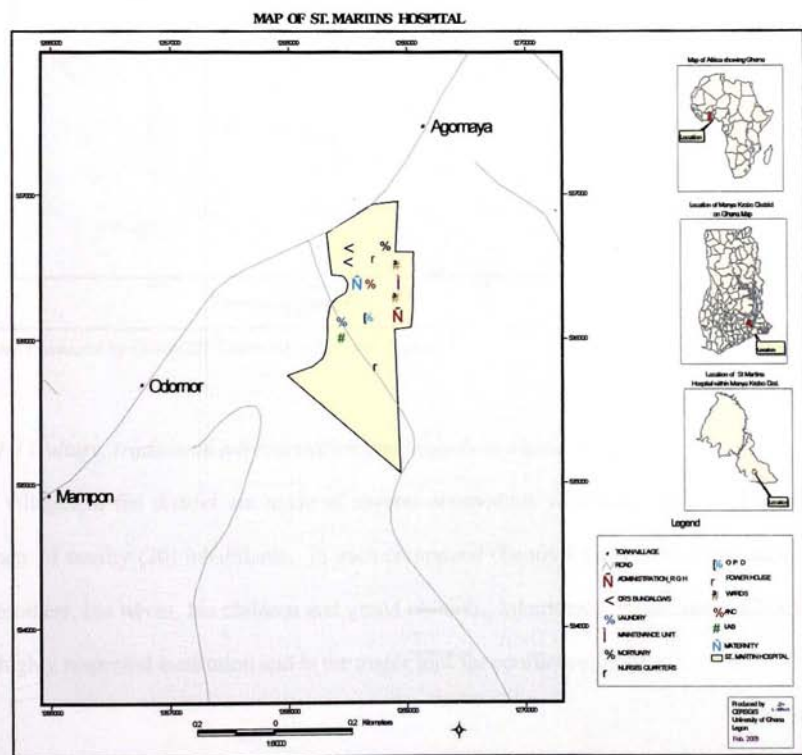


Source: Produced by CERGIS, University of Ghana, Legon

3.1.1 The Manya Krobo District

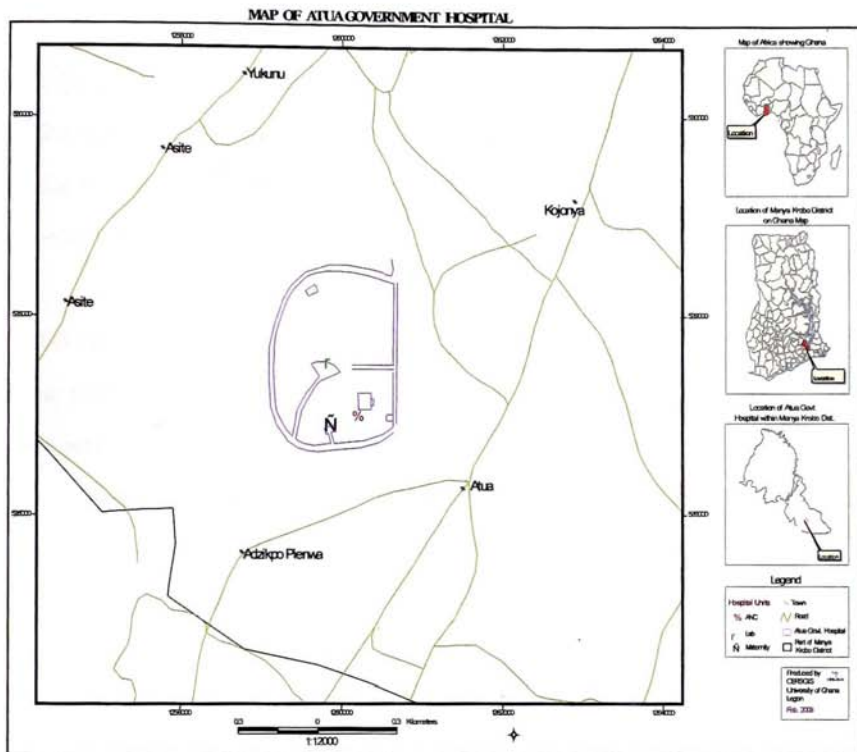
The Manya Krobo District is one of the 17 districts of the Eastern Region. It lies in the southeastern part of the Eastern Region between latitude $6^{\circ}05'S$ and $6^{\circ}30'N$ and longitude $0^{\circ}08'E$ and $0^{\circ}20'W$. It is bounded on the northeast by Kwahu North and northwest by Fanteakwa districts, on the east by Asuogyaman district, on the west by Fanteakwa and Yilo Krobo districts and on the south by North Tongu Districts. The District has an estimated population of 167,424 as projected from the 2000 Population census with a growth rate of 1.4. It covers a total surface area of 1476 sqkm. Odumase is the district capital and is situated 80 km from Accra. The Volta Lake, the biggest man made lake in the world, is found in the western part of the boundary.

Fig 3.2 The St Martins de Porres Hospital, Manya Krobo District



Source: Produced by CERGIS, University of Ghana, Legon

Fig 3.3 The Atua Government Hospital, Manya Krobo District



Source: Produced by CERSSGIS, University of Ghana, Legon

3.1.1.1 Culture, traditional administration and household characteristics

The villages in the district are made of several compounds with each compound having an average of twenty (20) inhabitants. In each compound (family house) is the compound head, his brothers, his wives, his children and grand children. Inheritance is patrilineal. Chieftaincy is a highly respected institution and is the major tool for conflict resolution.

The average household size in the district is 7.5. The large household size is a reflection of the social structure of the society; the numerous one's offspring the greater the respect accorded to

him. Children are sometimes also seen as a form of social security. Despite modernization and the erosion of the external family household composition, the household in the district maintains its traditional nature. The HIV epidemic, and rural-urban migration are, however, beginning to exact their impact on this system. Women now head forty percent (40%) of households in the urban areas of the district as a result of the above reasons.

3.1.1.2 Occupation

The four main occupations in the district are farming, fishing, trading and artisanship. There are also public and civil servants. Farming and fishing are traditionally in the domain of men. They prepare the land for sowing and do the weeding. Women and children take part in the sowing and harvesting. Crops grown include cassava, plantain, maize, cocoyam, yam and beans. Rice is grown in a few places in the district. Livestock (cattle, sheep, goats, and poultry) rearing is very common in the district.

3.1.1.3 Topography, climate and vegetation

The district is relatively flat to the southeast with isolated hills to the northeast. The landscape is generally undulating with several streams, most of which drain into the Volta lake. The climate is typically tropical with the major rainy season from March to July and the minor season from September to October. Annual rainfall varies from 1303.4mm in June to 165.6mm in September. Average temperature ranges from 12.2°C (rainy season) to 40°C (dry season). The moderate temperature and humidity and the double maxima rainfall have a bearing on the environment and the vector of the malaria parasite.

3.1.1.4 District health services

The District Health Administration provides technical and administrative support to health service providers. These include resource mobilization and distribution, training and research programmes. The District Health Administration ensures that services provided are in line with national policies.

There are 6 sub-districts (Odumase, Asesewa, Otrokper, Sekesua, Anyaboni, Kpong/Akuse) which provide mainly preventive services, and four hospitals, which serve as the first referral points namely: Atua Government hospital (one of the study sites), Akuse hospital, St. Martin's hospital (another study site) and Asesewa hospital.

The District is one of the highest HIV affected districts in Ghana. Sentinel surveillance data in the district over the years has shown the highest HIV prevalence in the country. HIV prevalence rates in the district ranged from 18% in 1992 to 8.8% in 2007 (NACP, 2008)⁹. The District, however, has a high level of commitment to addressing HIV and AIDS in the community, at the district health and traditional ruler levels. It was the first district in Ghana chosen to pilot the National Prevention of Mother-to-Child Transmission of HIV (PMTCT) and antiretroviral therapy program in 2001. These were among the reasons why the district was chosen for this study.

3.1.2. The Tema municipality

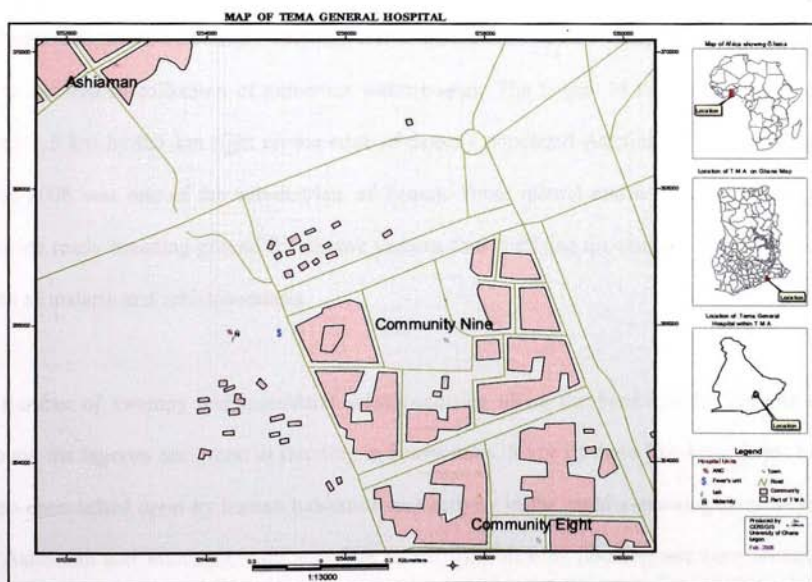
Tema Municipality is one of the 6 districts of the Greater Accra Region, located in the southeastern part of Ghana. The planned part of the Municipality is a vibrant commercial and

⁹ Details of trend of HIV prevalence can be seen in Fig 1.4.

industrial city. It is worth noting that Tema is the only purposefully planned city in the country. It has a large harbor – one of the world's biggest man-made harbors, which is the main seaport entry to Ghana.

The municipality is bounded in the North by the Eastern Region, on the East by the Dangme West District, on the Northwest by the Ga East District, on the Southwest by the Accra Metropolis and in the South by the Gulf of Guinea. Tema covers an area of 519 square kilometers, stretching between latitude $5^{\circ}37'N$ on the southern coastline and latitude $5^{\circ}52'N$ on its northern most limits, and longitude $0^{\circ}05'E$ on the eastern end and $0^{\circ}10'W$ on the western side (Fig 3.4)

Fig 3.4 The Tema General Hospital, Tema Municipal Assembly



Source: Produced by CERSGIS, University of Ghana, Legon

The Greenwich Meridian (longitude zero) passes through the district and is quite close to the Equator. On its approximately 20 km coastline can be found a large harbor, stretching nearly 2 km, and a military naval base. These, along with its numerous large as well as small industrial establishments make Tema very important for the economy and security of Ghana. These however, have attendant health implications such as for disease transmission (e.g. HIV) and occupational health problems.

3.1.2.1 Topography and demography

The area is mostly lowland. From its lowest parts, just 50 feet above sea level, mainly in the central parts (along the banks of the streams and rivers), the land rises gently easterly and westerly, with slight undulation, to about 400 feet in the higher parts. Many sections lie between 100 to 280 feet height only. Several irrigation dams built on these rivers and streams have resulted in collection of numerous water bodies. The largest of these is a linear lake, some 1.5 km by 0.5 km right on the edge of densely populated Ashaiman Metropolis (until June 2008 was one of the sub-districts of Tema). These natural and artificial water bodies provide ready breeding ground for disease vectors, thus fostering the transmission of diseases such as malaria and schistosomiasis.

A number of swampy and marshland areas occurring along the banks of the streams and around the lagoons are prone to flooding in heavy rains. Some of these low-lying lands have been encroached upon by human habitation and activity in the rapidly-growing suburbs such as Ashaiman and Manhean, with attendant health risks such as flooding and poor sanitation especially during the rainy season.

The population of Tema Municipality is estimated at 655,688 (projection from 2000 Census) making it the second largest populated district in the Greater Accra Region, and the third largest urban settlement in Ghana after Accra and Kumasi. Its population is about a fifth of the total population in the region and is growing at an estimated 4.4% annually (GSS, 2002).

3.1.2.2 Settlements and housing

The Municipality has urban, semi urban, as well as rural sections. The urban and semi urban sections are made up of several settlements, namely: Tema Township (made up of 26 communities), Manhean, Ashaiman, Kpone, Sakumono, Lashibi, Batsonaa, Adjiringanor, Otanor, Ashale Botwe, eastern part of Adenta, Frafraha and Ashiyie.

Rural Tema is made up of a number of settlements, including: Amrahia, Oyibi, Saduase, Kpone Bawaleshie, Apolonia, Kubekro, Katamanso, and Santeo. Some previously rural communities, such as Gbetsile, Kakasunanka No. 1 & 2, Adjei Kojo and Zenu, which were small villages until recently, are now fast growing into sub-urban areas.

Originally, the Tema city had a well laid out infrastructure. The residential communities, One through Twenty-Six all have master layout plans. The earlier built communities (One through Nine) followed approved well-spaced housing plans with adequate amenities. These accommodation units were mainly linked to work establishments and were well-managed by the Tema Development Corporation (TDC). As more immigrants trooped in, the job opportunities thinned out, whereas the demand for housing soared. This resulted in the deterioration of the originally well laid out infrastructure giving rise to the emergence of slums and semi-slums especially in Community One (Sites One and Two, Fishing Harbor.). The

attendant congestion predisposes to transmission of diseases such as tuberculosis and cholera. Initially, the earlier settlers in Community One as well as the other communities responded by constructing extensions to the existing houses in order to accommodate newcomers, until this no longer sufficed.

3.1.2.3 Health Institutions

There are six public health facilities including the Tema General Hospital, Tema Polyclinic, Tema Municipal Assembly Maternity Clinic; and four Health Centers namely Ashaiman, Manhean, Kpone and Oyibi) and about 84 private health facilities, including hospitals, clinics and maternity homes, spread all over the municipality. These private facilities cater mainly for the health needs of the industrial workers and their dependants.

3.2.0 Study design and summary of field procedures

The research was implemented by employing three different designs:

1. A prospective design to determine the associations between malaria and HIV infections during pregnancy and adverse maternal and perinatal outcomes;
2. A cross-sectional survey to document the choices HIV-positive mothers make regarding what to feed their infants; and
3. A qualitative investigation to explore the experiences and the challenges HIV-positive mothers face in implementing their feeding aspirations.

These components are summarized below:

3.2.1 The prospective study on adverse maternal and perinatal outcomes

This component of the study is detailed in sub-sections 3.2.1.1 through 3.2.1.5.

3.2.1.1 Study population and participants

The study population comprised pregnant women seeking antenatal care services from June 2005 to March 2008 at the Tema General Hospital in the Tema Municipality, the Atua Government Hospital, and the St Martins de Porres Hospital in the Manya Krobo District. From this population, the women who met the study's inclusion criteria and consented to enroll in the study were recruited. These women were encouraged to return and deliver at their designated hospitals for further data to be collected.

3.2.1.2 Sample size calculation for the prospective component of the study

The sample size determination was done using the Statcalc statistical module in the Epi Info software (Version 3.3.2). Epi Info is a public domain statistical software for epidemiology developed by Centers for Disease Control and Prevention (CDC). In the absence of any empirically documented local data on the main outcomes of the study (PTD, LBW, LAS, CMP, maternal anemia, maternal immunosuppression) among HIV-positive pregnant women, the findings from two Zimbabwean studies (Ticconi *et al.*, 2003; Noble *et al.*, 2005), one Kenyan study (Ayisi *et al.* 2004), one Tanzanian study (Villamor *et al.*, 2005), and a review by ter Kuile *et al.* (2004) were used.

The above studies provided data on four of the six outcomes – PTD, LBW, CMP, and maternal anemia. These formed the basis for the sample size calculation. The prevalence of PTD among HIV-positive pregnant women with no malaria (herein referred to as the unexposed group) was 10.7%; the prevalence of PTD in the exposed group (HIV-positive

pregnant women with malaria) was 25.7%. At 95% confidence level, with a statistical power of 80%, a sample size of 249 HIV-positive pregnant women was deemed adequate to test the hypothesis related to this outcome – PTD (Fliess, 1981). The minimum samples needed for the assessment of the other outcomes were similarly calculated. Illustration in Table 3.1 below is made of the outcome that gave the largest ‘minimum sample size’ after the calculations - PTD. This sample was therefore obviously considered adequate to test the hypotheses relating to the other outcomes.

Table 3.1. Sample size calculations (illustration made on one of six outcomes)

Hypothesis	Outcome of interest	Expected frequency of outcome in exposed group	Expected frequency of outcome in unexposed group	Confidence level	Statistical power	Minimum Sample size
¹⁰ Hypothesis 1 of 6	Preterm delivery	10.7	25.7	95%	80%	249

As shown in Table 3.1, the largest of the four samples was 249. To satisfy the apriori decided 1:2 ratio of exposed (HIV-positive pregnant women with malaria) to unexposed (HIV-positive pregnant women with no malaria), 63 HIV-positive pregnant women with malaria and 166 HIV-positive women without malaria needed to be enrolled and followed up at delivery.. With an anticipated participation rate of 95%¹¹, and attrition from all causes (attrition rate of 30% anticipated)¹², the 249 figure was upwardly adjusted and rounded up to 300.

A convenient sample of HIV-negative pregnant women two-fold the above sample – 600 were to be recruited as an additional comparison group. All the end of the first phase of the study, 443 HIV-positive pregnant women and 711 HIV-negative pregnant women – a total

¹⁰ Neonates of mothers infected with malaria and HIV during pregnancy have increased risk of preterm delivery

¹¹ This rate was informed by the experiences of an earlier study conducted by the investigator in 2005; unpublished data)

¹² Very high antenatal services but low institutional delivery is a very common phenomenon in this setting

1,154 pregnant women were recruited. Of these, 171 had malaria, and 983 had no malaria. Details of the study profile are given Fig 3.5.

3.2.1.3 Inclusion criteria

A pregnant woman attending the antenatal clinic was eligible to enroll into the study if she had not previously been registered at any of the antenatal clinics with her current pregnancy, if she had an established HIV status (positive or negative) or was willing to be tested, was 18 years of age or older, was resident in the study areas or surrounding townships, was willing to accept follow up visits, planned to stay in the study area for up to 6 months post-delivery, and willingly provided informed consent to be part of the study. All those who met these eligibility criteria were recruited into the study irrespective of gestation length.

3.2.1.4 Exclusion criteria

Pregnant women who had previously attended antenatal clinic at any of the three sites, those who were unwilling to give consent, as well as those younger than 18 years of age were excluded.

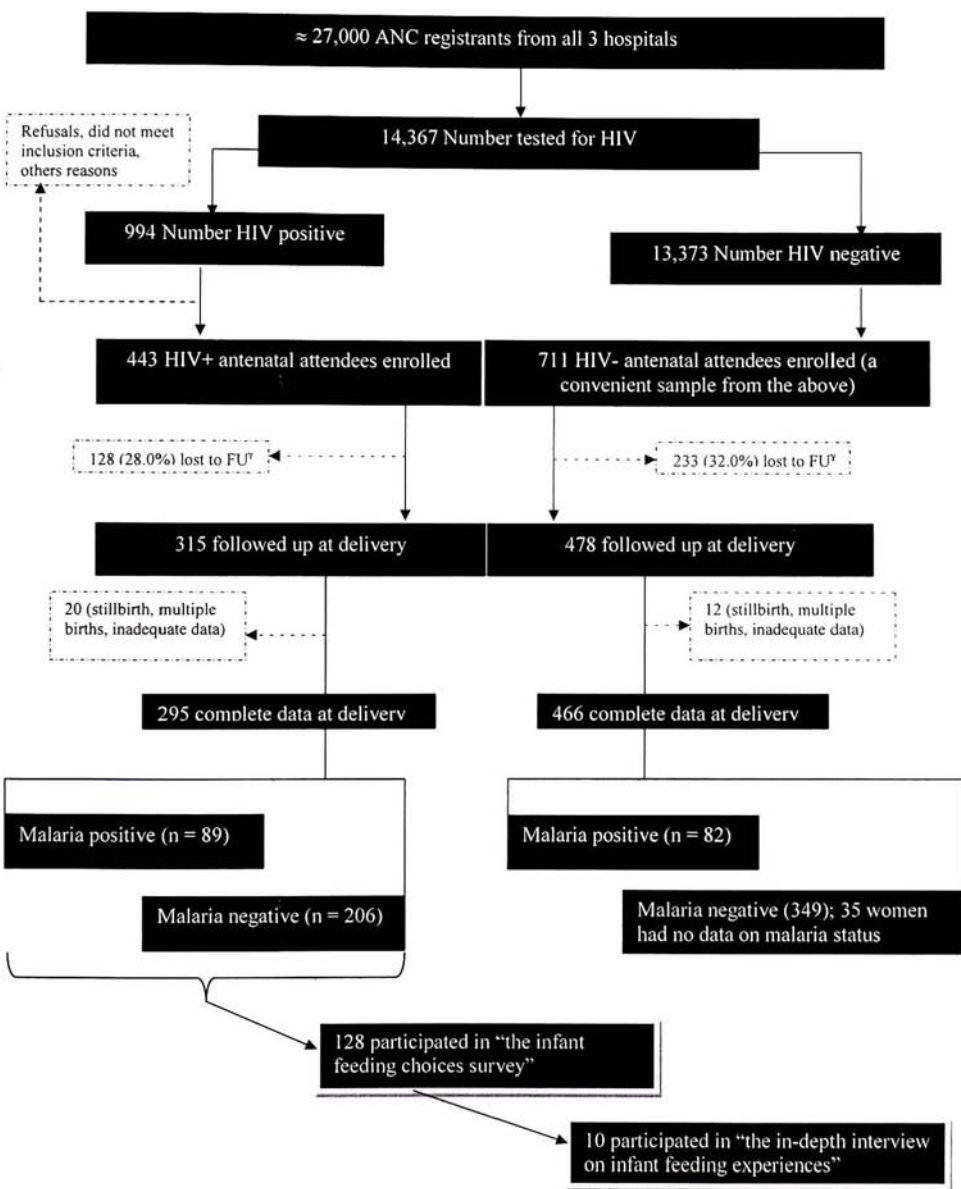
3.2.1.5 Sampling and follow-up procedures

Anticipating a low uptake of VCT services, all antenatal clients at the three study hospitals between June 2005 and March 2008 was approached for enrollment into the study. A total of 27002 pregnant women visited the three hospitals as new antenatal registrants throughout the period. A research nurse (running the PMTCT services) and research assistants aided the investigator to enroll all HIV-positive pregnant women who met the study's inclusion criteria. The investigator trained the nurses and research assistants on the methods, the inclusion criteria, as well as the objectives of the study. They (nurses and research assistants) were told to explain these to each study participant before enrollment. The women who consented to participate were asked if they had ever undertaken an HIV test during the antenatal period. If

their HIV status was already known/confirmed, they were enrolled as such; otherwise HIV test was done before enrollment. Two HIV-negative pregnant women were concurrently recruited for every HIV-positive woman as a comparison group. The information documented at recruitment included their background, socio-economic, socio-demographic characteristics, obstetric, and reproductive history. Clinical appraisals were carried out by the nurses, and 5ml blood samples collected by competent laboratory technicians for various determinations. Other information documented at recruited were their anthropometry (height, weight, MUAC, and triceps skinfold). All the above were documented on the first day of contact.

Follow-up data collection took place when the study participants returned to deliver at their designated hospitals. Of the 1,154 study participants enrolled into the study, seven hundred and ninety three (315 HIV-positive and 478 HIV-negative) turned up to delivery at the three hospitals. However, only 761 (295 HIV-positives and 466 HIV-negatives) had all the required data at delivery taken. These formed the sample for the follow-up data analysis. The details of the study profile are given below.

Fig 3.5 The study profile: June 2005 to August 2008



*High antenatal attendance and very low institutional delivery is a very common phenomenon in these settings

3.3 Documentation of infant feeding choices, experiences/challenges

A postpartum survey involving 128 of the 295 HIV-positive mothers (who had come back to deliver at the study hospitals) was conducted at postnatal clinics to document the infant feeding practices of these mothers. This took place during their postpartum period (specifically after three months). This phase of the data collection had questions on infant feeding choices/behavior, breastfeeding and breastfeeding initiation among others (Appendix 3).

3.3.1 Sample size for the infant feeding survey

Available data regarding the proportions of HIV-infected women accessing postnatal services from the Tema Municipal Health Administration Annual Reports (2002 – 2006); and the Manya Krobo District Health Directorate Annual reports (2000, 2003, and 2006), were used in the calculation of the sample size for the infant feeding choices survey.

At the Manya Krobo study site, the reports showed that the proportion of women accessing postpartum service who were HIV+ was 6.0¹³%. At the Tema General hospital, the proportion was 3.6¹⁴%. The sample size required for this study was determined as follows.

$$\text{Sample size} = N = \frac{Z^2 p (1-p)}{d^2}$$

Where:

N = minimum sample size

Z = normal deviate taken as 1.96 at 95% confidence level

p = proportion of HIV+ women accessing postnatal services

d = absolute amount of error tolerated (5% chance of error)

$$\text{Therefore, N for the Manya study site} = \frac{(1.96)^2 \times 0.064(1-0.064)}{(0.05)^2} = 68$$

$$\text{Analogously, N for Tema study site} = \frac{(1.96)^2 \times 0.036(1-0.036)}{(0.05)^2} = 58$$

¹³Proportion determined using data from the 2000, 2003, and 2006 annual reports.

¹⁴Proportion determined using data from the 2000 – 2006 annual reports

This gives a combined sample size of 126 for the two study sites. In all, 128 mothers were interviewed.

3.3.2 An investigation on infant feeding challenges and experiences

An exploratory qualitative study was conducted through in-depth interviews on a purposively selected sample of 10 HIV-positive mothers (Fig 3.5). The in-depth interviews were aimed at eliciting individual experiences on infant feeding practice and experiences. These were conducted by the investigator, with support from the nurses. The participants were purposively selected using the maximum variation technique, where person-related homogeneity was maintained but variation in the phenomenon (infant feeding behavior – exclusive breastfeeding, exclusive formula feeding, and mixed feeding) considered. The interviews were terminated after the 10th participant because, saturation¹⁵ was deemed to have been reached.

All 10 in-depth interviews were held using semi-structured interview guide (Appendix 5) that covered the following: infant's breastfeeding status, reasons for giving other feeds, issues on wet nursing, expressing breast milk for feeding, and influence of social pressure on feeding behavior. Also explored were the purchasing power of participants, perceptions on the cost of infant formula, and disclosure of HIV status to partner or close relative. Five of the ten interviews were conducted in English and the other half in Akan (through translators – nurse research assistants). All interviews were recorded in writing.

¹⁵ The main themes with respect to experiences and challenges were excessively being repeated by time the 10th participant was interviewed.

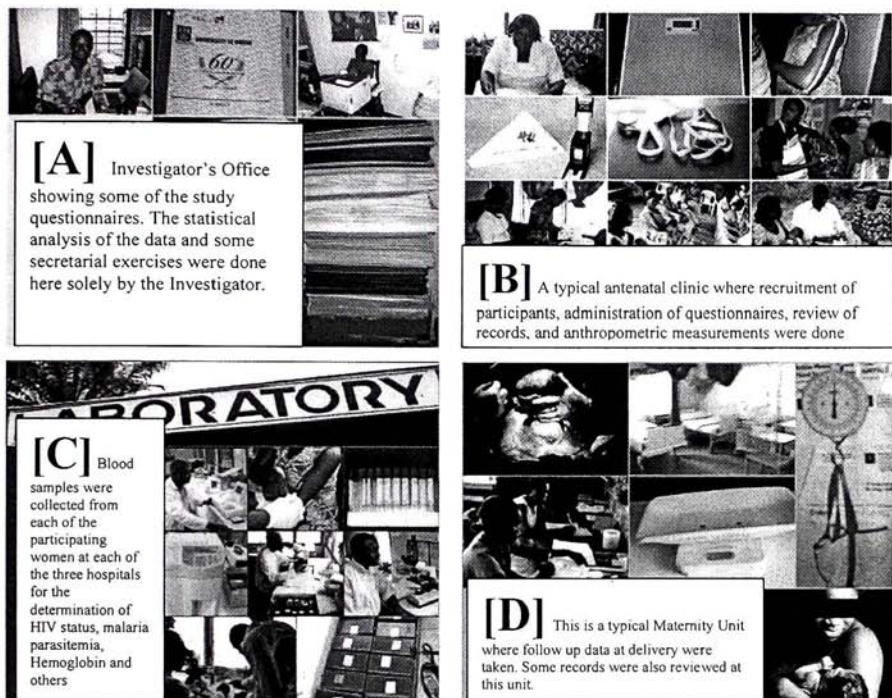
3.4.0 Ethical considerations

The research protocol met the guidelines for research involving human subjects of the Noguchi Memorial Institute for Medical Research (NMIMR). The study protocol was first vetted and reviewed by the Proposal Review Board of the School of Public Health for appropriateness and scientific content.

An ethical clearance was afterwards sought from the Institutional Review Board (IRB) of the Noguchi Memorial Institute for Medical Research. This was granted with the Federal Wide Assurance Number (FWA 00001824 IRB 0001276), and The NMIMR-IRB Identification Number (CPN 044/04-05 IORG 0000908).

Written informed consent, for those who were literate and verbal informed consent, for the illiterate was obtained from each study participant. Subjects were informed about the objectives and methods of the study. They were also assured of strict confidentiality with regards to any information obtained from them. The study participants were told that they would receive the same services whether or not they agreed to participate (details of this are given in Appendix 1 – Sample informed consent form).

Fig 3.6 Research implementation flow diagram



Source: Investigator

3.5.0 Community entry procedures

A series of meetings which provided information about the study to the community focal persons were held throughout the study sites (Fig 3.7). The meetings among other things sought to enhance community members' awareness of the impact of malaria on HIV-infected pregnant women and their offspring and the need to uptake PMTCT services. It was made clear during these meetings that participation in the study was voluntary.

Details of field procedures, including the use of the questionnaire, the nature of clinical and laboratory investigations were discussed with some of the opinion leaders and the healthcare

personnel. Additionally, two workshops were conducted for the chiefs and queen mothers of the Manya Krobo District to explain further the objectives of the project.

Fig 3.7 Snapshots of the community entry activities



Source: Investigator

3.6.0 Incentives for participants to enroll and to deliver at the designated study hospitals

Clients who consented to be interviewed were taken through counseling sessions during which they were counseled on the need to religiously attend antenatal clinics. They were also advised to report urgently to the hospital any time they felt unwell. Advice on the need to eat appropriately was given to each participant. To motivate women to deliver at the designated study sites, they were promised a number of the items required during delivery if they came back to deliver at their designated study sites (refer to Plate 3.1).

Plate 3.1 A list of required items for confinement

PREPARATION FOR CONFINEMENT	
Parazone	1
Rubber (Mackintosh)	2
Toilet Roll	1 or more
Pad (Fertex)	2 or more
Old Cloth	6 or more
Take Away (Rubber)	6 or more
Rubber Bucket	1
Mother's Soap	1
Mother's Towel	1
Mother's Sponge	1
Night Gown	1
Mother's cloth for use	
Baby's dresses	4 or more
Baby's Soap or (small key soap)	
Baby's Towel	1
Baby's Sponge	1
Beverage, biscuit or (bread)	
Cot Sheet	6
Dettol	1 bottle
Spirit	1 bottle
Pale with lid (small rubber bucket)	
Bag for Items or (Ghana must go)	
Antenatal Card	



GOOD LUCK

Enrolled study participants were assisted with some of these items when they came back to deliver. This was aimed at motivating them to deliver at the designated study sites. At the point of recruitment, they were informed about the Investigator's willingness and readiness to provide them with some of these items or their equivalent in cash not exceeding GH¢20.00. The figure was arrived at after a consultation with the PMTCT nurse providers, taking into consideration beyond what will be considered as an undue inducement.

3.7.0 Data Collection Techniques and Instruments

The study employed mainly quantitative data collection techniques and tools, and to a lesser extent qualitative methods in its implementation. These are summarized below.

3.7.1 Techniques

To a large extent, structured interviews were employed to elicit information from the study participants. In a few instances review of hospital records was done for corroboration.

3.7.2 Instruments

A two-phased structured questionnaire was designed by the investigator adapting a WHO assessment tool for research on infant feeding (WHO, 2001a). This two-phased questionnaire contained questions on subjects' background, socio-economic, socio-demographic, obstetric and reproductive history. Also included in the questionnaire were questions on the health seeking behaviour of the women, maternal and perinatal outcomes (Appendix 2 questionnaire). A semi-structured questionnaire to assess infant feeding choices was developed (Appendix 3). To aid in the administration of these questionnaires, an interviewer's guide in English was developed in very simple language explaining every question asked in the questionnaires (Appendix 4 Interviewer's guide). Finally, a semi-structured in-depth interviewer guide (Appendix 5) was also developed for the qualitative exploratory study. The various equipment – anthropometric, laboratory, and related logistics used in the implementation of the study are presented as Plates below.



Plate 3.2 Seca weighing scale

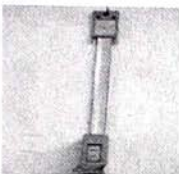


Plate 3.3 A wall-mounted microtome



Plate 3.4 Inelastic tape



Plate 3.5 Skinfold calipers



Plate 3.6 EDTA vacutainer tubes



Plate 3.7 A laptop computer and a digital camera



Plate 3.8 A printer



Plate 3.9 Research VAN



Plate 3.10 A set of questionnaire secured in a file

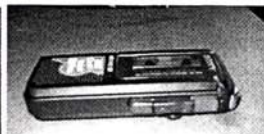


Plate 3.11 A micro-voice recorder

Source: *The Investigator*

3.8.0 Training

Prior to the field work, the research assistants, nurses and laboratory technicians were trained to ensure that all the questions were comprehended, all procedures delivered in a standardized way, and that responses were recorded adequately. There was a full-day training session at each of the study sites. The training centered on the following:

- introduction to the purpose and objectives of the study;
- familiarization with the data collection techniques and instruments;
- techniques of translating some of the questions into the local languages;
- probable ethical issues that might arise during the course of the data collection and

The need arose for a second training in June 2007 as a result of attrition in the number of nurses and assistants at the Manya Krobo study sites. The content of this training was unchanged.

3.9.0 Pre-testing

The data collection techniques and tools were pre-tested once on a sample of antenatal attendees at the Ashaiman Health Center. The needed modifications and validations were subsequently made before the actual data collection was initiated.

3.10 Actual data collection

The validated tools were then employed in the actual data collections as detailed below.

3.10.1 Laboratory

Blood samples (5ml) were collected from participating women at two time points: venous blood was taken both at recruitment and at delivery; cord blood was taken only at delivery into heparinized EDTA vacutainers for analysis.

3.10.1.1 Determination of maternal HIV status at recruitment

HIV serostatus was evaluated using the Determine® HIV-1/2 rapid test kit (Abbott Laboratories Diagnostics Division, IL, USA) Kit, as the initial screening test. Reactive sera were confirmed using the Oraquick HIV rapid test (Abbott Laboratories Diagnostics Division, IL, USA). These are immunochromatographic tests for the qualitative detection of antibodies to HIV-1 and HIV-2. The methods outlined in the test kits were strictly followed.

The principle of the test is, however, summarized here. Blood sample is added to the sample pad, and as the blood migrates through the conjugate pad, it reconstitutes and mixes with the selenium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized recombinant antigens and synthetic peptides at the patient window site. If antibodies to HIV/1 and or HIV/2 are present in the blood sample, the antibodies bind to the antigen-selenium colloid and to the antigen at the patient window, forming a red line at the patient window site. If antibodies to HIV/1 and/or HIV/2 are absent, the antigen-selenium colloid flows past the patient window and no red line is formed at the patient window site.

3.10.1.2 Determination of maternal and cord malaria parasitemia

Malaria parasitemia was determined using rapid test kit (Paracheck Pf, Orchid Biomedical Systems, India) that detects the presence of *P. falciparum*-specific protein (Pf. HRP-2) in whole blood specimen up to 14 days after the infection has been cleared. This test also utilizes the principle of immunochromatography. As the test sample flows through the membrane assembly of the dipstick after placing into the clearing buffer tube, the colored anti Pf HRP-2 antisera-colloidal gold conjugate (monoclonal) complexes the Pf HRP-2 in the lysed sample. This complex moves further on the membrane to the test region where it is immobilized by the anti Pf HRP-2 (monoclonal) antisera coated on the membrane leading to formation of a pink colored band which confirms a positive test result. Absence of this colored band in the test region indicates a negative test result, with a control band that serves to validate the test performance. The procedure outlined in the test kit was strictly followed.

3.10.1.3 Determination of maternal hemoglobin concentration

Maternal venous blood and infant cord blood hemoglobin concentrations were determined using an Automated Hematologic Analyzer, which measures hemoglobin by the formation of hemoglobincyanide. In addition the analyzer also directly measures the cell count for total red blood cells, white blood cells, and platelets.

3.10.1.4 Determination of maternal CD4+ count

Maternal CD4+ count was determined using the Becton Dickinson (BD) FACScout system, which measures absolute CD4 counts (Immunocytometry Systems, San Jose, CA), as outlined in the guidelines of the Centers for Disease Control and Prevention (CDC, 1997).

Plate 3.12 Venous blood being taken



Source: Investigator

3.10.2 Anthropometric methods

3.10.2.1 Height, weight, and birth weight

The height and weight measurements were recorded according to standard procedures (Frisancho; 1990). A Seca weighing scale weighing to the nearest 0.1 kg was used to take each subject's weight; height measurements were done using a wall-mounted microtoise (Raven

Equipment Ltd, England) measuring to the nearest 0.1 cm. Body Mass Index (BMI) in kgm^{-2} for each subject was then calculated from her weight and height measurements. At delivery, a research midwife weighed infants to the nearest 10 g on a standard Seca scale immediately after birth.

Plate 3.13 Height measurement



[Left] A subject's height being taken with a wall-mounted microtoise

Source: Investigator

Plate 3.14 Weight measurement



[Left] A subject's weight being taken using a Seca scale

3.10.2.2 Mid Upper Arm Circumference (MUAC)

This was measured at the mid-point of the left arm using a narrow flexible non-stretch steel tape. With the women in the standing position and the elbow flexed to 90°, the midpoint between the lateral projection of the acromial process (the tip of the elbow; refer to 'A' below) and the inferior border of the olecranon process of the ulna (the bony protrusion of the upper shoulder; refer to 'B' below) was identified. The mid point was then located and marked with a marker. With the tape now placed gently but firmly around the arm to avoid indentation of soft tissues, the MUAC was read with the arm hanging loosely at the side of the body (Jelliffe, 1969).

Plates 3.15a and 3.15b MUAC measurement



[Left] The mid-point of the upper arm being located with the aid of an inelastic tape [Right] an anthropometrist in the process of taking a subject's MUAC with the tape placed gently but firmly around the arm. This is done cautiously to avoid indentation of soft tissues

Source: Investigator

3.10.2.3 Triceps skinfold (TSF)

The TSF was measured using a skinfold caliper (Holtain Ltd CRYMYCH, UK), in the midline of the posterior aspect of the arm at the level mark (previously made during the MUAC measurement), with the arm hanging loosely.

Plates 3.16 Triceps skinfold measurement



Triceps skinfold being measured midway between the acromion and olecranon processes

Source: Investigator

3.11.0 Determination of Apgar score, and gestation length

3.11.1 Determination of Apgar score

Experienced midwives/nurses determined Apgar score at birth by monitoring five characteristic features of the neonate at one minute and at 5 minutes after birth. These are: a) heart rate and beat b) respiratory activity c) muscle tone d) reflexes and e) color. Scores are given to each of these depending on the degree as indicated in the Box 3.1 below. The sum of the scores at one minute and at 5 minutes gives the Apgar scores at these respective times.

Box 3.1 determination of Apgar score

Characteristic/Sign	Score		
	0	1	2
Heart rate or beat	Absent	Slow/below 100 per minutes	Over 100 beats per minutes
Respiratory activity	Absent	Weak cry	Good strong cry
Muscle tone	Limp	Some flexion at extremities	Well-flexed
Reflexes	No response	Grimace	Cough, sneeze
Color	Blue/pale	Body pink, but extremities blue	Completely pink

3.11.2 Determination of gestation length

Gestational length was determined by the nurses based on the recall of the last menstrual period of the study participant.

3.12.0 Derived variables

In this study a number of variables such as maternal age, weight, height, occupation, infection status, level of education among others were directly recorded by the investigator. Others such as morbidity profile, and socio-economic (SE) index score were derived using some of these already recorded variables. The derivations of these variables are explained below.

3.12.1 Morbidity profile

The morbidity profile of each subject was created based on the number of conditions presented with at the first antenatal visit. The conditions were:

- i. sore throat
- ii. fever
- iii. gastro-intestinal distress
- iv. nausea
- v. vomiting
- vi. oral candida
- vii. clinical anemia (assessed using palor)
- viii. sore mouth
- ix. tuberculosis
- x. anorexia
- xi. diarrhea
- xii. herpes

Using these 12 conditions, a subject's morbidity profile ranged from 0 (indicating she did not present with any of the 12 symptoms) to 12 (meaning she presented with all 12).

3.12.2 Determination of the socio-economic (SE) index score

Participants were assigned units based on the occupations as well as the level of education attained by themselves and that of their partners or caregivers. A summation of these four different units (from the occupation of subject, occupation of caregiver/partner; the level of education of subject, and the level of education of caregiver/partner) gave a subject her SE index score. This ranged from one (1) to twelve (12); subjects scoring between one and four were classified as low; scores five to eight were classified as middle; and scores nine to twelve as high.

Box 3.2. Socio-economic index score computation

Characteristic of subjects	Unit assigned*
Education	
Nil	0
Primary	1
JSS	2
SSS	3
Postsec/Poly/Tertiary	4
Occupation	
Not working at all	0
Peasant farmer	1
Services/student	2
Clerical	3
Professional/Tech/Admin	4

*The same criterion as in the partner was used for the partners/caregivers except that; the units assigned were halved in the case of the latter (partner/caregiver).

3.13.0 Outcome Measures

The main outcome measures of the prospective component of the study were grouped into maternal and infant outcomes.

The maternal outcomes included;

1. Maternal hemoglobin concentration in g/dl
2. Maternal CD4+ T-cell count (cells/mm³)

The infant outcomes included;

1. Gestation length,
2. Birth weight,
3. Cord blood malaria parasitemia,
4. Average Apgar score at 1 minute and at 5 minutes.

3.14.0 Maternal covariates

Maternal covariates included age, study site, HIV infection, peripheral malaria status, other morbidity conditions, duration of pregnancy in months at enrolment, gravidity, parity, CD4+ T-cell count and ARV use (for HIV+ subjects), use of any nutrient supplement, current weight in kg, MUAC/cm, triceps skinfold thickness/cm, HIV disease state (AIDS or HIV without AIDS defining symptoms), history of fever two weeks prior to enrollment, history of antimalarial use two weeks prior to enrollment, history of herbal drug use, hemoglobin concentration, and IPT use. These were selected in part on the basis of their theoretical importance. The covariates used in the multiple regression models were included if they were significantly associated with any of the outcome measures in the bivariate analyses, or if they were known to be associated with these outcomes based on previous studies.

3.15.0 Description of the study's data sets

The analyses that follow made use of three sets of data collected from antenatal attendees at the three Ghanaian hospitals between June 2005 and August 2008. All the three data sets were collected from pregnant women (HIV-positive, and HIV-negative women) presenting at the antenatal clinic at the Atua Government Hospital, St Martins *de Porres* Hospital and Tema General Hospital.

The first data set was collected at two time points (at recruitment and at delivery) by employing a study-specific questionnaire (interviewer-administered). At recruitment, information on the study participants' background, socio-demographic, and reproductive health history among others were documented. Thus, between June 2005 and March 2008, a total of 1154 (443 HIV-positive and 711 HIV negative) pregnant women accessing antenatal clinics from the three study hospitals were enrolled. Of the 1154 women, 361 (128 HIV-positive and 233 HIV-negative) were lost to follow-up before the second time point data collection – at delivery, and 32 cases excluded from the analysis as a result of multiple deliveries, still birth and inadequate data. In summary, this data set comprised 443 HIV-positive and 711 HIV-negative at recruitment, 295 HIV-positive, and 466 HIV-negative women on whom follow up data at delivery were available.

The second data set, aimed at providing information on the infant feeding choices and behavior of the HIV-positive women in the study area comprised 128 (themselves part of the study participants) who accessed postnatal services at the three study hospitals. They included 65 from the Tema study site and 63 each from the two Manya Krobo study sites.

The third data set documented infant feeding experiences of HIV+ nursing mothers. Data was collected by employing two qualitative techniques, non-participant observation at postnatal care, and in-depth interviews. This comprised ten HIV-positive mothers.

3.16.0 Data cleaning and entry

First, consistency checks were done on the questionnaire to assess unusual and unrelated responses. A data entry template with variable values appropriately defined to minimize data entry errors was created using the Statistical Package for Social Scientists, Version 15.0 (SPSS, 2007). This exercise was applied only to data sets one and two.

3.17.0 Data analysis

Statistical analyses were done using SPSS Version 15.0 (SPSS, 2007). Preliminary assessments of normality of distributions of key continuous variables including maternal CD4+ cell count, maternal hemoglobin, birth weight, gestational length, Apgar score were done using normal probability plots— Appendix 6. Appropriate measures of centrality (mean and median) and of dispersion (standard deviation, minimum, maximum, and standard error of the mean), as well as frequencies (absolute and relative) were computed and summarized in Tables.

Relationships between normally distributed continuous outcome variables with other variables were assessed using Pearson's correlation coefficient (r). For comparisons of proportions, the χ^2 and the Fishers exact tests were used as appropriate.

For comparisons of means of outcome variables (birth weight, gestation length and Apgar score), the ANOVA technique was used. During the various stages of these specific parametric analytic procedure, assessments were done to ascertain whether the data met the independence, and homogeneity of variance assumptions. The Welch F statistic was used as the robust test of equality of means where homogeneity of variance assumption was violated.

Post hoc tests (Hochberg's GT2 test was used where samples sizes were different and the Gaems-Hoewell procedure where homogeneity of variance assumption was violated.

Crude values of key continuous variables such as maternal CD4+ T cell counts which were found not to be normally distributed were analyzed using nonparametric techniques. The nonparametric analog of the ANOVA test (the Kruskal Wallis test) was used. The Mann Whitney U test was also used as a multiple comparison tool (Post Hoc test). In this singular instance, the level of significance was set at $p < 0.0167$ (which is 0.05 divided by the number of comparisons/tests).

The associations between adverse perinatal outcomes, and maternal infection status, as well as other factors were investigated using simple logistic, and multiple logistic regression techniques. Assessment of the strength of these associations was done using odds ratios (ORs) and their 95% confidence intervals (CI). Adjusted odds ratios (AOR) were computed controlling for a number of factors including maternal age, CD4 count, and gestation length. The covariates used in the multiple regression models were included if they were significantly associated with any of the outcome measures in the bivariate analyses, or if they were known to be associated with these outcomes based on previous studies.

3.17.1 Qualitative data analysis

The data from the in-depth interviews and participant observations were analyzed manually. This consisted of reading the jotted notes, synthesizing and grouping them into meaningful prose. These are presented as cases in Boxes 4.1 to 4.3.

3.18.0 Quality assurance

The following measures were put in place to ensure the quality and validity of the study data and findings:

- ⇒ Prior to the field work, the research assistants, nurses and laboratory technicians were trained to ensure that all the questions were comprehended, all procedures delivered in a standardized way, and that responses were recorded adequately. There was a full-day training session at each of the study sites;
- ⇒ Each day, the weighing scales and the skinfold calipers were checked for errors and calibrated before use;
- ⇒ Unannounced regular visits to the field sites were made to ensure that data were being collected through standardized procedure. During these visits, completed questionnaires were reviewed for consistency;
- ⇒ Effects of potential influential outliers were eliminated by using the median as a measure of central tendency and nonparametric analytic techniques where data were found not to be normally distributed.

CHAPTER FOUR

4.0 RESULTS

This chapter presents the findings of the study, organized into the following four themes:

4.1.0 Characteristics of the study participants; page 75;

4.2.0 Malaria, HIV infections during pregnancy and adverse perinatal outcomes; page 85;

4.3.0 Malaria, HIV infections during pregnancy and adverse maternal outcomes; page 106;

4.4.0 Infant feeding choices, experiences, and challenges faced by HIV-positive mothers; page 112.

4.1.0 Characteristics of the study participants

4.1.1 Background, socio-demographic, and other characteristics of study participants

Between June 2005 and March 2008, a total of 27,002 pregnant women as part of their usual antenatal endeavors, visited the three study hospitals (the Tema General Hospital, the Atua Government Hospital, and the St Martins de Porres Hospital) and were registered. Of these, a total of 1,154 pregnant women comprising 443 HIV-positive women and 711 HIV-negative women were recruited into the study. A little over 30% (361) of the 1154 enrolled were lost to follow up before delivery (128 HIV-positive and 233 HIV-negative). Thus 793 women returned and delivered at the designated study hospitals. Details of the study profile including the rates of the main perinatal outcomes by maternal HIV infection status are presented in Fig 4.1. Comparisons of the proportion of study participants recruited and followed up at delivery by study site and by HIV-serostatus are provided in Fig. 4.2.

Excluded from the analyses were 32 cases (7 babies who were products of multiple deliveries, 11 stillbirths, and 13 with missing/inadequate data). This left 761 (295 HIV-positive, and 466 HIV-negative) mother-infant pairs with adequate follow-up data for the analysis.

Other details of the characteristics of the overall study sample (1,154) are as in Table 4.1a. About one-third of these women were younger than 25 years, over 90% attended their first antenatal visit during the second and third trimesters of gestation (average gestation age: six months; ranging from one to nine months). Close to ten percent did not have any form of formal education, and most had not completed secondary schooling (72.7%). The majority were either married or cohabited with a partner (72.5%). About 27% were nulliparas, 38% primiparas, 20% were secundiparas, and 6% multiparas. The prevalence of primigravidity, secundi-gravidity and multigravidity among the study subjects were 30% 32.3% and 37% respectively.

Also included in Table 4.1a, are the details of the occupations and socio-economic index scores¹⁶ of the study participants. Services which included bakery, catering, food vending, hairdressing, tailoring formed the main source of income generating activity/occupation of the study participants. Their socio-economics status as operationally defined in this study was determined by assigning scores to four variables- the occupation, and educational level of subjects; and also the occupation and educational levels of their partners. Most of the participants were in the middle socio-economic stratum.

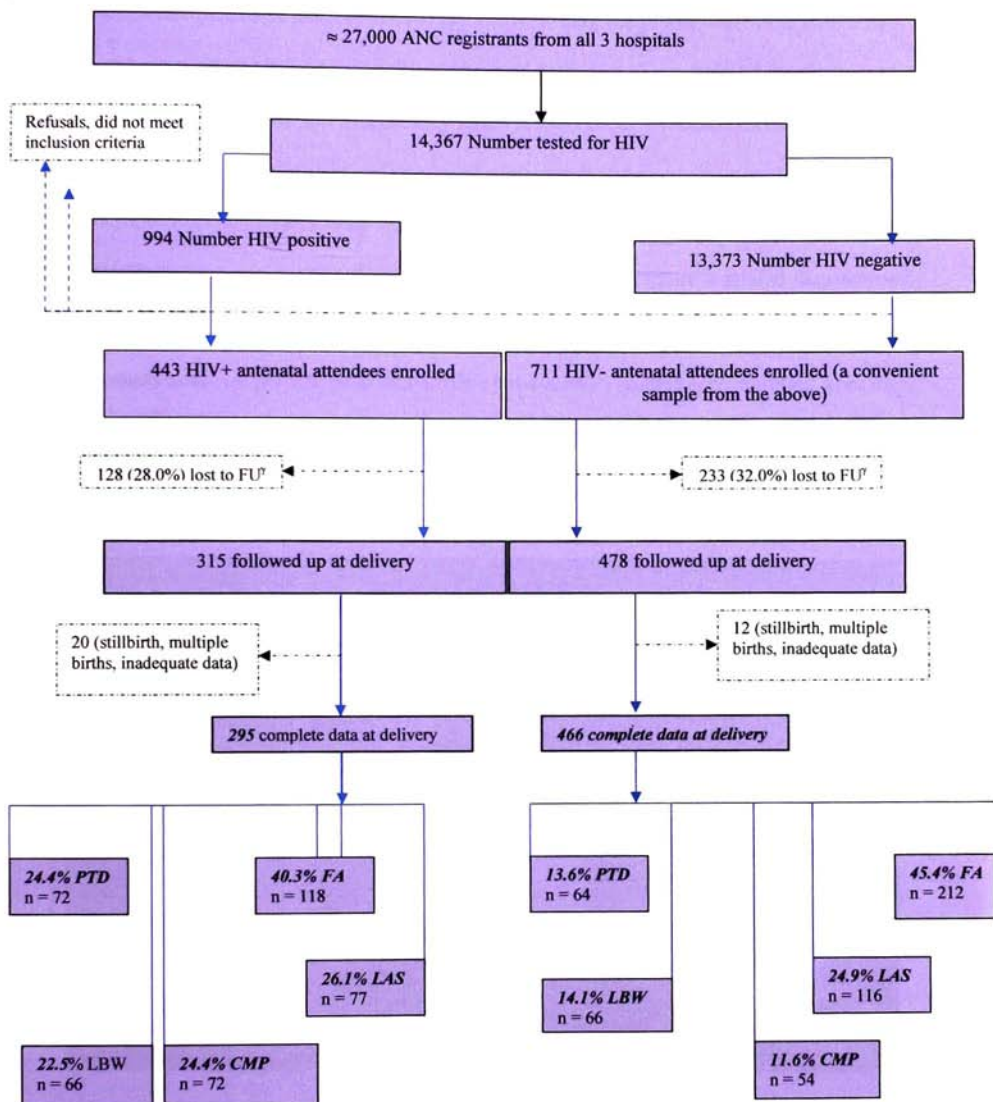
In Table 4.1b, an effort is made in comparing the baseline background and socio-demographic characteristics of the women on whom adequate data at delivery were available with that of

¹⁶ Assignment of scores done using four variables- the occupation, and educational level of subjects; and also the occupation and educational levels of their partners or caregivers (refer to Box 3.2 for details).

those who were lost to follow-up. These two groups of women did not differ significantly in terms of their age distribution, gestation length at first antenatal visit, occupation and socioeconomic stratification (Table 4.1b). They, however, differed significantly with respect to marital status, level of education, and place of residence (Table 4.1b).

In Table 4.2, remarkable differences in the distributions of the baseline demographic characteristics of the study participants are observed when comparisons were made by HIV-serostatus. HIV-negative participants were relatively younger ($p < 0.001$), initiated antenatal visit earlier than their HIV-positive counterparts ($p = 0.041$), and were more likely to be single/ not cohabiting compared to their HIV-positive counterparts ($p < 0.001$). The rest of the characteristics by HIV status are detailed therein.

Fig 4.1. Profile of study participants and the main adverse perinatal outcomes



[†]High antenatal attendance and very low institutional delivery is a very common phenomenon in these settings

4.1.2 Distribution of subjects at recruitment and at delivery by HIV sero-status and study sites

In Fig 4.2, a comparison is made at each study site regarding the proportion of the total study participants enrolled as well as those followed up at delivery. About 30% of the total 1154 subjects were enrolled from the Tema study site. Of this, about 25% had follow-up data at delivery documented. A little over one-third were each enrolled from the two study sites in the Manya Krobo. Follow up rates were slightly better in these sites (37.5% for Atua and 37.7% for St Martins) compared to 25% for the Tema site. In the same figure a related distribution showing how the 711 HIV-negative as well as the 443 HIV-positive were distributed among the three study sites. On per site basis more HIV+ but not HIV- women were enrolled from the Tema site.

Fig 4.2 Distribution of study participants at recruitment and at delivery by HIV status and study sites

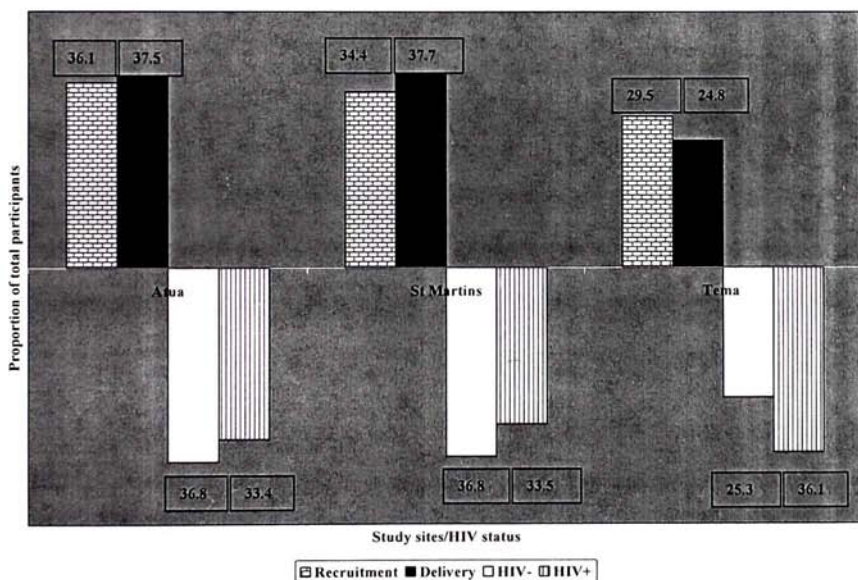


Table 4.1a Baseline background, and socio-demographic characteristics of all women at enrolment (N = 1154)

	All participants at enrolment
Age	
19 years or younger	113 (9.8)
20-24 years	277 (24.0)
25 years or older	762 (66.0)
Trimester at recruitment¹⁷	
First	110 (9.5)
Second	510 (44.2)
Third	527 (45.7)
Subject's level of education	
Nil	110 (9.5)
Primary	276 (23.9)
Middle/JSS	454 (39.3)
Secondary/Post secondary	244 (21.1)
Tertiary	67 (5.8)
Partner's level of education	
Nil	57 (4.9)
Primary	109 (9.4)
Middle/JSS	423 (36.7)
Secondary/Post secondary	343 (29.7)
Tertiary	161 (14.0)
Marital status	
Married	520 (45.1)
Cohabiting	316 (27.4)
Single	314 (27.2)
Divorced/Separated	4 (<0.01)
Religion	
Christian	809 (70.1)
Islam	322 (27.9)
Traditionalist	17 (1.5)
None	4 (0.3)
Place of residence	
Rural	760 (65.9)
Urban	394 (34.1)
Occupation of subject	
Not working	53 (14.4)
Peasant farming	10 (2.7)
Services	297 (80.5)
Clerical work	3 (0.8)
Professional/technical/administrative work	6 (1.6)
Occupation of partner	
Not working	17 (4.6)
Peasant farming	41 (11.1)
Services	219 (59.3)
Clerical work	56 (15.2)
Professional/technical/administrative work	36 (9.8)
Socio-economic index score of subject	
Low	99 (26.7)
Middle	252 (68.3)
High	18 (4.9)

¹⁷Baseline reproductive history of participants with follow up data. Average gestation age at recruitment: 6.27months; range (1 to 9 months) Parity: Nulliparous (26.8%) Primiparous (37.6%) Secundiparous (19.5%) Multiparous (6.1%); Gravidity Primigravid (30.8%) Secundigravid (32.3%) Multigravid (36.9%)

Table 4.1b Baseline background, and socio-demographic characteristics of women on whom complete data at delivery were available compared with those who were lost to follow-up

Characteristic	Participants at delivery	Participants lost to follow-up	P value ^{16a}
Age			
19 years or younger	79 (10)	31 (8.4)	0.587
20-24 years	181 (23.8)	88 (24.0%)	
20-24 years	501 (65.8)	248 (67.6)	
Trimester at recruitment			
First	69 (9.1)	39 (10.6)	0.540
Second	332 (43.9)	167 (45.5)	
Third	355 (47.0)	161 (43.9)	
Marital status			
Married	349 (45.9)	160 (43.4)	<0.001
Single	239 (31.4)	65 (17.6)	
Divorced/Separated	2 (0.3)	1 (0.3)	
Cohabiting	171 (22.5)	143 (38.8)	
None	1 (1.0)	3 (8.0)	
Religion			
Christian	468 (61.7)	331 (89.7)	<0.001
Islam	277 (36.5)	31 (8.4)	
Traditionalist	13 (1.7)	4 (1.1)	
None	1 (1.0)	3 (8.0)	
Place of residence			
Rural	471 (62.1)	280 (75.9)	<0.001
Urban	288 (37.9)	89 (24.1)	
Subject's level of education			
Nil	79 (10.4)	31 (8.4)	<0.001
Primary	172 (22.7)	101 (27.4)	
Middle/JSS	272 (35.9)	171 (46.3)	
Secondary/Post secondary	180 (23.7)	55 (14.9)	
Tertiary	55 (7.3)	11 (3.0)	
Partner's level of education			
Nil	45 (5.3)	12 (3.3)	0.040
Primary	68 (9.6)	39 (10.8)	
Middle/JSS	260 (36.6)	159 (44.2)	
Secondary/Post secondary	228 (32.1)	105 (29.2)	
Tertiary	110 (15.5)	45 (12.5)	
Occupation of subject			
Not working	143 (18.8)	53 (14.4)	0.431
Peasant farming	22 (2.9)	10 (2.7)	
Services	576 (75.7)	297 (80.5)	
Clerical work	5 (0.7)	3 (0.8)	
Professional/technical/administrative work	15 (2.0)	6 (1.6)	
Occupation of partner			
Not working	39 (5.1)	17 (4.6)	0.773
Peasant farming	74 (9.7)	41 (11.1)	
Services	434 (57.0)	219 (59.3)	
Clerical work	128 (16.8)	56 (15.2)	
Professional/technical/administrative work	86 (11.3)	36 (9.8)	
Subject's SE index score			
Low	186 (27.0)	76 (22.4)	0.117
Middle	471 (68.3)	252 (74.3)	
High	33 (4.8)	11 (3.2)	

^{16a}p value compares the differences in the characteristics of women on whom complete data at delivery were available and those who were lost to follow-up

Table 4.2 Baseline socio-demographic characteristics of women by HIV-sero status

Characteristic	HIV- participants N = 711 (100%)	HIV+ participants N = 443 (100%)	P value ¹⁸
Age categories			
19 years or younger	93 (13.1)	20 (4.5)	< 0.001
20-24 years	191 (26.9)	86 (19.4)	
25 years or older	425 (59.8)	337 (76.1)	
Trimester at recruitment¹⁹			
First	75 (10.7)	35 (7.9)	0.041
Second	325 (45.7)	185 (41.8)	
Third	304 (42.8)	223 (50.3)	
Marital status			
Married	314 (44.2)	206 (46.5)	< 0.001
Single	238 (33.5)	76 (17.2)	
Divorced/Separated	1 (0.1)	3 (0.7)	
Cohabiting	158 (22.2)	158 (35.7)	
Religion			
Christian	393 (55.3)	416 (93.9)	< 0.001
Islam	304 (42.8)	18 (4.1)	
Traditionalist	12 (1.7)	5 (1.1)	
None	2 (0.28)	4 (0.9)	
Place of residence			
Rural	425 (59.8)	335 (75.6)	< 0.001
Urban	284 (39.9)	108 (24.4)	
Subject's level of education			
Nil	182 (25.6)	110 (24.8)	< 0.001
Primary	265 (37.3)	94 (21.2)	
Middle/JSS	195 (27.4)	189 (42.7)	
Secondary/Post Secondary	66 (9.3)	49 (11.1)	
Tertiary	3 (0.4)	1 (0.2)	
Partner's level of education			
Nil	62 (8.7)	57 (12.9)	< 0.001
Primary	194 (27.3)	47 (10.6)	
Middle/JSS	251 (35.3)	229 (51.7)	
Secondary/Post secondary	143 (20.1)	92 (20.8)	
Tertiary	650 (91.4)	18 (4.1)	
Occupation of subject			
Not working	133 (18.7)	68 (15.3)	0.001
Peasant farming	18 (2.5)	14 (3.2)	
Services	536 (75.4)	356 (80.4)	
Clerical work	3 (0.4)	5 (1.1)	
Professional/technical/administrative work	21 (3.0)	0 (0.0)	
SE index score of subject			
Low	167 (23.5)	177 (40.1)	< 0.001
Middle	489 (67.6)	262 (59.2)	
High	63 (8.8)	4 (0.9)	

¹⁸ P value compares the differences in proportions of the various characteristics of HIV-positive participants to those who were HIV-negative

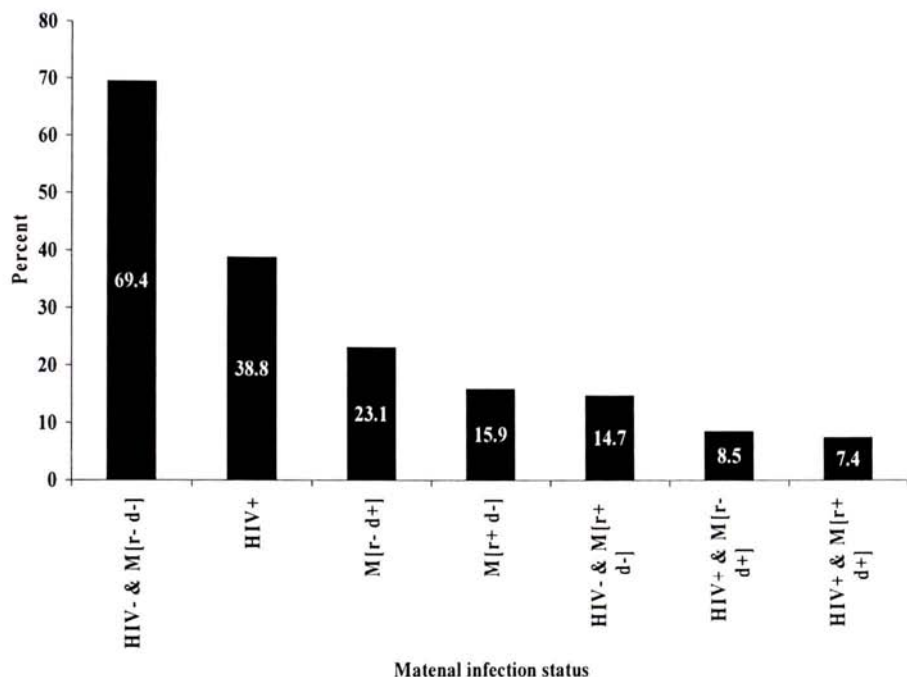
¹⁹Baseline reproductive history of participants: (HIV-negative: Primigravid [33.4%], Secundigravid [29.1%], Multigravid [37.5%]); (HIV-positive: Primigravid [26.8%], Secundigravid [37.3%], Multigravid [35.9%]) (HIV-: Nulliparous [38.2%], Primiparous [28.8%], Secundiparous [17.8%], Multiparous [15.2%]); (HIV+ Nulliparous [2.8%], Primiparous [56.0%], Secundiparous [23.1%], Multiparous [18.1%]); Mean duration of pregnancy at first antenatal visit HIV-negative (6 months, HIV-positive (6.5 months).

4.1.3 Maternal infection status and related clinical characteristics of the study participants

Fig 4.3, Table 4.3 and Appendices 7 – 9 provide information on the clinical characteristics of the study subjects. The distribution of the participants by malaria and HIV infection status throughout the study period is presented in Fig 4.3. In Table 4.3, a comparison of the baseline outcomes of the study participants on whom complete data at delivery were available is made with those of the participants who were lost to follow-up. With the exception of severe anemia (defined as hemoglobin concentration < 7.0 g/dl), the participants on whom follow-up data at delivery were documented were comparable to those who were lost to follow-up regarding these baseline clinical outcomes (Table 4.3).

These baseline outcomes were also compared by HIV sero-status. This is appended as one of the appendices (Appendix 7), while the results of the clinical appraisals done on the subjects at recruitments are presented in Appendix 8. Twelve different clinical conditions were documented. Sore throat, fever and gastrointestinal distress were more common (accounting for about two-third of the total prevalence; Appendix 8). The individual prevalence rates of other conditions like anorexia/loss of appetite, clinical anemia, diarrhea, herpes, oral lesions and TB were under 10%. Using these twelve clinical conditions assessed, a morbidity profile for each of the study participants was constructed theoretically ranging from zero (indicating the subject presented with none of the 12 conditions) to twelve (meaning the particular subject presented with all 12 conditions). The actual morbidity profile as presented in Appendix 9 ranged from zero to seven (with over 40% of the subjects presenting with none of the 12 assessed conditions, and as low as under one percent (0.4%) of the participants presenting with six or more co-morbidities).

Fig 4.3 Distribution of study participants by maternal infection status (N = 761)



Key: M[r]⇒ malaria positive at recruitment; M[d] ⇒ malaria positive at delivery; M[r+ d-] ⇒ malaria positive at recruitment and negative at delivery; M[r+ d+]⇒ malaria positive both at recruitment and at delivery



Table 4.3 Baseline outcomes of women on whom complete data at delivery were available compared with those who were lost to follow-up

Characteristic	Participants lost to follow-up	Participants at delivery	p-value
MUAC			
< 23.5cm	31 (8.9)	73 (9.6)	0.410
>23.5cm	316 (91.1)	688 (90.4)	
Morbidity profile			
< 4 conditions	352 (95.4)	708 (93.0)	0.077
4 or more conditions	17 (4.6)	53 (7.0)	
CD4+ count			
>350 cells/mm ³	69 (50.7)	162 (54.9)	0.214
<350 cells/mm ³	67 (49.3)	133 (45.1)	
Malaria infection			
Negative	320 (87.4)	637 (83.9)	0.071
Positive	46 (12.6)	122 (16.1)	
Herbal drug use			
No	244 (69.1)	492 (73.3)	0.089
Yes	109 (30.9)	179 (26.7)	
Clinical anemia			
Not anemic	349 (94.6)	710 (93.3)	0.244
Anemic	20 (5.4)	51 (6.7)	
Anemia/Hb concentration			
> 11g/dl	147 (40.7)	276 (36.8)	0.113
<11 g/dl	214 (59.3)	475 (63.2)	
Severe anemia			
Not anemic	351 (97.2)	744 (99.1)	0.022
Anemic	10 (2.8)	7 (0.9)	
HIV disease state			
Asymptomatic	140 (96.6)	273 (92.5)	0.252
Symptomatic	5 (3.4)	22 (7.5)	
Gravidity			
Primigravid	11 (31.4)	230 (30.3)	0.450
Secundigravid	107 (29.0)	248 (32.7)	
Multigravid	146 (39.6)	281 (37.0)	
Parity			
Nulliparous	90 (28.5)	177 (26.3)	0.136
Primiparous	97 (30.7)	254 (37.8)	
Secundiparous	77 (24.4)	133 (19.8)	
Multiparous	52 (16.5)	108 (16.1)	

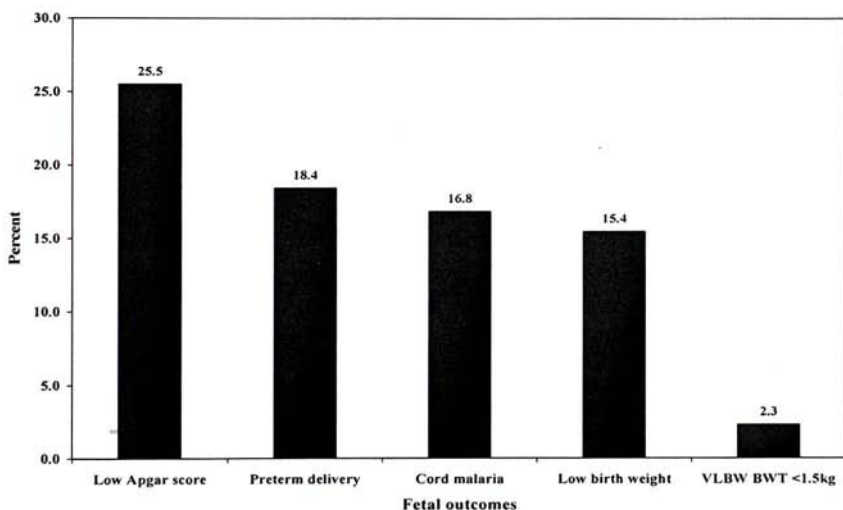
4.2.0 Adverse perinatal outcomes

4.2.1 Malaria and HIV infections during pregnancy and adverse perinatal outcomes

One of the objectives of this study was to document the associations between malaria and HIV infections during pregnancy and four adverse perinatal outcomes. These adverse perinatal outcomes were PTD, LBW, LAS, and CMP. To accomplish this, the study recruited 1154 (443

HIV-positive and 711 HIV-negative) antenatal attendees and prospectively collected data on perinatal outcomes at delivery. With an attrition rate of 34%, data on perinatal outcomes were available for 761 of the 1154 women recruited. Of this, 611 (80.3%) delivered vaginally, and 149 (19.6%) via emergency Cesarean section, one (< 0.1) through elective Cesarean section. Mean gestation length, birth weight, and Apgar score among the 761 neonates were respectively 38.1 weeks, 3.0 kg, and 6.9. The select group of neonates who were delivered before the 37th week did not differ markedly from the overall group with respect to average Apgar score (6.9 vs 6.8). The overall prevalence of the various adverse events assessed were: LAS (25.5%); PTD (18.4%), CMP (16.8%), and LBW (15.4%). These are presented in the figure below.

Fig 4.4 Prevalence of adverse perinatal outcomes at delivery (N = 761)



4.2.2 Association between adverse perinatal outcomes and maternal infection status stratified by gravidity

The associations between infant outcomes and some selected maternal outcomes stratified by maternal reproductive history are presented in Tables 4.4a and 4.4b. With respect to HIV infection and incidence of LBW, there were no gravidity-specific effects. Prevalence of LBW was significantly more among the HIV-positive primigravids than their HIV-negative counterparts ($p = 0.018$). This was also true in the select group of multigravid mothers, where the incidence of LBW in the HIV-positive women was also double that in the HIV-negative women ($p = 0.031$).

A comparable picture could be visualized with respect to maternal malaria infection at delivery (Table 4.4a). On the contrary, maternal malaria infection only at delivery was associated with LBW in the multigravid women ($p = 0.022$) but not in the primigravids ($p = 0.340$). In most cases, statistically significant associations were observed between the various adverse outcomes and the various maternal infections categories (Tables 4.4a and 4.4b). These observations suggest a tendency toward an increased frequency of adverse outcomes among women with both infections either at recruitment or at delivery.

Table 4.4a Associations between adverse perinatal outcomes and maternal infection status stratified by gravidity

	LBW		PTD	
	<i>Primi-gravid n (%)</i>	<i>Multi-gravid n (%)</i>	<i>Primi-gravid n (%)</i>	<i>Multi-gravid n (%)</i>
Maternal infection status				
P	0.018	0.031	<0.001	<0.001
HIV-	17 (48.6)	39 (46.4)	13 (30.2)	33 (38.8)
HIV+	18 (51.4)	45 (53.6)	20 (69.8)	52 (61.2)
P	<0.001	<0.001	0.040	0.042
Malaria parasitemia at enrollment	14 (41.1)	22 (26.2)	12 (27.9)	18 (21.2)
No malaria at enrollment	20 (58.9)	62 (73.8)	21 (72.9)	67 (78.8)
P	0.115	<0.001	0.071	0.093
Malaria parasitemia at delivery	11 (31.4)	33 (39.3)	11 (25.6)	26 (31.0)
No malaria at delivery	24 (68.6)	51 (60.7)	22 (74.4)	58 (69.0)
P	0.011	<0.001	0.183	0.025
HIV+ & malaria at enrollment	10 (55.6)	15 (33.3)	9 (34.6)	13 (25.0)
HIV+ but no malaria at enrollment	8 (44.4)	30 (66.7)	11 (20.8)	39 (75.0)
P	0.340	0.022	0.100	0.822
HIV+ & malaria at delivery	7 (38.9)	20 (44.4)	9 (36.0)	15 (28.8)
HIV+ but no malaria at delivery	11 (61.9)	25 (55.6)	11 (64.0)	37 (71.2)
P	<0.001	<0.001	0.004	0.001
HIV+ & malaria both at enrolment & at delivery	9 (36.0)	18 (21.4)	8 (24.2)	13 (15.3)
HIV+ but no malaria both at enrollment and at delivery	26 (64.0)	66 (78.6)	25 (75.8)	72 (84.7)

P = p value: indicates whether the proportions of the adverse events differed significantly by maternal infection status.

Table 4.4b Associations between adverse perinatal outcomes and maternal infection status stratified by gravidity

	Low Apgar score		Cord malaria	
	Primi-gravid n (%)	Multi-gravid n (%)	Primi-gravid n (%)	Multi-gravid n (%)
Maternal infection status				
P	0.199	0.710	0.003	0.001
HIV-	38 (57.6)	72 (59.0)	14 (41.2)	36 (40.9)
HIV+	28 (42.4)	50 (41.0)	20 (58.8)	52 (59.1)
P	0.639	0.009	0.001	<0.001
Malaria parasitemia at enrollment	16 (24.6)	26 (21.3)	15 (44.1)	27 (30.7)
No malaria at enrollment	49 (75.4)	96 (78.7)	19 (55.9)	61 (69.7)
P	0.002	0.131	<0.001	<0.001
Malaria parasitemia at delivery	23 (34.8)	35 (28.9)	30 (88.2)	82 (93.2)
No malaria at delivery	43 (65.2)	86 (71.1)	4 (11.8)	6 (6.8)
P	0.017	0.004	0.060	<0.001
HIV+ & malaria at enrollment	14 (50.0)	14 (28.0)	10 (50.0)	16 (30.8)
HIV+ but no malaria at enrollment	14 (50.0)	36 (72.0)	10 (50.00)	36 (69.2)
P	<0.001	0.737	<0.001	<0.001
HIV+ & malaria at delivery	16 (51.1)	16 (32.0)	18 (90.0)	50 (96.3)
HIV+ but no malaria at delivery	12 (42.9)	34 (68.0)	2 (10.0)	2 (3.8)
P	0.002	0.030	<0.001	<0.001
HIV+ & malaria both at enrolment & at delivery	12 (15.9)	14 (11.5)	12 (35.3)	24 (27.3)
HIV+ but no malaria both at enrollment and at delivery	54 (84.2)	108 (88.5)	22 (64.7)	64 (72.3)

P = p value: indicates whether the proportions of the adverse differed significantly by maternal infection status

4.2.3 Correlations among maternal and infant outcomes and some selected maternal characteristics

In Tables 4.5a and b, the correlational relationships between study outcomes and some selected maternal characteristics are presented. Maternal hemoglobin was positively and significantly associated with maternal MUAC ($r = 0.125$; $p < 0.001$), and maternal weight at recruitment ($r = 0.073$ $p < 0.05$), but negatively with morbidity profile ($r = -0.112$; $p < 0.001$). Of the infant outcomes, birth weight was positively and significantly correlated with gestation length ($r = 0.310$; $p < 0.001$), while gestational length as an outcome was also positively related with maternal weight at recruitment, and negatively with maternal hemoglobin at delivery, and duration of pregnancy at first antenatal visit (Table 4.5a). The maternal anthropometric measurements taken in this study (MUAC, and weight) were both not

significantly related with infant anthropometry (birth weight). Controlling for maternal HIV infection did not appreciably alter these results of the correlation analysis (Table 4.5b).

Table 4.5a. Relationship between maternal and infant outcomes and some selected maternal characteristics (Pearson correlations)

		Age of mother	Duration of pregnancy	MUAC	Weight	Morbidity profile	Hb at enrollment	Apgar score	Birth weight	Gestation length
Age of mother	r	1								
Pregnancy duration at enrollment	r	-.006	1							
MUAC	r	.273**	-.046	1						
Weight	r	.194**	.160**	.672**	1					
Morbidity profile	r	.042	-.128**	-.106**	-.115**	1				
Hb at recruitment	r	-.004	-.047	.125**	.073*	-.112**	1			
Apgar score	r	.062	.020	.024	.036	-.013	.037	1		
Birth weight	r	-.057	-.041	-.020	-.018	.020	.063	-.012	1	
Gestation length	r	-.062	-.094*	.004	.082*	-.020	.071	-.008	.310**	1

Table 4.5b. Relationship between maternal and infant outcomes and some selected maternal characteristics (controlling for HIV infection status)

		Age of mother	Duration of pregnancy	MUAC	Weight	Morbidity profile	Hb at enrollment	Apgar score	Birth weight	Gestation length
Age of mother	r	1								
Pregnancy duration at enrollment	r	-.036	1							
MUAC	r	.273**	-.045	1						
Weight	r	.210**	.166**	.672**	1					
Morbidity profile	r	.006	-.130*	-.095*	-.091*	1				
Hb at recruitment	r	.078*	-.016	.121*	.047	-.047	1			
Apgar score	r	.014	-.013	.020	.040	.011	.068	1		
Birth weight	r	-.042	-.010	-.035	-.036	.051	-.017	.023	1	
Gestation length	r	-.053	-.085*	-.011	.054	.010	.014	.060	.297*	1

** Correlation is significant at the 0.01 level 2-tailed. * Correlation is significant at the 0.05 level 2-tailed.

4.2.4 Association between maternal infection status and infant outcomes (birth weight, gestation length, Apgar score)

Attempts have been made in the previous sections to demonstrate the associations between some maternal factors and infant outcomes. Some associations particularly between maternal infection status and PTD, LBW, LAS, and CMP were observed (Tables 4.4a and 4.4b). To further explore the connection between malaria and HIV infections and such infant outcomes as birth weight, gestation length, and Apgar score, it was hypothesized that, these outcomes are associated with the following variants of maternal infection status.

- (i) HIV- & M [r- d-]:- women with no HIV, & also no malaria both at recruitment and at delivery
- (ii) HIV- & M [r+ d-]:- women with no HIV, but have malaria at recruitment & not at delivery,
- (iii) HIV+ & M [r- d+]:- women with HIV, no malaria at recruitment but have malaria positive at delivery,
- (iv) HIV+ & M [r+ d+]:- HIV-positive women with malaria both at recruitment and at delivery

Two approaches were then employed to test these hypotheses. In the first approach the parametric analytic procedure ANOVA was used to test the differences in the means of the three outcomes across the above four groups. The second approach made use of simple logistic and multiple logistic regression techniques. These are presented in sub-sections 4.2.5 through 4.2.8.4.

4.2.5 Association between maternal infection status and birth weight

The effect of no infection (HIV- & M [r- d-]), single maternal infection (HIV- & M [r+ d-], dual infection at recruitment (HIV+ & M [r+ d-]), at delivery (HIV+ & M [r- d+]), and at both time points (HIV+ & M [r+ d+]) on mean birth weight are presented in Table 4.6a. The outcome of this procedure (statistically described as Generalized Linear Model One [GLM 1]) supports the hypothesis that the mean birth weight of a neonate differs significantly by maternal infection status; $F(3, 722) = 11.23$; $p < 0.001$ (Table 4.6a).

Given the disparity in the sample sizes across the test groups, the Hochberg GT2 Post Hoc test was the appropriate choice for the multiple comparisons (Table 4.6b). These comparisons while affirming the findings above, specifically showed that compared to HIV-negative women without malaria at recruitment, HIV-negative women with malaria infection only at recruitment, on average delivered babies who weighed 0.123kg less; mean difference = 0.123kg; 95% CI (0.001 – 0.244); $p = 0.046$. Those dually infected at recruitment delivered babies weighing 0.195kg less; mean difference = 0.195kg; 95% CI (0.035 – 0.356), $p = 0.008$. These differences in mean birth weight were particularly marked in women dually-infected both at recruitment and at delivery. These women delivered babies weighing on average 0.563kg less than those of uninfected counterparts; mean difference = -0.563.5kg; 95% CI (-0.855 -0.272; $p < 0.001$; Table 4.6b). Collectively these findings demonstrate that maternal infection with HIV, and/ or malaria has a significant effect on birth weight.

4.2.6 Association between maternal infection status and gestation length

As was done with birth weight, the possible association between maternal infection status and gestation length was similarly evaluated. The results are presented in Tables 4.7a and b. The results also show the existence of statistically significant differences in gestation length across the four different groups. Of note here, is the violation of the homogeneity of variance assumption (Levene Statistic [4.321; df1:df2 (3: 739)]; $p = .005$). To ensure validity of the test outputs, a more robust test of equality of means (the Welch F statistic) was used. This again affirmed the hypothesis that significant differences exist in mean gestation length across the maternal infections categories; $F(3, 123) = 7.40$; $p < 0.001$. The violation of the homogeneity of variance assumption also informed the choice of the Post Hoc test. In this case, the Games-Howell test was chosen. On average, maternal infections (single or dual) were associated with

shorter gestation length. However, this was more pronounced and statistically significant in the group of women who were dually infected both at recruitment and at delivery. Compared to their HIV-uninfected, and malaria negative counterparts, this group of women delivered two (2) weeks earlier; mean difference = -2.08 weeks 95% CI (-3.28 – -0.88), $p < 0.001$. These differences persisted, but nevertheless attenuated when the malaria negative/HIV-uninfected group was replaced by single infection, or dual infection only at recruitment (Table 4.7b). Again this narrative can be visualized pictorially in Table 4.7b. All these put together show that maternal dual infection with HIV and malaria during the course of pregnancy has a significantly negative effect on gestation length. This was especially true in the group of women who were dually infected both at recruitment and at delivery.

4.2.7 Association between maternal infection status and Apgar score

Similar conclusions as in the above sections are made here regarding the effect of maternal malaria and HIV infection on neonate's Apgar score. Thus, newborns differed significantly regarding their average Apgar score depending on whether they were born to HIV/malaria uninfected mother, HIV-negative/malaria-positive mother, or a mother dually-infected with these conditions (Table 4.8a). In statistical terms, there was a significant reduction in Apgar corresponding to the degree of maternal infection burden; $F(3, 757) = 6.62$; $p < 0.001$ (Table 4.8a). Details of the Post Hoc test are presented in Table 4.8b. Collectively the results demonstrate that maternal dual infection with HIV and malaria at first antenatal visit (recruitment) and at delivery is associated with a low Apgar score.

Table 4.6a Associations between maternal infection status and birth weight

Maternal infection status	Birth weight						
	N	Mean	Standard deviation	95% CI for the Mean		Min	Max
				Lower bound	Upper bound		
HIV- & M [r- d-]	338	3.05	0.55	2.99	3.10	1.60	5.40
HIV- & M [r+ d-]	252	2.92	0.52	2.86	2.99	1.30	4.80
HIV+ & M [r- d+]	109	2.85	0.62	2.73	2.97	1.00	4.90
HIV+ & M [r+ d+]	27	2.48	0.57	2.26	2.71	1.60	3.70
Total	726	2.95	0.56	2.91	2.99	1.00	5.40

Overall Test: F (3, 722) = 11.24; p < 0.001

Table 4.6b Post Hoc analysis (Hochberg GT2 test); dependent variable (birth weight)

(I) Maternal infection status	(J) maternal infection status	Mean Difference (I-J)	p value	95% CI	
				Lower bound	Upper bound
HIV- M _[r- d-]	HIV- M _[r+ d-]	.12255	.046	.0014	.2437
	HIV+ M _[r- d+]	.19543	.008	.0351	.3558
	HIV+ M _[r+ d+]	.56349	.000	.2724	.8546
HIV- M _[r+ d-]	HIV- M _[r- d-]	-.12255	.046	-.2437	-.0014
	HIV+ M _[r- d+]	-.07288	.821	-.0940	.2398
	HIV+ M _[r+ d+]	.44094	.001	.1462	.7357
HIV+ M _[r- d+]	HIV- M _[r- d-]	-.19543	.008	-.3558	-.0351
	HIV- M _[r+ d-]	-.07288	.821	-.2398	.0940
	HIV+ M _[r+ d+]	.36806	.012	.0551	.6810
HIV+ M _[r+ d+]	HIV- M _[r- d-]	-.56349	.000	-.8546	-.2724
	HIV- M _[r+ d-]	-.44094	.001	-.7357	-.1462
	HIV+ M _[r- d+]	-.36806	.012	-.6810	-.0551

Table 4.7a Associations between maternal infection status and gestation length

Maternal infection status	Gestation length						
	N	Mean	Standard deviation	95% CI for the Mean		Min	Max
				Lower bound	Upper bound		
HIV- & M [r- d-]	332	38.24	1.81	38.05	38.44	32.00	44.00
HIV- & M [r+ d-]	269	38.16	2.36	37.87	38.44	32.00	44.00
HIV+ & M [r- d+]	111	38.01	2.02	37.63	38.39	32.00	42.00
HIV+ & M [r+ d+]	31	36.16	2.41	35.28	37.05	32.00	41.00
Total	743	38.09	2.12	37.94	38.24	32.00	44.00

Overall Test: Welch F (3, 123); $p < 0.001$

Table 4.7b Post Hoc analysis (Games-Howell test); dependent variable: gestational length

(I) Maternal infection status	(J) Maternal infection status	Mean Difference (I-J)	p value	95% CI	
				Lower bound	Upper bound
HIV-M _[r- d-]	HIV- M _[r+ d-]	.08784	.958	-.3625	.5382
	HIV+ M _[r- d+]	.23497	.699	-.3264	.7964
	HIV+ M _[r+ d+]	2.08269	.000	.8820	3.2834
HIV- M _[r+ d-]	HIV- M _[r- d-]	-.08784	.958	-.5382	.3625
	HIV+ M _[r- d+]	.14712	.928	-.4737	.7679
	HIV+ M _[r+ d+]	1.99484	.001	.7682	3.2215
HIV+ M _[r- d+]	HIV- M _[r- d-]	-.23497	.699	-.7964	.3264
	HIV- M _[r+ d-]	-.14712	.928	-.7679	.4737
	HIV+ M _[r+ d+]	1.84772	.002	.5817	3.1138
HIV+ M _[r+ d+]	HIV- M _[r- d-]	-2.08269	.000	-3.2834	-.8820
	HIV- M _[r+ d-]	-1.99484	.001	-3.2215	-.7682
	HIV+ M _[r- d+]	-1.84772	.002	-3.1138	-.5817

Table 4.8a Associations between maternal infection status and Apgar score

Maternal infection status	N	Mean	SD	Apgar score			
				95% CI for the Mean		Min	Max
				Lower bound	Upper bound		
HIV- & M [r- d-]	350	6.85	2.10	6.62	7.07	.00	10.00
HIV- & M [r+ d-]	269	7.05	2.37	6.77	7.34	.00	10.00
HIV+ & M [r- d+]	111	6.86	2.17	6.46	7.27	.00	10.00
HIV+ & M [r+ d+]	31	5.16	2.70	4.17	6.15	.00	9.00
Total	761	6.85	2.26	6.69	7.01	.00	10.00

Overall Test: $F(3, 757) = 6.62; p < 0.001$

Table 4.8b Post Hoc analysis (Multiple Comparisons, Dependent Variable: Apgar score)

(I) Maternal infection status	(J) Maternal infection status	Mean Difference (I-J)	p value	95% CI	
				Lower Bound	Upper Bound
HIV- M _[r- d-]	HIV- M _[r+ d-]	-.20633	.829	-.6848	.2721
	HIV+ M _[r- d+]	-.01915	1.000	-.6619	.6236
	HIV+ M _[r+ d+]	1.68442	.000	.5788	2.7901
HIV- M _[r+ d-]	HIV- M _[r- d-]	.20633	.829	-.2721	.6848
	HIV+ M _[r- d+]	.18718	.975	-.4785	.8528
	HIV+ M _[r+ d+]	1.89075	.000	.7716	3.0099
HIV+ M _[r- d+]	HIV- M _[r- d-]	.01915	1.000	-.6236	.6619
	HIV- M _[r+ d-]	-.18718	.975	-.8528	.4785
	HIV+ M _[r+ d+]	1.70357	.001	.5050	2.9022
HIV+ M _[r+ d+]	HIV- M _[r- d-]	-1.68442	.000	-2.7901	-.5788
	HIV- M _[r+ d-]	-1.89075	.000	-3.0099	-.7716
	HIV+ M _[r- d+]	-1.70357	.001	-2.9022	-.5050

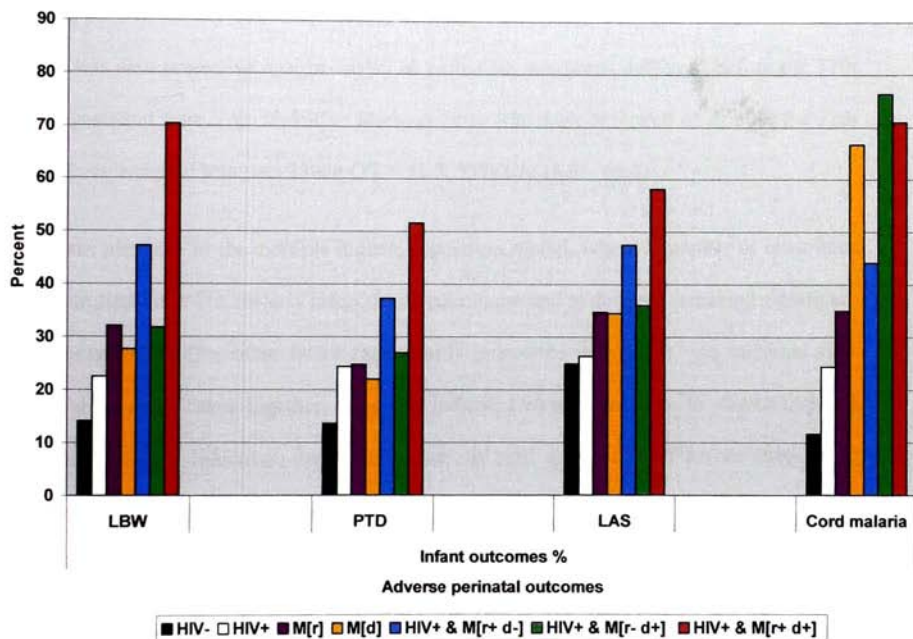
4.2.8 Associations between LBW, PTD, LAS, CMP and some selected maternal characteristics

This section examines the factors associated with the incidence of LBW, PTD, LAS, and CMP. Presented in Fig 4.5 are the prevalence rates of these adverse outcomes by maternal infection status.

Relating these adverse perinatal events to maternal infections status throughout the study period showed a clear trend. Overall, HIV-infected women were more likely to have an adverse perinatal outcome than uninfected women. To place these results in a broader context of maternal infections or dual infections at the two time points, the incidence of the above

adverse perinatal outcomes were compared against seven different maternal infection status (Fig 4.5). The incidence of these events was even more pronounced if the mother was at any point co-infected with malaria. Of all the groups compared, mothers who were co-infected with HIV and malaria both at their first antenatal visit and at delivery were worse off (Fig 4.5). In determining the risk factors of these adverse outcomes, simple logistic and multiple logistic regressions models were ran. Overall, women infected with HIV, malaria, or dually infected with these conditions either at recruitment or at delivery were more likely to have any of the adverse perinatal outcomes (Figs 4.6 – 4.9; Tables 4.9a – d).

Fig 4.5 Prevalence of adverse perinatal outcomes by maternal infection status



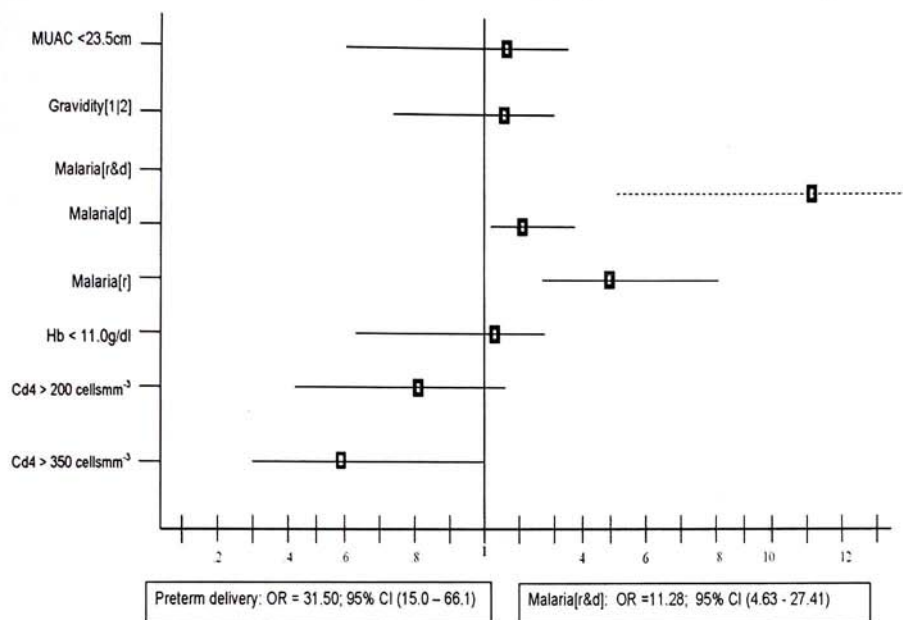
Key: LBW \Rightarrow low birth weight; PTD \Rightarrow preterm delivery; LAS \Rightarrow low Apgar score; M[r] \Rightarrow malaria positive at recruitment; M[d] \Rightarrow malaria positive at delivery; M[r+ d-] \Rightarrow malaria positive at recruitment and negative at delivery; M[r+ d+] \Rightarrow malaria positive both at recruitment and at delivery

4.2.8.1 Associations between LBW and some selected maternal characteristics

In Fig 4.5, the virtual profile suggests the existence of a negative association between LBW and maternal infection status. Incidence of LBW was higher in women with infection, and strikingly higher among women dually infected at two time points (at recruitment and at delivery). These findings are affirmed in Fig 4.6. This bivariate level analysis shows a significantly increased risk of LBW among HIV+ women who had malaria parasitemia at recruitment OR = 4.4; 95% CI (2.3 – 8.4), and at delivery OR = 2.5; 95% CI (1.1 – 3.7). This risk was statistically more pronounced in neonates whose mothers were dually infected with HIV and malaria at both time points – at recruitment and at delivery OR = 11.3; 95% CI (4.6 – 27.4; Fig 4.6). In accord with its generally protective effects on LBW, term delivery in this instance was also protective against LBW. In particular, newborns delivered before the 37th week of gestation were over 30-fold as likely as those who were delivered on or after the 37th week to have weighed less than 2500g OR = 31.5; 95% CI (15.0 – 66.1).

These risks persisted in the multiple logistic regression model, where a number of covariates were controlled for. PTD, malaria infection at recruitment and at delivery remained significant predictors of LBW. One other factor significantly associated with LBW was maternal HIV status (Table 4.9a). Taken together, these data indicate that neonates born to women exposed to malaria and HIV infections during pregnancy as well as those born before term are at particular risk of LBW.

Fig 4.6 Risk factors associated with LBW (bivariate analysis; ORs with their 95% CI)

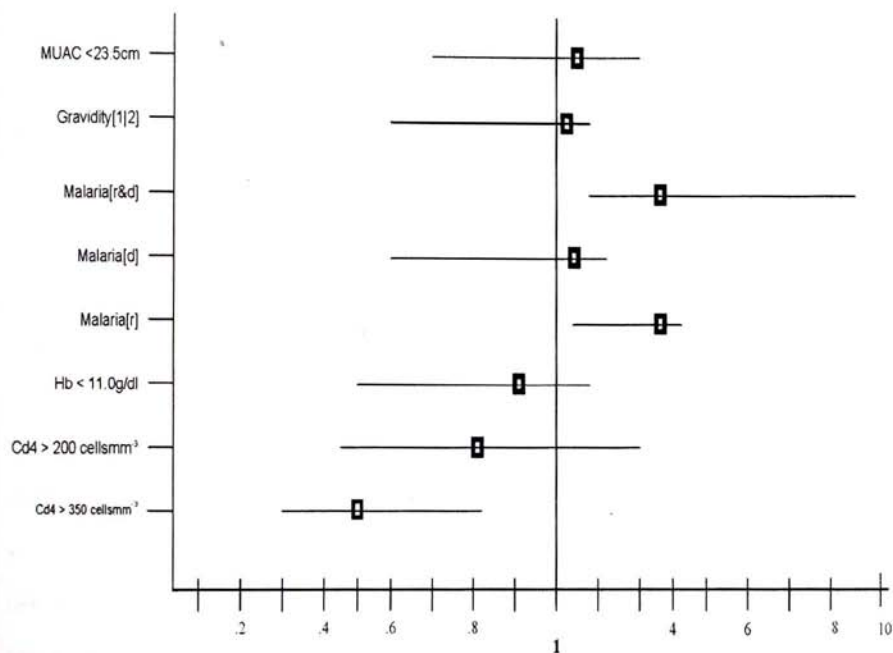


4.2.8.2 Associations between PTD and some selected maternal characteristics

In Fig 4.7, the associations between PTD and some clinical and nonclinical maternal factors are presented. Among HIV-positive women antibodies at recruitment, maternal CD4 count beyond a certain threshold (more than 350 cells per milliliter) were significantly protective against PTD. On the contrary, pregnant women with malaria had an increased risk of delivering preterm. Malaria infection (both at recruitment and at delivery) was associated with almost 4-fold risk of delivering before the 37th week of gestation OR = 3.96; 95% CI (1.8 – 8.5). Women with one-time malaria infection – recruitment, but not at delivery also had higher relative odds of delivery preterm (Fig 4.7). Maternal MUAC < 23.5cm, and maternal anemia (defined as hemoglobin concentration < 11.0g/dl) were both not significantly associated with PTD (Fig 4.7). These associations were further evaluated in a multiple logistic regression

model including maternal malaria infection at recruitment, at delivery, malaria infection at these two time points, HIV infection, and CD4 count as predictors. At this stage, malaria at recruitment, malaria at delivery, HIV status, were still significantly associated with PTB (Table 4.9b).

Fig 4.7 Risk factors associated with PTB (bivariate analysis; ORs with their 95% CI)



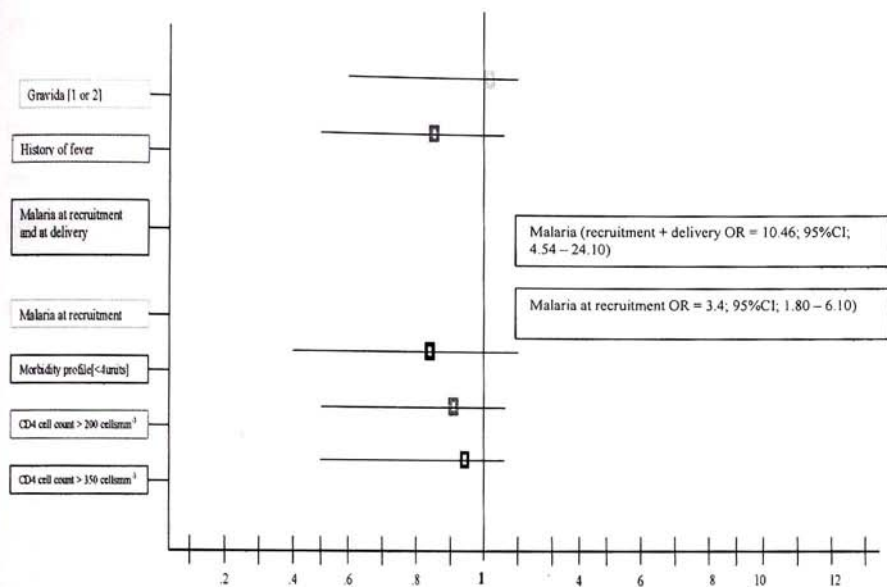
4.2.8.3 Associations between CMP and some selected maternal characteristics

To determine the association between maternal malaria and HIV co-infection and CMP, cord blood samples were collected at delivery and examined for the presence of malaria parasites. Of the 1154 women initially identified – at recruitment, cord blood samples were available for 727 (95.5) of the 761 whose follow-up data at delivery formed the basis for this analysis. Of these 727 samples examined, 122 (16%) were positive and the remaining 605 were negative for CMP; giving a CMP rate of 16.8%, Fig 4.4).

At the bivariate level, women whose infants had CMP were more likely to be co-infected with malaria at recruitment OR (95% CI) 3.3 (1.8 – 6.0); or dually infected both at recruitment and at delivery 10.5 (4.5 – 24.0). The risk was very high in neonates' whose mothers were malaria parasitemic at delivery 163.5 (54.2 – 493.2). No association was found between gravidity, history of herbal drug use and risk of CMP (Fig 4.8).

In multiple regression analysis with predictors including maternal infection status and CD4 count, this risk of delivering a neonate with cord blood malaria persisted among women who were infected with malaria at delivery but not at recruitment (Table 4.9c). In particular, the risk was very high for HIV-positive women with malaria infection at delivery to have neonates with CMP OR = 97.3; 95% CI (54.2 – 118.9).

Fig 4.8 Risk factors associated with CMP (bivariate analysis; ORs with their 95% CI)



4.2.8.4 Associations between LAS and some selected maternal characteristics

Fig 4.9 presents the probable risk factors for LAS. Newborns with average Apgar score lower than 7 units (herein referred to as LAS) were more likely to be born to HIV+ women with malaria at recruitment OR = 3.4; 95% CI (1.8 – 6.1), malaria at delivery OR = 2.0; 95% CI (1.1 – 3.4), malaria both at recruitment and at delivery OR = 4.7 95% CI (2.2 – 10.2). Compared to their multi-gravid counterparts, primi-gravid/secundi-gravid women had almost two-fold risk of delivering a neonate with average Apgar score lower than the upper three digits (< 7 units). Women who were anemic at recruitment, reported history of fever within the past two weeks and women with morbidity profile > 4 conditions were also at higher relative odds of delivering a neonate with a LAS. Nevertheless, these associations were not statistically significant (Fig 4.9).

As shown in Table 4.9d, the incidence of LAS was significantly higher among neonates born to women with malaria infection. Neonates of mothers who had malaria at recruitment were at increased risk of LAS compared with neonates born to women without malaria infection at recruitment OR = 3.3; 95% CI (1.7 – 6.5). There was also a marginally significant risk among mothers with malaria parasitemia at delivery to have delivered a baby with LAS; OR = 2.4; 95% CI (0.97 – 6.13; Table 4.9d)

Fig 4.9 Risk factors associated with LAS (bivariate analysis; ORs with their 95% CI)

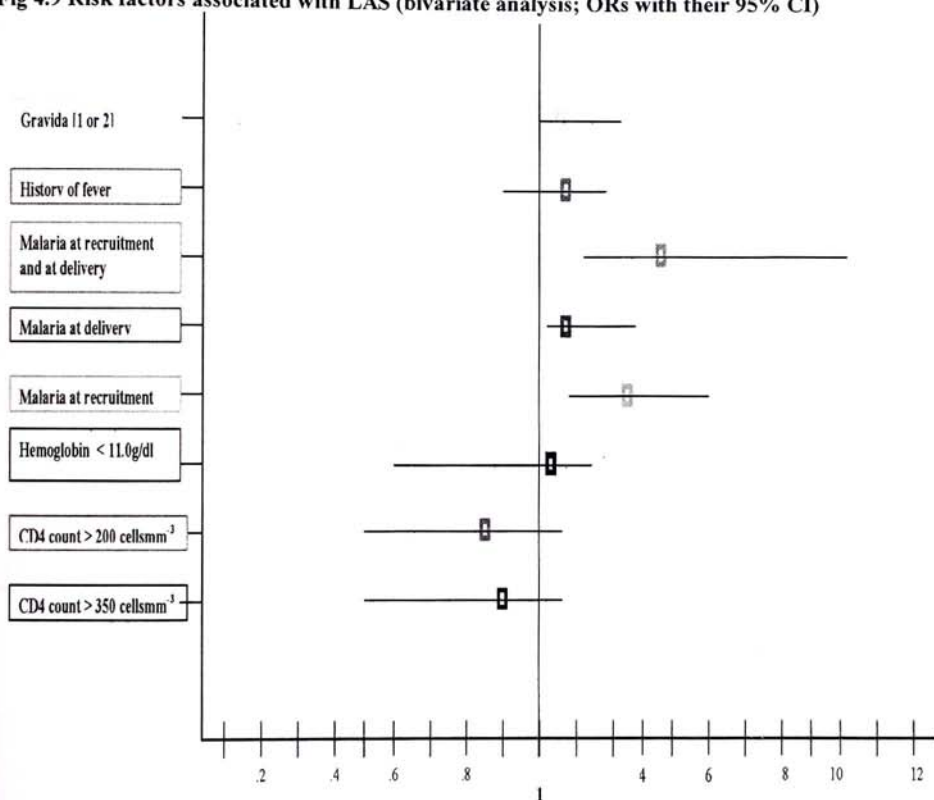


Table 4.9a Predictors of low birth weight (LBW): Multiple logistic regression analysis²⁰

Predictors	B (SE)	95% CI for the AOR		
		Lower bound	AOR	Upper bound
β_0	-5.15 (1.01)			
Malaria at recruitment	2.57 (0.72)	3.18	13.03*	53.33
Malaria at delivery	2.17 (0.83)	1.72	8.77*	44.76
CD4 count	0.21 (0.42)	0.54	1.24	2.82
HIV status	1.89 (0.99)	1.95	6.65*	46.47
PTD	3.66 (0.44)	16.22	38.74*	92.53

Model for LBW included the following variables: Malaria at recruitment, Malaria at delivery, CD4 count, HIV status, and PTD

Model Summary: -2 Log likelihood 146.09; Cox & Snell R Square .39; Nagelkerke R Square .60

*p value significant at .05 level

AOR = Adjusted Odds Ratio

Table 4.9b Predictors of preterm delivery (PTD): Multiple logistic regression analysis

Predictors	PTD	95% CI for the AOR		
		Lower bound	AOR	Upper bound
β_0	-2.46 (0.54)			
Malaria at recruitment	2.26 (0.62)	2.85	9.58*	32.27
Malaria at delivery	1.43 (0.62)	1.23	4.17*	14.18
CD4 count	-0.56 (0.30)	0.32	0.57	1.04
HIV status	2.41 (0.80)	2.33	11.13*	53.30

Model for PTD included the following variables: Malaria at recruitment, Malaria at delivery, CD4 count, HIV status, and malaria infection either at recruitment or at delivery

Model Summary: -2 Log likelihood 285.03; Cox & Snell R Square .08; Nagelkerke R Square .11

*p value significant at .05 level

AOR = Adjusted Odds Ratio

²⁰ Multicollinearity assessed; refer to footnote # 21

Table 4.9c Predictors of cord malaria parasitemia (CMP): Multiple logistic regression analysis²¹

Predictors	CMP B (SE)	95% CI for the AOR		
		Lower bound	AOR	Upper bound
β_0	-3.45 (0.69)			
Malaria at recruitment	0.83 (0.57)	0.75	2.30	7.04
Malaria at delivery	5.29 (0.66)	54.16	97.32*	118.92
CD4 count	-0.47 (0.52)	0.23	0.62	1.72
HIV status	.17 (1.30)	0.09	1.18	15.14
Malaria at either time point	1.29 (0.58)	1.16	3.61*	11.28

Model for CMP included the following variables: Malaria at recruitment, Malaria at delivery, CD4 count, HIV status, and malaria infection either at recruitment or at delivery

Model Summary: -2 Log likelihood 113.01; Cox & Snell R Square .50; Nagelkerke R Square.75

*p value significant at .05 level

AOR = Adjusted Odds Ratio

Table 4.9d Predictors of low Apgar score (LAS): Multiple logistic regression analysis

Predictors	LAS B (SE)	95% CI for the AOR		
		Lower bound	AOR	Upper bound
β_0	-1.89 (0.31)			
Malaria at recruitment	1.21 (0.34)	1.72	3.34*	6.49
Malaria at delivery	0.86 (0.49)	.97	2.36	6.13
Sex	0.52 (0.29)	.95	1.68	2.98
CD4 count	0.10 (0.29)	.63	1.10	1.95
HIV status	-0.35 (0.33)	.36	.70	1.36

Model for LAS included the following variables: Malaria at recruitment, Malaria at delivery, CD4 count, HIV status, and sex of newborn

Model Summary -2 Log likelihood Cox & Snell R Square.075 Nagelkerke R Square.111;

*p value significant at .05 level

AOR = Adjusted Odds Ratio

²¹ It did not escape my speculation that the inclusion in the model simultaneously, the variants of maternal infection categories such as malaria infection at recruitment, malaria infection at delivery could make the models prone to the biasing effect of collinearity. Of note here, the version of the SPSS used in the analysis did not have the option for producing collinearity diagnostics in logistic regression. Nevertheless, statistics such as tolerance and VIF values were obtained by running a linear regression analysis using the same outcome and predictors as suggested by Field (2005). The tolerance and VIF values showed that multicollinearity was not a cause for concern.

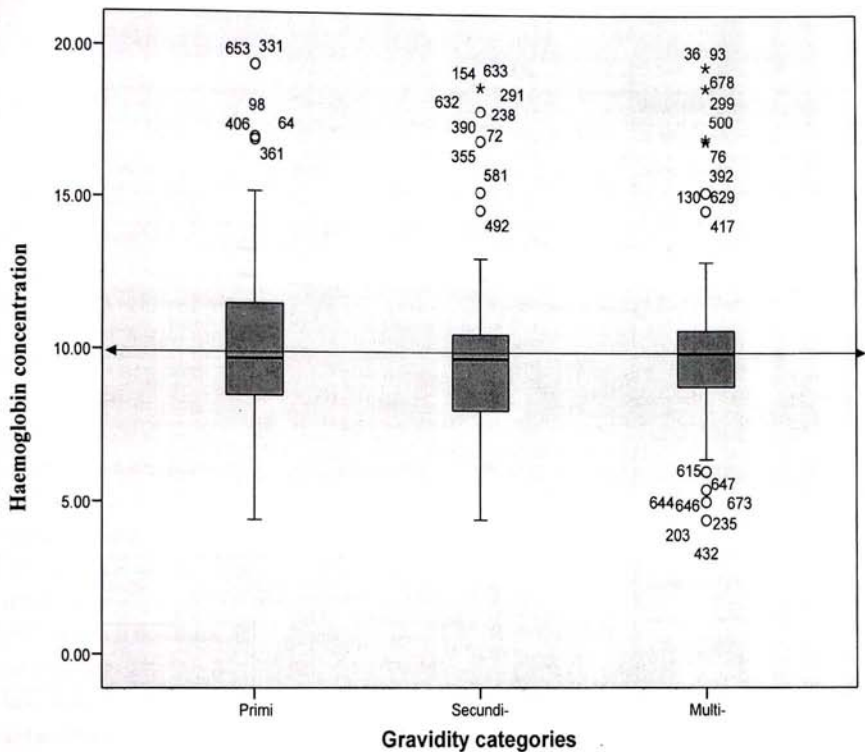
4.3.0 Adverse maternal outcomes

4.3.1 Malaria and HIV infections during pregnancy and maternal anemia

Of the total number of 761 participants on whom data at delivery were documented, hemoglobin data was recorded for 751 (98.7%) of them at recruitment, and 726 (95.4%) at delivery. Mean maternal hemoglobin concentration varied between 10.9g/dl range (6.5 – 15.3) for HIV-negative and 9.8g/dl; range (5.9 – 17.9) for HIV-positive at recruitment; 9.7g/dl range (4.4 – 19.4) for HIV- and 9.3g/dl range (5.9 – 19.4) for HIV-positive at delivery. Further examinations of the distributions of maternal hemoglobin concentration at childbirth by gravidity are presented in Fig 4.10. The lowest median hemoglobin was recorded among the primigravids, and the highest in the multigravids. These differences were not statistically significant ($p > 0.05$).

At recruitment 63% of the 761 mothers had hemoglobin concentration lower than 11.0g/d; defined here as maternal anemia, while 13.6% had hemoglobin levels lower than 9.0g/dl (moderately severe anemia). Anemia at delivery occurred in 77.8% of the mothers. In general, prevalence of this adverse maternal health outcome was higher among the HIV-positive women, and was higher in the women who were dually-infected with HIV and malaria. Details on these associations between maternal anemia and maternal infection status and other factors are given in Table 4.10, where statistically significant differences were observed between maternal anemia and maternal infection but not maternal receipt of IPTp.

Fig 4.10 Median maternal hemoglobin concentration at delivery by gravidity



KEY:

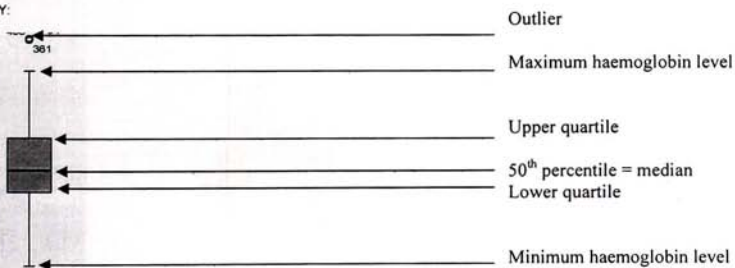


Table 4.10 Prevalence of maternal anemia (hemoglobin concentration < 11.0g/dl) by maternal infections status and IPT use

Maternal infection status	Prevalence by maternal infection category n (%)	χ^2 (p value) ²²⁾	Odds Ratio (²³ p value)
Overall	77.8%	NA	
HIV- negative	336 (78.0)	0.01 (0.916)	Reference group
HIV-positive	229 (77.6)		0.49 (0.242)
No malaria at delivery	420 (75.3)	9.12 (0.003)	Reference
Malaria positive at delivery	145 (86.3)		3.067 (0.001)
HIV+, no malaria both at recruitment and at delivery	136 (76.4)	7.94 (0.047)	Reference group
HIV+, malaria at delivery but not at recruitment	49 (84.5)		1.854 (0.215)
HIV+, malaria at recruitment but not at delivery	17 (60.7)		0.789 (0.681)
HIV+, malaria both at recruitment and at delivery	27 (87.1)		1.868 (0.040)
HIV-, no malaria both at recruitment and at delivery	238 (75.3)	10.48 (0.015)	Reference group
HIV-, malaria at delivery but not at recruitment	51 (94.4)		2.060 (0.055)
HIV-, malaria at recruitment but not at delivery	29 (80.6)		1.74 (0.063)
HIV-, malaria both at recruitment and at delivery	18 (72.0)		3.361 (0.006)
Malaria prophylaxis (IPTp with SP)²⁴			
Taken SP thrice	266 (78.2)	1.30 (0.728)	Reference group
Taken SP twice	198 (75.3)		0.986 (0.983)
Taken SP once	12 (70.6)		1.107 (0.865)
Never given SP	17 (81.0)		2.899 (0.067)

²²P value compares the differences in the proportion of maternal anemia by maternal infection status and also by IPT status

²³p value measures the significance of the odds ratio at 0.05 level

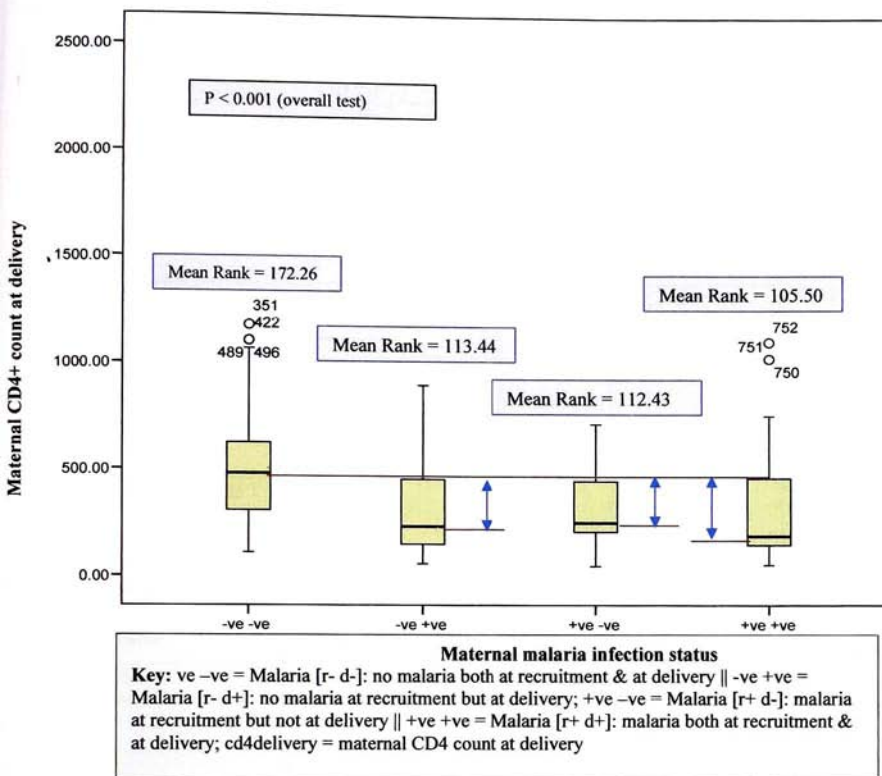
²⁴Similar finding by HIV status (data not shown)

4.3.2 Association between CD4 count at delivery and maternal infection status

Fig 4.11 presents the CD4 count and maternal malaria infection status, determined at two different time points – at recruitment and at delivery. Indicated in the figure are significant differences in maternal CD4 count by these infection categories (overall $p < 0.001$) as determined by the non-parametric Kruskal-Wallis test. The choice of the test was informed by the fact that the distribution of maternal CD4 count was not normally distributed.

A follow-up nonparametric Post Hoc Test (the Mann Whitney U Test) was performed to identify exactly where the differences lie. In doing this, each of the maternal malaria infection categories was compared to the reference group (HIV-negative women without malaria infection at both time points). This, as presented in Fig 4.11 shows that maternal CD4 count for each of the three groups were significantly lower when compared with that of the reference group without malaria and HIV infections.

Fig 4.11 Associations between maternal CD4 count at delivery and maternal malaria infection status (Kruskal-Wallis test)



↕ → P < 0.001

Table 4.11 below presents outputs of further analysis that compared the proportions of study participants who were immunosuppressed by maternal malaria infections categories. Episode of malaria either at recruitment or at delivery was associated with about 50% higher rate of immunosuppression ($\chi^2_{(3)} = 34.3$; $p < 0.001$).

Table 4.11 Prevalence of low CD4+ cell count at delivery by maternal infections status and IPT use

Maternal infection status	CD4+ count <350 n (%)	χ^2 (²⁵ P)	CD4+ count <200 n (5)	χ^2 (P)
Overall	43.4% ²⁶	NA	19.4% ²⁷	NA
No malaria at recruitment and at delivery	53 (29.8)	34.33 (<0.001)	22 (12.4)	23.32 (<0.001)
Malaria at recruitment but not at delivery	17 (60.7)		5 (18.5)	
Malaria at delivery but not at recruitment	38 (67.2)		15 (27.3)	
Malaria at recruitment and also at delivery	19 (61.3)		14 (48.3)	
	CD4+ count <350		CD4+ count <200	
Malaria prophylaxis (IPTp with SP)				
Never given SP	1 (100.0)	2.90 (0.408)	1 (100.0)	4.890 (0.180)
Taken SP once	37(43.0)		17 (20.2)	
Taken SP twice	58 (44.6)		23 (18.0)	
Taken SP thrice	0 (0.0)		0 (0.0)	

²⁵P value compares the differences in the proportion of maternal anemia by maternal CD4+ count and also by IPT status

²⁶ Corresponding rate at recruitment = 45.4%

²⁷ Corresponding rate at recruitment = 26.4%

4.4.0 Infant feeding choices, experiences, and challenges faced by HIV+ mothers

To document the infant feeding choices, experiences and challenges faced by HIV-positive mothers, as they strive to implement their chosen feeding options, a separate survey was conducted among a select group of 128 HIV-positive mothers with infants aged three months or older. In addition, an exploratory qualitative technique employing in-depth interviews of 10 of these HIV-positive mothers was done. The background, socio-demographic characteristics, and reproductive history of these 128 mothers are presented in Table 4.12. Details of the characteristics of the 10 mothers, and findings from the in-depth interviews are given in the later sections.

Table 4.12 Background, socio-demographic characteristics and reproductive history of mothers who participated in the infant feeding choices survey (N = 128)

Characteristic	Frequency	Percent
Study hospitals		
Atua Government Hospital	65	50.8
St Martins de Porres Hospital	17	13.3
Tema General Hospital	46	35.9
Marital status		
Single	23	18.0
Married	56	43.8
Divorced/Separated	3	2.3
Widowed	2	1.6
Cohabiting	44	34.4
Residence		
Rural	79	61.7
Urban	49	38.3
Level of education		
No formal education	33	25.8
Primary	31	24.2
Junior High School	54	42.2
Senior High school, Vocational Training, Post-Sec	9	7.0
Tertiary	1	0.8
Age bracket²⁸		
24 years or younger	17	13.3
25-35 years	82	64.1
36 years or older	29	22.7
Parity²⁹		
Primiparous	37	28.9
Secundiparous	32	25.0
Multiparous	59	46.1
Gravidity		
Primigravid	20	15.6
Secundigravid	24	18.8
Multigravid	84	65.6

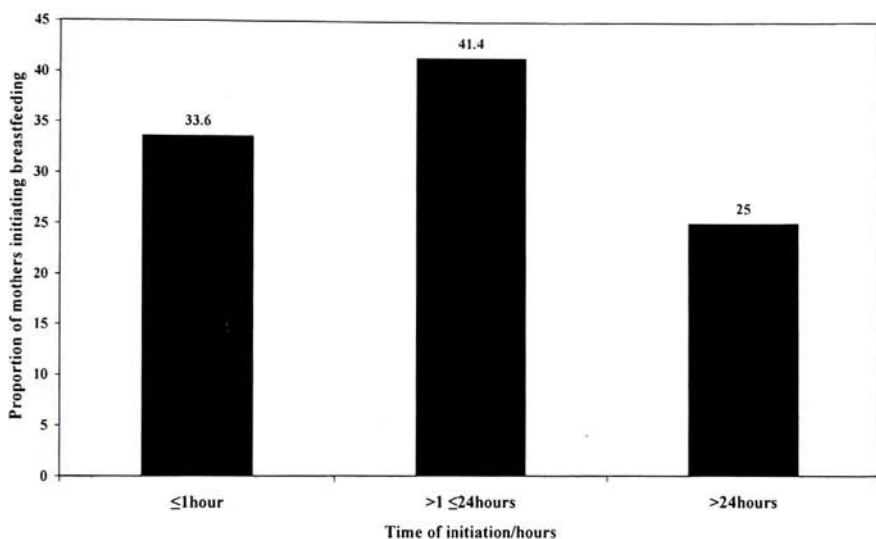
²⁸ Mean age (range): 31 (19-43)

²⁹ All except one woman delivered through spontaneous vaginal delivery

4.4.1 Breastfeeding initiation by HIV-positive mothers

Ninety six (96) of the 128 mothers who participated in the survey had during the recruitment phase of the study declared their intentions to breastfeed. The distribution of these 96 participants by time breastfeeding was initiated is presented in Fig 4.12. A little over one-third (33.6%) initiated breastfeeding within an hour of delivery. Twenty-five percent of these 96 mothers introduced breast milk to their infants only after 24 hours of delivery (Fig 4.12).

Fig 4.12 Breastfeeding initiation among HIV-positive mothers

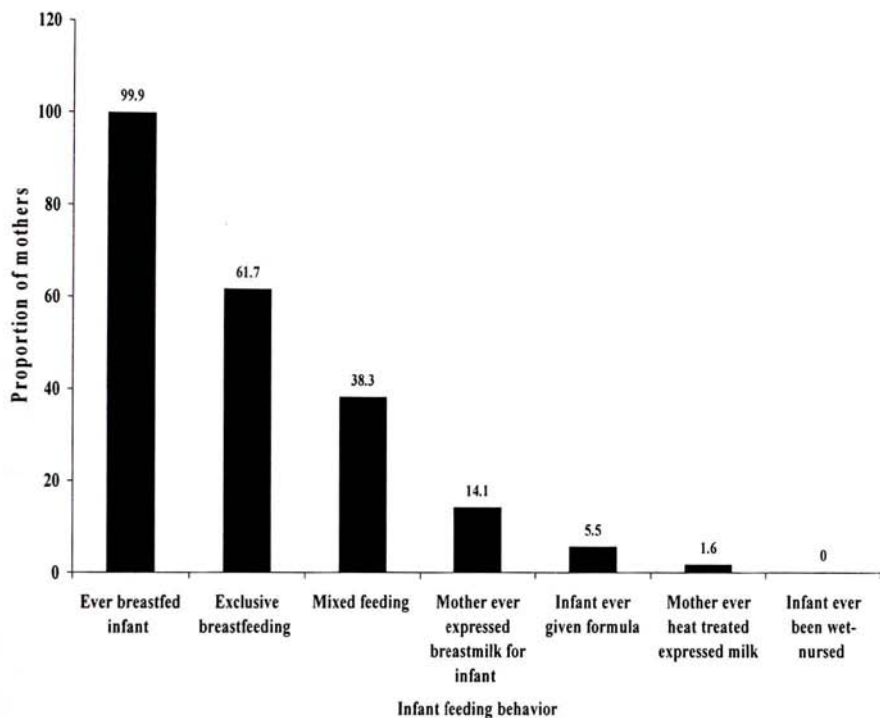


4.4.2 Infant feeding behavior of HIV-positive mothers

A questionnaire item explored the practices of seven different kinds of infant feeding behaviors (Fig 4.13a). These were “ever breastfed” (99.9%), “exclusively breastfed for up to three months” (61.7%), “mixed-fed or infant ever given other foods in addition to breast milk” (38.3%), “ever expressed breast milk with the intention to feed the infant” (14.4%), “ever

given formula to infant” (5.5%), “ever heat-treated expressed breast milk” (1.6%), and infant “ever been wet-nursed” (0%).

Fig 4.13a Infant feeding behavior of HIV-positive mothers (N = 128)



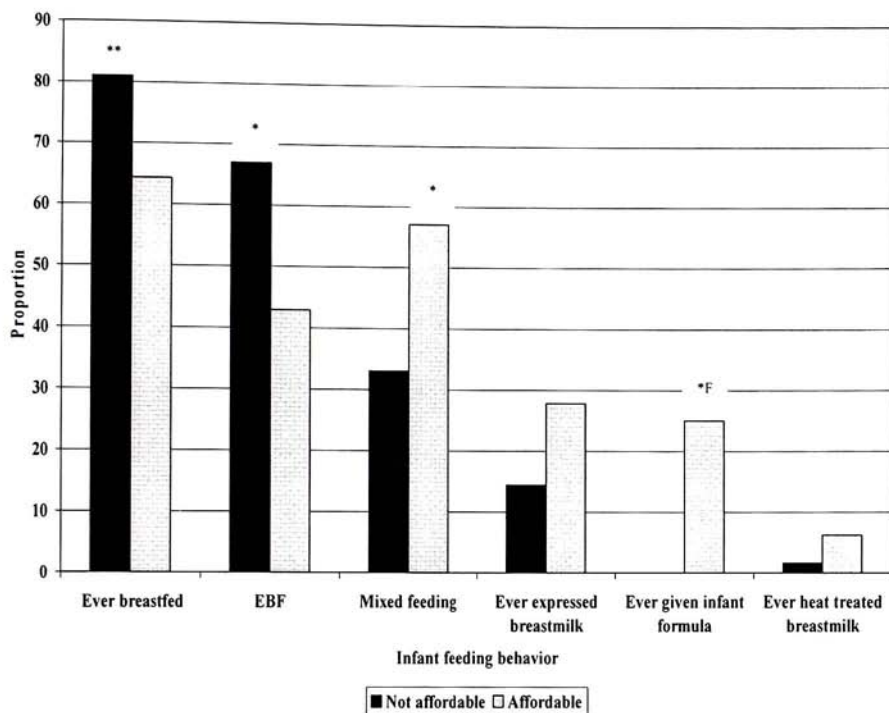
The various infant feeding choices made by mothers, the associations between perceptions on replacement feeding cost, and also formula feeding related stigma on feeding behavior are presented in Figs 4.13b – c. Differences in the choices of these feeding behaviors by level of education, place of residence, whether or not they were married, and whether they had

disclosed their HIV status to partner or relative perceptions are presented in Appendices 11a to 11c.

Women who had no formal education or had less than nine years of formal education were more likely to have breastfed their infant with breast milk compared to those with more than nine years of formal education ($p < 0.05$) – Appendix 11a. None of the mothers who perceived the cost of infant formula to be expensive introduced it to their infants (Fig 4.13b).

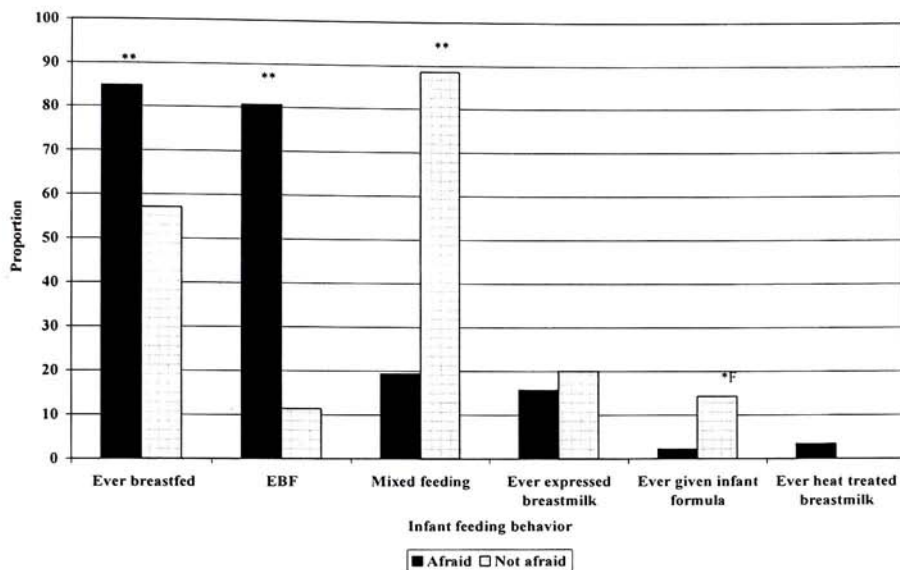
A substantial percentage of women were concerned about the social repercussions or stigma if they did not breastfeed. Of those women who chose to EBF, a significant proportion did so because, they were concerned about the stigma associated with failure to breastfeed (Fig 4.13c). Others did so because formula feeding was perceived to be unaffordable (Fig 4.13b). Mixed feeding, defined as giving breast milk as well as other non-breast milk foods was significantly influenced by perceptions on formula feeding-related stigma and cost (Figs 4.13 b and c).

Fig 4.13b Infant feeding behavior by perceptions on replacement feeding cost



[*]: differences statistically significant at $p < 0.05$; [**]: differences statistically significant at $p < 0.001$; [F]: p from Fisher's Exact Test

Fig 4.13c Infant feeding behavior by fear that not breastfeeding will result in stigma



[*]: differences statistically significant at $p < 0.05$; [**]: differences statistically significant at $p < 0.001$; [F]: p from Fisher's Exact Test

The above factors were further evaluated using logistic regression (Table 4.13). At this level, perception on cost of replacement feeding was still associated with EBF behavior. At a bivariate level analysis, mothers who perceived the cost of replacement feeding to be expensive were almost three-times as likely as those who felt it was affordable to exclusively breastfeed, OR = 2.7; 95% CI (1.15 – 6.25). There was even a higher propensity to exclusively breastfeed if mothers felt that choosing only formula feeding could lead to stigmatization OR = 7.50; 95% (CI 2.30 – 24.44). In multiple logistic regression model, mothers with nine or more years of formal education were on average 80% less likely to exclusively breastfeed OR = 0.21; 95% CI (0.05 – 0.88). On the contrary, perception on stigma related to formula feeding OR = 15.62; 95% CI 3.94 – 61.98), and cost of infant formula (OR = 4.60; 95% CI 1.40 –

15.14) were the significant predictors of exclusive breastfeeding of infants. This model included cost of replacement feeding; fear that replacement feeding may lead to stigmatization; HIV-sero status disclosure to partner; residency; education; and belief in the benefits of breastfeeding.

Table 4.13 Some potential predictors of infant feeding choice by HIV-positive mothers

<i>Infant feeding type</i>	<i>EBF n</i>	<i>Other! n</i>	<i>Total N</i>	<i>p-value</i>	<i>OR¹</i>	<i>95% CI¹</i>	<i>OR²</i>	<i>95% CI²</i>
Factors								
Cost of replacement feeding								
Not affordable	67	33	100	0.020 (τ)	2.70	1.15 - 6.25	4.60	1.40 - 15.14
Affordable	12	16	28					
Afraid that replacement feeding may lead to stigmatization								
Yes	75	35	110	<0.001 (τ)	7.50	2.30 - 24.44	15.62	3.94 - 61.98
No	4	14	18					
HIV-sero status disclosed to husband								
No	67	41	108	0.863 (τ)	1.09	0.41 - 2.86	1.42	0.32 - 6.325
Yes	12	8	20					
Rural residency								
Yes	52	27	79	0.225 (τ)	0.64	0.31 - 1.32	0.65	0.188 - 2.22
No	27	22	49					
Nine or more years of formal education								
Yes	35	29	64	0.102 (τ)	0.55	0.27 - 1.12	0.21	0.05 - 0.88
No	44	20	64					
Believes in the benefits of breastfeeding								
No	4	4	8	0.07 (F)	0.24	0.06 - 1.09	0.33	0.05 - 1.96
Yes	73	18	91					
Regular maternal income								
No	63	37	100	0.573 (τ)	1.28	0.54 - 3.03	Not included in model	
Yes	16	12	28					
Afraid of HIV disclosure repercussions								
No	10	4	14	0.428 (τ)	1.64	0.48 - 5.56	Not included in model	
Yes	69	45	114					

p (τ) = p value for Chi Square test; p (F) = p -value for Fisher's exact test; EBF = Exclusive breastfeeding; Other! = Any other mode of infant feeding (mixed or formula). OR¹ = Odds Ratio Estimate from bivariate cross-tabulation/simple logistic regression analysis; CI¹ = 95% Confidence Interval for OR¹; OR² = Odds Ratio Estimate from multiple logistic regression model containing (Cost of replacement feeding, Afraid that replacement feeding may lead to stigmatization, HIV-sero status disclosed to husband, Residency, Education, Believes in the benefits of breastfeeding); CI² = 95% Confidence Interval for OR².

4.4.3 Infant feeding experiences, and challenges faced by HIV-positive mothers.

On the assumption that documentation of HIV-positive women's experiences/challenges on infant feeding would enhance our understanding of the relevance of the various infant feeding options available to HIV-positive women in Ghana today, this phase of the study explored the experiences, practices, and challenges faced by the women. These experiences are summarized below.

4.4.3.1 Socio-demographic characteristics of the 10 study participants

Ten (10) of the 128 HIV+ mothers on whom information on infant feeding choices were available constituted the sample for this qualitative investigation. The 10 mothers were between 25 and 43 years of age. Seven of them were from rural areas in the Manya Krobo District, while three (3) were from Tema Municipal area and its environs. Eight (8) of them had no formal education; one had completed JSS, and the other a vocational school. One of the 10 was widowed; two were single mothers, and the rest married/cohabiting. Seven of the women were living in an extended family; two were living in a nuclear family, and one living alone. One had a permanent income from self-employment (boutique/hairdressing), another from petty trading, and eight (8) were not employed. All but two had disclosed their HIV+ status to either a partner or close relative.

The following are condensed narratives on three of the 10 women. These are presented here as cases because their experiences and challenges emerged as representative of the 10 in that, they bring up the recurring experiences and challenges that were revealed from the interviews.

4.4.3 .2 Case One: Opted to do exclusive formula feeding for six months*

Box 4.1. Infant feeding experiences of "Mamunatu" (Fictive name)

Mamunatu is a 34 year old widow with some vocational training from one of the vocational schools in Accra. She currently lives with the mum in Nungua, a suburb of Accra. She got married to a divorcee, for close to a decade without an issue. During the course of their connubial coexistence, she observed her husband take some "pills"; something he did slavishly. She one day mastered courage and asked him what medications he was taking; but was shut up instantaneously. "Mind your business he thundered". One day when the husband was at work, Mamunatu sneaked into his room, picked the container and dashed to a nearby chemical store to seek help as to the identity of the medicine. It is worth noting that, until very recently, antiretroviral drugs were very uncommon, and so the Chemist could not identify it. She dashed back home with the container disappointed. Mamunatu's husband finally died when she was pregnant for him.

Mamunatu, until recently was self-employed (owned a boutique and a hair dressing salon). Her late husband was also gainfully employed in one of the industries in Tema. During her last pregnancy, she tested positive for HIV. The results came as a great shock to her as she had not experienced signs of the infection. She instantaneously told the doctor that she was going to abort it. However, after a short counseling, she agreed to keep it, and was hence referred to *St Martins de Porres Hospital in Agomanya*. After a comprehensive counseling, she agreed to carry the pregnancy, opted for elective Caesarean section and exclusive formula feeding for six months. During the first three after delivery, she enjoyed the full support of her in-laws who at this point were not aware of her HIV status. Mamunatu had no serious financial difficulties during those three months of replacement feeding, and so was able to do exclusive formula feeding.

Challenge:

After months of serous internal deliberations, Mamunatu mastered courage and disclosed her status to her in-laws during the third month after delivery.

"This marked the beginning of my misery" she said. When I told them this, they ceased all communications with me, no more financial remittances; they literally cut of links with me. My boutique is also no more functional because someone made away with my 3 million old Ghana cedis. I am so broke now. I am so much worried, I can't even reason for myself. I am, rejected, dejected and abandoned. I don't go for ARVs anymore even though I know the importance. Why because I don't even have trotro fare to go to St Martins. I regret disclosing my status to my in-laws. Is it a crime to disclose your status? Is this the price I have to pay for disclosing my status? Doctor, what should I do?" The impact of Mamunatu's disclosure of her HIV-status to her in-laws on her chosen option is obvious.

*It is very important to note that, the above case was the only one of the few (who opted for replacement feeding) to have done so exclusively for three months. She had planned to do so for six months but for the challenges indicated above

4.4.3 .3 Case two: Opted for exclusive breastfeeding for six months

Box 4.2 Infant feeding experiences of "Yaa Mansa" (Fictive name)

Yaa Mansa is 42 years old, married and is living alone with her cohabitant, and many children in Odumase, the provincial capital of the Manya Krobo District/Traditional Area. She is a housewife cum petty trader (sells tomatoes, and "momoni" – salted fish). "My husband is a peasant who hasn't been to school but has a degree in drinking" Yaa Mansa herself is an illiterate; we interacted through an interpreter (her nurse counselor). She is on ART and is closely monitored by her nurse counselor, who also happens to be her adherence monitor. Yaa Mansa during her several antenatal visits was counseled to come back to deliver at the hospital, which she did. Before, during, and after delivery, she was given the necessary ARVs and counseling. She opted to do exclusive breastfeeding, which she initiated within an hour after delivery. She ceased breastfeeding abruptly at six months for the singular reason that she might transmit the virus to her child. When asked about other reasons for choosing breastfeeding she said, "Breastfeeding was the best choice for me. No one does wet nursing or express breast milk here. I couldn't have chosen formula feeding. What reasons will I give to the people around me for not breastfeeding the baby? Everyone in this community does breastfeeding". More so the nurse counselor tells me formula feeding is very, very expensive. She has disclosed her status to close family members. She appreciated the counseling given by the nurse, and strongly believes in the benefits of exclusive breastfeeding.

Challenge:

"I am highly stigmatized at home and in my area after disclosing my status to my husband". A man she claimed is a drunkard. This man comes to the house most of the time after drinking to insult me; he literally broadcasts my status to the people in the area. This is a serious problem to me. These days, people around my area call me all kinds of names behind my back. Some even say I will give the sickness to my baby. But for the nurse counselor who encouraged and advised me those people who talk about me do not even know their HIV status and that the medicine I am taking will prevent the MTCT. If I knew that disclosure of my status to him was going to lead to this disgrace, I would not have..."

4.4.3.4 Case three: Opted for EBF but ended up doing mixed feeding

Box 4.3 Infant feeding experiences of "Boyelli Nyaa" (Fictive name)

Boyelli Nyaa is the first of two wives, and has four children. She is 25 years old, with no formal education, she sales garden eggs and onions in their local market. She is one of the settlers in Ogame, just a stone's throw from the *St Martins de Porres Hospital*. During her first pregnancy, she tested positive for HIV and was counseled on infant feeding. She became very confused by the information she received, but finally decided to breastfeed because, as she put it, "*breastfeeding is the only acceptable option here*". She did not tell anybody about her HIV status and lived in constant worry that people might find out. After delivery, her mother in-law came to stay with her to help her with household chores. Her first kids were twins; they are five years old now (both still alive and look very healthy).

She is currently nursing an infant seven months old. She delivered at hospital and was given Nevirapine tabs and syrup. She opted to do exclusive breastfeeding after counseling. She was, however, unexpectedly caught doing mixed feeding when her nurse counselor paid her a surprise visit at home. This she said was an influence by her sister. Incidentally her sister after delivery had the problem of "dry breast" – failure of milk to flow from her breast she explained. The sister had no other alternative but to formula-feed. This Boyelli Nyaa indicated, influenced her feeding behavior.

Challenge:

Obviously her failure to exclusively breastfeed was occasioned by the experience with her sister and her environment as a whole. To some extent failure to appreciate intricacies of infant feeding counseling may have played a role. Another challenge to Boyelli Nyaa has been her refusal to disclose her status to anyone. *Being an orphan (both of my parents are dead), I am afraid that disclosure will lead to untold consequences, I might be sacked from the house, I have no where to go to. My only sibling is in the "North". "My main challenge is how I can continue with this denial without being exposed... What should I do?"*

CHAPTER FIVE

5.0 DISCUSSIONS

This is the penultimate chapter of the thesis. It discusses in detail the findings of the research organized into four broad themes. Sub-section 5.1 deals with the characteristics of the study participants. In sub-sections 5.2 and 5.3 malaria and HIV infections during pregnancy and adverse maternal and perinatal outcomes are discussed. Finally in sub-section 5.4 the infant feeding choices, experiences, and challenges faced by HIV-positive mothers in implementing their feeding intentions are dealt with.

5.1.0 Background, socio-demographic and clinical characteristics of the study participants.

This study was conducted at three public hospitals; two in the Manya Krobo District (Eastern Region) and one in the Tema Municipality (Greater Accra Region) of Ghana. The study was implemented in a dynamic policy environment with regard to perinatal HIV prevention, and malaria treatment/prevention. Within the period that this study was implemented, there was the shift from the "opt in" to the "opt out" antenatal HIV testing strategies, the shift from the short-course antiretroviral prophylaxis to Highly Active Antiretroviral Therapy (HAART) for pregnant women depending on their CD4 count and other factors, and also the change from Chloroquine monotherapy to Artesunate-Amodiaquine (AS-AQ) combination therapy for malaria treatment. All these took place in the setting where the intermittent preventive antimalarial treatment in pregnancy with SP was being implemented.

Presently at all the three hospitals, programs have been established to deliver both short-course antenatal antiretroviral therapy and full HAART to HIV-positive pregnant women (GHS, 2007) and also to provide IPTp during pregnancy in accordance with recent international

policy (WHO/AFRO, 2003). The successful adoption and implementation of these programs can be attributed to the systemic structures that have since the year 2001 been put in place in these areas. It is worthy of note that, the first National PMTCT Pilot Program and Antiretroviral Therapy Program were introduced in the Manya Krobo district in 2001. Presently this district, the TMA, and most others in Ghana, have a high level of commitment to addressing the issues of HIV and malaria at both the health facility and at the community levels.

Of 1,154 pregnant women who were recruited into the study, about 30% were lost to follow-up (LTFU) before delivery. It is, however, worth noting that in terms of age distribution, gestation length at first antenatal visit, occupation, and socio-economic stratification, those women on whom follow data were available did not differ significantly from those who were lost to follow-up. Also speculating that the baseline clinical outcomes of this group of women on whom data at delivery were available might differ from those who did not come back to deliver at the study hospitals a similar comparison was made. This analysis again showed that, with the exception of severe anemia, the two groups of study participants were comparable. On this premise, I proceed to discuss the study findings with confidence that the 761 women on whom the main analysis were based, to a large extent represent the overall sample of 1,154 women enrolled into the study.

I, however, acknowledge though that, if an intention to treat analysis had been done where all those lost to follow-up will have been included in the denominators during the calculation of the various estimates of effect, possibly different conclusions will have been made. Nevertheless, this approach which works on the assumption that none of those lost to follow-up suffered the adverse outcomes of interest can open the door to a misleading presentation of

study results. It is also worthy of note that, the other alternative strategies available in dealing with this problem by imputing outcomes to those lost to follow-up, in general, all make unverifiable assumptions that may introduce bias in the estimates of treatment effect (Hollis and Campbell, 1999).

The characteristics of the 761 women on whom data at delivery were available are presented in Table 4.1b. Of particular concern is the fact that over 90% of these pregnant women attended their first antenatal visit during their second or third trimester. This, however, is not a strange phenomenon. It has been previously noted that in the African setting, it is not uncommon for more than 10% of women making their first antenatal clinic visit after 36 weeks of gestation, while some even present to maternity health care settings for the first time in early labor (De Cock et al., 2000).

Marriage is an important institution for procreation in many parts of the world. In many traditional societies in Ghana where children are regarded as an asset and social security in old age, marriage is very much encouraged. It was not surprising to find that the majority were either married or cohabited with a partner (68.4%). Senah in his paper titled "*Maternal Mortality in Ghana: the other side*" asserts that in kinship-based societies such as ours, the mathematics of kinship enjoins every adult kin not only to procreate, but to do so prolifically (Senah, 2003). The author in substantiating this, quotes Sarpong, as having observed particularly among the Asantes the offering of prayers appealing to the gods and their ancestral spirits to bless the bride with the womb of an elephant (Sarpong, 1974). In similar vein, the Gas he indicates specifically request for ten children (Senah, 2003). It is in this respect of numerous progeny that Fortes has commented that the childless Ghanaian is regarded with pity not unmixed with scorn (Fortes, 1960).

5.2.0 Malaria and HIV infections during pregnancy and adverse perinatal outcomes

This study evaluated the effect of HIV on maternal and perinatal outcomes taking into account the effect of malaria. Elsewhere a series of studies have demonstrated that malaria and HIV infections during pregnancy are associated with several adverse outcomes (Steketee et al., 2001; Ayisi et al., 2003; Ticconi et al., 2003; Abrams et al., 2004; Villamor et al., 2005)

This current study employed two approaches in assessing the associations between these infections and the outcomes of interest. The findings presented in the previous chapter, are discussed in detail below.

5.2.1 Association between maternal infection status and birth weight/LBW

The evaluation on the effect of maternal infection on mean birth weight supports the study's hypothesis that the mean birth weight of a neonate differs significantly by maternal infection status. Overall, this study's findings demonstrate that maternal infection with HIV, and/ or malaria has a significant effect on birth weight. Several studies conducted in non-Ghanaian settings have reported similar findings (Steketee et al., 1996b; Leroy et al., 1998; Verhoeff et al., 1999b; Ayisi et al., 2003; Ticconi et al., 2003; Villamor et al., 2005). For instance, in the study by Ayisi *et al.* (2003), it was reported that compared with women with no malaria or HIV, maternal HIV infection was associated with a 99g reduction in mean birth weight. A dig into past literature revealed that this finding of Ayisi et al. was consistent with findings from other studies in the region (Braddick et al., 1990; Mmiro et al., 1993), although the reduction in the latter studies did not translate into a greater risk of LBW in either gravidae.

The second approach which employed simple and multiple logistic regression techniques revealed that the risk of LBW was highest in women dually infected at two time points (at

recruitment and at delivery). This risk was statistically more pronounced in neonates whose mothers were dually infected with HIV and malaria at both time points – at recruitment and at delivery OR = 11.3; 95% CI (4.6 – 27.4) (Fig 4.8). This observation was also reported by Villamor *et al.* (2005), who found HIV infection to be an independent risk factor for LBW. In the study by Ticconi *et al.* (2003), it was specifically reported that infants born to HIV-positive mothers were more likely to have LBW (<2500 g) or VLBW (<1500 g). This partly confirmed the results of a previous study, which found birth weight <2500 g to be associated with HIV infection on univariate analysis, but disappeared after controlling for gestational age (Castetbon *et al.*, 1999). In this current study, the risks persisted in the multiple logistic regression model, where a number of covariates including PTD were controlled for. After controlling for gestational age, malaria infection at recruitment and at delivery, as well as HIV remained significant predictors of LBW (Table 4.6).

Taken together, these findings indicate that neonates born to women exposed to malaria and HIV infections during pregnancy are at particular risk of LBW. Neonates of mothers who had malaria at both time points were worse off. This may reflect the effect of chronic malaria infection on fetal growth as reported previously by Menendez *et al.* (2000). Malaria infection is thought to impact on birth weight in a number of ways. One way is through malaria-induced anemia, and the other is through the effects of placental infection (Ibhanesebhor and Okolo, 1992; Okoko *et al.*, 2002; Kassam *et al.*, 2006). Researchers had previously hypothesized that, a high density parasitemia, chronic infection in the placental blood, and the associated cellular immune response may result in the consumption of glucose and O₂ that would have gone to the fetus (Menendez *et al.*, 2000). The ultimate effect of this on the weight of unborn fetus is obvious. Histopathologic studies done with infected placentas have also found thickening of the cytotrophoblastic membranes (Ismail *et al.*, 2000; Guyatt and Snow, 2004). This according

to the researchers has the potential of interfering with nutrient transport to the fetus, and subsequently leading to LBW.

In the study by Ayisi *et al.* (2003), dual infection with malaria and HIV among primigravidae was associated with a threefold increased risk of LBW, almost a threefold increased risk of prematurity, and approximately a twofold increased risk of small for gestational age (SGA) when compared with uninfected women. Dreyfus *et al.* (2001) in an earlier investigation in Tanzania had reported that *P. falciparum* malaria parasitemia during pregnancy was also significantly associated with lower birth weight but with similar risk of LBW among both primiparas and multiparas, in contrast with the more recent findings by Ayisi *et al.* (2003).

In the present study the rates of LBW was comparable in both HIV-positive primigravidae and multigravidae. This observation may be explained by a previously reported finding that, the HIV infection erodes the gravidity-specific pattern of adverse outcomes previously reported among African women in malaria endemic areas, in which primigravidae are more affected than multigravidae (Friis *et al.*, 2004).

In the last 1990s, a meta-analysis of studies examining the relation of HIV infection to pregnancy outcomes concluded that HIV-infected women were at higher risk of LBW than are uninfected women (Brocklehurst and French, 1998). A study that examined this relation stratified by stage of disease found that symptomatic HIV-positive women tended to have a higher risk of LBW than do asymptomatic women (Ryder *et al.*, 1989). Very few of the HIV-positive study participants in this current study were symptomatic (3.1%), limiting the power of the study to compare incidence of LBW by maternal HIV disease status.

Maternal nutritional status measured by MUAC has been previously reported to be significantly and independently associated with the risk of low birth weight (Adebami et al., 2007; Rollins et al., 2007). In this present study, maternal nutrition (measured by maternal BMI, MUAC, and weight) was not significantly associated with newborn's weight. Even though it is biologically plausible to hypothesize that poor maternal nutrition would lead to fetal malnutrition, this thinking does not obscure the fact that not all malnourished mothers give birth to malnourished babies and some well-nourished mothers sometimes give birth to malnourished babies. Regarding the former case, Naismith had remarked that the fetus is a 'perfect parasite' and that it takes fairly extreme forms of maternal malnutrition to significantly affect the quantity and quality of nutrients transferred to the fetus (Naismith, 1969). This current finding of lack of association between maternal nutritional status and birth weight is not unfounded. In explaining this, a number of factors, including maternal infection, and placental insufficiency need to be considered. Placental function for instance if defective in terms of transferring nutrients to the fetus can lead to LBW, but this cannot be detected by maternal anthropometry (WHO, 1995).

More than 80% of the subjects in this current study were given at least one dose of malaria prophylaxis (SP) according to the Ministry of Health standards of prenatal care in Ghana. Some studies on chemoprophylaxis trials found antimalarial drugs such as SP (Schultz *et al.*, 1994), to be very effective for improving birth weight and reducing the risk of LBW. Several other studies (Taha et al., 1995; Marti et al., 2007; Rollins et al., 2007) have evaluated the influence of maternal malaria and HIV infections on adverse birth outcomes including LBW among HIV-positive women on ART. In a study among pregnant women on ART, maternal HIV infection was associated with an approximate 45% increased risk of having a LBW baby (Rollins *et al.*, 2007), and in the study by Marti *et al.*, LBW rate was 28% (Marti *et al.*, 2007).

These rates were far higher than that reported in this current study. It may be worthwhile implementing another research to study the particular effects of ART and SP on LBW among pregnant women in Ghana.

5.2.2 Association between maternal infection status and gestation length/PTD

To examine the existence of an association between maternal infection status and gestation length in this study, the ANOVA technique was first used. This shows that on average, maternal infections (single or dual) were associated with shorter gestation length. However, this was more pronounced and statistically significant in the group of women who were dually infected both at recruitment and at delivery. Compared to their HIV-uninfected, and malaria negative counterparts, this group of women delivered two (2) weeks earlier; mean difference = -2.08 weeks 95% CI (-3.28 – -0.88; $p < 0.001$).

Six of numerous studies reviewed by *ter Kuile* (2004), examined the effect of dual infection with malaria and HIV on birth outcomes including PTD (Steketee et al., 1996b; Leroy et al., 1998; Weng et al., 1998; Verhoeff et al., 1999b; Ayisi et al., 2003; Ticconi et al., 2003). Although differences in study design limited direct comparisons between these studies, the review reported an increased risk of preterm birth with both HIV and malaria, with the greatest risk in women with dual infection (*ter Kuile et al.*, 2004). All these seven studies reported on gestational age; suggesting that the effect on birth weight reflects a combined effect of shortened gestational age and IUGR (Steketee et al., 1996b; Leroy et al., 1998; Weng et al., 1998; Verhoeff et al., 1999b; Ayisi et al., 2003; Ticconi et al., 2003). In a separate but related study in Malawi, Abrams et al. after examining risk factors and mechanisms of PTD in malaria-exposed pregnant women reported that HIV was associated with PTD, while malaria was not (Abrams et al., 2004), contrary to the findings by Noble et al. where both maternal

HIV infection, and malaria history, among Zimbabwean women were associated with preterm delivery (Noble *et al.*, 2005).

In the current analysis, the effect of maternal infection persisted, but nevertheless attenuated when the comparisons were made between maternal single infection versus dual infection at two time points, or dual infection only at one time point (only at recruitment) versus dual infection at two time points. Put together, the data demonstrate that maternal dual infection with HIV and malaria during the course of pregnancy has a significantly negative effect on gestation length.

In the second approach, associations between PTD and some clinical and non-clinical maternal factors were assessed using simple and multiple logistic regression techniques. PTD is defined as labor resulting in birth before 37 completed weeks (259 days) of gestational age. This definition, promulgated by the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO), originated from a statistical analysis of the distribution of gestational age at birth, based on the first day of the last menstrual period (WHO, 1976). This definition was used for this analysis.

Among women with CD4 count greater than 350 cells/mm³ was significantly less likely to deliver before term. On the contrary, maternal malaria infection had an increased risk of delivering preterm. These associations after a further evaluation using multiple logistic regression models showed malaria infection, HIV infection, and CD4 count as significant predictors. Although the precise effect of malaria infection on PTD is uncertain, malaria-infected placentas according to some authorities have been shown to frequently carry

antibodies, cytokines and macrophages which are indicative of active immune-response, and this response may stimulate early labor (Ismail et al., 2000; Guyatt and Snow, 2004).

The current PTD rate of 18.4% was lower than those reported by earlier studies whose study participants were on antiretroviral therapy (ART). At the initiation of our study, ART uptake was low (4.9%) and only 10 of the 62 HIV-positive women who delivered prematurely were on ART. Even though the benefits of ART are known, concerns have been raised that maternal receipt of these drugs during pregnancy may be associated with adverse outcomes including PTD (Tuomala et al., 2002; Thorne and Newell, 2003; Saraceni et al., 2005; Suy et al., 2006; Marti et al., 2007; Thorne and Newell, 2007). In the studies by Marti et al. and Thorne and Newell among HIV-positive women receiving antiretroviral therapy, premature delivery rates were 29% and 24.9% respectively (Marti et al., 2007; Thorne and Newell, 2007). One possible explanation for the low rates of PTD in my study in relation to these other studies is the fact that most (97%) of the women in were asymptomatic. Further studies controlling for the effect of ART on PTD are needed to shed more light on this.

5.2.3 Associations between CMP and maternal infection status

To determine whether maternal HIV and malaria infections affect the probability that a woman would infect her fetus with malaria perinatally, cord blood samples were examined for possible infection. The CMP rate among HIV-positive study participants was 24.4%. This prevalence of cord parasitemia in babies born to HIV-infected women from this current study was comparable to that reported for HIV-positive Malawian women, 26% (Steketee *et al.*, 1996b) but higher than that in children born to HIV-negative women: 9% in Zaire (Fischer *et al.*, 1995), 7% in Malawi (Redd *et al.*, 1996), and 10.4% in Kenya (Malhotra *et al.*, 2006).

According to De Silva and colleagues, cord blood may become infected with malarial parasites through maternal transfusion into fetal circulation either at the time of delivery or during pregnancy, direct penetration through the chorionic villi, and penetration through premature separation of the placenta (De Silva *et al.*, 1982). However, the effectiveness of the placenta to restrain malaria parasite passage to the fetus and the remarkable capacity of the fetus to resist infection has been demonstrated (Miller and Telford, 1996). The resistance may reflect among other things; a) the physical barrier of the placenta to infected red cells, b) the passive transfer of maternal antibodies, and c) the poor environment afforded by the fetal red cells for plasmodial replication (De Silva *et al.*, 1982; Miller and Telford, 1996). The free passage or the high prevalence of cord blood parasitemia may therefore mean that placental barriers are no more very effective when infected with malaria, and or HIV.

The definition of cord malaria in this present study was the presence of *P. falciparum* in cord blood at delivery. Other earlier reports from both malaria-endemic and non-endemic areas showed varying prevalence of cord malaria ranging from 8% to 33% (Jelliffe, 1966; Akindele *et al.*, 1993; Tobian *et al.*, 2000). The condition in some cases has been shown to be strongly associated with placental malaria (Uneke, 2007c). In corroboration with this finding, this current data show statistically significant associations between cord malaria and maternal malaria infection. In the study by Tobian *et al.*, an association was noted between neonatal parasitemia and early mortality, and in Malawi, cord parasitemia was found to be associated with preterm delivery (Tobian *et al.*, 2000). The strong association between cord parasitemia and neonatal mortality that was found according to Villamor *et al.* indicate that, among HIV-infected women, the transplacental passage of *P. falciparum* is not only more frequent compared with HIV-uninfected but is also more detrimental for survival (Villamor *et al.*, 2005).

In this study, HIV-positive women whose infants had CMP were more likely to be co-infected with malaria at recruitment OR (95% CI) 3.3 (1.8 – 6.0); or dually infected both at recruitment and at delivery 10.5 (4.5 – 24.0). These associations suggest that preventing infection, avoiding treatment failure if infected and preventing re-infection in women who present with malaria parasitemia at the first antenatal visit could decrease the burden of this adverse outcome. No association was found between gravidity, history of herbal drug use and risk of CMP.

5.2.4 Associations between Apgar score/LAS and some selected maternal characteristics

The prevalence of low Apgar score and its attendant risk factors have not been established in many sub-Saharan countries including Ghana. In this study, prevalence of low Apgar score was 25.5% among all the neonates, and 26.1 % among the group of neonates born to HIV-positive women. A previous study by Ondoa-Onama and Tumwine found maternal factors to be significantly associated with low Apgar scores including presence of infections during pregnancy (Ondoa-Onama and Tumwine, 2003).

There is limited data on the influence of infections such as malaria and HIV during pregnancy on low Apgar score. Two studies have reported on low Apgar score and its associated factors among women infected with HIV (Tuomala et al., 2002; Ticconi et al., 2003). In the Tuomala et al. study, rates of low Apgar scores was associated with HIV but independent of maternal receipt of ART during pregnancy (Tuomala *et al.*, 2002). The role of malaria was not considered. In the study by Ticconi *et al.* (2003) to investigate the effect of isolated or concomitant infection with malaria and HIV on neonatal outcome among pregnant Zimbabwean women, malaria and HIV infections were independently associated with increased risk of low Apgar score.

This current study demonstrates that the newborns' Apgar scores differed significantly with respect to whether they were born to HIV-negative mothers without malaria, HIV-negative mothers with malaria, or a mother dually-infected with HIV and malaria. In statistical terms, there was a significant decrement in Apgar score corresponding to the degree of maternal infection burden. Compared to their HIV-uninfected, and malaria negative counterparts, women dually infected with malaria and HIV both at recruitment and at delivery had neonates with significantly reduced Apgar scores. Collectively these findings demonstrate that maternal dual infection with HIV and malaria at first antenatal visit (at recruitment) and at delivery is associated with a low Apgar score.

5.3.0 Malaria and HIV infections during pregnancy and adverse maternal outcomes

Malaria in pregnancy is one of the major causes of maternal morbidity worldwide. A recent review recognized a complex interaction between pregnancy and the malaria parasite – all seem to favor the parasite and disadvantage the pregnant woman (RCOG, 2005).

5.3.1 Malaria and HIV infections during pregnancy and maternal anemia

Recent estimates suggest that in malaria-endemic sub-Saharan Africa, approximately 25 million women become pregnant and are at increased risk of infection with *Plasmodium falciparum*, each year particularly in their first two pregnancies (WHO, 2004). This results in maternal anemia (Brabin et al., 2001; Steketee et al., 2001). Both HIV (Mocroft et al., 1999), and malaria (Guyatt and Snow, 2001) are known causes of maternal anemia. Several studies describe a negative effect of the combined impact of HIV and malaria on maternal hemoglobin concentrations (Verhoeff et al., 1999a; Ayisi et al., 2003; Ticconi et al., 2003).

This study documented the prevalence of maternal anemia (defined as hemoglobin concentration lower than 11.0g/dl) at first antenatal visit to be 63% while prevalence of moderately severe maternal anemia (defined as hemoglobin less than 9.0g/dl) was 13.6%. Anemia at delivery occurred in 77.8% of the mothers. The time between delivery and taking blood for hemoglobin estimation could affect the maternal postpartum hemoglobin levels because of volume redistribution resulting from the effects of labor (Ayisi *et al.*, 2003). In this study, however, the blood sample for hemoglobin estimation was taken immediately after delivery, to prevent this effect. Some earlier studies conducted by Geelhoed and colleagues at the Holy Family Hospital, Berekum, Ghana, reported a rather low prevalence (< 30%) of anemia at during antenatal visit, and 13.3% at childbirth (Geelhoed *et al.*, 2006b, 2006a). The investigators attributed this significant reduction in the prevalence of anemia their intervention at that time – chloroquine prophylaxis. Being cognizance of the findings of several other African studies with reports on anemia prevalence in pregnancy to be over 50% (van den Broek, 1998; van den Broek *et al.*, 1998; Lassey *et al.*, 1999; Verhoeff *et al.*, 1999a), I attribute the excellently low anemia rates in the Geelhoed *et al.* (2006) study to the subjectivity of the method they used in assessing anemia. A qualitative paper method was employed in measuring haemoglobin as a percentage before converting to g/dl units.

Overall, the prevalence of maternal anemia was high (77.8%), was higher in the women who were dually-infected with HIV and malaria at delivery (84.5%) and strikingly higher in women who were dually-infected both at recruitment and at delivery (87.1%). These differences were statistically significant. Ayisi and colleagues in their study to determine the effect of dual infection with HIV and malaria on birth outcomes and maternal anemia among women delivering at a large public hospital in Kisumu, Western Kenya, found that both HIV and malaria were significant risk factors for postpartum maternal anemia, and HIV-

seropositive women with malaria were twice as likely to have anemia than HIV-seronegative women with or without malaria (Ayisi *et al.*, 2003). A review by ter Kuile *et al.* (2004) on the burden of co-infection with HIV and malaria in pregnant women in sub-Saharan Africa, showed that HIV-infected women experienced consistently more severe anemia than uninfected women (ter Kuile *et al.*, 2004). The high prevalence of anemia in the current study is rather disappointing given that such interventions as distribution of insecticide-treated bed nets, IPTp, and offer of hematenics at ANC are all geared toward reducing the some of these burdens. It may be alluring to speculate that the interventions are not very effective; however, the inevitable negative impact of pregnancy-related hemodilution on maternal hemoglobin concentration must be noted. It was not within the precincts of this study to evaluate the effectiveness of the various interventions mentioned above. Other studies looking at these issues could have policy implications.

5.3.2 Association between CD4 count at delivery and maternal infection status

Some interactions between HIV infection, CD4 cell count and malaria infection have already been reported; including increased incidence of both symptomatic and asymptomatic malaria (Whitworth *et al.*, 2000; Atzori *et al.*, 2003) a higher risk of malaria treatment failure (Van geertruyden and D'Alessandro, 2007), and more severe malaria attacks (Chandramohan and Greenwood, 1998). In 2004, Hisaeda *et al.* demonstrated that infection with malaria parasites induce total immune suppression even in HIV-uninfected individuals (Hisaeda, 2004).

In this study, degree of immunosuppression was measured by absolute CD4+ cell count (immunosuppressed [CD4+ cell count < 350 cells/mm³], seriously immunosuppressed [CD4+ cell count < 200 cells/mm³]). The results demonstrate a negative effect of malaria infection status on maternal CD4+ count. This finding is consistent with those of Mermin *et al.* (2006)

who showed that malaria was associated with a more rapid decline in CD4+ cell count (Mermin *et al.*, 2006). In this particular study, Mermin *et al.* showed that the mean difference in CD4 cell decline per each additional malaria episode was 40.5 cells/mL per year (95% CI: 13.1 - 68.0; $p = 0.0038$). Clearly as in this current study, the decrement in CD4+ count in the study by Mermin *et al.* was attributed to malaria.

In the recent past, concerns have been raised about the use of absolute CD4 cell count in determining the degree of immunosuppression instead of CD4 cell percentage. In an editorial, Gandhi argues that the absolute CD4 cell count may be less accurate than the CD4 cell percentage for assessing the degree of immunosuppression, and hence should be used to guide therapy for HIV-infected patients (Gandhi, 2007). Almost spontaneously, McGovern *et al.* presented findings that do not provide evidence to support the hypothesis of Gandhi, according to which CD4 cell percentage should be used to guide therapy for HIV-infected patients (McGovern, 2007). In fact, McGovern *et al.* (2007) found that, the CD4 cell count was a better predictor of the risk of developing an AIDS-defining illness than the CD4 cell percentage. Absolute CD4 cell count, McGovern *et al.* suggest, should continue to be used to guide therapy decisions for all HIV-infected patients. In line with this and also in line with evidence-based recommendations from the World Health Organization (WHO, 2006), CD4 < 350 cell/mm³ is used as a marker for the initiating of HAART among pregnant women. The decision to use maternal CD4 cell count < 350 cells/mm³ as a measure of immunosuppression was also informed by this recommendations.

Further analysis to compare the proportions of study participants who were immunosuppressed by the above four maternal malaria infections categories revealed strikingly similar findings, where an episode of malaria either at recruitment or at delivery was

associated with about 50% higher rate of immunosuppression. This observed association may in part be explained by possible impaired immune responses to malaria in particular, and CD4 cell activity – as a result of HIV infection. In a previous study, increased susceptibility of HIV- positive pregnant women to malaria (Mount *et al.*, 2004) was attributed to immunosuppression or depletion of CD4 cells and impairment of cytokine functions (Moore *et al.*, 2000). Apart from the combined effect of HIV and malaria, malaria alone may also have a direct effect on CD4 cells. Indeed, a reversible decrease in lymphocytes and the absolute and relative CD4 counts have been observed in HIV-negative patients with malaria (Greenwood *et al.*, 1977; Lisse *et al.*, 1994). This is in line with findings from a study by Shah *et al.* which showed that after successful antimalarial treatment, absolute CD4 count increased significantly in adult patients with uncomplicated malaria, regardless of their HIV-1 status (Shah *et al.*, 2004).

In Ghana like many countries with limited resources, CD4 cell count is one of the markers used in monitoring the progression of HIV-1 infection, to decide on antiretroviral treatment, and to assess its impact (WHO, 2006). However, findings of this present study, supported by those of previous studies, are suggestive that malaria parasitemia may be an important confounding factor for the correct evaluation of the degree of immune depression in HIV-positive individuals. For effective interventions, malaria needs to be included in routine assessment of HIV-related immunosuppression.

5.4.0 Infant feeding choices, experiences, and challenges faced by HIV-positive mothers

Findings on the choices HIV-positive women make regarding what to feed their infants, the challenges and experiences they go through implemented their feeding aspirations are discussed here.

5.4.1 Breastfeeding and breastfeeding initiation by mothers

It was refreshing to note that 75% of the 128 mothers who participated in this second phase of the study had declared their intentions to breastfeed before delivery. The benefit of breastfeeding is very well publicized. Interactions both with the PMTCT nurse counselors and the HIV-positive mothers revealed that the socio-cultural context in which these women make their infant feeding decisions is one in which breastfeeding is highly valued. As in most parts of Ghana, breastfeeding in the Manya Krobo and Tema is culturally normative, and there is no evidence in this study to suggest that this fundamental cultural practice is being eroded, even in this era of HIV. Leshabari *et al.* (2007b) in a study that explored infant feeding decision making among HIV-positive Tanzanian women describe the failure of a mother to breastfeed as 'a significant failure', pointing to the substantial failure to live up to practices deeply embedded in a culturally constituted moral universe. These authors further noted that, in addition to putting the life of the child at risk and violating the rules of good motherhood, not breastfeeding an infant is interpreted as an act of disrespect to the lineage.

A little over one-third (33.6%) initiated breastfeeding within an hour of delivery; and 25% initiated breastfeeding after. Given the national norm, and the fact that the three hospitals where the study was conducted have been declared Baby Friendly Hospitals, this particular observation is rather below expectation. The low rates, nevertheless, could be attributed to decisions taken apriori by mothers not to breastfeed. Breastfeeding initiation rates in HIV-

negative women in these areas were not assessed in this study. If initiation rates in HIV-negative are found to be comparable to that of their HIV-positive counterparts, a relook at the impact of the Baby Friend Hospitals label on this outcome would be warranted.

5.4.2 Infant feeding behavior of HIV-positive mothers

A questionnaire item explored the practices of seven different kinds of infant feeding behaviors. Close to 100% of the participants had introduced their infants to breastmilk. In keeping with the result of a previous study from Nigeria (Sadoh *et al.*, 2008), over one-third (38.3%) of the mothers in this study who opted to breastfeed had introduced to their infants water and other kinds of foods. Similar findings have been reported by Abiona *et al.* (2006) where participants of a focus group discussion argued that breast milk is 'food' and that, just as an adult drinks water after eating, a baby should be given water after being breastfed. To ensure that HIV-positive mothers who choose to breastfeed do so exclusively, these beliefs and attitudes in relation to giving infants water, and other foods to the infant without a doubt need to be addressed.

In this present study, none of the infants was wet-nursed. This is also in line with findings of a Nigerian study where participants in a focus group discussion noted that wet-nursing is very rare these days (Sadoh *et al.*, 2008). Wet nursing was thought of by technical experts as an alternative infant feeding option in HIV-positive mothers. The limited literature on its feasibility especially in the African continent clearly shows that this option is not popular. One other issue worth investigating is the role of nurse counselors in this business of HIV and infant feeding. Are counselors well informed to help women make informed choices? This is a question that deserves an investigation.

The financial cost of feeding with infant formula is estimated to be about GH¢20.00 per month. The costs of fuel, safe water, and utensils are not considered in the derivation of this cost. In low-income families these (costs of fuel, safe water, and utensils) have been noted to be important (Rea et al., 2007). Given that a significant proportion of the women in this present study were from underprivileged settings, infant formula was not thought of as a feasible feeding option for most of the mothers. About 6% indicated having ever given formula to their infants; only one doing so exclusively in this study. It is only in rare cases – when mothers have the economic means to purchase it, that infant formula is used. Other reasons for opting for infant formula noted in this current study stems from the notion that, only mothers who are well to do, opt for formula feeding. This behavior has the potential of spilling over to affect HIV-negative nursing mothers. Efforts at addressing this through the various health communication channels discussed above should be vigorously pursued.

Education, perception on stigma that may stem from failure to breastfeed, and also perceptions on cost of infant formula were revealed in this study to have significant influences on exclusive breastfeeding behavior. Mothers with nine or more years of formal education were on average 80% less likely to exclusively breastfeed. On the contrary, perception on stigma related to formula feeding and cost of infant formula were the significant predictors of exclusive breastfeeding of infants. This information will be useful to HIV counselling service providers in these districts. If efforts are made to address these issues in these areas, infant feeding practices may be positively enhanced.

Apart from the cost factor, further interactions with both the PMTCT nurse counselors and the HIV-positive mothers revealed that nurse counselors in these settings do not feel comfortable

providing helpful instructions about formula feeding in the name of this initiative. The importance of hospital breastfeeding policy and attitudes of health personnel in affecting breastfeeding practices has been repeatedly documented (Knodel et al., 1990; Williamson, 1990; Weng et al., 2003). This current finding, though anecdotal, is worrying as the Baby Friendly Hospital Initiative in reality does not preclude the use of replacement feeding in situations that are medically indicated (WHO/UNICEF, 1989). The implications of such attitudes health workers on this infant feeding need to be looked at.

5.4.3 Experiences, and challenges faced by HIV+ mothers in implementing their infant feeding intentions.

The qualitative investigation has given a snapshot of the experiences and challenges that HIV-positive mothers in the Manya Krobo and Tema Municipality face as they attempt to implement their infant feeding intentions. These experiences manifest a variety of hardships regarding the choosing, implementing, and sustaining their infant feeding intentions. The few, who managed to implement their feeding options religiously, did not do so without challenges.

For instance, Mamunatu who had delivered by caesarean section opted to do exclusive formula feeding, managed to do so for three months. She nevertheless had challenges after disclosing her HIV-status to her caretakers. The repercussions of which was outright rejection by her caretakers leading to her premature cessation of formula feeding at three months.

Disclosure of HIV status to the partner is usually a major condition for successful replacement feeding. However, in this study, disclosure of HIV-positive status to a partner in contrast to previous studies resulted in problems. For instance a study in Uganda found that women who succeeded in adhering to replacement feeding had family support (Matovu *et al.*, 2002). In this study, however, as illustrated by the experiences of *Yaa Mansa*, who but for the intervention

of her nurse counselor would have ceased breastfeeding even though her personal circumstance was not AFASS for replacement feeding. One probable reason for the differences in reactions to disclosure partner notification in the Ghanaian situation compared to that in the Ugandan study is the magnitude of HIV epidemic. The massive HIV publicity in Uganda has possibly led to the appreciation of the HIV problem better.

Most of the women interviewed in the present study were well aware that the HIV can be transmitted to their infants through breastfeeding. Nevertheless, the majority decided to breastfeed their babies. As Senah rightly remarked, the factors which promote good health and precipitate ill health are not purely biological, but can be social, economic, and cultural, and that these elements can work together or against one another in the life of an individual (Senah, 2003). These dynamics can be likened to the decision making processes of these women with regard to what to feed their infants. In other words, the decision to breastfeed or not to do so is not merely linked to knowledge of medical risks of MTCT through breastfeeding. In microbiological phraseology, Dubos sums this up aptly when he argued that the prevalence and severity of microbial diseases are conditioned more by the ways of life of people than they are by the virulence of specific etiologic agents (Dubos, 1985). In conclusion, this qualitative component of the present study has demonstrated that the responsibility of a mother's intentions and her possibility to put her intentions into action is not only determined by the so called knowledge of medical risks, but also social and cultural nuances of the community. As the popular saying goes, "*knowledge does not necessary lead to behavior change*". As such, any strategy designed on HIV and infant feeding must recognize these dynamics.

5.5.0 Limitations and needed improvements in subsequent studies

This study has a number of limitations which need to be discussed. The first limitation relates to the loss to follow up of the study participants. This could affect the representativeness of this sample to all the participants who were originally enrolled and introduce some bias in outcome measures. It is, however, worth noting that this group of women on whom data at delivery were available did not differ significantly from those who did not come back to deliver at the study hospitals in terms of their occupation, socio-economic, and clinical profile, and may therefore be representative of the rest of the women who were enrolled into the study.

I note that if an intention to treat analysis had been done where all those lost to follow-up will have been included in the denominators during the calculation of the various estimates of effect, possibly different conclusions will have been made. Nevertheless, this approach which works on the assumption that none of those lost to follow-up suffered the adverse outcomes of interest can open the door to a misleading presentation of study results. It is also worthy of note that, the other alternative strategies available in dealing with this problem by imputing outcomes to those lost to follow-up, in general, all make unverifiable assumptions that may introduce bias in the estimates of treatment effect (Hollis and Campbell, 1999).

The second limitation of this study is the inability of the investigator to measure HIV viral load, and malaria parasite density. This was due to lack of the needed logistics. These variables could have shed more light on the interactions between HIV and malaria.

The third limitation of the study relates to the failure of to capture all episodes of parasitemia, since there were only two scheduled periods for blood sampling – at recruitment and at

5.5.0 Limitations and needed improvements in subsequent studies

This study has a number of limitations which need to be discussed. The first limitation relates to the loss to follow up of the study participants. This could affect the representativeness of this sample to all the participants who were originally enrolled and introduce some bias in outcome measures. It is, however, worth noting that this group of women on whom data at delivery were available did not differ significantly from those who did not come back to deliver at the study hospitals in terms of their occupation, socio-economic, and clinical profile, and may therefore be representative of the rest of the women who were enrolled into the study.

I note that if an intention to treat analysis had been done where all those lost to follow-up will have been included in the denominators during the calculation of the various estimates of effect, possibly different conclusions will have been made. Nevertheless, this approach which works on the assumption that none of those lost to follow-up suffered the adverse outcomes of interest can open the door to a misleading presentation of study results. It is also worthy of note that, the other alternative strategies available in dealing with this problem by imputing outcomes to those lost to follow-up, in general, all make unverifiable assumptions that may introduce bias in the estimates of treatment effect (Hollis and Campbell, 1999).

The second limitation of this study is the inability of the investigator to measure HIV viral load, and malaria parasite density. This was due to lack of the needed logistics. These variables could have shed more light on the interactions between HIV and malaria.

The third limitation of the study relates to the failure of to capture all episodes of parasitemia, since there were only two scheduled periods for blood sampling – at recruitment and at

delivery. Monthly measures of parasitemia could have provided the most accurate data on incidence rates of malaria parasitemia. There was therefore the possibility of women being misclassified as malaria aparasitemic during the course of pregnancy. Such misclassifications nevertheless, would be expected to bias the study findings toward the null hypothesis.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

This chapter finalizes and summarizes the findings of the study presented in two thematic sections as per the broad objectives of this research. They are herein referred to as the study's conclusions. Following these are the recommendations the researcher intends to communicate to fellow researchers, the Ministry of Health/Ghana Health Services, and other policy makers. Finally recommendations on the future directions of this research are considered from academic research viewpoints.

6.1.0 Conclusions

6.1.1 Malaria and HIV infections during pregnancy and adverse maternal and perinatal outcomes.

This study demonstrates that women infected with HIV and/or malaria and their newborns are at heightened risk of adverse maternal and perinatal outcomes.

1. Specifically, the findings show that maternal infection with HIV and/or malaria during the course of pregnancy has a significant negative effect on birth weight, gestation length, and cord parasitemia. In particular, neonates born to women exposed to HIV and/or malaria infections during pregnancy were at particular risk of preterm delivery, low birth weight, cord blood malaria parasitemia, and low Apgar score.
2. The risks of the above adverse perinatal outcomes were more pronounced in women dually infected with HIV and malaria at first antenatal visit, and also at delivery.
3. With respect to umbilical cord blood parasitemia, this study indicates that in pregnant women, co-infection with malaria and HIV increases the chance that the offspring will be infected with malaria. The strongest risk factors for umbilical cord parasitemia were maternal malaria parasitemia at either at first antenatal visit, or at delivery. This is

suggestive that preventing malaria infection, successful treatment, and avoiding re-infection could decrease the risk of this adverse outcome.

4. Investigations on the associations between maternal infections with malaria and/or HIV and maternal anemia revealed that women infected with malaria were significantly more prone to being anemic than uninfected counterparts.
5. By HIV-infection status, the study participants did not differ significantly with respect to maternal anemia.
6. Dual infection with HIV and malaria particularly at delivery was significantly associated with maternal anemia at child birth.
7. Finally, the study has also demonstrated an association between maternal malaria infection and maternal immunosuppression.

6.1.2 Infant feeding choices, experiences and challenges faced by HIV+ mothers

1. This investigation on infant feeding choices by HIV-positive mothers has revealed that breastfeeding as a fundamental cultural practice is highly valued in the Manya Krobo District and Tema Municipality.
2. The study, however, shows that mothers in the study areas face various individual-level, community-level, and service-related barriers in choosing and implementing their feeding intentions. Such barriers include social pressure to mix-feed, local norms such as water supplementation, and "*the Baby Friendly Hospital Initiative*".

3. These challenges presented here may not be unique to only the mothers of the Manya Krobo District and Tema Municipality, but may be experienced by other mothers in various parts of Ghana.

6.2.0 Recommendations

6.2.1 Malaria and HIV infections during pregnancy and adverse maternal and perinatal outcomes.

In areas where both malaria and HIV are co-endemic, routine screening of pregnant women for both malaria and HIV at antenatal visits, successful treatment of women who are found to have malaria and avoidance of re-infection during the course of the pregnancy may reduce the incidence of the various adverse outcomes investigated in this study.

In the light of the above findings, innovative integration of malaria management in PMTCT programs in areas where both infections are co-endemic may bring some synergy into these interventions, which are currently vertical in nature. While malaria control programs could specifically consider malaria interventions for pregnant women with HIV, PMTCT programs could also consider the possibility of taking advantage of contacts with healthcare systems to deliver malaria prevention interventions.

6.2.2 Infant feeding choices, experiences and challenges faced by HIV-positive mothers

At present, the WHO advises that unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for infant and mother, exclusive breastfeeding should be practiced. These findings are suggestive that the ideal circumstances for replacement feeding are unlikely for some of the women in the Manya Krobo District, and Tema Municipality. The various challenges experienced by the mothers in this current study reinforce the fact that the social and cultural nuances of the community is important in decision individuals take. It is

therefore recommended that national PMTCT policy makers and PMTCT service providers recognize the social and cultural contexts of mothers before giving out recommendations.

6.2.3 Recommendations for future research

Further longitudinal studies with multiple follow-up data collection time points during the course of pregnancy, as well as deployment of methodologically robust analytic techniques to control for the effect of maternal HIV viral load, malaria parasite density, and maternal uptake of antiretroviral treatment may shed further light on these issues.

At present, mass IPTp and ARV are being rolled out in these areas. This may provide an opportunity to assess whether the incidence of these adverse outcomes in pregnant women and their neonates can be reduced in areas where the control programs are implemented simultaneously. Another interesting bit of research as a follow-up to this study will be to investigate the effectiveness of the existing SP prophylaxis programme in pregnancy, as mothers continue to get malaria and experience adverse pregnancy and perinatal events related to malaria.

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APPENDICES

APPENDIX 1. SAMPLE INFORMED CONSENT FORM

TITLE: Malaria and HIV infections in pregnancy: maternal, perinatal, and infant health issues.

Institutional affiliation:

School of Public Health, College of Health Sciences, University of Ghana, Legon

Funding Source:

Teaching and Learning Innovation Fund (TALIF) Project # CHSR/001/2005, School of Public Health, University of Ghana, Legon

Background

Greet! My name is..... I am a researcher from the School of Public Health. I am conducting a research on the influence of malaria and HIV infections on maternal and perinatal health. This academic research is part of student project work, PhD Degree in Public Health.

Procedures:

We would be collecting information at various time points during the course of your pregnancy, at delivery, and after delivery. If you agree to enroll in this study, we will ask you to provide information about yourself, your health, your dietary intake, health seeking behavior, and infant feeding practices. In addition your body measurements (weight, height, arm circumference, and skinfold thickness) will be taken and clinical appraisals done by a trained nurse. We shall also take 5ml of your blood to determine HIV status, malaria status, hemoglobin level, and others.

Risks and Benefits

You may feel uneasy with some of the questions we will be asking you. However they will be helpful to us and to the providers of healthcare in Ghana if you could answer all the questions. After our clinical appraisals and laboratory determinations, all women who require immediate medical attention will be referred to the appropriate quarters for management. All participants will be given incentives towards the cost of delivery in the chosen facility (study site). The information you provide will contribute to the efforts aimed at mitigating the effects of malaria and HIV on pregnant women and their children.

Right to refuse:

Giving us consent to participate in this study is voluntary and not under any obligation if you do not want to do so. Refusal to enroll will not affect the privilege you derive from any of the Health Institutions in this community. You are also at liberty to withdraw from the study anytime after enrollment, if you so wish.

Anonymity and Confidentiality

Be assured that the information collected will be handled with strict confidentiality and will be used purely for academic purposes. All your responses will not be shared with anybody who is not part of the study team, and data analysis will be done at the aggregate level to ensure anonymity.

Before taking consent

Do you have any questions that you wish to ask? Yes/No..... (If yes, questions to be noted below)

If you have questions later, you may contact **Mr. Amos Laar on 0244982176, School of Public Health, University of Ghana, Legon, Accra.**

Consent

I....., having understood the study, after having the consent form thoroughly explained to me in English/Twi/GaDagbme language do hereby agree to enroll and participate in this study.

Signature/Thumbprint of Respondent Date

Interviewer's statement:

I, the undersigned, have explained to the subject in the language that she understands the procedures to be followed in this study and the risks and benefits involved. She has agreed to participate in the study.

Signature of Interviewer Date

Name and signature of witness.....Date

APPENDIX 2. TWO-PHASED QUESTIONNAIRE

[Phase one]

SECTION A₀. RECRUITMENT FORM:

- 01. Questionnaire no.....
- 02. Date
- 03. Subject Code.....
- 04a. Contact address/directions to place of residence

Name of research assistant

.....
Date.....

Name of Supervisor

.....
Date.....
.....
.....

A04b. Alternate contact addresses:

05 Telephone no(s) :.....

06 Study Area: (1) Atua (2) St Martin's (3) Tema General Hospital

A. BACKGROUND INFORMATION

A1 Age..... , A2 Duration of pregnancy in months

A3. Marital status:

- (1). Single (2). Married (3). Divorced/Separated (4). Widowed (5) Cohabiting

A4. Religion:

- (1). None (2). Christian (3). Muslim (4) Traditionalist (5) Other.....

A5. Place of residence:

- (1) Urban (2) Rural

A6. Subject's level of education:

- (1). Nil (1). Primary (2). Middle/JSS (3). Secondary/Vocational/Post-secondary (4) Tertiary

A7. Caregiver/partner's educational level:

- (1). Nil (2). Primary (3). Middle/JSS (4). Secondary/Vocational/Post-secondary (5) Tertiary

A8. Occupation before infection:

- (1). None (2). Farmer (3). Teacher (4).Trader (5). Secretary/ accounts clerk
(6). Work in a hotel (7) Music industrial (8) Marketing agent (9) Other.....

A9. Current Occupation:

- (1). None (2). Farmer (3). Teacher (4).Trader (5).Secretary/Accounts clerk
((6). Work in a hotel (7) Music industrial (8) Marketing agent (9) Other.....

A10. Occupation of Caregiver/partner:

- (1). None (2). Farmer (3). Teacher (4) Trader (5). Secretary/Accounts clerk
(6). Work in a hotel (7) Music industrial (8) Marketing agent (9) Other.....

A11. Relationship to Caregiver:

- (1). Spouse (2). Parent (3). Child (4). Other family member (5). Friend (6).
Other.....

A12. Reproductive health history:

1. gravidity-----
2. parity-----
3. no. of children alive-----

B. HEALTH-SEEKING BEHAVIOR

B1. Which health facilities are available in this area?

- (a) Clinics (b) Pharmacies/drug stores (c) indigenous healers (d) healing churches

B2. Which of these have you accessed in the last 3 months?

- (a) Clinics (b) Pharmacies/drug stores (c) indigenous healers (d) healing churches

B3. What health problems did you take

there?.....

.....

.....

B.4 Where do you normally go for ANC services?

.....

B5. Which other facility do you use for ANC

services?.....

B6. Why do you use these other

facilities?.....

B7a. HIV status: Positive Negative (If negative go to Section C)

B7. Do you go for ARV treatment? YES NO

B8. If YES, when did you start the treatment?

B9. Identify 3 main problems you encounter in going for ARV treatment

a.

b.

...

c.

...

B10. Suggest ways to improve ARV treatment at this facility

You can write here!



C. DIETARY SURVEY

C1. Do you have problems with eating?

1). NO (2). YES (If NO skip question C2)

C2. What problems?

C3. Do you use any nutrient supplement? 1). NO (2). YES (If NO skip question C4)

C4. If yes specify

C5. Have you stopped consuming any food item lately?

(1). NO (2). YES (If NO, skip question C6)

C6. Name these items and the reasons why you stopped consuming them

ITEM	REASONS

C7. Have you started consuming any food item that you were not consuming before?

(1). NO (2). YES (If NO, skip question C8)

C8. Name these items and the reasons why you have started consuming them.

ITEM	REASONS

C9. During the past 24 hours, what foods did you consume? (The table below should be completed by the interviewer, indicating the types and amounts of all foods and snacks the subject has consumed over the past 24 hours).

24-hour dietary assessment recall form (to be repeated for one more week day and one weekend day).

Time	Description of Food and Drink	Quantity/Estimated Portion size
Breakfast		
Snack		
Lunch		
Snack		
Supper		
Snack		

D. ANTHROPOMETRIC MEASUREMENT

- D1. Current weight in kg.....
D2. Height in cm: D3. BMI in kg/m²:.....
D4. MUAC/cm..... C5. Triceps skinfold measurements/cm.....

E: CLINICAL AND LABORATORY INFORMATION

E1. HIV first diagnosed (date)

E2 HIV disease state

- (1) HIV Positive with no AIDS (2) HIV Positive with AIDS

E3. Clinical appraisal results:

- (1). No symptoms (2). Diarrhoea (3). Skin rashes (4). Anorexia (5). Anal discharge (6). Vomiting
(7). Sore throat/cough (8). Oral lesion (9) Anaemia (10) Tuberculosis (11) Candidiasis
(12) Fever/Malaria (13) Other.....

E4. History of fever over the past two weeks: (1) YES (2) NO

E5. History of antimalarial use: (1) YES (2) NO

E5b. If YES, name(s) of drug(s).....

E6. History of herbal drug use: (1) YES (2) NO

E7. If YES, name(s) of drug(s).....

E8. Axillary temperature in degrees centigrade: at recruitment

E9 Hemoglobin in g/dl: at recruitment

E10. Malaria status: 1. Positive 2. Negative

E11b. Date diagnosed.....

E11. Classification of malaria disease state:

- (1) Parasitemic with clinical malaria, (2) Parasitemic without clinical malaria

E13 CD4+ cell count (cells/mm³) at recruitment

[Phase two]
FOLLOW-UP AT DELIVERY

Samples to be taken during delivery

- ❖ Cord blood (5ml) in EDTA vacutainer
- ❖ Venous blood (5ml) in EDTA vacutainer

Name of research officer

.....

Date.....

Name of Supervisor

.....

Date.....

Questionnaire no.....

Participant's (Mother's) full name.....

Address of mother as in recruitment form:

F01. Date of delivery

F02. Study Area: (1) Atua (2) St Martin's (3) Tema General Hospital

F03. Mother's age

F04. Gestational age

F05. Live birth OR Still birth

F06. Birth weight

F07. Apgar score at 1 minute.....5minutes.....

F08. Condition of baby at delivery.....

F09. Fetal abnormality.....

F11. Sex of newborn.....

F12. Type of delivery.....

F13. Mother's body temperature at delivery.....

F15. Condition of mother at delivery.....

F16i. Peripheral malaria status at delivery 1. Positive 2. Negative [Note: use venous blood]

F16iii. Cord blood malaria status at delivery 1. Positive 2. Negative [Note: use cord blood of baby]

F17. Classification of mother's malaria disease state:

(i) Parasitemic with clinical malaria (ii) Parasitemic without clinical malaria

F18. CD4 count of mother at delivery.....

F19. Hemoglobin in g/dl:

i. of mother at delivery (use venous blood).....

ii. of infant at delivery (uses cord blood).....

F20. IPT uptake

To be done in the Labor Ward

To be done in the Labor Ward

To be done in the Lab

APPENDIX 3 - FOLLOW-UP QUESTIONNAIRE ON INFANT FEEDING POST-DELIVERY

Background: This phase of the questionnaire is designed to ASSESS INFANT FEEDING PRACTICES, AS WELL AS THE HEALTH OF OUR ENROLLED STUDY PARTICIPANTS AND THEIR INFANTS. It is also designed to quantify the determinants of INFANT FEEDING CHOICES among them. The questions are grouped into six sections: Section 1 **BASELINE**; Sections 2 deals with **INFANT FEEDING PRACTICES**; Section 3 **INFANT HEALTH**; Section 4 **MATERNAL HEALTH**; Section 5 **BREASTFEEDING CESSATION**; and section 6 **DETERMINANTS OF INFANT FEEDING CHOICES**.

A. BACKGROUND, FIRST VISIT AFTER BIRTH (reconcile with that at recruitment)

A1. Questionnaire no-----

A2. Date -----/-----/-----

A3. Contact address/directions to place of residence

A4. Telephone no(s): Home-----Mobile-----

A6. Study Area:

(1) Atua

(2) St Martin's

(3) Tema General Hospital

A7. Type of delivery [of index child]

(a) Spontaneous Vaginal Delivery (b) Elective Caesarean section (c) Emergency caesarean section

A8 .Number of people living in the household -----

(B) INFANT FEEDING PRACTICES**[Food items given to infant]**

B1. Did you ever breastfeed your infant? Yes [] No []

B1.1 If NO, go to SECTION C Question 1. Before that, tell us how your child has been fed since birth

B1.2 If yes, how soon after delivery was your infant first put to the breast? (in hours) -----

B2. Did your infant receive anything to eat/drink before he was first put to the breast?

Yes [] No [] Don't know []

B3. Food items given to infant

	Before any breast milk		Since birth	
	Given	Reason	Given	Reason
Breast milk				
Other milk				
Unsure if other food given				
Water or Glucose water				
Tea or Juice				
Formula				
Cereals or porridge (home prepared or commercial)				
Vegetables or fruits				
Pharmaceutical medicines				
Traditional medicines				
ORS				
Cooking oil				

Probe all the items listed in the table.

Other food specified 1: _____

Other food specified 2: _____

B4. Was the feeding pattern typical of the way the infant was fed since birth?

Yes [] No [] Don't know []

Wet-nursing practices]

B5. Has anyone else (beside yourself) ever breastfed this infant since birth?

Yes [] No []

B5.1. If no, go to **QUESTION B9**

B6. Who beside the mother has breastfed this infant? (*Ask the question and tick only the answers given. Do not prompt.*)

(a) Sister [] (b) Mother [] (c) Other family member [] (d) Neighbour []

(e) Other (specify) -----

B7. Number of days on which this occurred? (days)-----

B8. Why did the other person breastfeed your infant? (*Ask the question and tick only the answers given. Do not prompt, except to ask "Are there any other reasons?"*)

(a) Mother ill/weak [] (b) Breast or nipple difficulty [] (c) Not enough milk []

(d) Work [] (e) Had to go out/be separated from infant [] (f) Advised by husband []

(g) Advised by other family member [] (h) Did not want to infect infant with HIV []

(i) Other (specify) -----

[Expressed milk]

B9. Have you ever expressed your breast milk since birth? Yes [] No []

B10. Number of days on which this occurred since birth? (days)-----

B11. Have you heat treated your breast milk since birth? Yes [] No []

B12. Number of days on which this occurred since birth? (days)-----

B13. Why did you express milk? (*Ask the question and tick only the answers given. Do not prompt, except to ask "Are there any other reasons?"*)

(a) To relieve breast pain/engorgement [] (b) To relieve pain due to cracked nipples. []

(c) Thought milk was bad/unsafe/contaminated [] (d) To heat-treat before feeding. []

(e) Had to be separated from infant [] (f) To wean/stop breastfeeding. []

(g) Other (specify) -----

(C) INFANT HEALTH

C1. Infant weight (in g) -----

C2. Infant age (months) -----

D3. Has the infant shown any of the following signs since birth?

D2.1. Mouth sores? Yes [] No []

D3.2. Sore with white patches on the inside of the mouth (Oral thrush) Yes [] No []

D3.3. Fast or difficult breathing? Yes [] No []

D3.4. Fever? Yes [] No []

D3.5. Diarrhea? Yes [] No []

D3.6. Other problem (specify) -----

C6. What did you do differently as a result of the above? (*Ask the question and tick only the answers given*)

(a) Stopped breastfeeding Yes [] No [] (b) Stopped non-human milks Yes [] No []

(c) Stopped other liquids Yes [] No [] (d) Stopped solid foods Yes [] No []

(e) Began giving non-human milks Yes [] No [] (f) Began giving other liquids Yes [] No []

(g) Began giving solid foods Yes [] No []

(D) MATERNAL HEALTH

D1. Since your birth, have you ever been sick? Yes [] No []

D2.1. If yes, specify what sickness-----

D2.2. Did you seek treatment for this condition at the health centre? Yes [] No []

D2.7. Did you change the way you fed your child during that time? Yes [] No []

D3. What did you do differently? (*Ask the question and tick only the answers given.*)

(a) Stopped breastfeeding []

(b) Stopped non-human milks []

(c) Stopped other liquids []

(d) Stopped solid foods []

(e) Began giving non-human milks []

(f) Began giving other liquids []

(g) Began giving solid foods []

(h) Other specify-----

[Breast health and breastfeeding related difficulties]

D4. Since birth, have you experienced any difficulty with your breast or with breastfeeding health problem? Yes [] No []

If yes, check any of the following that applies

Breast enlarged?	Yes []	No []
Skin of the breast red/hot	Yes []	No []
An abscess on the breast?	Yes []	No []
Skin of the nipple broken (cracked)?	Yes []	No []
Skin of the nipple broken with pus?	Yes []	No []
Skin of the nipple broken and bleeding?	Yes []	No []
Skin of the nipple flaking?	Yes []	No []
Itching?	Yes []	No []
Pain affecting the nipple during feeding?	Yes []	No []
Breast pain persisting between feeds?	Yes []	No []

D5. Was breastfeeding stopped from the affected breast during the episode? Yes [] No []

(E) CESSATION OF BREASTFEEDING

If the mother has not reported any breastfeeding in the last few days, ask:

E1. Have you completely stopped breastfeeding your infant every day and every night? Yes [] No []

E2. How old was your infant when you completely stopped breastfeeding him every day and every night?(age in months)-----

E3. Do you still put your child to the breast occasionally (less than once per day and night, e.g. when your child starts crying)? Yes [] No []

E4. Why did you stop breastfeeding your infant? (Ask the question and tick only the answers given. Do not prompt, except to ask "Are there any other reasons?")

- | | | |
|---|---------|--------|
| (a) Infant old enough | Yes [] | No [] |
| (b) Infant no longer wanted to breastfeed. | Yes [] | No [] |
| (c) To encourage infant to eat solid food. | Yes [] | No [] |
| (d) Pregnancy. | Yes [] | No [] |
| (e) Fear of transmitting HIV. | Yes [] | No [] |
| (f) Mother can afford replacement feeding. | Yes [] | No [] |
| (g) Advised by health provider. | Yes [] | No [] |
| (h) Advised by husband or partner. | Yes [] | No [] |
| (i) Resumption of sexual relationship. | Yes [] | No [] |
| (j) Advised by other person. | Yes [] | No [] |
| (k) Separation from infant due to work. | Yes [] | No [] |
| (l) Separation from infant for other reasons. | Yes [] | No [] |
| (m) Mother too sick to breastfeed. | Yes [] | No [] |
| (n) Infant too sick to breastfeed. | Yes [] | No [] |
| (o) Infant not growing well. | Yes [] | No [] |
| (p) Other reason (specify) ----- | | |

E5. How did you stop breastfeeding your infant? (Ask the question and tick only the answers given. Do not prompt, except to ask "Are there any other reasons?")

(a) Put something on breast. Yes [] No []

- (b) Sent infant to relative or friend or neighbor. Yes [] No []
- (c) Took medicine to stop milk Yes [] No []
- (d) Gave infant other milk or food. Yes [] No []
- (e) Gave infant a feeding bottle. Yes [] No []
- (f) Did nothing special. Yes [] No []
- (g) Other method (describe) -----

E6. Did you encounter any problems when you stopped? Yes [] No []

E7. What problems did you encounter when you stopped breastfeeding your infant? (Ask the question and tick only the answers given. Do not prompt, except to ask "Is there any other reason?")

- (a) Infant cried or unhappy. []
- (b) Breast pain. []
- (c) Breast engorgement. []
- (d) Mother became ill. []
- (e) Infant became ill. []
- (f) Disapproval by partner or family or neighbors. []
- (g) Disapproval by health worker. []
- (h) No food or milk to feed the infant. []
- (i) Other problems (specify) -----

F: DETERMINANTS OF INFANT FEEDING CHOICES

F1. YES or NO to the following questions:

- a. Fear of HIV? Yes [] No []
- b. Husband aware of your HIV status? Yes [] No []
- c. Ashamed of not breastfeeding? Yes [] No []
- d. Belief in the benefits of breast-feeding? Yes [] No []
- e. Supportive home environment? Yes [] No []
- f. Regular maternal income? Yes [] No []
- g. Consider cost of replacement foods expensive? Yes [] No []
- h. The number of antenatal home visits -----

F2. Do you have regular supply of the following?

- a. Fuel for cooking Yes [] No []
- b. Electrical power Yes [] No []
- c. Access to safe water Yes [] No []
- d. Supplies of formula at clinics Yes [] No []
- e. Access to infant formula storage facilities Yes [] No []

APPENDIX 4 INTERVIEWER'S GUIDE TO APPENDICES 2 AND 3

Interviewer's guide

This study is a hospital-based, prospective in design involving pregnant women attending antenatal clinics at the following Hospitals: The Atua Government hospital, St Martin *de Porres* Hospital (in the Manya Krobo District), and the Tema general hospital (in the Tema Municipality).

The overall goal of the study is to determine the influence of malaria and HIV infections during pregnancy on the health of the pregnant woman and her unborn baby. Methods are detailed in the protocol. Briefly, the data collection techniques to be employed will include desk review of hospital records, and structured interviews. Malaria parasitemia, HIV-sero status, CD4 cell count, haemoglobin concentration, and maternal anthropometrics (weight height, body mass index, arm circumference, triceps skinfold) will be measured. Assessment of their dietary intake will also be done as detailed in the protocol.

Some of the tools to be used in gathering this information are the structured questionnaires described above (Appendices 2, and 3). The first phase of the two-phased questionnaire (Appendix 2) is divided into six sections (section A₀ is the recruitment form, section A is intended to collect background and socioeconomic information of the study participants, section B; health-seeking behavior, section C; dietary information, section D; anthropometric measurement, and section E; biochemical/clinical data).

Section A₀ will be filled by the recruiting nurse/research assistant, sections A-C by a trained interviewer and sections D and E by a trained anthropometrist/phlebotomist/lab technician. Most of the questions in all the sections are self-explanatory and should be filled in as appropriate. This guide all the same, tries to explain to the comprehension of the research assistant as to what each question seeks to gather, by providing more information on every question in the questionnaire.

SECTION A₀. RECRUITMENT FORM:

A01. Questionnaire no (already filled in)

A02. Date : Date (day/month/year) of recruitment to be filled in as appropriate

A03. Subject Code: Subject to be given a 2-digit sequential code or serial number at each study site.

A04a. Contact address/directions to place of residence (to be filled in as appropriate in the space provided.

Directions should be taken in such a way as to allow the location of the place during follow-up by a different research assistant should the need arise)

A04b. Alternate contact addresses (second address to be provided in case of movement). Thus address of most probable place respondent will move to, or address of person to contact in case of movement from the current place of residence.

A05 Contact phone no(s): to be filled in as appropriate (both the respondent's phone number and that of the person to contact in case of movement).

A06 Study Area: To be checked as appropriate

A07. Age: Age in completed years to be filled in as appropriate

A09. Duration of pregnancy in months: To be filled in as appropriate

NOTE: Conclude and thank respondent after every section

SECTION A: BACKGROUND AND SOCIOECONOMIC INFORMATION

A1. Marital status:

(1) – (4) to be checked as appropriate. (5) Cohabitation applies to unmarried partners who are staying together

A2. Religion:

To be checked as appropriate

A3. Place of residence:

To be checked as appropriate

A4. Subject's level of education:

To be checked as appropriate

A5. Caregiver/partner's educational level:

To be checked as appropriate

A6. Occupation before infection:

To be checked as appropriate or written in the 'other' option if not one of those provided

A7. Current Occupation:

To be checked as appropriate or written in the 'other' option if not one of those provided

A8. Occupation of Caregiver:

To be checked as appropriate or written in the 'other' option if not one of those provided

A9. Relationship to Caregiver:

To be checked as appropriate or written in the 'other' option if not one of those provided

A10. Gravidity: number of pregnancies a woman has had. This is to be checked as appropriate

A11. Parity: Deliveries at 28 weeks gestation or more whether live or stillborn. This is to be checked as appropriate

NOTE: Conclude and thank respondent after every section

SECTION B: HEALTH-SEEKING BEHAVIOR

B1. Name two common health problems that affect you: To be filled as appropriate

B2. What are the causes of? Causes to be filled as appropriate

B3. Which of the above problems are curable? To be filled as appropriate

B4. Which of them are preventable? To be filled as appropriate

B5. Which health facilities are available in this area?

To be checked as appropriate or written in the '*other*' option if not one of those indicated

B6. Which of these have you accessed in the last 3 months?

To be checked as appropriate or written in the '*other*' option if not one of those indicated

B7. What health problems did you take there? To be filled as appropriate

B8. Where do you normally go for ANC services? To be filled as appropriate

B9. Which other facility do you use for ANC services? To be filled as appropriate

B10. Why do you use these other facilities? To be filled as appropriate in the space provided

B11. Do you go for ARV treatment? To be checked as appropriate

B12. If YES, when did you start the treatment? Date (month and year) participant started treatment to be filled in the space provided

B13. Why did you choose this facility for the treatment? Reasons to be written in the space provided

B14. How much do you pay for the treatment? Amount in Ghanaian cedis to be written in the space provided

B15. How would you describe cost of ARV treatment? To be checked as appropriate

B16. Identify 3 main problems you encounter in going for ARV treatment

3 problems respondent encountered during her ARV (antiretroviral) treatment to be written in the space provided

B17. Would you advise other pregnant sero-positives to go for ARV treatment? To be checked as appropriate

B18. Why to B17 above? Probe and write in the space provided the reason for the choice in question B17.

B19. Suggest ways to improve ARV treatment at this facility: Respondent's views as to how to improve ARV treatment to be written down in the box provided.

NOTE: Conclude and thank respondent after every section

SECTION C. DIETARY SURVEY

- C1. Do you have problems with eating?** To be checked as appropriate (If NO skip question C2)
- C2. What problems?** If yes probe and fill in the space problems the respondent has with respect to eating
- C3. Do you use any nutrient supplement?** To be checked as appropriate (If NO skip question C4)
- C4. If yes specify.** If yes, probe and write in the space provided the various nutrient supplements the respondent takes
- C5. Have you stopped consuming any food item due to your present condition?** To be filled in as appropriate (If NO, skip question C6)
- C6. Name these items and the reasons why you stopped consuming them.** Food items and reasons why respondent stopped consuming them to be filled in the table provided
- C7. Have you started consuming any food item that you were not consuming before your present condition?** To be checked as appropriate (If NO, skip question C8)
- C8. Name these items and the reasons why you have started consuming them.** Food items and reasons why respondent started consuming them to be filled in the table provided

C9. 24 hours: The purpose of this question is to have an idea about the amount of foods consumed over the past 24-hours. To achieve this objective, respondents are supposed to begin recalling foods consumed starting from the immediate past meal. The precaution here is that, you (the research assistant) should enquire about the type and amounts of foods consumed by the respondent. Time column refers to meal (breakfast, lunch, dinner or snack). With regard to the column for portion size, you are required to find out from the respondent an estimate of food consumed using the common household measures (spoons, ladles etc) to be provided. For instance, if a respondent consumed maize porridge ask her to estimate the amount in ladles. Whether 2 or 3 soup ladleful, 1½ teaspoonful of sugar, a tablespoonful of Nido, etc). Where the food was bought from food vendors, please indicate the name, state of food and amount bought. The table below should thus be completed by the interviewer, indicating the types and amounts of all foods and snacks the subject has consumed over the past 24 hours).

Time	Description of Food and Drink	Quantity/Estimated Portion size
Breakfast		
Snack		
Lunch		
Snack		
Supper		
Snack		

NOTE: Conclude AND THANK RESPONDENT AFTER EVERY SECTION

D. ANTHROPOMETRIC MEASUREMENT

(D1, D2, D4 and D5 to be measured according to the procedures provided in the protocol. Procedures will be made available to the research assistant. C3. BMI in kg/m². To be left blank

SECTION E. CLINICAL AND BIOCHEMICAL DATA

E1. HIV first diagnosed (month/year to be filled as appropriate)

E2 HIV disease state:

HIV without AIDS: A laboratory confirmed HIV seropositive without any of the minor signs [(persistent cough for at least one month, generalised pruritic dermatitis, recurrent herpes zoster, oro-pharyngeal candidiasis, chronic progressive and disseminated herpes simplex infection and generalised lymphadenopathy), MOH, 2000] of AIDS or with less than two of the major signs (weight loss of more than 10% of body weight, chronic diarrhoea for at least one month and prolonged fever for at least one month) of AIDS.

HIV with AIDS: A person is said to have AIDS when he or she has two of the major signs and one minor sign plus evidence of HIV by the ELISA method, or when he or she has three major signs with or without a minor sign plus evidence of HIV by the ELISA method (MOH, 2000).

E3. Classification of HIV disease stage: to be left blank

E4. Reported complications:

To be checked as appropriate or written in the 'other' option if not one of those provided

E5. History of fever over the past two weeks: To be checked as appropriate

E6. History of antimalarial use: To be checked as appropriate

E6b. If YES, name(s) of drug(s): Probe and write down names of antimalaria drugs used

E7. History of herbal drug use: To be checked as appropriate

E8. If YES, name(s) of drug(s): Probe and indicate names of herbal drugs respondent uses

E8b. For how long have you been taking them? To be filled as appropriate

E9. Axillary temperature in degrees centigrade: To be measured with a clinical thermometer and filled in the space provided

E10. Malaria status: To be checked as appropriate after performing rapid malaria test (test kit will be provided)

E10b. If positive, date diagnosed: Date (day/month/year) test is performed to be indicated

E11. Classification of malaria disease state:

Parasitemic without clinical malaria. A subject presenting with any level of malaria parasitemia without fever ($<37.5^{\circ}\text{C}$) and no signs of nausea, lassitude, headaches, or body aches (Smith et al., 1994).

Parasitemic with non-severe clinical malaria. A person with any level of parasitemia who seeks medical attention for signs or symptoms that include fever documented by the physician (axillary temperature $\geq 37.5^{\circ}\text{C}$ by digital thermometer), reports of fever within the preceding 2 days, nausea, lassitude, headaches, or body aches.

E12 Hemoglobin at recruitment in g/dl: Hemoglobin concentration to be filled as appropriate after hemocue determinations

E13 CD4+ count at recruitment in n/ μl : To be left blank

NOTE: Conclude and thank respondent after every section

[Phase two of Interviewer's guide]

FOLLOW-UP AT DELIVERY

Samples to be taken during delivery

- ❖ Cord blood (5ml) in EDTA vacutainer
- ❖ Venous blood (5ml) in EDTA vacutainer

Questionnaire no..... (please refer to recruitment form; should be the same #).

Address of mother as in recruitment form: (As in recruitment form)

F01. Date of delivery (dd/mm/yy)

F02. Study Area: (1) Atua (2) St Martin's (3) Tema General Hospital (tick as appropriate)

F03. Mother's age (age in completed years)

F04. Gestational age (in completed weeks)

F05. Live birth OR Still birth (as appropriate)

F06. Birth weight kg..... (use baby Seca scale provided)

F7. Apgar score at 1, and 5 minutes..... || (to be filled using grid provide by midwife)

F8. Condition of baby at delivery..... (to be filled as good or bad)

F9. Fetal abnormality..... (present or absent)

F11. Sex of newborn..... (as appropriate)

F12. Type of delivery..... (SVD, CS, other)

F13. Mother's body temperature at delivery..... (in degrees centigrade)

F15. Condition of mother at delivery..... (good/ bad)

F16i. Peripheral malaria status at delivery 1. Positive 2. Negative [Note: use venous blood]

F16iii. Cord blood malaria status at delivery 1. Positive 2. Negative [Note: use cord blood of baby]

F17. Classification of mother's malaria disease state:

(i) Parasitemic with clinical malaria (ii) Parasitemic without clinical malaria

F18. CD4 count of mother at delivery.....

F19. Hemoglobin in g/dl:

iii. of mother at delivery (use venous blood).....

iv. of infant at delivery (uses cord blood).....

F20. IPT uptake (total number of doses taken before delivery)

[Phase three]

QUESTIONS ON INFANT FEEDING CHOICES AND PRACTICES

All the SIX SECTIONS (Section 1 BASELINE; Sections 2 deals with INFANT FEEDING PRACTICES; Section 3 INFANT HEALTH; Section 4 MATERNAL HEALTH; Section 5 BREASTFEEDING CESSATION; and section 6 DETERMINANTS OF INFANT FEEDING CHOICES) of this questionnaire are self-explanatory and should be completed as appropriate.

NOTE: USE THIS ONLY FOR HIV+ MOTHERS WHO HAD THEIR RECRUITMENT AND FOLLOW UP DATA AT DELIVERY TAKEN.

13. Did your infant receive anything to eat/drink before he was first put to the breast?

14. Food items given to infant before any breast milk

- Breast milk
- Other milk
- Unsure if other food given
- Water or Glucose water
- Tea or Juice
- Formula
- Cereals or porridge (home prepared or commercial)
- Vegetables or fruits
- Pharmaceutical medicines
- Traditional medicines
- ORS
- Cooking oil
- Other foods specified

15. Was the feeding pattern typical of the way the infant was fed since birth?

16. Food items given to infant since birth with reasons

- Breast milk
- Other milk
- Unsure if other food given
- Water or Glucose water
- Tea or Juice
- Formula
- Cereals or porridge (home prepared or commercial)
- Vegetables or fruits
- Pharmaceutical medicines
- Traditional medicines
- ORS
- Cooking oil
- Other foods specified

17. Was the feeding pattern typical of the way the infant was fed since birth?

Wet-nursing practices

18. Has anyone else (beside you) ever breastfed this infant since birth?

19. Who beside the mother has breastfed this infant?

20. Why did the other person breastfeed your infant?

Expressed milk

21. Have you ever expressed your breast milk since birth?

22. Number of days on which this occurred since birth? (days) -----

23. Have you heat treated your breast milk since birth?

24. Number of days on which this occurred since birth? (days) -----

25. Why did you express milk?

EXPLORE THESE

- (1.) Dependence on close kin
- (2.) Social pressure
- (3.) Pressure from family and friends
- (4.) Cultural acceptance of feeding method chosen
- (5.) Any traditional or cultural rites after delivery
- (6.) Residence:
- (7.) Education:
- (8.) Marital status:
- (9.) Living with extended family members:
- (10.) Living with partner alone:
- (11.) Living alone:
- (12.) Has permanent income from employment:
- (13.) Purchasing power
- (14.) Not employed:
- (15.) HIV sero-status disclosed to partner or close relative:
- (16.) Ashamed of not breastfeeding
- (17.) Belief in the benefits of breast-feeding
- (18.) Consider cost of replacement foods expensive
- (19.) Fuel for cooking

- (20.) Electrical power
- (21.) Access to safe water
- (22.) Supplies of formula at antenatal clinics

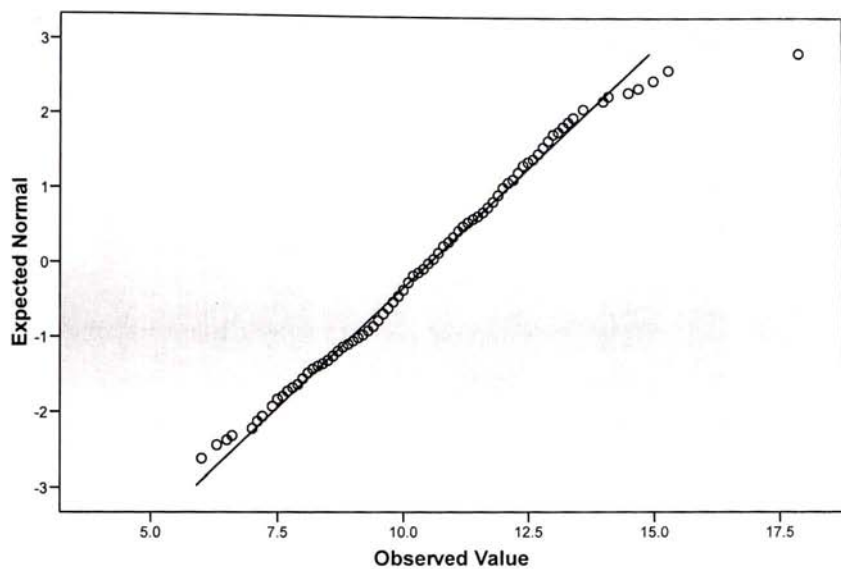
23. Record narrative of infant feeding experiences and challenges here



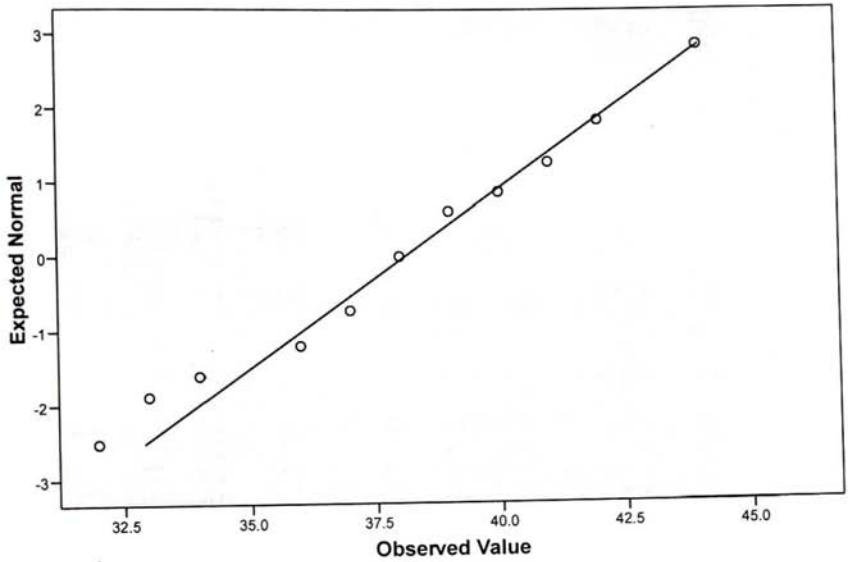
APPENDIX 6 DISTRIBUTIONS OF KEY CONTINUOUS VARIABLES

Appendix 6a. Distribution of maternal hemoglobin

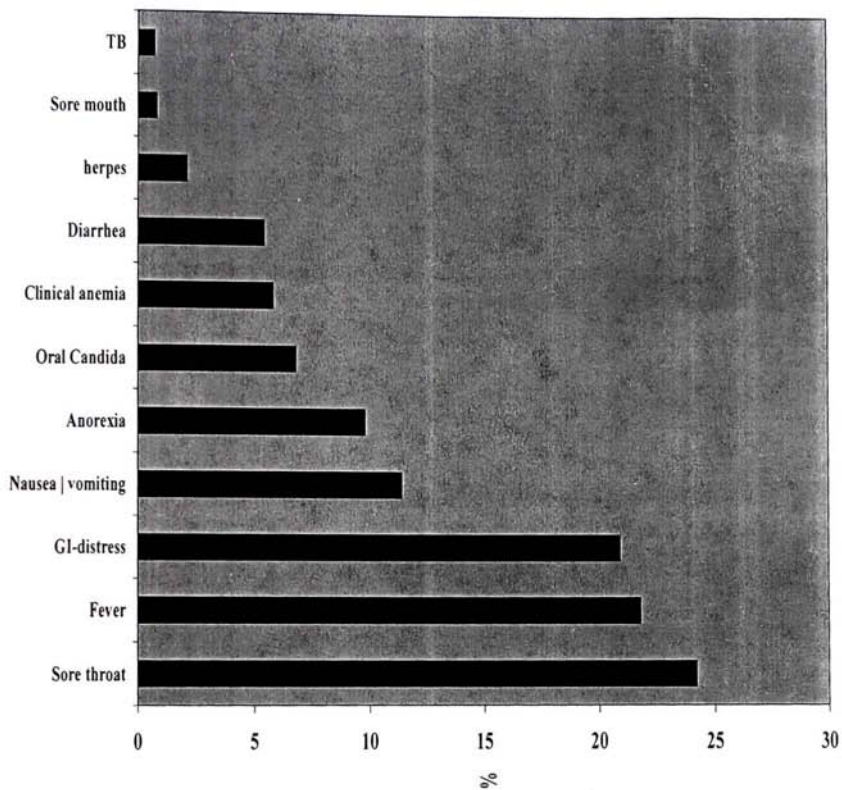
Normal Q-Q Plot of Hemoglobin



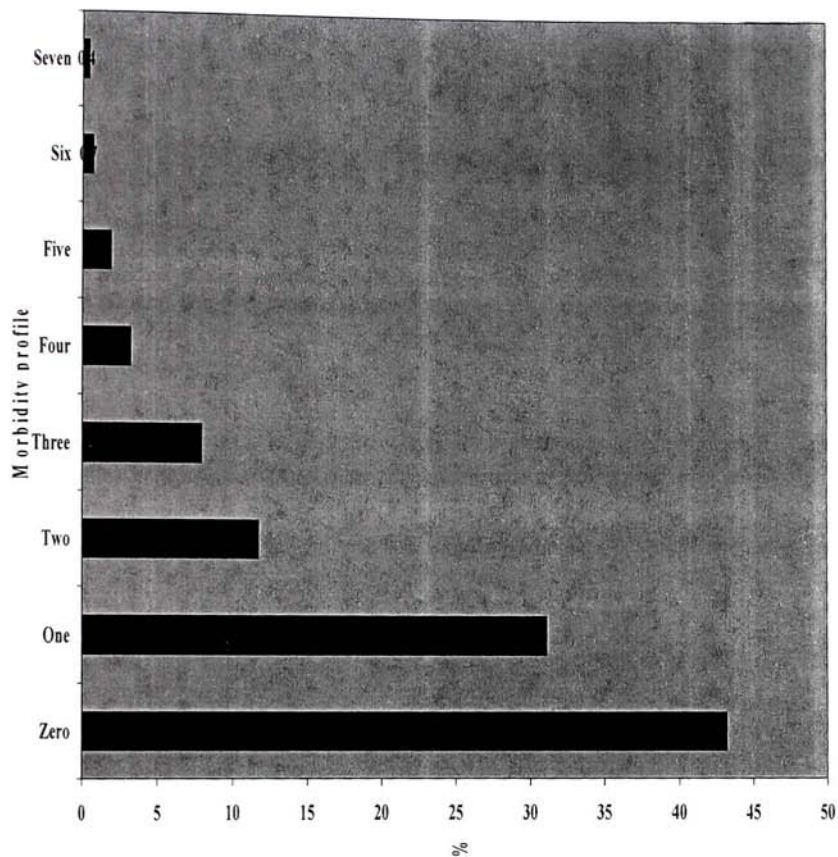
Normal Q-Q Plot of FUGesage



Appendix 7 Clinical presentations of study participants at enrollment

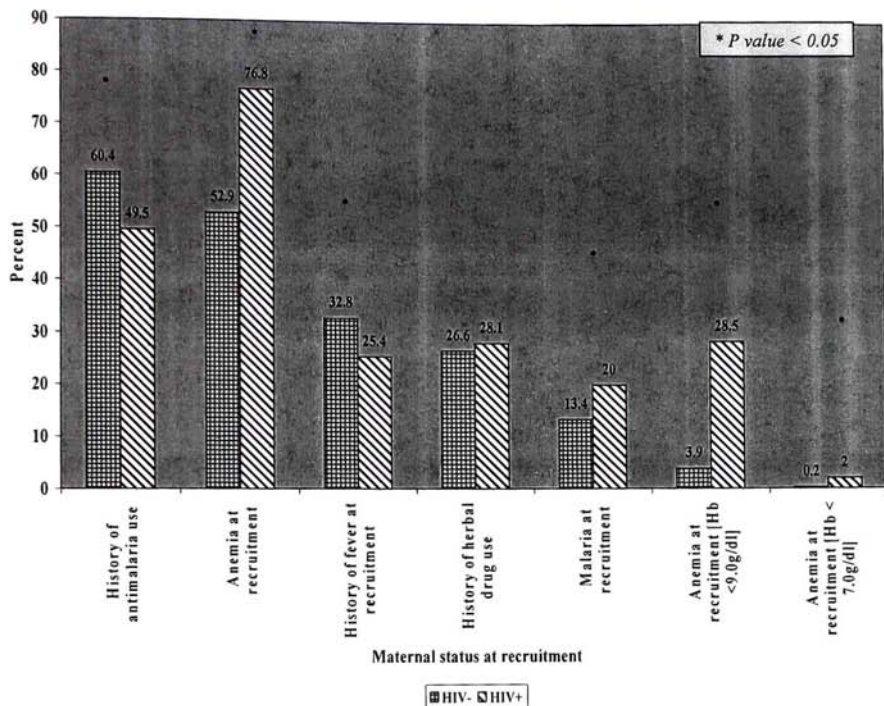


Appendix 8 Morbidity profile¹ of study participants at enrollment

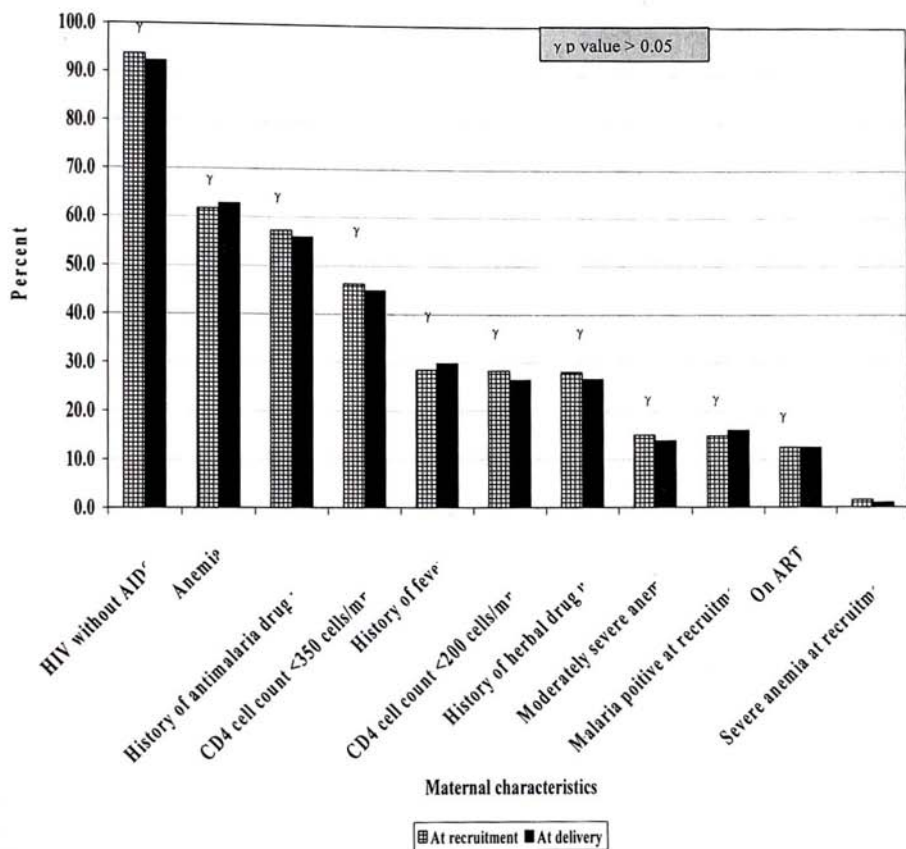


¹ Morbidity profile was computed using the twelve clinical conditions indicated in Appendix 8. Each of the study participants was given a score relating to the number of conditions the subject presented with. No condition means zero score, 12 conditions conditions represented a score of 12.

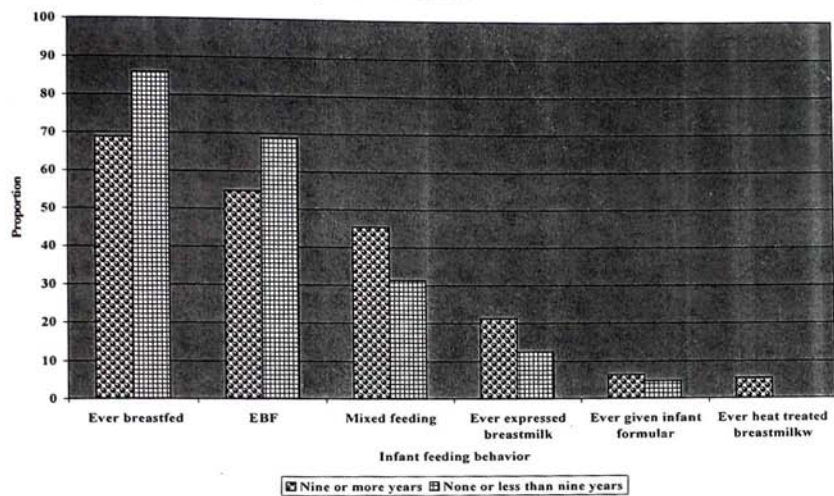
Appendix 9 Baseline outcomes of all women on whom data at delivery were available by HIV status



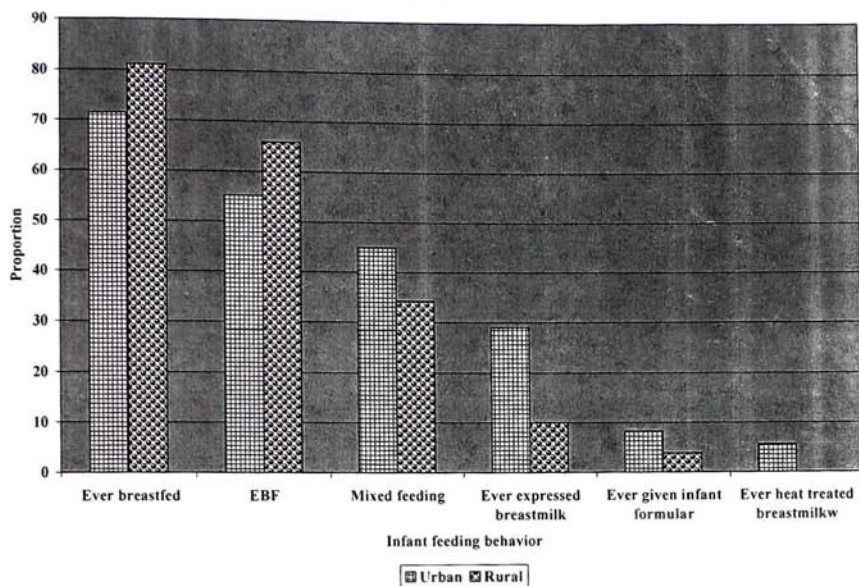
Appendix 10 Baseline outcomes of HIV+ women at enrolment compared with those on whom data at delivery were available.



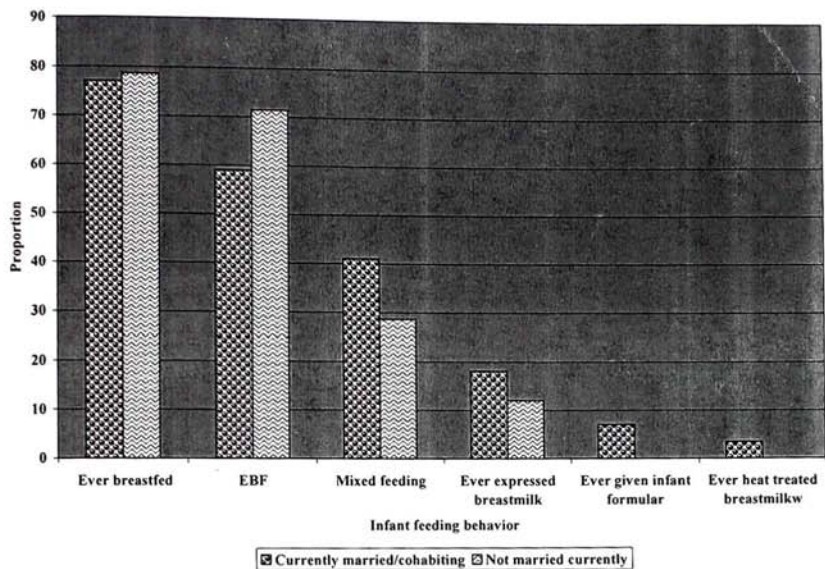
Appendix 11a. Infant feeding behavior by level of education



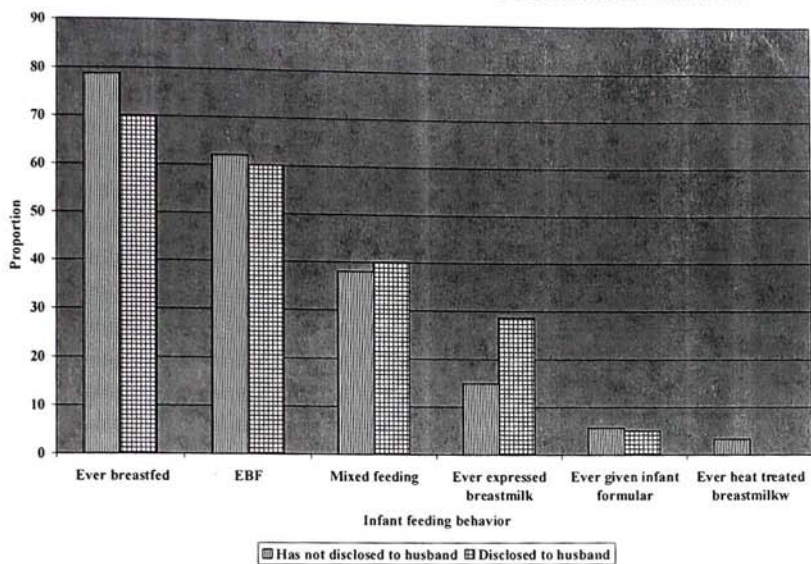
Appendix 11b Infant feeding behavior by place of residence .



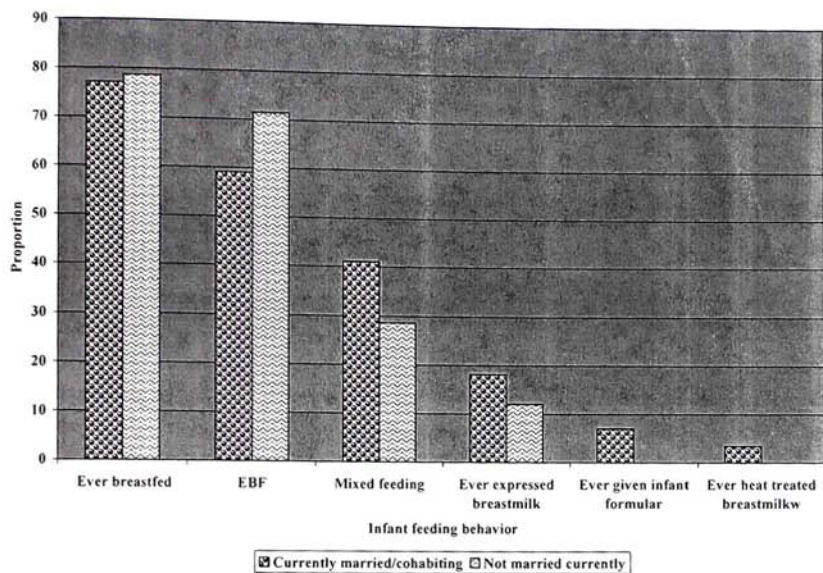
Appendix 11c Infant feeding behavior by marital status



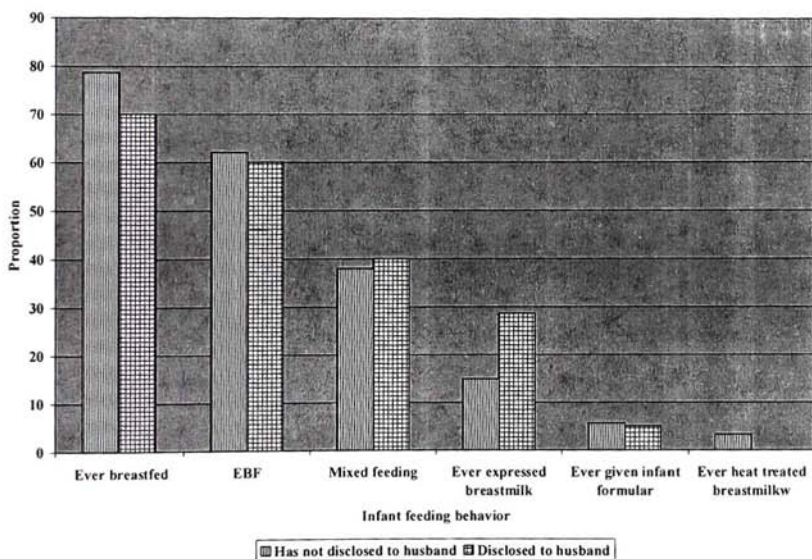
Appendix 11d Infant feeding behavior by disclosure of HIV-sero status to husband/cohabitant



Appendix 11e Infant feeding behavior by marital status



Appendix 11f Infant feeding behavior by disclosure of HIV-sero status to husband/cohabitant



INFANT FEEDING CHOICES AND EXPERIENCES OF HIV-POSITIVE MOTHERS FROM TWO GHANAIAN DISTRICTS

¹Laar AK., ²Ampofo W., ¹Tuakli JM., and ¹Quakyi IA.

¹School of Public Health, College of Health Sciences, University of Ghana, Legon

²Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon

RATIONALE & OBJECTIVES

Documentation of the feeding choices and experiences of HIV-positive mothers is needed to improve infant feeding counselling. The feeding behaviour and experiences of mothers receiving infant feeding counselling at two Ghanaian districts were explored.

MATERIALS & METHODS

A postpartum survey involving 128 HIV-positive mothers, and in-depth interviews involving a purposively selected sample of 10 HIV-positive mothers were conducted.

FINDINGS

Exclusive breastfeeding rate was 62%. About six percent of the infants were given breast milk and infant formula, while 33% received breast milk and other feeds. Perceived stigma of formula feeding (odds ratio [OR] 7.50; $p < 0.05$), and perceived cost of infant formula (OR 0.37; $p < 0.05$) were significantly associated with exclusive breastfeeding for three months. In our multiple regression analysis, perceived stigma of formula feeding (OR 15.62; $p < 0.05$), and perceived cost of infant formula (OR 4.60; $p < 0.05$) were significantly associated with exclusive breastfeeding. Social pressure to mix-feed, local norms and "*the baby friendly hospital initiative*" also influenced infant feeding implementation efforts of mothers.

CONCLUSION

Mothers face various barriers in implementing their feeding intentions. Policy makers and service providers in these districts need to address these issues in order to improve feeding practice.

Key words: Infant feed choices, infant feeding experiences, HIV-positive mothers, Ghana

*Address of Corresponding Author:

Amos Kankponang Laar, School of Public Health, College of Health Sciences, University of Ghana, Box LG 13, Legon, Accra. Tel: +233- 244- 982176 e-mail: aklaar@yahoo.com OR alaar@ug.edu.gh

Introduction

Infant feeding in settings where Human Immunodeficiency Virus (HIV) is a public health problem and especially where breastfeeding is routinely practised is a worrying issue. Not only are health workers expected to counsel HIV-positive mothers on safer infant feeding methods as per national and international guidelines, HIV-positive women are expected to understand complex information provided by health workers, and make informed and healthy choices for themselves and their infants.

In guiding health workers, a series of international guidelines have been developed over time depending on prevailing knowledge. The first generation guidelines informing infant feeding indicated that where it is acceptable, feasible, affordable, sustainable and safe (AFASS), replacement feeding should be adopted and breastfeeding avoided (WHO et al., 2003). However, upon reviewing accumulating evidence, a technical consultation convened by WHO on behalf of the Inter-Agency Task Team (IATT) in October 2006 updated these guidelines (WHO, 2006). The review of substantial body of new evidence and experience regarding HIV and infant feeding since the previous technical consultation in October 2003 (WHO et al., 2003), and since the Glion¹ and Abuja² calls to action on the prevention of mother-to-child transmission (PMTCT) of HIV gave birth to the 14-point second generation guidelines. This includes the following:

- 1. The most appropriate infant feeding option for an HIV-infected mother depends on her individual circumstances, including her health status and the local situation, but should take consideration of the health services available and the counselling and support she is likely to receive;*
- 2. Exclusive breastfeeding is recommended for HIV-infected mothers for the first six months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time;*
- 3. When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended;*
- 4. At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed. All breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided.*

The principal factor considered in the evolution of the guidelines was the risk of perinatal transmission of HIV. The general range of HIV transmission through breastfeeding of any kind without any interventions is 5-20% (WHO et al., 2004). The consultation was also aware of the possible benefits of exclusive breastfeeding in relation to HIV transmission suggested by the work of Coutsooudis and colleagues (Coutsooudis et al., 1999). Since then, other

¹ 4 UNFPA and WHO. The Glion Call to Action on Family Planning and HIV/AIDS in Women and Children, 3-5 May 2004.

² 5 Call to Action: Towards an HIV-free and AIDS-free Generation. Prevention of mother-to-child transmission. High-level global partners forum, Abuja, Nigeria, December 3, 2005.

studies have shown that exclusive breastfeeding carries a lower risk of HIV transmission than mixed breastfeeding. A risk of about 4% was reported in South Africa (Coovadia et al., 2007) and 1.3% (HIV transmission rate between six weeks and six months) in Zimbabwe (Iliff et al., 2005). Against this background and in the midst of the confusion regarding what HIV-positive mothers should feed their infants, health workers are reminded that exclusive breastfeeding for the first six months is preferred to mixed feeding. Mixed feeding carries a higher risk of HIV transmission than exclusive breastfeeding (Coovadia et al., 2007).

Before and after the evolution of the first generation recommendations, some authorities contend that no single guideline can be universally applicable, and that every guideline ought to be implemented taking into consideration individual circumstances (Bobat, 2000; Coutsooudis, 2005; Leshabari et al., 2006; Bland et al., 2007; Leshabari et al., 2007a; Leshabari et al., 2007b).

In 2005, Gara *et al.* reported that the level of education and employment status as well as the opinions of family members and health care personnel were the major factors that influenced the choice of method for infant feeding (Gara et al., 2005). Other studies on the choice of infant feeding method show that while HIV-positive women commonly make a distinct choice to exclusively breastfeed or exclusively replacement feed during pregnancy, they often end up practising mixed feeding early in the baby's life. The multiplicity of factors leading to this behavior have been documented in various studies from non-Ghanaian settings to include social stigma, scorn and suspicion, harsh economic circumstances, technological barriers (electricity and refrigeration requirements), and more importantly the cultural usages and nuances of any given community (Thairu et al., 2005; Abiona et al., 2006; Leshabari et al., 2007a; Leshabari et al., 2007b; Rollins, 2007; Sadoh et al., 2008).

To date virtually no studies have focused specifically on the choices, experiences and challenges HIV-positive mothers in Ghana face. Working on the assumption that the factors influencing particular feeding choices or the challenges mothers face may show setting specificity, with cultural usages and nuances playing significant roles, this study explored HIV+ women's choices, experiences and practices as it relates to infant feeding in the social and cultural context of the Manya Krobo and Tema areas. The study investigated the following research questions:

- i. What choices do HIV+ women in the Manya Krobo and Tema areas make regarding infant feeding?
- ii. What challenges do they face in implementing their feeding options?
- iii. What experiences can they share regarding HIV and infant feeding?

Methodology

The study sites

This study was conducted at three public hospitals in Ghana; the Tema General Hospital in the Tema Municipality, Greater Accra region, Atua Government Hospital and St Martins de Porres Hospital both in the Manya Krobo District, Eastern region. All the three study hospitals provide PMTCT services to both urban and rural populations; such as VCT, and infant feeding counselling. The two sites in the Manya Krobo district were the first national pilot PMTCT sites in Ghana.

Service data on the HIV prevalence rates among pregnant women in the Tema municipality show a range from 2.6% in 1999, 6.5% in 2002, 3.6% in 2006, to 2.2% in 2007 (NACP, 2008). Related service data indicate that the proportion of HIV-infected women accessing postnatal services at the Municipality is 3.6% (Tema-Municipal-Health-Administration, 2002-2006). In the Manya Krobo District HIV prevalence rates among pregnant women in the district over the years have consistently been above the national average ranging from 18% in 1992 to 8.9% in 2007 (NACP, 2008). The proportion of HIV-infected women accessing postnatal services at the district is 6.0% (District-Health-Directorate-Manya-Krobo, 2000 - 2006). Between June 2005 and March 2008, a total of 27,000 antenatal clients were registered at the three study hospitals. Of these, 14,367 Number tested for HIV, of which 994 were HIV-positive, giving a combined HIV prevalence of 6.9% (Laar, 2009).

Study design, population and summary of field procedures

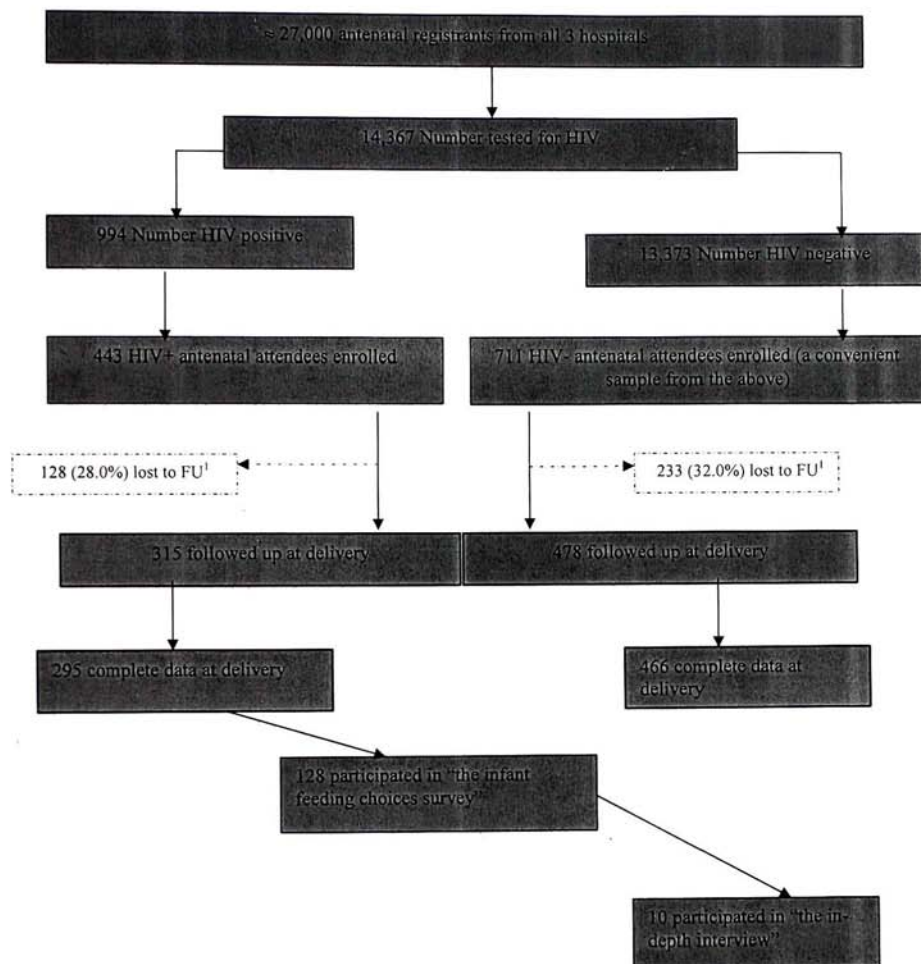
The documentation of infant feeding choices, experiences and challenges faced by HIV-positive mothers was part of a prospective study on the influence of HIV and malaria infections on maternal and perinatal health among 443 HIV-positive and 711 HIV-negative antenatal attendees, from three public hospitals in Ghana. At their first antenatal visit, the investigator with assistance from trained nurses and research assistants collected information on the background, socio-economic, socio-demographic characteristics, obstetric, and reproductive history of the study participants. Also assessed at this point were the infant feeding intentions of these expectant mothers. All the women were counselled by trained nurse counsellors, who were thoroughly informed about the purpose of the study. Seven hundred and sixty-one (295 HIV-positive and 466 HIV-negative) of the 1154 women who were enrolled had their follow up data at delivery taken. This paper concentrates on the infant feeding choices and experiences of 128 of the 295 HIV-positive mothers who were available for a postpartum interview.

Documentation of infant feeding choices, experiences/challenges

A postpartum survey involving 128 of the 295 HIV+ mothers at postnatal clinics was conducted to document the infant feeding practices of these mothers. This took place during their postpartum period (specifically after three months). This phase of the data collection had questions on infant feeding choices/behaviour, breastfeeding and breastfeeding initiation. An exploratory qualitative study was conducted through in-depth interviews on a sample of 10 HIV-positive mothers (Diagram 1). The in-depth interviews were aimed at eliciting individual experiences on infant feeding practice and experiences. These were conducted by the first author, with support from experienced nurse research assistants. The participants were purposively selected using the maximum variation technique, where person-related homogeneity was maintained but variation in the phenomenon (infant feeding behaviour – exclusive breastfeeding, exclusive formula feeding, and mixed feeding) considered.

In all ten in-depth interviews were held using semi-structured interview guides that covered the following: infant's breastfeeding status, infant's mixed feeding status, and reasons for giving other feeds, issues on wet nursing, expressing breast milk for feeding, and influence of social pressure on feeding behaviour. Also explored were the purchasing power of participants, perception of the cost of infant formula, and disclosure of HIV sero-status to partner or close relative. Five of the ten interviews were conducted in English and the other half in Akan (through competent translators – nurse research assistants). All interviews were recorded in writing.

Diagram¹. The study profile: June 2005 to August 2008



¹ FU = Follow-Up

Ethical issues

The research protocol met the guidelines for research involving human subjects of the Noguchi Memorial Institute for Medical Research (NMIMR). The study protocol was first reviewed and vetted by the Proposal Review Board of the School of Public Health for appropriateness and scientific content. An ethical clearance was afterwards sought from the Institutional Review Board (IRB) of the Noguchi Memorial Institute for Medical Research (*FWA 00001824, NMIMR-IRB CPN 044/04-05, IRB 0001276*).

Written informed consent, for those who were literate and witnessed verbal informed consent, for the illiterate was obtained from each study participant. Subjects were informed about the objectives and methods of the study. They were also assured of strict confidentiality with regards to any information obtained from them.

Data analysis

Statistical analysis was carried out using SPSS Version 15.0 (SPSS, 2007). Associations between maternal characteristics and infant feeding choice were assessed using Chi Square test (χ^2) and the Fishers exact tests as appropriate. Further evaluations of these associations were done using logistic regression technique, where odds ratios (ORs) and their 95% confidence intervals (CI) were computed to measure the strength of the associations.

The data from the in-depth interviews were analyzed manually. This consisted of appraising the jotted notes, and synthesizing them into meaningful themes by the first author. Certain portions of the participants' responses were also reported verbatim where it was deemed necessary. This exercise was edited by the rest of the co-authors with a few modifications to enhance readability.

Results

The background, socio-demographic characteristics, and reproductive history of the 128 mothers are presented in Table 1. The mean age of the participants was 31 years (range 19-43 years). All but one of the women had vaginal deliveries. A little over a quarter (28.9%) was primiparous and 46% multiparous, and attended the first antenatal care at 25 weeks gestation (range 4-36 weeks). About a quarter did not have formal education. The majority were either married or cohabited with a partner (Table 1).

The ten mothers who constituted the sample for the qualitative investigation were aged between 25 and 43 years. Seven of them were from rural areas in the Manya Krobo District, while three (3) were from Tema Municipal area. Eight (8) of them had no formal education; one had completed Junior High School, and the other a vocational school. One of the 10 was widowed; two were single mothers, and the rest married/cohabiting. Seven of the women were living with extended family members; two were living in a nuclear family, and one living alone. One had a permanent income from self-employment (boutique/hairdressing), another from petty trading. The other eight (8) were not employed. All but two had disclosed their HIV-positive status to either a partner or close relative.

Table. 1 Background, socio-demographic characteristic and reproductive history of mothers who participated in the infant feeding choices survey (N = 128)

Characteristic	Frequency	Percent
Study hospitals		
Atua Government hospital	65	50.8
St Martins de Porres Hospital	17	13.3
Tema General Hospital	46	35.9
Marital status		
Single	23	18.0
Married	56	43.8
Divorced/Separated	3	2.3
Widowed	2	1.6
Cohabiting	44	34.4
Residence		
Rural	79	61.7
Urban	49	38.3
Level of education		
No formal education	33	25.8
Primary	31	24.2
Junior High School	54	42.2
Seniour High school, Vocational Training, Post-Sec	9	7.0
Tertiary	1	0.8
Age bracket		
24 years or younger	17	13.3
25-35 years	82	64.1
36 years or older	29	22.7
Parity		
Primiparous	37	28.9
Secundiparous	32	25.0
Multiparous	59	46.1
Grauidity		
Primigravid	20	15.6
Secundigravid	24	18.8
Multigravid	84	65.6
Type of delivery		
Spontaneous Vaginal delivery	127	99.3
Caesarean Section	1	0.77

Breastfeeding, breastfeeding initiation and infant feeding behaviour of mothers

Ninety six (96) of the 128 mothers who participated in the postpartum survey had declared their intentions antepartum to breastfeed. The distribution of these participants by time breastfeeding was initiated is presented in Fig 1. About one-third (33.6%) initiated breastfeeding within an hour of delivery.

Among the 128 mothers, a questionnaire item explored the practices of seven different kinds of infant feeding behaviours over a three month recall period (Fig 2). These were "ever breastfed" (99.9%), "exclusively breastfed for up to three months" (61.7%), "mixed-fed or infant ever given other foods in addition to breast milk" (38.3%), "ever expressed breast milk with the intention to feed the infant" (14.4%), "ever given formula to infant" (5.5%), "ever heat-treated expressed breast milk" (1.6%), and infant "ever been wet-nursed" (0%).

Fig 1. Breastfeeding initiation among mothers

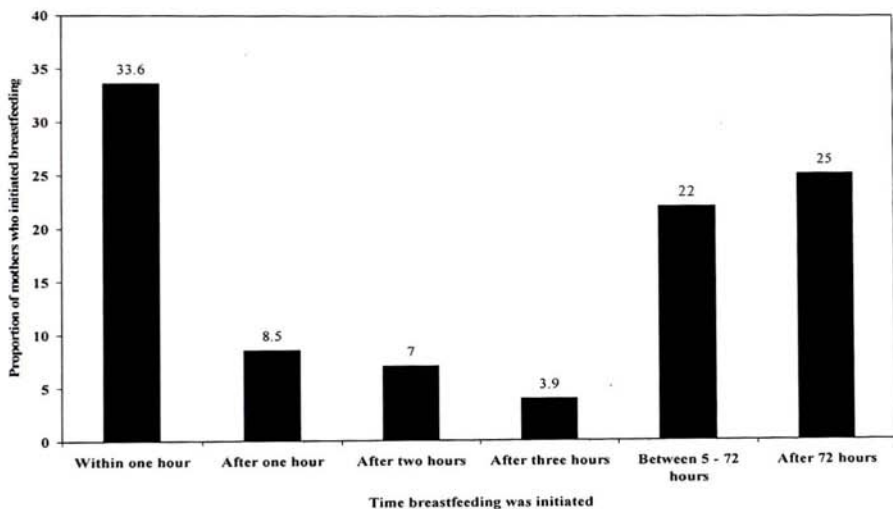
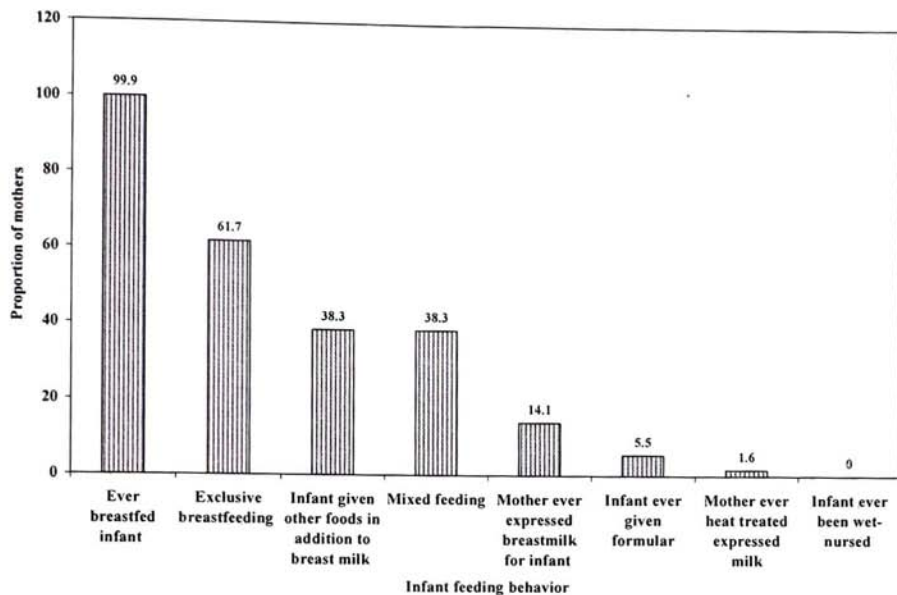


Fig 2. Infant feeding choices of HIV+ mothers (all 128 mothers)



Perception on cost of replacement feeding was associated with EBF behavior. At a bivariate level analysis, mothers who perceived the cost of replacement feeding to be expensive were almost three-times as likely as those who felt it was affordable to exclusively breastfeed, OR = 2.7; 95% CI (1.15 – 6.25). There was even a higher propensity to exclusively breastfeed if mothers felt that choosing only formula feeding could lead to stigmatization OR = 7.50; 95% (CI 2.30 – 24.44). In multiple logistic regression model, mothers with nine or more years of formal education were on average 80% less likely to exclusively breastfeed OR = 0.21; 95% CI (0.05 – 0.88). On the contrary, perception on stigma related to formula feeding OR = 15.62; 95% CI 3.94 – 61.98), and cost of infant formula (OR = 4.60; 95% CI 1.40 – 15.14) were the significant predictors of exclusive breastfeeding of infants. This model included Cost of replacement feeding; Fear that replacement feeding may lead to stigmatization; HIV-sero status disclosure to partner; Residency; Education; and Belief in the benefits of breastfeeding.

Table 2. Some potential predictors of infant feeding choice

Infant feeding type	EBF n	Other n	Total N	p-value	OR ²	95% CI ²
Factors						
Cost of replacement feeding						
Not affordable	67	33	100	0.020 (†)	4.60	1.40 - 15.14

Affordable	12	16	28			
Afraid that replacement feeding may lead to stigmatization						
Yes	75	35	110	<0.001 (τ)	15.6	3.94 - 61.98
No	4	14	18		2	
HIV-sero status disclosed to husband						
No	67	41	108	0.863 (τ)	1.42	0.32 - 6.325
Yes	12	8	20			
Rural residency						
Yes	52	27	79	0.225 (τ)	0.65	0.188 - 2.22
No	27	22	49			
Nine or more years of formal education						
Yes	35	29	64	0.102 (τ)	0.21	0.05 - 0.88
No	44	20	64			
Believes in the benefits of breastfeeding						
No	4	4	8	0.07 (F)	0.33	0.05 - 1.96
Yes	73	18	91			
Regular maternal income						
No	63	37	100	0.573 (τ)		Not included in model
Yes	16	12	28			
Afraid of HIV disclosure repercussions						
No	10	4	14	0.428 (τ)		Not included in model
Yes	69	45	114			

p (τ) = p value for Chi Square test; p (F) = p -value for Fisher's exact test; EBF = Exclusive breastfeeding; Other! = Any other mode of infant feeding (mixed or formula). OR^1 = Odds Ratio Estimate from bivariate cross-tabulation/simple logistic regression analysis; CI^1 = 95% Confidence Interval for OR^1 ; OR^2 = Odds Ratio Estimate from multiple logistic regression model containing (Cost of replacement feeding, Afraid that replacement feeding may lead to stigmatization, HIV-sero status disclosed to husband, Residency, Education, Believes in the benefits of breastfeeding); CI^2 = 95% Confidence Interval for OR^2 .

Infant feeding experiences and challenges faced by mothers

We present below the condensed narratives on three of the 10 women whose experiences and challenges were recorded during the in-depth interviews. Those presented here bring up the recurring experiences and challenges that were revealed from the interviews. Social pressure to mix-feed, local norms such as water supplementation, negative repercussions of disclosure of HIV status or partner notification, and *"the baby friendly hospital initiative"* were the issues that influenced infant feeding choices and implementation efforts.

One theme that came up was the notion that, mothers who disclose their HIV status suffer negatively from this commendable behaviour. This is evidenced by the only mother in this study who opted to do exclusive formula feeding for six months. She ended up doing so for three months. According to her, her choice was successfully implemented for the first three months with fiscal support from her in-laws (her husband had died of an unidentified cause a couple of months before she delivered). This mother after months of debating on whether or not to disclose her status to her benefactors, finally mastered courage and did. This (disclosure) in her own words marked the beginning of her misery. *"When I told them this, they ceased all communications with me, no more financial remittances; they literally cut off links with me. I regret disclosing my status to my in-laws". Is it a crime to disclose your status?* She asked.

In a related case, a mother who opted to exclusively breastfeed for six months could not implement this because of both partner and community members' stigmatizing behaviour towards her. This mother morosely narrated that she was highly stigmatized at home and in my area after disclosing her HIV status to her husband, a man she claimed is an alcohol addict. *"He comes to the house most of the time after his daily bout of drinking to verbally abuse here. He literally broadcasts my status to the people in the area. This is a serious problem to me. These days, people around my area call me all kinds of names behind my back. Some even confront me that I should stop breastfeeding for I will give the sickness to my baby. If I knew that disclosure of my status to him was going to lead to this disgrace, I would not have..."*. When asked about the reason why she chose to breastfeed given that she was aware that she was HIV-positive, this is what she said, *"Breastfeeding was the best choice for me. No one does wet nursing or expresses breast milk in this community. I couldn't have chosen formula*

feeding. I also didn't want to be asked by people around me for reasons for my not breastfeeding the baby. Everyone in this community does breastfeeding. More so my nurse counsellor tells me infant formula is very, very expensive". I didn't know my partner would broadcast my HIV status to the community. I wouldn't have, if I knew he was going to do that...." It is also noteworthy that, there have been conscious efforts by nurse counsellors in all the three hospitals to frown on the AFASS of infant formula. The Prevention of Mother-To-Child Transmission of HIV (PMTCT) "In-charges" assert that, being signatories to the *Baby-friendly Hospital Initiative*, it is binding on them to not display infant formula at their facilities.

The issues of water supplementation, peer pressure to mix-feed, and naiveté of some mothers regarding the appropriateness of feeding choices are illustrated in the experience of a mother who antenatally opted to do exclusive breastfeeding but ended up doing mixed feeding after delivery. To some extent, her failure to appreciate the intricacies of infant feeding practices played a role. She indicated she singlehandedly adopted the practice of formula feeding and water supplementation when she had problems of "milk flow", a condition her sister had previously experienced. Her sister who was incapable of lactating after undergoing a Caesarean section was advised to formula-feed. She saw this as a successful practice and hence adopted it for her infant for she felt she was not producing enough milk for her infant. Another challenge this mother faced was her refusal to disclose her status to anyone. This she indicates troubles her mentally and makes her not enjoy the act of nourishing her son with breast milk. She believes there is a possibility that that feeding option could transmit the virus to him, justifying the intermittent introduction of infant formula. When asked why she was not sticking to formula alone, she replied that she did not have the means. Having lost both parents in her childhood, she indicated she was very afraid that disclosure to her partner for financial support could lead to untold consequences. *"I might be sacked from the house, I have no where to go to."*

Discussion

Breastfeeding intentions, breastfeeding initiation and infant feeding choices of mothers

It was refreshing to note that three out of four of the mothers who participated in the postpartum survey had declared their intentions to exclusively breastfeed for six months during the antepartum survey. The benefit of breastfeeding is very well publicized in medical literature. Interactions both with the PMTCT nurse counselors and the HIV-positive mothers revealed that the socio-cultural context in

which these women make their infant feeding decisions is one in which breastfeeding is highly valued. As in most parts of Ghana, breastfeeding in the Manya Krobo and Tema is culturally normative, and there is no evidence in this study to suggest that this fundamental cultural practice is being eroded, even in this era of HIV. Leshabari et al. in a study that explored infant feeding decision making among HIV-positive Tanzanian women describe the failure of a mother to breastfeed as 'a significant failure', pointing to the substantial failure to live up to practices deeply embedded in a culturally constituted moral universe (Leshabari et al., 2007b). These authors further noted that, in addition to putting the life of the child at risk and violating the rules of good motherhood, not breastfeeding an infant is interpreted as an act of disrespect to the lineage. These interpretations of the value attached to breastfeeding with certainty can be extrapolated to the communities in which this current study was conducted. This fundamental cultural practice of attaching particular importance to breastfeeding in the Manya Krobo and Tema, if well harnessed could positively affect infant feeding practice.

About one-third (33.6%) initiated breastfeeding within an hour of delivery. Given the national norm, and the fact that the three hospitals where the study was conducted are signatories to "The Baby Friendly Hospital Initiative", this particular observation is rather below expectation. The initiative enjoins signatory institutions to support mothers to initiate breastfeeding within an hour after birth. Further interactions with both the PMTCT nurse counselors and the HIV+ mothers revealed that nurse counselors in these settings do not feel comfortable providing helpful instructions about formula feeding in the name of this initiative. The importance of hospital breastfeeding policy and attitudes of health personnel in affecting breastfeeding practices has been repeatedly documented (Knodel et al., 1990; Williamson, 1990; Weng et al., 2003). In reality, however, the Baby Friendly Hospital Initiative does not preclude the use of replacement feeding in situations that are medically indicated (WHO/UNICEF, 1989). In addressing this problem, we suggest that supportive supervisions and refresher training be given to this group of health workers. In their bid to significantly increase the rates of exclusive breastfeeding, health workers need to be reminded of the other options available to nursing mothers as enshrined in the guidelines for infant feeding for HIV-positive mothers (WHO, 2006).

A questionnaire item explored the practices of seven different kinds of infant feeding behaviors. These were "ever breastfed", "exclusive breastfeeding for up to three months", "mixed-feeding", "ever expressed breast milk with the intention to feed the infant", "ever given formula to infant", "ever heat-treated expressed breast milk" and "wet-nursing". As indicated earlier, in Many Krobo and in the Tema, breastfeeding is normal practice. Not surprisingly, close a 100% of the participants had ever breastfed but not exclusively with breast milk. In keeping with the result of a previous study from Nigeria (Sadoh et al., 2008), a sizeable proportion (38.3%) of the mothers in this study who opted to breastfeed had introduced to their infants water and other kinds of foods. Similar findings have been reported by Abiona et al. where participants of a focus group discussion argued that breast milk is 'food' and that, just as an adult drinks water after eating, a baby should be given water after being breastfed (Abiona et al., 2006). In fact, most infants are given water from birth, in part due to cultural perceptions that infants need water to survive. To ensure that HIV-positive mothers who choose to breastfeed do so exclusively, these beliefs and attitudes in relation to giving infants water, and other foods, without a doubt need to be addressed. Both formal and informal interactions between researchers, health workers and community members through durbars could help in reshaping some of these long held attitudes.

In this present study, none of the infants was wet-nursed. As indicated by one of the mothers *"Breastfeeding was the best choice for me. No one does wet nursing or express breast milk here. I couldn't have chosen formula feeding. What reasons will I give to the people around me for not breastfeeding the baby? Everyone in this community does breastfeeding.* This is also in line with findings of a Nigerian study where participants in a focus group discussion noted that wet-nursing is very rare (Sadoh et al., 2008).

The financial cost of feeding with infant formula is estimated to be about GH¢20.00 per month. The costs of fuel, safe water, and utensils are not considered in the derivation of this cost. In low-income families these (costs of fuel, safe water, and utensils) have been noted to be important (Rea et al., 2007). Given that a significant proportion of the women in this present study were from underprivileged settings, infant formula was not thought of as a feasible feeding option for most of the mothers. About 6% indicated having ever given formula to their infants; only one doing so exclusively

in this study. It is only in rare cases – when mothers have the economic means to purchase it, that infant formula is used. Other reasons for opting for infant formula noted in this current study stems from the notion that, only mothers who are well to do, opt for formula feeding. This behaviour has the potential of spilling over to affect HIV-negative nursing mothers. Efforts at addressing this through the various health communication channels discussed above should be vigorously pursued.

Education, perception on stigma that may stem from failure to breastfeed, and also perceptions on cost of infant formula were revealed in this study to have significant influences on exclusive breastfeeding behaviour. Mothers with nine or more years of formal education were on average 80% less likely to exclusively breastfeed. On the contrary, perception on stigma related to formula feeding and cost of infant formula were the significant predictors of exclusive breastfeeding of infants. This information will be useful to HIV counselling service providers in these districts. If efforts are made to address these issues in these areas, infant feeding practices may be positively enhanced

Experiences/challenges faced by mothers in implementing infant feeding intentions.

The in-depth interview component of this investigation has given a snapshot of the experiences and challenges that HIV-positive mothers in the Manya Krobo and Tema Municipality face as they make attempts at implementing their infant feeding intentions. These experiences manifest a variety of hardships regarding the choosing, implementing, and sustaining the feeding intentions. The few, who managed to implement their feeding options religiously, did not do so without challenges.

For instance, the only mother who had delivered by caesarean section opted to do exclusive formula feeding for six months, managed to do so for only three months because of the following reasons. Her challenges included stigmatization, discrimination, cessation of *communications and financial remittances by her in-laws*. Disclosure of HIV status to the partner is usually a major condition for successful replacement feeding. However, in this study, disclosure resulted in problems. For instance a study in Uganda found that women who succeeded in adhering to replacement feeding had family support (Matovu et al., 2002). In this study, however, as illustrated by the experiences of one of the mothers, *“I am highly stigmatized at home and in my community after disclosing my status to my husband...”*

All the women interviewed in the present study had been informed by their PMTCT nurse counsellors that the HIV can be transmitted to their infants through breastfeeding. They were also counselled on the other options available to them. The majority opted to breastfeed their infants for various socio-cultural and economic reasons outlined earlier. As Senah rightly remarked in his paper titled "*Maternal Mortality in Ghana: the other side*", the factors which promote good health and those that precipitate ill health are not purely biological, but can be social, economic, and cultural (Senah, 2003). This dynamics can be likened to the decision making processes of these women with regard to what to feed their infants. A decision to breastfeed or not to do so is not merely linked to knowledge of medical risks of mother-to-child transmission of HIV through breastfeeding as Leshaberi et al. (2007) put it, but can be occasioned by social and cultural nuances of the community. In contributing to making the current global infant feeding guidelines useful in this locale, we call that such guidelines modified taking cognizance of all these issues.

Conclusions

This investigation on infant feeding choices by HIV-positive mothers has revealed that breastfeeding as a fundamental cultural practice is highly valued in the Manya Krobo District and Tema Municipality..

The study also shows that mothers in the study areas face various individual-level, community-level, and service-related barriers in choosing and implementing their feeding intentions. Such barriers include social pressure to mix-feed, local norms such as water supplementation, and "*the baby friendly hospital initiative*". These challenges presented here may not be unique to only the mothers of the Manya Krobo District and Tema Municipality, but may be experienced by other mothers in various parts of Ghana. HIV counselling service providers in these districts need to address these issues in order to improve infant feeding practice.

Recommendations

At present, the WHO advises that unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for infant and mother, exclusive breastfeeding should be practiced. These findings are suggestive that the ideal circumstances for replacement feeding are unlikely for a lot of the women

in the Manya Krobo District, and Tema Municipality. We therefore recommend that these guidelines be modified to address the issues discussed. The issues also need to be brought to the knowledge of PMTCT service providers in these areas.

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Infant feeding behavior and challenges faced by HIV-positive mothers from two Ghanaian districts

Laar A. K.

RATIONALE & OBJECTIVES

Documentation of the feeding behavior and challenges faced by HIV-positive mothers may improve infant feeding counseling. The feeding behavior and experiences of mothers receiving infant feeding counseling at two Ghanaian districts were explored.

MATERIALS & METHODS

A survey involving 128 HIV-positive mothers with infants aged three to twelve months was conducted. Additionally, in-depth interviews involving 10 of these mothers were done.

RESULTS & FINDINGS

Seventy-five percent of the mothers who participated in the survey had declared their intentions to exclusively breastfeed before delivery. However, by the third month, about one-third of the mothers had introduced other supplementary feeds to their infants. About 62% of the infants were exclusively breastfed for three months. Formula feeding rate was 5.5%, but only one of these mothers exclusively formula-fed for three months. Social pressure to mix-feed, local norms such as water supplementation, belief about the quality of breast-milk, fear of transmitting the virus to baby, and "*the baby friendly hospital initiative*" were some of the impediments to mothers implementing their feeding intentions.

CONCLUSION

Breastfeeding is still highly valued in these districts. Mothers, however, face various impediments implementing their feeding intentions.

Mr. Amos Kankponang Laar, PhD Student, School of Public Health, College of Health Sciences, University of Ghana, Box LG 13, Legon, Accra. Tel: +233- 244- 982176 e-mail: aklaar@yahoo.com OR alaar@ug.edu.gh; Fax #: None.

¹Laar AK, ²Ampofo WK, ¹Tuakli JM, ⁴Owusu WB, ⁶Amenyah RN, ¹Soyiri IN, ¹Kuranchie P, ³Senah K, ⁵Valerie PM, ¹Amuah P, and ¹Quakyi IA. **Prevalence of poor perinatal outcomes among HIV+ women in the Manya Krobo District & Tema Municipality**

¹School of Public Health, College of Health Science, University of Ghana, Legon, ²Noguchi Memorial Institute for Medical Research, College of Health Science, University of Ghana, Legon, Legon, ³Department of Sociology, University of Ghana, Legon, ⁴Department of Nutrition and Food Science, University of Ghana, Legon, ⁵Africa AIDS Watch, Inc. Washington D.C., ⁶Family Health International, Ghana.

Background: HIV and malaria infections are associated with poor perinatal outcomes. Identification of setting-specific factors related to poor perinatal outcomes among HIV+ women could inform policies to improve perinatal outcomes.

Objectives: To determine the prevalence and correlates of preterm delivery (PTD), low birth weight (LBW) and stillbirth (SB) among HIV+ women delivering at three public hospitals in Ghana.

Methods: Data on socio-demographics, perinatal outcomes, malaria parasitemia, hemoglobin, and CD4+ count were collected from women enrolled in a prospective study in three public hospitals in Ghana on the interaction between HIV and malaria infections during pregnancy.

Results: HIV+ (346) antenatal clients were enrolled. For 162 (46.8%) clients, data at delivery were taken. Prevalence of maternal malaria parasitemia was 47/346 (13.6%) at recruitment and 18/162 (11.1%) at delivery. Overall, 38 (23.5%) of the infants presented with at least one perinatal outcome. PTD and SB occurred in 22 (13.6%), and 8 (4.9%) deliveries respectively. Of the 154 live birth 26 (16%) weighed < 2500g. Seventy infants (43.2%) were anemic (Hb < 11.0g/dl), and 8% of them severely anemic (Hb < 8.0g/dl). Statistically significant correlates included maternal presentation with four or more morbid conditions, OR (95% CI), 1.68 (1.04-2.73); cord blood parasitemia, 3.26 (1.22-8.72); maternal malaria at recruitment, 3.26 (1.40-7.63); pregnancy in the teenage age, 4.1 (1.15-14.43); and symptomatic AIDS, 5.71 (1.77-18.46).

Conclusions/recommendations: Pregnant women with malaria and AIDS are at elevated risk of adverse perinatal outcomes. Routine screening of both HIV and malaria and anticipatory care of pregnant women at risk of adverse pregnancy outcomes may reduce the incidence of some of these adverse outcomes.

*Amos Kankponang Laar, PhD student, Department of Population, Family and Reproductive Health, School of Public Health, College of Health Sciences, University of Ghana, Box LG 23, Legon. E-mail: alaar@ug.edu.gh

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Appendix 112d: A paper presented at the 1st Annual College of Health Sciences Scientific Conference, Accra International Conference Center, September 26-28, 2007

¹Laar AK, ²Ampofo WK, ¹Tuakli JM, ⁴Owusu WB, ⁶Amenyah RN, ¹Soyiri IN, ¹Kuranchie P, ³Senah K, ⁵Valerie PM, ¹Amuah P, and ¹Quakyi IA. **Are poor maternal anthropometrics at first prenatal visit associated with adverse perinatal outcomes?**

¹School of Public Health, Legon, ²NMIMR, Legon, ³Department of Sociology, Legon, ⁴Department of Nutrition and Food Science, Legon, ⁵Africa AIDS Watch, Inc. Washington, D.C., ⁶Family Health International, Ghana.

ABSTRACT

Background: Among HIV-uninfected populations, maternal anthropometry is one of the strongest predictors of pregnancy outcomes. Short maternal stature and low pre-pregnancy weight are known determinants of adverse pregnancy outcomes.

Objectives: In a prospective study of 346 pregnant HIV-infected Ghanaian women, we examined the incidence of preterm delivery (PTD), low birth weight (LBW) and stillbirth in relation to maternal anthropometry at first prenatal visit.

Subjects and methods: Anthropometric measurements taken at recruitment included height, weight, and mid upper arm circumference (MUAC).

Results: At baseline, close to a third (29%) were primigravids, 26.3% nulliparous, and 165 (48%) had CD4 cell counts < 350/mm³. Symptomatic HIV was present in 23 (7%) of them. There were 22 (13.6%) PTD and 8 (4.9%) stillbirths among the 162 newborns. Of the 154 live births, 16% were LBW. Maternal weight, body mass index (BMI) and MUAC at the first visit were not associated with fetal death or preterm delivery. However, compared with their taller counterparts, women with short stature < 150 cm had a higher incidence of stillbirth RR (95% CI), 3.26, (1.77-14.78); LBW, 1.78 (0.78-4.49) and preterm delivery, 1.54 (0.52-4.63). Our findings show no evidence of a linear association between maternal anthropometrics and that of the newborn. After stratification by HIV disease state, and CD4 status, however, statistically significant associations were found between maternal weight, BMI, and MUAC and adverse perinatal outcomes among women with HIV and AIDS.

Conclusion: We conclude that, except women with HIV/AIDS, and compromised immune status, maternal anthropometric status at the first prenatal visit are poor predictors of adverse pregnancy outcomes among HIV+ women.

*Amos Kankponang Laar, PhD student, Department of Population, Family and Reproductive Health, School of Public Health, College of Health Sciences, University of Ghana, Box LG 23, Legon. E-mail: alaar@ug.edu.gh

Abstract # 056 pp 77

^aLaar AK, ^bAmpofo WK, ^cTuakli JM, ^cAmenyah RN ^dQuakyi IA. Fetal anemia and umbilical cord parasitemia in newborns of HIV+ women.

^aDepartment of Population, Family and Reproductive Health, School of Public Health, College of Health Sciences, University of Ghana, Legon.

^bNoguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon

^cGhana AIDS Commission, Accra Ghana

^dDepartment of Biological Environmental and Occupational Health Sciences, School of Public Health, College of Health Sciences, University of Ghana, Legon.

ABSTRACT

Objective: To determine clinical factors associated with fetal anemia and cord parasitemia in newborns of HIV+ women from two Ghanaian districts.

Methods: We enrolled HIV+ antenatal attendees at their first antenatal visit, documented their background and socio-demographic characteristics and prospectively collected information on birth outcomes, parasitological, hematological and immunological indices.

Results: Subjects with complete data at recruitment and delivery formed the basis for this analysis. Prevalence of fetal anemia (cord hemoglobin level <11.0g/dL) and cord parasitemia (presence of *P. falciparum* in cord blood at delivery) were respectively 43.2% and 8.6%. Maternal malaria parasite rates were 10.5% at recruitment and 11.1% at delivery. Clinical factors found to be associated with fetal anemia were maternal malaria at delivery OR (95% CI) 3.0 (1.05-8.35); CD4+ T cell counts > 350 cells/mm³ 0.56 (0.30-1.00); maternal anemia at recruitment 1.70 (0.99-3.76); malaria infection at two time points 4.22 (1.01-21.56); symptomatic AIDS 3.83 (1.77-15.00). Umbilical cord parasitemia was associated with malaria parasitemia at recruitment 6.30 (1.12-21.81); maternal malaria parasitemia at delivery 43.75 (11.22-70.62); malaria infection at two time points 54.75 (9.50-315.51); and malaria infection at one time point 8.50 (2.53-28.56). Other factors such as primigravidity, teenage pregnancy, use of nutrient supplements, and herbal drugs were not associated with either fetal anemia or cord parasitemia.

Conclusions: Malaria infection in women with HIV may lead to fetal anemia and also transplacental transfer of the malaria parasites. Prevention of malaria infection during pregnancy may reduce the incidence of these adverse perinatal outcomes among HIV+ women.

*Amos Kankponang Laar, PhD student, Department of Population, Family and Reproductive Health, School of Public Health, College of Health Sciences, University of Ghana, Box LG 23, Legon. E-mail: alaar@ug.edu.gh

