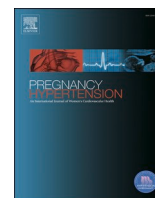




Contents lists available at ScienceDirect

# Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: [www.elsevier.com/locate/preghy](http://www.elsevier.com/locate/preghy)

## Impact of antenatal care on severe maternal and neonatal outcomes in pregnancies complicated by preeclampsia and eclampsia in Ghana

Titus K. Beyuo<sup>a</sup>, Emma R. Lawrence<sup>b</sup>, Samuel A. Oppong<sup>a,\*</sup>, Emily K. Kobernik<sup>c</sup>, Mary Amoakoh-Coleman<sup>d</sup>, Diederick E. Grobbee<sup>e</sup>, Joyce L. Browne<sup>e,1</sup>, K.W.M. Bloemenkamp<sup>f,1</sup>

<sup>a</sup> Department of Obstetrics and Gynaecology, University of Ghana Medical School, P.O. Box 4236, Accra, Ghana

<sup>b</sup> Department of Obstetrics and Gynecology, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor, MI 48109 USA

<sup>c</sup> Department of Learning Health Sciences, University of Michigan, 1111 East Catherine Street, Ann Arbor, MI 48109 USA

<sup>d</sup> Department of Epidemiology, Noguchi Memorial Institute for Medical Research, University of Ghana, Ghana

<sup>e</sup> Julius Global Health, Julius Center for Health Science and Primary Care, University Medical Center Utrecht, Utrecht University, the Netherlands

<sup>f</sup> Wilhelmina's Children Hospital, UMC Utrecht, Department of Obstetrics, Division Woman and Baby, Utrecht, the Netherlands

### ARTICLE INFO

#### Keywords:

Antenatal care  
Prenatal care  
Hypertensive disorders of pregnancy  
Preeclampsia  
Eclampsia  
LMIC

### ABSTRACT

**Objectives:** To explore how specific measures of antenatal care utilization are associated with outcomes in pregnancies complicated by preeclampsia and eclampsia in Ghana.

**Study Design:** Participants were adult pregnant women with preeclampsia or eclampsia at a tertiary hospital in Ghana. Antenatal care utilization measures included timing of first visit, total visits, facility and provider type, and referral status. Antenatal visits were characterized by former and current World Health Organization recommendations, and by gestational age-based adequacy.

**Main Outcome Measures:** Composites of maternal complications and poor neonatal outcomes. Multivariate logistic regressions identified associations with antenatal care factors.

**Results:** Among 1176 participants, median number of antenatal visits was 5.0 (IQR 3.0–7.0), with 72.9% attending  $\geq 4$  visits, 19.4% attending  $\geq 8$  visits, and 54.9% attending adequate visits adjusted for gestational age. Care was most frequently provided in a government polyclinic ( $n = 522$ , 47.2%) and by a midwife ( $n = 704$ , 65.1%). Odds of the composite maternal complications were lower in women receiving antenatal care at a tertiary hospital (aOR 0.47,  $p = 0.01$ ). Odds of poor neonatal outcomes were lower in women receiving antenatal care at a tertiary hospital (aOR 0.56,  $p < 0.001$ ), by a specialist Obstetrician/Gynecologist (aOR 0.58,  $p < 0.001$ ), and who attended  $\geq 8$  visits (aOR 0.67,  $p = 0.04$ ). Referred women had twice the odds of a maternal complication (aOR 2.12,  $p = 0.007$ ) and poor neonatal outcome (aOR 1.68,  $p = 0.002$ ).

**Conclusions:** Fewer complications are seen after receiving antenatal care at tertiary facilities. Attending  $\geq 8$  visits reduced poor neonatal outcomes, but didn't impact maternal complications. Quality, not just quantity, of antenatal care is essential.

### 1. Introduction

Hypertensive disorders of pregnancy (HDP), which include gestational hypertension, preeclampsia, and eclampsia, complicate 10% of pregnancies worldwide [1–3]. Failure to timely identify and manage HDP can lead to significant maternal morbidity, including seizure,

stroke, acute kidney injury, and death [4]. In low- and middle-income countries (LMIC), HDP account for 10–15% of maternal deaths [1,2]. Due to an increasing burden of comorbid medical conditions in reproductive-aged women and the greater complexity of managing HDP, hypertensive disorders have overtaken postpartum hemorrhage as the leading cause of maternal mortality in many LMICs [3].

**Abbreviations:** HDP, hypertensive disorders of pregnancy (HDP); LMIC, low- and middle-income countries; WHO, World Health Organization; RCT, randomized control trial; KBTH, Korle Bu Teaching Hospital; HELLP, Hemolysis Elevated Liver enzymes and Low Platelets; ICU, intensive care unit.

\* Corresponding author.

**E-mail addresses:** [emmarl@med.umich.edu](mailto:emmarl@med.umich.edu) (E.R. Lawrence), [saoppong@ug.edu.gh](mailto:saoppong@ug.edu.gh) (S.A. Oppong), [d.e.grobbee@umcutrecht.nl](mailto:d.e.grobbee@umcutrecht.nl) (D.E. Grobbee), [jbrowne@umcutrecht.nl](mailto:jbrowne@umcutrecht.nl) (J.L. Browne), [stafverloskunde@umcutrecht.nl](mailto:stafverloskunde@umcutrecht.nl) (K.W.M. Bloemenkamp).

<sup>1</sup> Shared senior authorship.

<https://doi.org/10.1016/j.preghy.2023.07.177>

Received 2 November 2022; Received in revised form 26 July 2023; Accepted 27 July 2023

Available online 14 August 2023

2210-7789/© 2023 International Society for the Study of Hypertension in Pregnancy. Published by Elsevier B.V. All rights reserved.

While HDP may not be entirely preventable, associated morbidity and progression to severe preeclampsia and eclampsia may be reduced with quality and timely antenatal care and obstetric management [5]. Early initiation of antenatal care is important to establish accurate dating and identify risk factors for HDP, including chronic hypertension, history of HDP in a prior pregnancy, and obesity [6]. The risk of developing HDP can be reduced with the initiation of oral aspirin in women with risk factors [7] and calcium supplementation in regions with low calcium consumption [8]. Continued, frequent engagement in antenatal care throughout the second and third trimester allows regular monitoring of blood pressures, which may facilitate earlier detection of HDP [6]. In instances of preeclampsia with severe features that necessitate prompt delivery, antenatal care allows for identification, referral, and management of these cases. In instances of gestational hypertension or preeclampsia without severe features prior to term, regular antenatal care allows for continued close monitoring of blood pressure, laboratory values, and symptoms [6].

In 2016, the World Health Organization (WHO) increased their 2002 recommendations from four antenatal visits in a pregnancy to eight antenatal visits, with first contact in the first 12 weeks' gestation and subsequent contacts at 20, 26, 30, 34, 36, 38 and 40 weeks' gestation. The overarching goal of this change was to reduce stillbirths and pregnancy complications, and to support a positive pregnancy experience [9]. A 2018 systematic review demonstrated a reduction in the occurrence of HDP in women who received more antenatal care [10]. Among women who do develop HDP, there is very limited research on the impact of antenatal care on maternal and neonatal health outcomes. To fill this gap, our study describes the timing and quantity of antenatal care attended by a group of women who developed preeclampsia and eclampsia, and explores how aspects of antenatal care, including timing, frequency, and type of provider, is associated with clinical outcomes in pregnancies complicated by preeclampsia and eclampsia.

## 2. Methods

This is a secondary analysis of data collected as part of a randomized control trial (RCT) that evaluated the impact of magnesium sulfate duration on efficacy of seizure prophylaxis among women with preeclampsia with severe features and eclampsia [11,12]. The published study protocol provides trial details (<https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=4690>) [11]. Apart from duration randomization to 12 versus 24 h of magnesium sulfate, women received the standard of care at Korle Bu Teaching Hospital (KBTH), with all clinical care decisions made by the on-call obstetrics team. Ethical approval was granted by the Scientific and Technical Committee of the KBTH (KBTH-IRB 00096/2018) and the University of Michigan (HUM00139104). Written informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

This study was conducted at the Korle Bu Teaching Hospital in Ghana's capital city of Accra. KBTH is a large tertiary care teaching hospital that provides antenatal care and labor and delivery services for women living in Accra, as well as referral cases across southern Ghana. KBTH conducts approximately 9,500 deliveries each year. HDP are currently the leading cause of maternal mortality at KBTH [3]. The government of Ghana provides free antenatal care services in all public health facilities for all pregnant women, implemented through the National Health Insurance Scheme. Pregnant women only need to show evidence of pregnancy to register for this free service.

Participants were adult pregnant patients admitted to KBTH with a diagnosis of preeclampsia with severe features or eclampsia. Exclusion criteria were the presence on admission of acute renal failure, Hemolysis Elevated Liver enzymes and Low Platelet (HELLP) Syndrome, pulmonary edema, a co-morbid maternal diagnosis of renal disease or seizure disorder, and age 17 or younger.

Outcome variables were two composites of maternal and neonatal

outcomes. A composite of severe maternal complications was defined as any one of the following: development of pulmonary edema, development of acute kidney injury, intensive care unit (ICU) admission, or maternal death. A composite of poor neonatal outcomes was defined as any one of the following: stillbirth, birthweight <1500 g, five-minute APGAR < 7, neonatal ICU (NICU) admission, or livebirth with death before discharge.

Predictor variables were all available measures of antenatal care utilization, including gestational age at first antenatal visit, number of total antenatal visits, facility and provider type of primary antenatal care, and referral to KBTH (versus received antenatal care at KBTH). See Supplemental Table 1 for definitions of facility and provider types in Ghana. Gestational age at first antenatal visit was categorized based on whether the first visit occurred in the first trimester—defined as prior to fourteen weeks and zero days' gestation. The total number of antenatal visits was categorized both as  $\geq 4$  visits and as  $\geq 8$  visits, based on prior and current WHO recommendations. Using WHO's schedule of recommended visits [9], an "adequate antenatal care visits" variable was created, defined as achieving a minimum number of recommended antenatal care visits based on gestational age at delivery.

Potential confounder variables included in the adjusted models were age, parity (nulliparous vs multiparous), marital status (married vs not married), and health insurance status (insured vs not insured). These variables were selected by the authors based on their clinical and sociodemographic relevance [13]. Gestational age at delivery was included as a confounder for models evaluating total number of antenatal care

**Table 1**  
Demographic and antenatal care characteristics.

Characteristic	n (%) or median (IQR)
Age, years	31.0 (27.0, 35.0)
Parity group	
Nulliparous	376 (32.0)
Multiparous	798 (68.0)
Marital status	
Married	847 (73.1)
Not Married	312 (26.9)
Health insurance status	
Insured	1100 (96.2)
Not Insured	43 (3.8)
Gestational age at delivery, weeks	36.6 (33.3, 38.9)
Gestational age at first antenatal care visit, weeks	16.0 (11.7, 21.0)
First antenatal care visit in first trimester	444 (40.4)
Number of total antenatal care visits	5.0 (3.0, 7.0)
$\geq 4$ antenatal care visits	791 (72.9)
$\geq 8$ antenatal care visits	210 (19.4)
Adequacy of antenatal care visits based on WHO recommendations <sup>a</sup>	
Adequate	645 (54.9)
Inadequate	531 (45.2)
Level of facility for primary antenatal care	
Government tertiary hospital	230 (20.8)
Government regional/district hospital	137 (12.4)
Government polyclinic	522 (47.2)
Private hospital	157 (12.4)
Maternity home	60 (5.4)
Type of primary caregiver for antenatal care	
OBGYN specialist	259 (24.0)
Medical officer	118 (10.9)
Midwife	704 (65.1)
Referred	844 (74.6)

Note: Data missing for parity (n = 2), marital status (n = 17), health insurance status (n = 33), gestational age at delivery (n = 37), gestational age at first trimester visit (n = 98), first trimester visit (n = 78), number of antenatal care visits (n = 91), level of facility for primary antenatal care (n = 70), primary caregiver (n = 95), referral (n = 45).

WHO = World Health Organization.

<sup>a</sup> Defined as achieving a minimum number of recommended antenatal care visits based on the WHO schedule of recommended visits and the woman's gestational age at delivery.

visits, having  $\geq 4$  visits, having  $\geq 8$  visits, and referral status [14].

Data was extracted from the medical record and supplemented by direct interview of participants, including past medical history, past obstetric history, and history of the index pregnancy. Data on antenatal care factors included level of facility where antenatal care was received and type of primary antenatal care provider. During the admission for labor and delivery, extracted data including mode and timing of delivery and occurrence of maternal complications. Neonatal information was collected from delivery through discharge, including gestational age at delivery, birthweight, outcome of delivery, NICU admission, APGAR score, and status at discharge.

Data was collected using paper forms, entered into REDCap for data storage and organization, and downloaded into SAS 9.4 (SAS Institute Inc., Cary, N.C) for analysis. First, sociodemographic and antenatal care factors were described for the total population. The normality of continuous variables was determined using Shapiro-Wilk test and assessing skewness and kurtosis. Non-normally distributed numerical variables (age, gestational age at delivery, gestational age at first antenatal care visit, and number of antenatal visits) were presented using medians and interquartile range. Unadjusted bivariate analyses were performed to compare sociodemographic and antenatal care factors across composite outcomes using Wilcoxon Rank test, Chi-squared, and Fisher's exact test where appropriate. For each antenatal care variable, separate multivariable logistic regression models were performed to identify associations between the antenatal care factor and each of two outcomes: composite of severe maternal complications (yes vs no) and composite of poor neonatal outcomes (yes vs no). Possible confounders were identified based on epidemiological and clinical knowledge. Each model was adjusted for age, parity, marital status, and insurance status. Models evaluating total number of antenatal care visits, having  $\geq 4$  visits, having  $\geq 8$  visits, and referral status were also adjusted for gestational age at delivery. Missing data were assumed to be missing completely at random and were not included in statistical comparisons. All statistical tests were two-sided and a p-value  $< 0.05$  was considered statistically significant.

### 3. Results

Between October 2018 and October 2020, 1,176 total pregnant participants were enrolled. Of these, 1,060 (90.1%) had a diagnosis of preeclampsia with severe features and 116 (9.9%) had eclampsia. Participants had a median age of 31.0 years (interquartile range (IQR): 27.0, 35.0), and most were married (n = 847, 73.1%) and had public insurance through Ghana's National Health Insurance Scheme (n = 1090, 95.4%). Median gestational age at delivery was 36.6 weeks (IQR: 33.3, 38.9), with 36.4 % (n = 431) delivering between 32.0 and 37.0 weeks

and 16.7% (n = 197) delivering prior to 32.0 weeks (Table 1).

Antenatal care was initiated at a median of 16.0 weeks (IQR 11.7, 21.0), and 40.4% (n = 444) had an antenatal visit in the first trimester. The median number of antenatal visits was 5.0 (IQR 3.0, 7.0), with 72.9% (n = 791) attending  $\geq 4$  visits and 19.4% (n = 210) attending  $\geq 8$  visits. Half of participants (n = 645, 54.9%) had an adequate number of antenatal care visits based on their gestational age at delivery and the WHO recommended schedule of visits (Table 1, Figure 1). All antenatal care visits had both a corresponding blood pressure and a urine protein level recorded. The most common type of facility for prenatal care was a government polyclinic (n = 522, 47.2%) and the most frequent type of provider was a midwife (n = 704, 65.1%). The majority (n = 844, 74.6%) were referred from another institution to KBTH for hospital admission.

Overall, the composite of severe maternal complications was experienced by 148 participants (12.7%) (Table 2, Supplemental Table 2). Although the number of antenatal care visits (uOR 0.85, p < 0.01),  $\geq 4$  antenatal care visits (uOR 0.48, p < 0.001), and  $\geq 8$  antenatal care visits (uOR 0.48, p = 0.01) were all associated with decreased odds of the composite of severe maternal complications in the unadjusted analysis (Table 2), these relationships were no longer significant in the final adjusted model (Table 3). Patients achieving WHO-defined adequate antenatal care visits, the gestational age at first antenatal care visit, and type of healthcare provider for antenatal care were also not significantly associated with the composite of severe maternal complications. Receiving antenatal care at a government tertiary hospital was associated with a 53% decreased odds of experiencing the severe maternal complication composite (aOR 0.47, 95% CI 0.26–0.85, p = 0.01). Compared to patients who received their antenatal care at KBTH, those who were referred to KBTH for labor and delivery or postpartum care had 2.0 higher odds of experiencing a severe maternal complication (aOR 2.00, 95% CI 1.16–3.45, p = 0.01).

Among 1218 babies born to the participants, poor neonatal outcomes were experienced by 58.2% (n = 707) (Table 2, Supplemental Table 2). In the final adjusted model, patients achieving WHO-defined adequate antenatal care visits and attending  $\geq 4$  antenatal care visits were not significantly associated with the composite of poor neonatal outcomes. However, attending  $\geq 8$  antenatal care visits was associated with 33% lower odds of experiencing a poor neonatal outcome (aOR 0.67, 95% CI 0.46–0.97, p = 0.04). In addition, receiving antenatal care at a tertiary hospital was associated with a 44% decreased odds of experiencing a poor neonatal outcome (aOR 0.56, 95% CI 0.41–0.77, p < 0.001) and receiving care from an OBGYN specialist resulted in a 42% decreased odds of a poor neonatal outcome (aOR 0.58, 95% CI 0.43–0.77, p < 0.001). Compared to attendants, women who were referred had 68% increased odds of a poor neonatal outcome (aOR 1.68, 95% CI

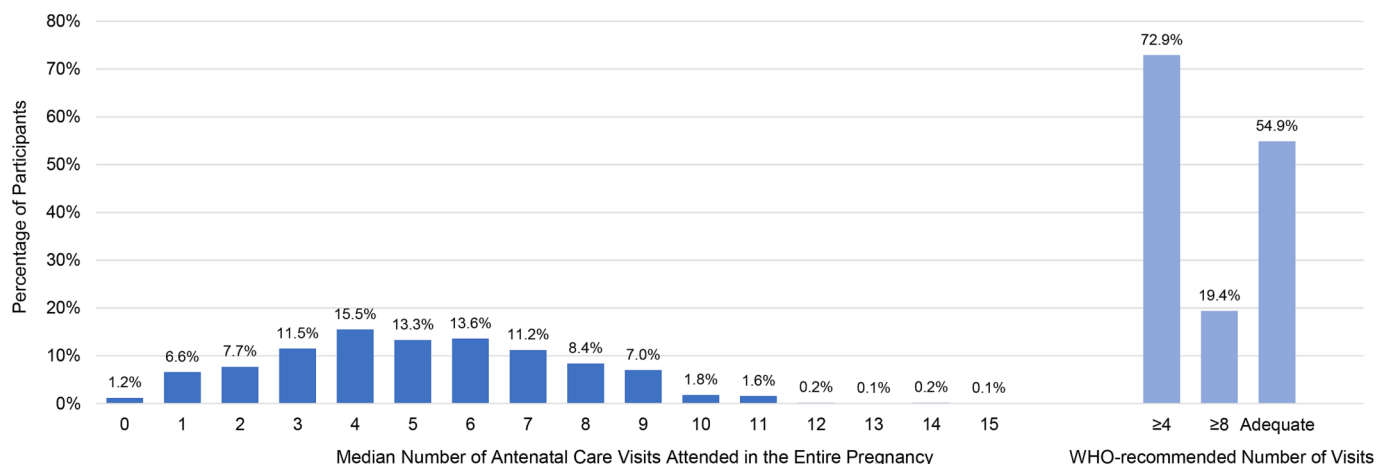


Fig. 1. Number of antenatal care visits attended, grouped by total number during pregnancy and by WHO recommendations.

**Table 2**  
Unadjusted bivariate analysis of sociodemographic and antenatal characteristics across composites of severe maternal complications and poor neonatal outcomes.

Characteristic	Maternal Complication Composite <sup>a</sup>			Poor Neonatal Outcome Composite <sup>b</sup>		
	Yes (n = 148)	No (n = 1,018)	P-value	Yes (n = 707)	No (n = 508)	P-value
Age, years <sup>c</sup>	32.0 (28.0, 35.0)	31.0 (27.0, 35.0)	0.35	31.0 (27.0, 36.0)	31.0 (27.0, 35.0)	0.48
Parity group <sup>d</sup>			0.19			0.79
Nulliparous	40 (27.2)	332 (32.7)		228 (32.3)	168 (33.1)	
Multiparous	107 (72.8)	685 (67.4)		477 (67.7)	340 (66.9)	
Marital status <sup>d</sup>			0.37			0.60
Married	111 (76.0)	727 (72.5)		503 (72.0)	366 (73.4)	
Not Married	35 (24.0)	276 (27.5)		196 (28.0)	133 (26.7)	
Health insurance status <sup>d</sup>			0.02			0.87
Insured	131 (92.9)	961 (96.8)		663 (96.4)	478 (96.2)	
Not insured	10 (7.1)	32 (3.2)		25 (3.6)	19 (3.8)	
Gestational age at delivery, weeks <sup>c</sup>	37.0 (33.9, 39.0)	33.9 (30.6, 36.0)	< 0.001	34.0 (31.4, 36.6)	38.4 (37.1, 39.9)	<0.001
Gestational age at first antenatal care visit, weeks <sup>c</sup>	16.0 (11.0, 20.1)	16.0 (12.0, 21.3)	0.29	16.0 (11.7, 21.0)	15.9 (11.3, 21.0)	0.48
First antenatal visit in first trimester <sup>d</sup>	52 (40.0)	387 (40.4)	0.93	258 (39.8)	203 (41.8)	0.49
Number of total antenatal care visits <sup>c</sup>	4.0 (3.0, 6.0)	5.0 (3.0, 7.0)	< 0.001	4.0 (3.0, 6.0)	6.0 (4.0, 8.0)	<0.001
≥4 antenatal care visits <sup>d</sup>	75 (58.6)	707 (74.7)	< 0.001	425 (65.7)	399 (83.5)	<0.001
≥8 antenatal care visits <sup>d</sup>	14 (10.9)	194 (20.5)	0.01	76 (11.8)	146 (30.5)	<0.001
WHO-defined adequate antenatal care visits <sup>d</sup>	79 (53.4)	559 (54.9)	0.73	401 (56.7)	271 (53.4)	0.24
Facility for primary antenatal care <sup>d</sup>			0.30			<0.001
Government tertiary hospital	18 (13.7)	209 (21.7)		106 (16.3)	138 (28.2)	
Government regional/district hospital	18 (13.7)	118 (12.2)		99 (15.2)	43 (8.8)	
Government polyclinic	69 (52.7)	450 (46.6)		299 (45.9)	237 (48.4)	
Private hospital	19 (14.5)	136 (14.1)		105 (16.1)	55 (11.2)	
Maternity home	7 (5.3)	52 (5.4)		42 (6.5)	17 (3.5)	
Type of primary caregiver for antenatal care <sup>d</sup>			0.16			0.002
OBGYN specialist	23 (18.3)	232 (24.6)		132 (20.8)	144 (29.8)	
Medical officer	18 (14.3)	97 (10.3)		70 (11.0)	49 (10.1)	
Midwife	85 (67.5)	616 (65.2)		434 (68.2)	290 (60.0)	
Referred <sup>d</sup>	128 (87.1)	708 (72.7)	< 0.001	541 (79.1)	320 (65.7)	<0.001

Data presented as n (%) or median (interquartile range).

<sup>a</sup> Composite of maternal complication is defined as “Yes” to pulmonary edema or acute kidney injury or hemodialysis or ICU admission or maternal death.

<sup>b</sup> Composite of poor neonatal outcome is defined as “Yes” to stillbirth or birthweight < 1500 g or 5-minute APGAR < 7 or yes to NICU admission or livebirth with death before discharge; calculated among 1218 births.

<sup>c</sup> Data presented as median interquartile range and comparisons tested using Wilcoxon Rank test.

<sup>d</sup> Comparisons between outcome groups tested using Chi-squared or Fisher’s exact test.

1.20–2.35, p = 0.002).

#### 4. Discussion

In a population of Ghanaian women with preeclampsia and eclampsia, we found that only half of participants had an adequate number of antenatal care visits based on their gestational age at delivery and the WHO-recommended schedule of visits. Achieving adequate antenatal care visits was not associated with improved health outcomes. Meeting the current WHO recommendations to attend ≥8 antenatal visits was associated with lower odds of a poor neonatal outcome; however, it was not associated with a lower rate of the maternal complication composite. The odds of experiencing a severe maternal complication were lower in women who received their antenatal care at a tertiary hospital, while the odds of experiencing a poor neonatal outcome were lower in women who received their antenatal care at a tertiary level hospital and by an OBGYN specialist. Compared to attendants, women who were referred to KBTH had twice the odds of having a severe maternal complication and a poor neonatal outcome.

This study demonstrates the importance of frequent antenatal care in reducing poor neonatal outcomes; however, the frequency of antenatal care alone is not sufficient to reduce serious maternal complications. Having an adequate number of antenatal care visits was not associated with maternal or neonatal health outcomes. Although antenatal care is universally recommended and valued, results from evidence-based evaluation of antenatal care has been varied. Many studies have shown a relationship between fewer antenatal visits and worse pregnancy outcomes, including low birthweight, preterm birth, and neonatal death [15–17], while others have failed to demonstrate improved outcomes associated with number of antenatal visits [18]—particularly in low-risk populations [19]. A 2010 Cochrane Review evaluated the impact of reduced antenatal visits and found no adverse perinatal outcomes in high-income countries, but significantly higher rates of perinatal mortality in LMICs [20].

Our findings demonstrate the protective benefits of receiving antenatal care at a tertiary facility and by an OBGYN specialist. Provider and facility type may be proxy for quality of care, reflecting settings of improved monitoring, earlier detection of HDP, and, subsequently, improved outcomes. Alternatively, this finding could be explained by unmeasured factors that predispose certain groups of pregnant women to receive care at tertiary facilities. These findings reinforce the importance of risk stratification early in antenatal care to identify higher-risk patients who may benefit from early referral to tertiary-level, specialist care. This must be carefully balanced with the potential for overcrowding at tertiary facilities and the need to build capacity for quality care at primary and secondary care levels.

Most studies of antenatal care have focused on quantitative differences in the number of prenatal visits [10,15]. However, our results suggest that in pregnant women at risk of developing preeclampsia and eclampsia, not only is the quantity of antenatal care essential, but so is the quality. While of critical importance, evaluating the quality of antenatal care is more difficult [21]. Though no single metric currently exists, proposed metrics for evaluating antenatal care quality include early initiation of prenatal care, monitoring of specific physical and laboratory parameters, provision of prenatal and intrapartum education, promotion of breastfeeding and family planning education, and a

**Table 3**

Antenatal care factors associated with composites of maternal complications and poor neonatal outcomes.

Characteristic	Maternal Complication <sup>a</sup>			Poor Neonatal Outcome <sup>b</sup>		
	uOR (95% CI)	aOR (95% CI)	P- value	uOR (95% CI)	aOR (95% CI)	P-value
Gestational age at first antenatal care visit	0.99 (0.96, 1.01)	0.98 (0.95, 1.01) <sup>c</sup>	0.12	0.99 (0.98, 1.01)	0.99 (0.97, 1.01) <sup>c</sup>	0.29
First antenatal care visit in first trimester	0.98 (0.68, 1.43)	1.09 (0.74, 1.61) <sup>c</sup>	0.65	0.92 (0.72, 1.17)	0.96 (0.75, 1.23) <sup>c</sup>	0.74
Number of total antenatal care visits	0.85 (0.79, 0.92)	0.95 (0.87, 1.04) <sup>d</sup>	0.27	0.79 (0.75, 0.84)	0.94 (0.88, 1.00) <sup>d</sup>	0.06
≥4 antenatal care visits	0.48 (0.33, 0.70)	0.78 (0.50, 1.22) <sup>d</sup>	0.27	0.38 (0.28, 0.51)	0.83 (0.56, 1.22) <sup>d</sup>	0.34
≥8 antenatal care visits	0.48 (0.27, 0.85)	0.79 (0.42, 1.49) <sup>d</sup>	0.47	0.30 (0.22, 0.41)	0.67 (0.46, 0.97) <sup>d</sup>	0.04
WHO-defined adequate antenatal care visits	0.94 (0.67, 1.33)	1.03 (0.71, 1.49) <sup>c</sup>	0.87	1.15 (0.91, 1.44)	1.20 (0.95, 1.53) <sup>c</sup>	0.13
Primary antenatal care facility						
Government tertiary hospital	0.56 (0.33, 0.97)	<b>0.47</b> ( <b>0.26</b> , <b>0.85</b> ) <sup>c</sup>	<b>0.01</b>	0.61 (0.45, 0.83)	<b>0.56</b> ( <b>0.41</b> , <b>0.77</b> ) <sup>c</sup>	<b>&lt;0.001</b>
Government regional/district hospital	1.00 (0.57, 1.74)	0.95 (0.53, 1.71) <sup>c</sup>	0.85	1.83 (1.23, 2.71)	<b>1.96</b> ( <b>1.29</b> , <b>2.97</b> ) <sup>c</sup>	<b>0.002</b>
Government polyclinic	REF	REF	REF	REF	REF	REF
Private hospital	0.91 (0.53, 1.57)	0.94 (0.54, 1.64) <sup>c</sup>	0.83	1.51 (1.05, 2.19)	<b>1.47</b> ( <b>1.01</b> , <b>2.15</b> ) <sup>c</sup>	<b>0.045</b>
Maternity home	0.88 (0.38, 2.01)	0.86 (0.37, 1.98) <sup>c</sup>	0.72	1.96 (1.09, 3.53)	<b>1.88</b> ( <b>1.04</b> , <b>3.40</b> ) <sup>c</sup>	<b>0.04</b>
Type of primary caregiver for antenatal care						
OBGYN specialist	0.72 (0.44, 1.17)	0.61 (0.36, 1.03) <sup>c</sup>	0.06	0.61 (0.46, 0.81)	<b>0.58</b> ( <b>0.43</b> , <b>0.77</b> ) <sup>c</sup>	<b>&lt;0.001</b>
Medical officer	1.35 (0.78, 2.34)	1.35 (0.76, 2.38) <sup>c</sup>	0.30	0.96 (0.64, 1.42)	0.94 (0.63, 1.41) <sup>c</sup>	0.77
Midwife Referred	REF (1.53, 4.18)	REF ( <b>1.23</b> , <b>3.66</b> ) <sup>d</sup>	REF <b>0.007</b>	REF (1.52, 2.57)	REF ( <b>1.20</b> , <b>2.35</b> ) <sup>d</sup>	REF <b>0.002</b>

uOR = unadjusted odds ratio; aOR = adjusted odds ratio.

<sup>a</sup> Composite of maternal complication is defined as “Yes” to pulmonary edema or acute kidney injury or hemodialysis or ICU admission or maternal death.<sup>b</sup> Composite of poor neonatal outcome is defined as “Yes” to stillbirth or birthweight < 1500 g or 5-minute APGAR < 7 or yes to NICU admission or livebirth with death before discharge.<sup>c</sup> Multivariable logistic regression models are adjusted for age, parity, marital status, and health insurance status.<sup>d</sup> Multivariable logistic regression models are adjusted for age, parity, marital status, health insurance status, and gestational age at delivery.

positive patient experience with a perception of respectful maternity care [22–24]. Despite all women in our study developing a serious complication of pregnancy, either preeclampsia or eclampsia, many began their antenatal care as low-risk pregnancies. This highlights the importance of every pregnant woman receiving early, quality antenatal care. Comprehensive history-taking and risk-stratification provide the

opportunity to initiate daily aspirin and calcium supplementation, which reduces the risk of developing preeclampsia in select women [7]. Further, if complications develop, accurate confirmation of dating, known trends in blood pressures, and serial assessment of fetal well-being are all essential to informed management of complications. Finally, benefits of quality care extend to women being well-counseled, trusting their healthcare providers, and having a positive pregnancy experience even in the face of complications. In women with preeclampsia and eclampsia, who have elevated risks of recurrence in future pregnancies [4], this counseling and trust is critical for future reproductive outcomes.

Strengths of this study include a large population of high-risk participants, including a large number of pregnancies complicated by eclampsia. Extensive clinical information was collected, including occurrence and timing of each antenatal visit, and this data was linked to outcomes during labor and delivery and in the immediate postpartum period. Limitations of the study include data collection at a single urban tertiary care hospital, which may limit generalizability to other facilities in dissimilar locations. A large proportion of participants were referred from other facilities, which may represent an especially complicated population. Although data was collected on whether blood pressure and urine protein were checked at each antenatal visit, additional information on quality of antenatal care is not available for analysis. Finally, given the observational nature of data collection on antenatal care utilization, we are unable to determine if antenatal care variables caused the observed differences in clinical outcomes. Additional research is needed to untangle the complex impact that unmeasured and unmeasurable factors, including socioeconomic status and patient agency, have on both antenatal care utilization and clinical outcomes.

## 5. Conclusion

Overall, severe maternal morbidity and mortality resulting from HDP remain high in many LMICs despite known interventions and management protocols. This may be due in part to limited access to and utilization of quality antenatal care. In a population of high-risk Ghanaian women with preeclampsia and eclampsia, we demonstrate that the frequency of antenatal care alone may not be sufficient to reduce severe maternal and neonatal complications. In pregnant women at risk of developing preeclampsia and eclampsia, the quality of antenatal care is essential—not just quantity. Our findings highlight the importance of risk stratification of pregnancies early in antenatal care and referral to tertiary-level, specialist care for the highest risk patients. Importantly, preeclampsia and eclampsia often develop in previously low-risk patients. Thus, every pregnant woman should have access to quality evidence-based antenatal care to optimize detection and management if complications develop.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We thank Hassan Kaleem and Andrew Owusu for leadership in data collection and entry.

### Data statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Funding

This work was supported by the Rudi Ansbacher Research Award, University of Michigan Department of Obstetrics and Gynecology and

Women's Health Leadership Board Innovation Fund, University of Michigan.

#### Contributors:

**Titus Beyuo:** I declare that I participated in the conceptualization, study protocol development, data collection and management, data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest. Titus Beyuo was supported by a VECD Global Health Fellowship funded by the Fogarty International Center (FIC) of the National Institutes of Health (D43 TW009337).

**Emma R. Lawrence:** I declare that I participated in the study protocol development, data collection and management, data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**Samuel Oppong:** I declare that I participated in the conceptualization, study protocol development, data collection and management, data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**Emily K. Kobernik:** I declare that I participated in the data analysis, data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**Mary Amoakoh-Coleman:** I declare that I participated in the data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**Diederick E. Grobbee:** I declare that I participated in the data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**Joyce L. Browne:** I declare that I participated in the data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

**K.W.M. Bloemenkamp:** I declare that I participated in the data interpretation, and manuscript editing and review for this study and that I have seen and approved the final version of the manuscript. I have no conflicts of interest.

#### References

- [1] L. Duley, The global impact of pre-eclampsia and eclampsia, *Semin. Perinatol.* 33 (3) (2009) 130–137.
- [2] World Health Organization, WHO recommendations for Prevention and treatment of pre-eclampsia and eclampsia, 2011. [https://apps.who.int/iris/bitstream/handle/10665/44703/9789241548335\\_eng.pdf;jsessionid=476A1D103CE06844B2BD636E94D8E7DD?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/44703/9789241548335_eng.pdf;jsessionid=476A1D103CE06844B2BD636E94D8E7DD?sequence=1). (Accessed February 15, 2022).
- [3] K. Adu-Bonsaffoh, S.A. Oppong, G. Binlinla, S.A. Obed, Maternal deaths attributable to hypertensive disorders in a tertiary hospital in Ghana, *Int. J. Gynaecol. Obstet.* 123 (2) (2013) 110–113.
- [4] L.C. Chappell, C.A. Cluver, J. Kingdom, S. Tong, Pre-eclampsia, *Lancet* 398 (10297) (2021) 341–354.
- [5] E. Haelterman, R. Qvist, P. Barlow, S. Alexander, Social deprivation and poor access to care as risk factors for severe pre-eclampsia, *Eur. J. Obstet. Gynecol. Reprod. Biol.* 111 (1) (2003) 25–32.
- [6] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Obstetrics, Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222, *Obstet Gynecol* 135(6) (2020) e237–e260.
- [7] T.T. Xu, F. Zhou, C.Y. Deng, G.Q. Huang, J.K. Li, X.D. Wang, Low-Dose Aspirin for Preventing Preeclampsia and Its Complications: A Meta-Analysis, *J. Clin. Hypertens. (Greenwich)* 17 (7) (2015) 567–573.
- [8] T.S. Patrelli, A. Dall'asta, S. Gizzo, G. Pedrazzi, G. Piantelli, V.M. Jasonni, A. B. Modena, Calcium supplementation and prevention of preeclampsia: a meta-analysis, *J. Matern. Fetal Neonatal Med.* 25 (12) (2012) 2570–2574.
- [9] World Health Organization, WHO recommendations on antenatal care for a positive pregnancy experience, 2016. [https://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/). (Accessed 28 July 2022).
- [10] G. Dutra, L.D.C. Dutra, G. Fonseca, M.B.D. Nascimento Junior, E.E.S. Lucena, Prenatal Care and Hypertensive Gestational Syndromes: A Systematic Review, *Rev Bras Ginecol Obstet* 40 (8) (2018) 471–476.
- [11] T. Beyuo, E. Lawrence, E.S. Langen, S.A. Oppong, Open-labelled randomised controlled trial of 12 hours versus 24 hours modified Pritchard regimen in the management of eclampsia and pre-eclampsia in Ghana (MOPEP Study): study protocol, *BMJ Open* 9 (10) (2019) e032799.
- [12] T.K. Beyuo, E.R. Lawrence, E.K. Kobernik, S.A. Oppong, A novel 12-hour versus 24-hour magnesium sulfate regimen in the management of eclampsia and preeclampsia in Ghana (MOPEP Study): A randomized controlled trial, *Int. J. Gynaecol. Obstet.* 159 (2) (2022) 495–504.
- [13] I.N. Okedo-Alex, I.C. Akamike, O.B. Ezeanosike, C.J. Uneke, Determinants of antenatal care utilisation in sub-Saharan Africa: a systematic review, *BMJ Open* 9 (10) (2019) e031890.
- [14] K. Beeckman, F. Louckx, K. Putman, Determinants of the number of antenatal visits in a metropolitan region, *BMC Public Health* 10 (2010) 527.
- [15] G.R. Alexander, M. Kotelchuck, Assessing the role and effectiveness of prenatal care: history, challenges, and directions for future research, *Public Health Rep.* 116 (4) (2001) 306–316.
- [16] K. Raatikainen, N. Heiskanen, S. Heinonen, Under-attending free antenatal care is associated with adverse pregnancy outcomes, *BMC Public Health* 7 (2007) 268.
- [17] R.G. Cox, L. Zhang, M.E. Zotti, J. Graham, Prenatal care utilization in Mississippi: racial disparities and implications for unfavorable birth outcomes, *Matern. Child Health J.* 15 (7) (2011) 931–942.
- [18] K. Fiscella, Does prenatal care improve birth outcomes? A critical review, *Obstet Gynecol* 85 (3) (1995) 468–479.
- [19] E.B. Carter, M.G. Tuuli, A.B. Caughey, A.O. Odibo, G.A. Macones, A.G. Cahill, Number of prenatal visits and pregnancy outcomes in low-risk women, *J. Perinatol.* 36 (3) (2016) 178–181.
- [20] T. Dowswell, G. Carroli, L. Duley, S. Gates, A.M. Gulmezoglu, D. Khan-Neelofur, G. G. Piaggio, Alternative versus standard packages of antenatal care for low-risk pregnancy, *Cochrane Database Syst. Rev.* 10 (2010) CD000934.
- [21] L. Benova, Ö. Tunçalp, A.C. Moran, O.M.R. Campbell, Not just a number: examining coverage and content of antenatal care in low-income and middle-income countries, *BMJ Glob. Health* 3 (2) (2018) e000779.
- [22] World Health Organization, Integrated Management Of Pregnancy And Childbirth: Managing Complications in Pregnancy and Childbirth, 2017. <https://apps.who.int/iris/bitstream/handle/10665/255760/9789241565493-eng.pdf>. (Accessed 28 July 2022).
- [23] B. Chalmers, V. Mangiaterra, R. Porter, WHO principles of perinatal care: the essential antenatal, perinatal, and postpartum care course, *Birth* 28 (3) (2001) 202–207.
- [24] J.P. Vogel, M.A. Bohren, O. Tunçalp, O.T. Oladapo, R.M. Adanu, M.D. Balde, T. M. Maung, B. Fawole, K. Adu-Bonsaffoh, P. Dako-Gyeke, E.T. Maya, M.C. Camara, A.B. Diallo, S. Diallo, K.T. Wai, T. Myint, L. Olutayo, M. Titiloye, F. Alu, H. Idris, M. A. Gulmezoglu, W.H.O. Research Group on the Treatment of Women During Childbirth, How women are treated during facility-based childbirth: development and validation of measurement tools in four countries - phase 1 formative research study protocol, *Reprod. Health* 12 (2015) 60.