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FACTORS ASSOCIATED WITH DETECTION AND REPORTING OF SUSPECTED YELLOW FEVER CASES IN THE GREATER ACCRA REGION

BY

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DECLARATION

I, **Magdalene Norkai Sayah,** declare that except for other peoples' investigation which have been fully acknowledged, this dissertation is my original work and has not been presented either in part or whole elsewhere for another degree.

Signature .....

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(Academic Supervisor)

DEDICATION

This dissertation is dedicated to my husband Mr Florent A. Sayah and my two angels Yanisse and Yanelle Sayah for hanging in there while Mummy went to school.

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ABSTRACT

Introduction:

Yellow fever is a viral heamorrhagic fever transmitted primarily by the *Aedes aegyptii* mosquito and is characterized mainly by fever and jaundice. It is endemic in Africa and South America. The possibility of eradicating yellow fever is quite remote but a drastic of disease burden can be attained through vaccination of populations living in or visiting places considered to be high-risk areas in endemic countries. The WHO surveillance case definition for a suspected case of yellow fever is any case presenting with acute onset of fever, with jaundice appearing within 14 days of onset of the first symptoms. WHO recommended strategy for controlling yellow fever is through detection, reporting, preventing and controlling outbreaks and vaccination with the 17D yellow fever vaccine. A number of factors affect the detection and reporting of suspected cases but these can be improved through heightened surveillance.

Objective:

The main objective of this study was to assess the factors associated with detection and reporting of suspected yellow fever cases in the Greater Accra Region and how to possibly improve on the rate of reporting of suspected cases.

Methods:

The study is a cross sectional survey of clinicians who are directly involved in attending to patients and district disease control/surveillance officers in the Greater Accra region. Clinicians were selected from government, quasi-government and private facilities. Disease control officers were selected from the 21 operational districts in the Greater Accra Region. A structured anonymous questionnaire (Appendix 1) was administered to all participants in the study. Data entry and analysis were done using Epi Info and STATA 14 respectively.

Results

In all, 371 clinicians and 18 disease control officers were interviewed. Out of the 371 clinicians inter viewed, 87.6% had detected fever with jaundice cases in their consulting rooms within the last 12 months but only 10.8% had reported any suspected yellow fever case. Investigation of fever with jaundice cases as well as reporting of suspected cases had significant influence on the detection of yellow fever as well as case notification ($p<0.001$). Clinicians who had identified 1 to 3 fever with jaundice cases were 1.15 (*CI* 1.07-1.23, $p<0.001$) times more likely to detect yellow fever as compared to those who identified no case. However after adjusting for the sending of notification forms, the association between identification of fever with jaundice and detection of yellow fever was no longer significant (p=0.092). The unadjusted odds of detecting yellow fever cases among those who did not send notification forms were 82.0% lower than those who sent notification forms (*OR*=0.18, 95% *CI*=0.09-0.38). After controlling for the identification of fever with jaundice, the association between sending of notification forms and detection of yellow fever was no longer significant (p=0.0865). Additional factors found to be associated with reporting of suspected yellow fever cases were sensitization (*AOR* 15.02, *CI*=3.88 – 58.14, $p<0.001$), availability of reporting tools (*AOR* 7.41, *CI*=2.76- 19.89, $p<0.001$) and number of fever with jaundices recorded (*AOR* 0.05, *CI*=0.04-0.19, $p<0.001$).

Conclusion and Recommendations

Although clinicians in the Greater Accra Region see a lot of fever with jaundice cases in their consulting rooms, which is the surveillance case definition for a suspected yellow fever case, this does not translate to the number of suspected cases reported. Only one-tenth of cases that fit the suspected yellow fever case definition seen get reported and investigated and the main reasons

for non-reporting are that clinicians do not suspect yellow fever cases (53.2%) or are unaware of the reporting system (25.2%). It is recommended that District Health Directorates should further sensitize clinicians on the application of the surveillance case definition for yellow fever and the need to report all such and Public Health Units in facilities and districts should make case notification forms readily available and accessible in all consulting rooms and wards.

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LIST OF ABBREVIATIONS

DC/SO	Disease Control/Surveillance Officer
DHA	District Health Administration
DHF	Dengue Heamorrhagic Fever
DHMT	District Health Management Team
GHS	Ghana Health Service
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
IDSR	Integrated Disease Surveillance and Response
IHR	International Health Regulations
NPHRL	National Public Health and Reference Laboratory
PHU	Public Health Unit
WHO	World Health Organization
YF	Yellow Fever

CHAPTER ONE

1.0 Introduction

Yellow fever is a viral heamorrhagic disease transmitted primarily by the *Aedes aegyptii* mosquito. It is caused by the yellow fever virus, a reemerging virus that is endemic in several sub-Saharan African and South American countries. According to the World Health Organisation, 47 countries i.e. 34 countries in Africa and 13 countries in South America are endemic for or have areas that are endemic for yellow fever (Tomori, 2002).

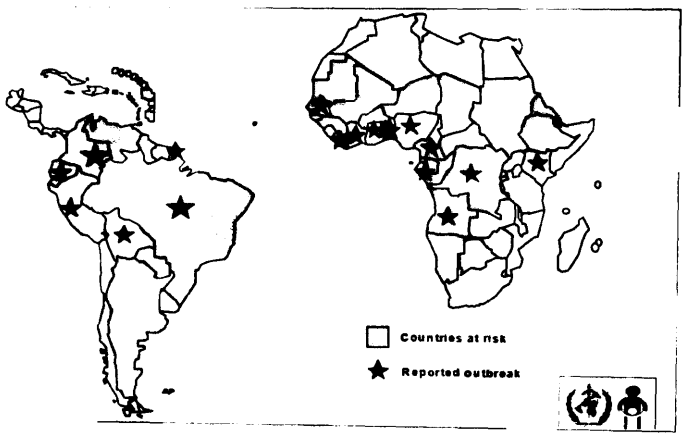


Fig. 1: **Map showing YF endemic countries** (Tomori, 2002)

The clinical presentation ranges from a mild asymptomatic self-limiting disease, through mild ailment with flu-like symptoms, to a very severe disease including fever with jaundice or haemorrhage and death. Overall mortality ranges from 20–50% (New IHR 2005: 58th World

Health Assembly 2005). Due to its severity and the high risk of widespread outbreaks, most countries which are in the endemic regions, implement case based surveillance. In this type of surveillance, yellow fever is often associated with clinical cases of acute febrile jaundice (Makiala-Mandanda et al., 2017). However, this clinical syndrome is common to several endemic diseases, particularly malaria and viral hepatotropic infections. In a study conducted in the Democratic Republic of Congo (DRC), viral hepatitis serological markers were diagnosed in 218 (43.7%) patients. The seroprevalences were 16.7% for HAV, 24.6% for HBV, 2.3% for HCV, and 10.4% for HEV, and 26.1% of HBV- positive patients were also infected with HDV (Makiala-Mandanda et al., 2017).

Studies have shown that there are three main transmission cycles depending on which host and vector species are involved in the transmission (Garske, Van Kerkhove, Yactayo, Ronveaux, Lewis, Staples, Perea, Perraut, et al., 2014). In the sylvatic cycle, tree-dwelling *Aedes aegyptii* mosquitoes convey the virus to non-human primate hosts. When humans encroach on these forests habitats, infections in humans may occur. On the other hand, in the urban transmission cycle, humans remain the main hosts whiles transmission occurs via domestic mosquito species. When yellow fever is introduced into urban areas, extensive outbreaks may occur, which may be very challenging to control. Intermediate transmission is the third type of transmission and is usually found in sub Saharan Africa. This usually occurs in rural habitats along the edges of forests with both humans and primates being affected. This type of transmission is usually driven by both domestic and semi-domestic mosquito species. Although eradication of yellow fever is not attainable due to the forest reservoir, a high level of control is reachable due to the

availability of an effective and safe vaccine that confers life-long immunity from a single dose (Garske, Van Kerkhove, Yactayo, Ronveaux, Lewis, Staples, Perea, Ferguson, et al., 2014).

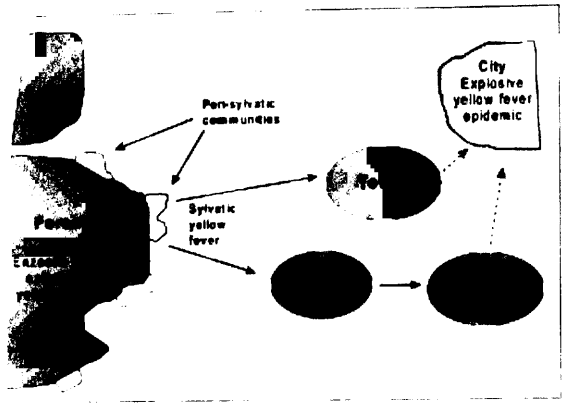


Fig 2. **Cycles of YF transmission**
(Garske, Van Kerkhove, Yactayo, Ronveaux, Lewis, Staples, Perea, Perraut, et al., 2014)

Even though eradication of yellow fever is not very feasible, a drastic reduction in the number of cases can be achieved through vaccination of people living in or visiting high-risk rural areas in endemic countries. A modelling research based on African data sources puts the burden of yellow fever in 2013 at 84,000 – 170,000 severe cases and 29,000 – 60,000 deaths (World Health Organisation, 2016). Detection and reporting of all suspected yellow fever cases is therefore mandatory by WHO for all endemic countries. The coming into force of the International Health Regulation (IHR 2005) in 2007 also mandates all countries to report all yellow fever cases.

WHO recommended strategy for controlling yellow fever is through detection, reporting, preventing and controlling outbreaks and vaccination with the 17D yellow fever vaccine (WHO, 2015a). The main aim of yellow fever surveillance is to detect outbreaks early enough to put in control measures that would be effective enough to stop further spread of the outbreak. At risk populations can be identified through continuous surveillance so that appropriate interventions can be planned and implemented. The burden of disease is however not easy to estimate using the usual surveillance methods because there are many asymptomatic or pauci-symptomatic cases, and even when some signs and symptoms show, they cannot be easily distinguished from other infections like malaria and other viral heamorrhagic fevers (Makiala-Mandanda et al., 2017).

Effective surveillance of yellow fever should be both active and passive and the Integrated Disease Surveillance and Response (IDSR) method should be employed in order to detect and report as many suspected cases as possible. A number of factors affect the detection and reporting of suspected cases and these become enhanced by a weak surveillance system.

1.1 Problem Statement

The resurgence of yellow fever has been confirmed by new epidemics in many countries in Africa and South America e.g. in Angola (2015-2016) and Brazil (2016-2017). These transmissions have been autochthonous but some imported cases have also been reported in Asia. The possibility of spreading beyond the borders of endemic countries exists and this has become a matter of global concern. Presently, there are about 1 billion people, from 49 endemic

countries, that are considered to be at risk (Ortiz-Martínez, Patiño-Barbosa, & Rodriguez-Morales, 2017).

Assessing the burden of disease of yellow fever has always been a challenge due to the wide range of the severity of clinical symptoms, with non-specific symptoms seen in the majority of infections. Like many infectious agents, YF virus only causes disease in a percentage of persons it infects and severe illness only signifies the tip of the iceberg comparative to the total number of infections, which is the more critical element for virus transmission (Johansson, Vasconcelos, & Staples, 2014).

In addition, there are a substantial number of challenges in the surveillance and health care systems across most of the affected regions. It is also evident that yellow fever is considerably underreported. Estimates from data based on previous serological surveys conducted in children in Nigeria during the early 1990s, placed the burden of disease at 200,000 cases and 30,000 deaths annually. This data is still used as the basis for some recent studies to quantify the burden of disease of yellow fever, or the cost-effectiveness of vaccines (Tuboi, Costa, da Costa Vasconcelos, & Hatch, 2007). As is evident from the recent Angolan outbreak, as of 4 April 2016, a total of 1562 suspected YF cases and 501 lab-confirmed cases and 225 deaths (case fatality rate: 14.4%) have been reported. The urban Angolan outbreak of YF has exposed 2 important challenges confronting the control of the disease. These are (i) the risk of national/ international spread of the outbreak, and (ii) YF global vaccine supply (Nishino K., 2016).

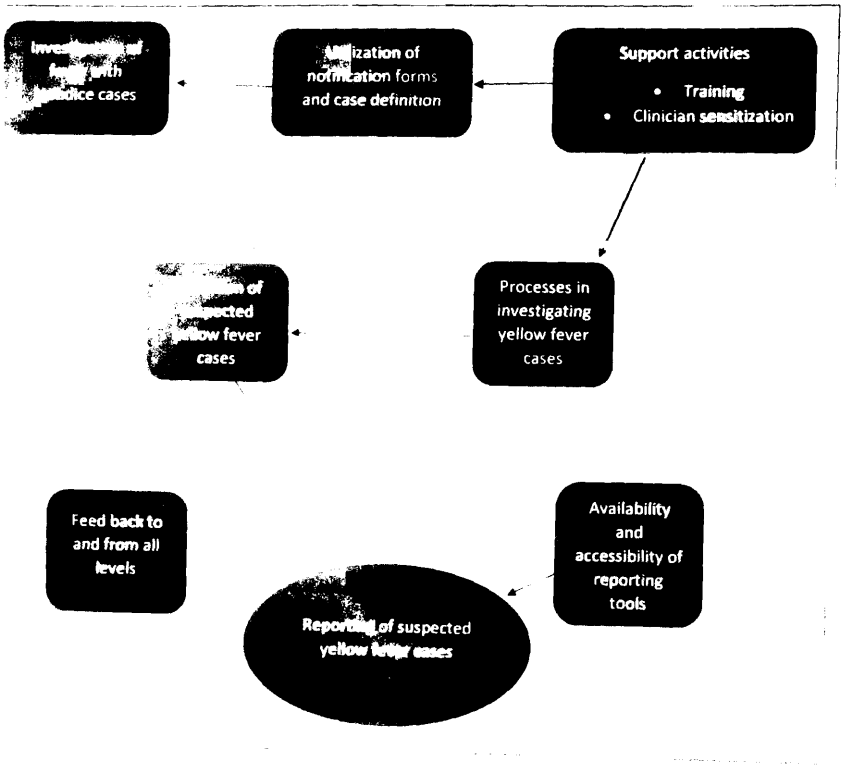
Surveillance of yellow fever therefore requires both active and passive case search. For effective surveillance, the WHO surveillance case definition for yellow fever which is *"any case presenting with an acute onset of fever, with jaundice appearing within 14 days of onset of the first symptoms"* ("Yellow fever surveillance and outbreak response: revision of case definitions, October 2010," 2010). The surveillance case definition for yellow fever has been simplified and made sensitive enough to capture all suspected cases.

These case definitions are to be provided in all consulting rooms at health facilities and also at the offices of the District Health Management Teams (DHMT). Clinicians are therefore expected by these case definitions, to notify the public health units of any suspected case. Case notification forms are expected to be provided in the consulting rooms. Upon notification, disease control/surveillance officers are expected to follow up on the patient and collect blood sample together with a filled case based form for investigation.

As part of their duties, Disease control/surveillance officers have to regularly review consulting room registers in health facilities in their catchment areas to follow up on cases that match the surveillance case definition for suspected yellow fever and other notifiable diseases. Many conditions such as severe malaria in children, typhoid, chronic liver disease like hepatitis B, C and E, schistosomiasis or even exposure to some toxic agents present with symptoms that mimic a suspected yellow fever case. In applying the surveillance case definition, all such cases should be suspected for yellow fever and investigated. Hence surveillance systems should be strong enough to detect Viral Haemorrhagic Fevers in a timely manner. Health facilities should also be prepared to promptly treat the initial cases because the case fatality ratios (CFRs) are usually very high among index cases (Ahmed et al., 2016).

Measles and yellow fever share the same surveillance indicators and reporting channels. The primary surveillance performance indicator for both measles and yellow fever is that every district should report at least one suspected case each of both diseases in a year. It is expected that with the sensitive case definition, this indicator should be easily met. However, percentage district reporting for yellow fever in the Greater Accra region has always been far below the target of 80%. Measles surveillance performance indicators have always been above that of yellow fever. Even for districts that have had confirmed cases before or districts bordering districts that are having outbreaks, reporting is still very low. This study therefore seeks to assess some of the factors that affect effective detection and subsequent reporting of suspected yellow fever cases in the Greater Accra Region.

Fig. 3: Factors affecting detection and reporting of suspected Yellow Fever cases



In the conceptual framework, investigation of a maximum number of fever with jaundice cases and the utilization of case notification forms by clinicians would lead to high detection rates of suspected yellow fever cases. Other supporting activities such as training of disease control or diseases surveillance officers and clinician sensitization of the surveillance case definition of a suspected yellow fever case would enhance overall processes in detecting and reporting suspected cases.

Feedback to and from all reporting levels is essential to future reporting of cases. Feedback to reporting facilities, clinicians and the sub district level is usually poor. Clinicians and disease control officers at these level become demoralized and are therefore not interested in investigating or reporting suspected cases. Also, availability and accessibility of reporting tools greatly enhance reporting of suspected cases.

1.3 Research Question

- What are the health service related factors associated with detection and reporting of suspected yellow fever cases in the Greater Accra Region?

1.4 General Objective

- To examine factors associated with detection and reporting of suspected yellow fever cases in the Greater Accra Region

1.5 Specific Objectives

1. To assess factors associated with detection of suspected yellow fever cases
2. To examine factors associated with reporting of suspected yellow fever cases
3. To determine the proportion of fever with jaundice cases reported as suspected yellow fever cases

CHAPTER TWO

2.0 Literature Review

2.1 Increasing risk of urban outbreaks

Yellow fever is now considered a reemerging infectious disease of significant global concern. It has reappeared as a threat to global public health. During the last outbreaks in Angola (2015-2016) and Brazil (2016-2017), a lot of cases were also reported from areas that had high vaccination coverages. Several factors, including (i) the vast borders of some endemic countries coupled with loose migratory laws and the ease of travel, (ii) extensive distribution of the *Aedes mosquitoes* and (iii) the nonexistence of effective health policies and surveillance systems, favor this complicated epidemiological scenario of reemergence (Ortiz-Martínez et al., 2017). Many African cities are fast becoming urbanized and highly populated thereby increasing the possibility of large urban outbreaks of yellow fever.

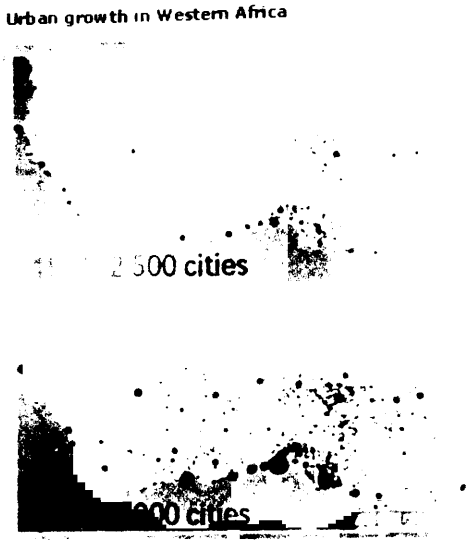


Fig. 4: Urban growth in West Africa (Bhatt et al., 2013)

According to WHO, there are a growing number of poorly planned shanty towns in Africa which are congested. Sanitary conditions in such towns are very poor with bad road networks and no potable water. Most of the people who live in such areas do not have access to potable water thereby storing water in containers which usually serve as breeding sites for the *Aedes aegypti* mosquito, which is the primary vector for the transmission of urban yellow fever (WHO, 2015). Furthermore, there are no public sanitation services and therefore empty cans, abandoned vehicle tires and derelict vehicles are left ajar and these serve as breeding places for the mosquitoes.

Urbanization substantially increases the density, larval development rate, and adult survival time of the Aedes mosquito, which in turn bring about a rise in vector capacity, and subsequently, disease transmissibility (Li et al., 2014).

There has been a study increase in the number of countries reporting suspected yellow fever cases to WHO over the last 10 years, especially in West Africa where 93 % of the countries have reported suspected cases in the past 4 years i.e. 2012 – 2016 (WHO, 2015b). This indicates a 30% increase compared to the period of 1995-1999 and brings to light a perturbing increase in the circulation of the virus in human populations which have rather low head immunity. The geographical spread of the virus is alarming and multiple outbreaks may occur concurrently in several places. This emphasizes the need to improve the response capacity of countries as well as the support capabilities of the international community (WHO, 2015b).

2.2 Burden of Yellow Fever

In a study carried out by Johansson et al (2014), data on asymptomatic infections of yellow fever, mild illness, severe disease characterized by fever with jaundice or hemorrhagic symptoms, and mortalities from 11 researches in Africa and South America which were carried out between 1969 and 2011 was compiled and analysed. The results showed that for YF virus infections, the probability of a suspected case not showing symptoms was 55%, those with mild disease was 33% and severe disease 12%. The probability of dying for people suffering from severe disease was 47%. This demonstrates that in outbreak conditions where only severe cases may be primarily detected, it is projected that for every severe case identified, there may be up to seventy infections that are either asymptomatic or causing mild disease. As it is, only the most

severe cases are usually identified and reported. These estimates will therefore help people to better understand the disease burden of yellow fever and the estimation of the potential risk of spread in outbreaks situations (Johansson et al., 2014).

2.3 Global issues on yellow fever surveillance

Throughout history, before vaccines were developed, yellow fever outbreaks have been known to have serious impact on countries where they have occurred. Yellow fever was known to be *"decimating populations, paralyzing industry and trade, and holding the peoples of these regions in a state of perpetual dread of the Yellow Jack"*(Tomori, 2002). Through development of the yellow fever vaccine and eradication of the vector in countries like Cuba, UK and North America, yellow fever has been eradicated in these countries leaving a few endemic areas in Africa and South America.

Although yellow fever is endemic in Africa and South America, some cases have also been reported in Europe and Asia. Most of these cases were imported from Africa or South America. According to Bae, Hi-Gung et al (2005), the under reporting of yellow fever cases in the various regions and lack of international interest leads to an underestimation of the continual risk of transmission in Africa and South America. Travellers who have not been vaccinated are at risk without the effective protection of the YFV 17D vaccine (Bae et al., 2005). Yellow fever is a disease of public health concern globally due to urbanisation, industrialisation and international travel. In 2010, the *Aedes* mosquito, the known vector for yellow fever usually found in the tropics was found in Northern Europe. Investigations showed that they were usually found around corporate facilities where tires were imported from USA (Enserink, 2010).

There was an upsurge of yellow fever in the 1980s after several years of subsiding. Several reasons were attributed to this resurgence. These include interruption of immunization campaigns that had been instituted in the early 1960s in Francophone countries, urbanization, migration, deforestation and perhaps, climate change.

Africa has 34 yellow fever endemic countries; out of these, 23 are considered to be at high risk for an outbreak. It is not easy to estimate the burden of yellow fever using the conventional surveillance systems because there are many cases that do not present with the usual symptoms and those that present with symptoms are barely distinguishable from other infections such as malaria (which is very common in these parts), typhoid, schistosomiasis and even the dreaded Ebola Virus Disease. Underreporting of suspected yellow fever cases is of great concern since the true number of cases is estimated to be 10 to 250 times what is now being reported (Jentes et al., 2011).

In controlling outbreaks, it is imperative to promptly detect cases and to respond rapidly through emergency vaccination campaigns. WHO recommends that every country that is at risk of yellow fever should have at least one national laboratory where basic yellow fever blood tests can be run. For yellow fever, one laboratory-confirmed case in a community where the head immunity is low, is considered an outbreak. A confirmed case in any context must be fully investigated, especially in areas where most of the people living in that community have been vaccinated. Investigation teams must evaluate and respond to the outbreak with both emergency measures and long-term immunization plans (Jentes et al., 2011).

Case based surveillance has therefore been instituted in endemic countries through Integrated Disease Surveillance and Response (IDSR). This has proven to be more effective compared to the weekly or monthly reporting that was in place. According to WHO, in 2015 the case-based surveillance system identified 7299 suspected YF cases worldwide. Out of these, 6342 had blood samples tested in national laboratories.

According to Tomori (2002), yellow fever cases are on the increase again in Africa due to a number of factors including 1) break down of health care delivery systems; 2) lack of appreciation of the full impact of yellow fever disease on the socio-economic development of affected communities; 3) inadequate political commitment to yellow fever control by governments of endemic countries; 4) poor or inadequate disease surveillance systems; 5) inefficient disease control measures, and 6) avoidable poverty .together with misplaced priorities in resource allocation.

Subsequently, for yellow fever to cease being a public health problem, African countries should ensure that they attain the target of at least 80% coverage for routine yellow fever immunization. Also a there should be a reliable and sustainable disease surveillance system with a responsive disease control programme (Tomori, 2002).

The main aim of YF surveillance is early detection and control of outbreaks. The strategy being promoted in the African Region for an effective control of yellow fever is the establishment of a case-based surveillance system together with laboratory confirmation of cases and a robust vaccination programme. A total of 19 countries in Africa have established case-based surveillance; however, performance of this surveillance varies. Countries that have not yet put in

place a case-based surveillance system continue to report weekly aggregations of suspected cases to a central level.

According to WHO, performance of the key indicator in yellow fever surveillance has greatly improved but a lot of countries are still not meeting the target of 80%. Shortage of reagents in the lab has always caused a general fall in the number of suspected cases reported (International & Uni, 2008).

Yellow fever is a compulsory notifiable disease because of its high epidemic potential worldwide and it therefore requires immediate reporting. A research conducted in Brazil has shown that routinely, surveillance of YF is passive; however during epidemics, the active form of surveillance is employed. The Vector Borne Diseases Branch of the Brazilian Ministry of Health reveals that the overall annual incidence of YF since the 1930s has been 0.02 cases/100 000 persons/year with a case fatality rate (CFR) of approximately 45%. The actual number of persons infected with the yellow fever virus is however underestimated due to the lack of an effective surveillance system and underreporting of asymptomatic, mild and less severe forms of yellow fever which accounts for about 90% of all infections (Tuboi et al., 2007). The May 2016 edition of the WHO fact sheet on yellow fever says that a modelling study which uses African data sources projected the burden of yellow fever in 2013 to be 84 000–170 000 severe cases and 29 000–60 000 deaths. According to Bosa et al (2016), case-based YF surveillance among YF suspect cases and the malaria negative acute febrile illness pool could greatly increase the detection of YF cases (Bosa et al., 2016).

2.4 Dengue Heamorrhagic Fever and Yellow Fever

Dengue Heamorrhagic Fever (DHF), a viral heamorrhagic fever like yellow fever is also caused by a flavirus and spread by the Aedes Aegiptae mosquito. DHF and YF both have similar geographical distributions and similar impacts on society. Work done on DHF shows that the real public health impact of DHF and YF alike, occurs during epidemics of this disease. Owing to week surveillance practices, the early stages of epidemic transmissions usually go undetected. Before the epidemic is recognized, cases are usually not reported. However, getting to the peak of the epidemic when index cases have been identified, there is a hike in reporting of suspected cases. Control efforts are then directed at vaccination and emergency mosquito control activities. These efforts are most often misdirected, and are too little and too late to have any impact on the epidemic. The public health impact of DF/DHF or YF epidemics is therefore is sometimes amplified because surveillance and public health planning are poor and emergency response plans are not effectively executed (Gubler, 2002).

The successful *Aedes aegypti* control program in South America was part of the global success story against infectious diseases during the 1950s and 1960s. This resulted in some level of complacency among government and public health officials and the general public which eventually led to the erroneous perception that DF and YF were no longer diseases of public health importance. This ultimately led to the breakdown of public health infrastructure needed to deal with DF and YF and other vector-borne diseases. The effect DHF/YF outbreaks is felt more because clinical management of severe cases is not up to standard with no triage plans for patients. This results in overburdening of clinics and hospitals by patients with DF or with mild non-dengue illness, an overworked medical staff, sub-standard care for patients with the lethal

DHF/dengue shock syndrome, and often increased case fatality which eventually leads to the social distraction of the lives and activities of affected communities.

Table 1:

Estimated burden of dengue in 2010, by continent

	Apparent	Inapparent
	Millions (credible interval)	**Millions (credible interval)**
Africa	15.7 (10.5 - 22.5)	48.4 (34.3 - 65.2)
Asia	66.8 (47.0 – 94.4)	204.4 (151.8 – 273.0)
Americas	13.3 (9.5 - 18.5)	40.5 (30.5 - 53.3)
Oceania	0.18 (0.11 - 0.28)	0.55 (0.35 - 0.82)
Global	**96 (67.1 - 135.6)**	**293.9 (217.0 – 392.3)**

(Bhatt et al., 2013)

The financial burden of viral heamorrhagic fevers such as yellow fever and DHF have been difficult to quantify especially in developing countries. However, in Thailand the annual economic burden of DHF on the country has been estimated to range between US $31.5 and $51.5 million, based on which epidemic activities were undertaken. Nearly 45% of these costs are paid by the patients and their relatives; this financial burden also contributes immensely to the social impact of DHF and YF epidemics. These figures are gross miscalculations of the true economic impact of dengue because they do not measure the entire cost of large epidemics of flu-like illness on the economy. Some other losses incurred include lost work and productivity, absenteeism from work and school, loss of revenue from tourism and social disruption.

Moreover, the burden of these diseases caused by the virus during inter-epidemic periods has been completely ignored because of poor surveillance practices (Gubler, 2002).

While the historical spread of this disease is well documented, the potentially enormous burden of ill-health attributable to dengue across much of the tropical and sub-tropical areas remains poorly estimated. In a study conducted by Bhatt et al using cartographic methods, they estimated that there are 390 million (95% *CI*= 284-528) dengue infections per year, of which 96 million (67-136) show symptoms (any level of clinical or sub-clinical severity). This infection total is more than three times the burden of dengue estimated by the World Health Organization (Bhatt et al., 2013).

2.5 Hepatitis E and Yellow Fever

Hepatitis E virus (HEV) disease is a waterborne disease that is transmitted through the fecal-oral route whiles Yellow fever (YF) is transmitted to humans through infected *Aedes* mosquitoes which is the vector. Though the mode of transmission of the two diseases are different, they have very similar clinical presentations (i.e. fever, jaundice, malaise, and dark urine). However, they differ in severity and disease outcome. A cross-sectional survey was conducted by Ahmed et al (2016) to estimate the measure association of concomitant YF and HEV infection in Darfur States during the outbreak of YF in 2012 in the region. Findings showed that there was concomitant outbreaks of YF and HEV at the same time with very weak statistical correlation between the two infections during the outbreak period. This poor correlation results proves that clinicians and care providers in tropical areas have to deal with clinical case definitions used for

disease surveillance very carefully since the occurrence of HEV infection is comparatively more common and this increases the likelihood of misclassification and missing of suspected YF cases, especially the index case, in a season or outbreak. This further establishes how important it is for clinicians, epidemiologists, and other healthcare providers to carefully set the operational surveillance case definitions and management plans, especially during heath emergencies and disease outbreaks (Ahmed et al., 2016).

CHAPTER THREE

3.0 Methodology

3.1 Study Design and Location

The study was a cross sectional survey of clinicians and disease control/disease surveillance officers involved in clinical practice and surveillance activities respectively in government, quasi-governmental and private hospitals in the Greater Accra Region of Ghana. The Greater Accra Region was chosen because of its low surveillance performance indicators and also because of its cosmopolitan nature and the rates of rural-urban migration to and from the region.

The study population was made up of clinicians who are directly involved in attending to patients within the past one year in the region and the disease control/surveillance officers who have been working in the region for at least one year. One year was chosen to reduce recall bias. The population of the Greater Accra region is 4,010,054 (GSS, 2012) with a doctor to patient ratio of one doctor to 9,939 patients (MOH, 2009). The region currently has 16 administrative and 21 operational districts with about 827 hospitals. These hospitals are classified as government, quasi-government and private facilities.

3.2 Study Variables

The main construct for the study is the dependent variable, reporting of suspected yellow fever cases. The independent variables such as availability and accessibility of reporting tools, support activities, investigation of jaundice cases, processes involved in investigating and reporting a suspected case and feedback to all levels are used in the study to establish the determinants of detection and reporting of suspected yellow fever cases by clinicians and disease control officers.

Table 2: Independent variables and indicators

Independent Variable	Indicator
Availability and accessibility of reporting tools	Availability of: Printed case definition in the consulting room Case notification forms in the consulting room Case investigation form Line listing form Weekly and monthly IDSR forms
Support activities	Number of trainings held Number of clinician sensitization
Investigation of jaundice cases	Proportion of jaundice cases investigated for yellow fever
Processes involved in investigating and reporting a suspected case	Availability of cold chain equipment Availability of transportation for sample collected
Feedback to all levels	Feedback sent to sub district and reporting facilities and clinicians

3.3 Sample size determination

The sample size determination was based on the formula;

$n = Z^2P(1-P)/d^2$

where n = sample size,

Z = Z statistic for a level of confidence (at 95% Confidence Interval)

P = expected prevalence and

d = precision [this is fixed at 5% (i.e. 0.05)]. There is no information about the prevalence of underreporting or an estimate of unreported suspected YF cases in the Greater Accra Region. Therefore assuming 50% (i.e. 0.5) of underreporting in the region and a precision of 0.05 at 95% confidence interval, the maximum sample size obtained using the formula is 384.

3.4 Sampling and data collection

The required sample size of 384 for the study was obtained by a convenient sampling of clinicians from the total population of clinicians involved in clinical practice in about 827 facilities and the total population of disease control/surveillance officers in the Greater Accra Region. Eighteen out of the 21 district control officers of the 21 operational districts were interviewed. Facilities from which clinicians were selected was grouped into government, quasi-government and private hospitals. The facilities in which questionnaires were administered was selected from these three levels. The inclusion criteria for a clinician to participate in the study was that s/he must be directly involved in the management of patients for at least one year. Clinicians who are only involved with administrative work was excluded from the study. A structured anonymous questionnaire (Appendix 1) was administered to all participants in the

3.5 Data Collection Techniques and Tools

Data collection was from May 22, 2017 to July 2, 2017. A semi-structured self-administered anonymous questionnaire (Appendix 1) was distributed to 384 clinicians in 31 different hospitals. The questionnaire was a two paged document that contained three sections. A separate three paged questionnaire was administered to the disease control officers. Information was collected on availability and accessibility of reporting tools, support activities such as clinician sensitization, investigation of jaundice cases, processes involved in investigating and reporting a suspected yellow fever case such as availability of cold chain equipment and transportation for sample collected and feedback to and from all levels.

The questionnaire was delivered to the doctors and prescribers in their consulting rooms after permission was sought from the head of the facility. A brief explanation of the study objectives, overview of the questionnaire and assurance of confidentiality was provided to the clinicians before their participation. Agreement to complete the questionnaire was taken as an informed consent to take part in the study.

3.6 Quality Control

The survey questionnaire was pretested to determine its appropriateness and suitability for the study. The pretesting resulted in correction, rephrasing and rearrangement of sentences and sections in the questionnaire. In order to ensure uniformity of the process, the two research assistants involved in the study were trained on how to explain the study objectives and overview of the questionnaire to the clinicians. To improve the response rate, the questionnaires were made with mainly checkboxes and a comment sections. The clinicians and disease control

officers were requested to complete the questionnaires in the presence of the investigator or study assistants. However, doctors who preferred to complete the questionnaires later were given some time and revisited in a few days for collection. Questionnaires not completed after revisit was considered a non-response.

3.7 Data Processing and Analysis

All questionnaires were cross-checked, edited and numbered before data entry. A data entry template was created for the questionnaire using Epi Info 7 and data entered unto this template. Data was then cleaned by running frequencies to check for double entries and inconsistencies. All errors thus detected were corrected before data analysis begun.

Data was analysed using STATA Version 14. Descriptive statistics was performed using frequencies and proportions. Chi squared test and simple logistic regression was used to test for the association between the dependent variables (detection and reporting of suspected YF cases) and independent variables. Multiple regression was used to test for the strength of association between the variables that prove significant in the analysis using the Chi squared test. The results was expressed as chi-squared, p-values, odd ratios and corresponding confidence intervals. A p-value ≤ 0.05 was considered statistically significant.

The proportion of clinicians and disease control/surveillance officers reporting suspected yellow fever cases was calculated by dividing the number of clinicians and disease control/surveillance officers who had reported a suspected yellow fever case in the past one year prior to the study divided by the total number of clinicians and disease control/surveillance officers who had seen a

patient with fever and jaundice but did not report. The factors perceived by clinicians and disease control/surveillance officers as contributing to low detection and reporting of suspected yellow fever cases were determined by multiple response to questions such as lack of time and heavy workload, unaware of the reporting procedure, availability of reporting tools, lack of training/sensitization, availability of cold chain equipment and transportation for collected samples, poor feedback and lack of confidence in the reporting system.

3.8 Ethical considerations

Ethical approval was sought from the Ghana Health Service Ethical Review Committee of the Research and Development Division of the Ghana Health Services for the conduct of the study. The identity of the clinicians and disease control officers who completed the questionnaires were kept confidential and their consent was sought before participation in the study. There was minimal or no risk associated with participation in this study and no compensation was paid to the participants.

CHAPTER FOUR

4.0 RESULTS

This chapter presents the results of the study. It provides information about reporting of yellow fever (YF) cases by both clinicians and Surveillance officers as well as identifies the factors that are associated with detection and reporting of suspected yellow fever cases in the Greater Accra Region.

4.1 Surveillance and Reporting Information by Clinicians

A total of 371 questionnaires were administered to clinicians in Greater Accra region and all were successfully recovered. Table 4.1 presents the surveillance and reporting information of clinicians. Approximately, 56.6% of the clinicians attended sensitization workshops as compared to 43.4% who never attended any clinician sensitization workshop on IDSR or surveillance of priority diseases as at the time of the study. Majority of the clinicians (77.9%) had case definition posters or booklets in their consulting room with more than half (51.5%) having access to case notification forms. Also, more than two-thirds of the respondents (69.8%) sent no notification forms of other diseases to the Public Health Unit (PHU) within a month with just a few (30.2%) that sent at least one notification form. About 65.2% of the clinicians reported that they had good inter-personal relationship with the disease control/surveillance officers as opposed to those who were neutral. However, approximately 89.2% of the clinicians sent no notification forms for suspected YF cases to the disease control/surveillance officer. More than three-quarters of the clinicians (87.3%) were able to detect cases of fever with jaundice relative to the few (12.7%)

that did not. About two-thirds of the clinicians (67.7%) were working in government facilities as opposed to those working in both quasi-government (8.6%) and private facilities (23.7%).

Table 4.1 Surveillance and Reporting Information by Clinicians (n=371)

Characteristics	Frequency	Percent (%)
Attended Sensitization workshops		
Yes	210	56.6
No	161	43.4
Availability of reporting tools		
Yes	289	77.9
No	82	22.1
Accessibility of reporting tools		
Yes	191	51.5
No	180	48.5
Number of case notification forms sent to PH unit monthly		
None	259	69.8
1-3	110	29.7
4-6	2	0.5
Relationship with Public Health Unit		
Cordial	242	65.2
Neutral	98	26.4
Others	31	8.4
Case notification forms sent for suspected YF cases		
None	331	89.2
1-3	40	10.8
Number of fever with Jaundice cases recorded		
None	46	12.4
1-3	317	85.4
4-6	5	1.4
7-9	3	0.8

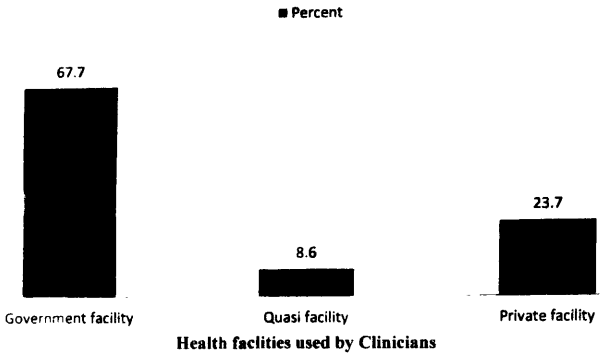


Figure5: Type of health facilities used by Clinicians in Greater Accra Region

4.1.1 Surveillance and Reporting Information of Disease Control or Surveillance Officers

Questionnaires were also administered to 18 Surveillance or Disease Control officers in addition to the clinicians. Approximately 83.3% provided case definition tools to clinicians with only 66.7% receiving reports from the clinicians. More than half (53.6%) responded that they reviewed records in the consulting room registers daily as compared to the few who reviewed records twice a week (16.7%) and on weekly basis (27.8%). About 61.1% confirmed that they were able to identify cases of fever with jaundice within the last 6 months as at the period the study was conducted with only 44.5% of those cases investigated. More than half (55.6%) of the Disease Control/Surveillance officers never gave feedbacks to the clinicians after doing record review or investigating cases. All the officers surveyed confirmed that they had yellow fever case based forms, weekly IDSR forms, access to DHIMS II and access to internet for reporting of diseases/events. Table 4.2 summarized the above findings.

Table 4.2 Surveillance and Reporting Information of Surveillance Officers (n=18)

Characteristics	Frequency	Percent (%)
Provision of case definition/notification tools		
Yes	15	83.3
No	3	16.7
Receives notification or reports from clinicians		
Yes	12	66.7
No	6	33.3
Number of times consulting room registers are reviewed		
Daily	10	55.6
Twice a week	5	27.8
Weekly	3	16.7
Sign in registers after reviewing the records		
Yes	13	72.2
No	2	11.1
Sometimes	3	16.7
Identified fever with jaundice case within the last 6months		
Yes	10	55.6
No	8	44.4
Number of fever with Jaundice cases investigated		
All	5	27.8
Some	3	16.7
None	10	55.6
Have notification forms		
Yes	12	66.7
No	6	33.3
Have Yellow Fever case based forms		
Yes	18	100
Have weekly IDSR forms		
Yes	18	100
Monitor timeliness and completeness of forms from facilities/sub district		
Yes	18	100
Have access to DHIMS II		
Yes	18	100
Have access to internet		
Yes	18	100

4.2 Proportion of fever with jaundice cases reported as suspected cases of yellow fever by clinicians

According to WHO definition of suspected yellow fever, a case that is characterized by acute onset of fever followed by jaundice within two weeks of the onset of the first symptoms can be considered to be a suspected case. In that light, the suspected cases of yellow fever in Greater Accra region as shown by Figure 2 was approximately 88.0% since approximately 87.6% cases of fever with jaundice were detected by the clinicians in the region. However, Figure 3 brought to light that out of the 88.0% suspected cases; only 10.8% were reported to the Public Health Unit.

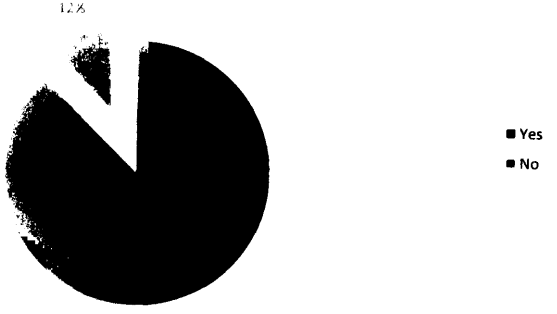


Figure 6: Distribution of detected suspected Yellow Fever cases in Greater Accra Region from Jaundice cases by Clinicians

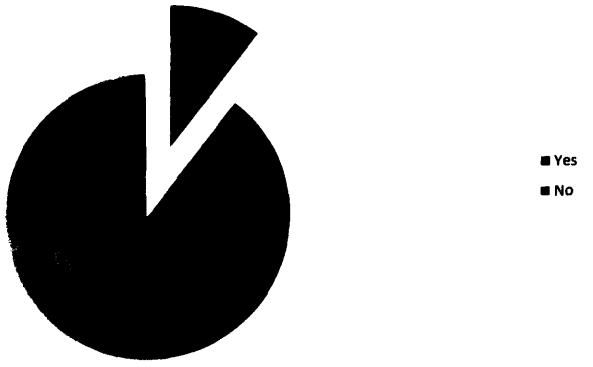


Figure 7: Distribution of reported suspected Yellow fever cases by Clinicians

4.3 Reasons for non-notification according to clinicians

The reasons why clinicians hardly notify PHU or Disease Control officers on suspected yellow fever cases were further determined. It was discovered that more than half (53.2%) of them asserted that they do not suspect yellow fever; whereas others attributed non-notification of suspected unawareness of reporting procedures (25.2%), poor feedbacks (9.0), lack of sensitization (6.9%), heavy load (3.9) and lack of confidence in the reporting system (1.8%). Table 4.3 presents the reasons for non-notification by clinicians.

Table 4.3 Reasons for non-notification according to clinicians

Reasons for non-notification	Frequency	Percentage
Do not suspect Yellow fever	177	53.2
Unaware of the reporting procedure	84	25.2
Poor feedback	30	9.0
Lack of sensitization	23	6.9
Heavy work load	13	3.9
Lack of confidence in the reporting system	6	1.8

4.4 Evaluation processes involved in investigating suspected Yellow fever cases by Disease Control/Surveillance officers

About 14 out of the 18 of the Disease Control officers responded that they took blood samples upon suspecting yellow fever; with more than half (61.1%) confirming that fill three case based forms for every blood sample taken as compared to those who fill two forms (38.9%). Majority of the officers (88.9%) send blood samples taken the same a day to the lab with none of them batch processing samples. All of the officers responded that they always filled case based forms for samples taken, probed vaccination status before filling case based forms, maintained the cold chain in storing and transporting sample and had means of transport in sending sample to the next level. About 77.8% received feedbacks for sample sent for testing and all also gave back test to clinicians. However, only 5 out of the 18 officers were able to report suspected yellow fever case in the last 12 months.

Table 4.4 Evaluation process involved in investigating suspected Yellow fever cases by Surveillance or Disease Control Officers (*n*=18)

Characteristics	Frequency	Percent (%)
Evaluating processes involved in investigating		
Take blood sample for suspected YF		
Yes	4	22.2
No	14	77.8
Always fill a case based form for samples taken		
Yes	18	100
Number of filled case based forms		
3	11	61.1
2	7	38.9
Keep copy of cased based forms		
Yes	18	100
Probe vaccination status before filling case based forms		
Yes	18	100
Length of time used in keeping sample before sending to the next level		
Same day	16	88.9
Within 3 days	2	11.1
Batch processing of sample		
No	18	100
Maintain the cold chain in storing and transporting sample		
Yes	18	100
Means of transportation used in sending sample to the next level		
Yes	18	100
Received feedback for sample sent for testing		
Yes	14	77.8
No	4	22.2
Gives back to the clinician who notified or requested for the test		
Yes	14	77.8
No	4	22.2
Reported suspected YF cases in the last 12 months		
Yes	5	27.8
No	13	72.2

4.5 Factors associated with detection of suspected yellow fever cases

A key objective of the study was to identify the factors that influence the detection of suspected yellow fever cases. Hence, a bivariate analysis was carried out to examine the association between possible factors and detection of YF cases. It was revealed that investigation of fever with jaundice cases ($p<0.001$) as well as reporting of suspected cases ($p<0.001$) had significant influence on the detection of yellow fever as well as notification. Results of the bivariate association are presented in Table 4.5.

Table 4.5 Factors associated with detection of suspected yellow fever cases (n = 371)

Variable	Detected Yellow Fever Cases		χ^2
	Yes	No	*P*-value
Identification of fever with jaundice cases			
None	16(34.8)	30(65.2)	<0.001
1-3	30(9.1)	301(90.9)	
Utilization of notification cases definition			
Yes	32(11.1)	257(89.9)	0.146
No	14(17.1)	68(82.9)	
Sending of notification forms			
Yes	30(75.0)	10(9)	<0.001
No	35(10.6)	296(89.4)	
Attended sensitization workshops			
Yes	32(15.2)	178(84.3)	0.058
No	14(8.7)	147(91.3)	

4.5.1 Logistic regression analysis on significant factors that affects the detection of suspected yellow fever

In order to further explore the strength of association between the two significant factors and the detection of yellow fever, simple and multiple regression models were fitted so as to compute both the crude and adjusted odds ratios respectively.

Table 4.6 Logistic regression of significant factors that influence the detection of suspected yellow fever cases

Variable	Crude *OR*(95% *C.I*)	*P-value*	Adjusted *OR* (95% *CI*)	*P-value*
Identification of fever with jaundice (*ref*: None)*				
1-3 fevers with jaundice	1.15 (1.07-1.23)	<0.001	1.12 (0.01-1.41)	0.092
Sending of notification forms (*ref*: Yes)**				
No	0.18 (0.09-0.38)	<0.001	1.23 (0.11-14.00)	0.865

***Adjusted for Sending of notification forms**
***Adjusted for Identification of fever with jaundice**

Table 4.7 Factors associated with reporting of suspected yellow fever cases (n = 371)

Variable	Reported Cases of YF		χ^2
	Yes	No	*P-value*
Attended sensitization workshops			
Yes	199(94.8)	11(5.2)	<0.001
No	133(82.6)	28(17.4)	
Availability of reporting tools			
Yes	272 (94.1)	17(5.9)	<0.001
No	60(73.2)	22(26.8)	
Accessibility of reporting tools			
Yes	180(94.2)	11(5.8)	0.002
No	152(84.4)	28(15.6)	
Relationship with PH unit /DH Administrator			
Cordial	219(90.5)	23(9.5)	0.016
Neutral	82(83.7)	16(16.3)	
Others	37(100.0)	0(0.0)	
Number of fever with jaundice case			
None	30(65.2)	16(34.8)	<0.001
1-3	298(94.0)	19(6.0)	
4-6	1(20.0)	4(80.0)	
7-9	3(100.0)	0(0.0)	

4.6.1 Logistic regression of significant factors that influence the reporting of yellow fever cases

Also, the strength of the association of all the significant factors was further assessed by estimating both the crude and adjusted odds ratios from a fitted logistic model. The most significant variables that influenced the reporting of suspected yellow fever cases were number of fever with Jaundice cases recorded (*OR*=31.7, 95% *CI*=2.78-362.73) attending of sensitization workshops (*OR*=15.02, 95% *CI*=3.88-58.14) and availability of reporting tools (*OR*=7.41, 95% *CI*=2.76-19.89).

Table 4.8 Logistic regression of significant factors influence the reporting of yellow fever cases (n = 371)

Variable	Crude *OR*(95% *C.I*)	*P-value*	Adjusted *OR* (95% *CI*)	*P-value*
Attended Sensitization workshops	**(*ref*:No)**			
Yes	3.81(1.83-7.91)	<0.001	15.02(3.88-58.14)	0.001
Availability of reporting tools	**(*ref*: No)**			
Yes	5.87(2.94-11.72)	<0.001	7.41(2.76- 19.89)	0.001
Accessibility of reporting tools	**(*ref*: No)**			
Yes	3.01(1.45-6.26)	0.003	0.71(0.19-2.74)	0.623
Relationship with Public Health Unit/DH Administrator (*ref*: Cordial)				
Neutral	1.86(0.93-3.69)	0.077	0.43(0.12-1.52)	0.190
Number of fever with Jaundice cases recorded (*ref*: None)				
1-3	0.12(0.06-0.26)	<0.001	0.05(0.04-0.19)	0.001
4-6	7.50(0.77-72.87)	0.082	31.7(2.78-362.73)	0.005

CHAPTER FIVE

5.0 DISCUSSION

The objective of this study was to determine factors associated with detection and reporting of suspected yellow fever cases in the Greater Accra Region and the proportion of fever with jaundice cases that are reported as suspected yellow fever cases.

5.1 Interpretation of fitted regression model

5.1.1 Identification of fever with jaundice (*ref*: None)

Clinicians who had identified 1 to 3 fever with jaundice cases were approximately 1.15 times more likely to detect yellow fever as compared to those who identified no case. This can also be interpreted as the chance of detecting yellow fever case among clinicians who identified 1 to 3 fevers with jaundice cases were approximately 15% greater than those who did not identify any case. After adjusting for the sending of notification forms, the association between identification of fever with jaundice and detection of yellow fever was no longer significant (p=0.092)

5.1.2 Sending of notification forms (*ref*: Yes)

The odds of detection of yellow fever cases among those who did not send notification were 82% lower than those who sent notification forms. (*OR*=0.18, 95% *CI*=0.09-0.38). After controlling for the identification of fever with jaundice, the association between sending of notification forms and detection of yellow fever was no longer significant (p=0.0865).

5.2 Interpretation of significant factors influencing the reporting of yellow fever cases

5.2.1 Attending of Sensitization workshops (*ref*: No)

Clinicians who attended sensitization workshops approximately 15 times more likely to report on suspected cases relative to those who did not (*OR*=15.02, 95% *CI*=3.88-58.14) were.

5.2.2 Availability of reporting tools (*ref*: No)

Clinicians with reporting tools such as case notification forms were approximately 7.41 times more likely to report on suspected yellow fever cases as opposed to those who did not have (*OR*=7.41, 95% *CI*=2.76-19.89).

5.2.3 Accessibility of reporting tools (*ref*: No)

Clinicians who had access to reporting tools were approximately 3 times more likely to report on suspected yellow fever cases as compared to those who did not have a reporting tool (*OR*=3.01, 95% *CI*=1.45-6.26).

5.2.4 Number of fever with Jaundice cases recorded (*ref*: None)

Clinicians who were able to identify fever with jaundice case were 88% times less likely to reporting on suspected yellow fever cases relative to those who identified no fever with jaundice case (*OR*=0.12, 95% *CI*=0.06-0.26). Adjusted analysis showed that the chance of reporting suspected yellow fever cases by a clinician who identified 4 to 6 cases of fever with jaundice is higher than those who recorded 1 to 3 cases.

5.3 Factors associated with reporting of suspected yellow fever cases

Another principal aim of this study was to determine the factors that influence the reporting of suspected yellow fever cases by clinicians. Similarly bivariate associations were conducted. It was found that attending sensitization workshops ($p<0.001$), availability of reporting tools ($p<0.001$), accessibility of reporting tools ($p<0.01$), relationship with public health or DH administrator ($p<0.05$) and number of fever with jaundice cases identified ($p<0.001$) were significant factors affecting the reporting of suspected yellow fever cases by clinicians

5.4 Proportion of fever with jaundice cases reported as suspected yellow fever cases

The use of the surveillance case definition is paramount in the detection and subsequent reporting of suspected yellow fever cases. Findings in this study indicate that proportion of fever with jaundice cases, which is the WHO case definition for yellow fever, detected in consulting rooms that were reported as suspected yellow fever cases was only 10.8%. This is an indication that suspected yellow fever cases are grossly underreported. This finding is in concordance with results of the study by Johansson et al, 2014 in which outbreaks in Africa and South America were evaluated. It was found out that for yellow fever virus infections, the probability of being asymptomatic was 0.55 (95% credible interval [CI] 0.37– 0.74), mild disease 0.33 (95% CI 0.13–0.52) and severe disease 0.12 (95% CI 0.05–0.26). The study therefore concluded that during yellow fever outbreaks only the severe cases may initially be detected. They estimated that for every confirmed case identified, there could be from one to as much as seventy mild or asymptomatic case (Johansson et al., 2014).

This implied that only 1.4% of cases get recognized and reported. According to Johansson et al., 2014, "*like many infectious agents, yellow fever (YF) virus only causes disease in a proportion of*

individuals it infects and severe illness only represents the tip of the iceberg relative to the total number of infections, the more critical factor for virus transmission" (Johansson et al., 2014).

Often times, yellow fever cases are misclassified because of the vast number of differential diagnosis. Findings in this study showed that 86.7% of clinicians detected fever with jaundice cases in their consulting rooms but do not report them as suspected yellow fever cases. Studies conducted in Dhafur, Sudan by Ahmed et al (2012) showed that concomitant outbreaks of yellow fever and hepatitis E, which is one of the differentials of yellow fever, occurred during the outbreak of yellow fever in 2012 at the same time with very weak statistical correlation between the two infections during the outbreak period, with Cramer's V correlation 0.05 and insignificant p value of 0.86. This correlation indicated that clinicians in yellow fever endemic areas are to apply the surveillance case definition very carefully since prevalence of hepatitis E infection is relatively common and this increases the possibility of misclassifying or missing yellow fever cases, especially the index case in an outbreak. This is also in congruence with findings by Otshudiema et al, during the 2015 -2016 outbreak in the DRC, malaria, viral hepatitis, and typhoid fever are common differential diagnoses among suspected yellow fever cases and this leads to underreporting of the disease (Otshudiema et al., 2017).

5.5 Factors Associated with Detection and Reporting of Suspected YF Cases

In assessing the factors that were associated with detection of suspected yellow fever, two factors, i.e., identification of fever with jaundice case and sending of notification forms were found to be significant from the bivariate analysis with $p<0.001$. But upon adjusting for each value in the regression model, the adjusted odd ratios of 1.12 (0.01-1.41) p=0.092 and 1.23(0.11-14.00) p=0.865 showed that none of the factors considered to be associated with the detection of

suspected yellow fever cases in this study were significant. However, clinician sensitization, availability of reporting tools and number of fever with jaundice cases recorded were found to be significant factors associated with the reporting of suspected yellow fever cases with adjusted odds ratios 15.02(3.88-58.14), 7.41(2.76- 19.89) and 0.05(0.04-0.19) respectively and p values of <0.001.

5.6 Sensitization and YF surveillance system in the Greater Accra Region

Detection and reporting of suspected yellow fever cases and the general surveillance of yellow fever depends largely on the Public Health Units (PHU) of districts and facilities. The PHU has the mandate to train/sensitize clinicians on the use of the surveillance case definitions and the need to report all suspected cases. The PHU is also supposed to provide reporting tools such as case notification forms, to ensure that samples of suspected cases are taken and sent to the National Public Health and Reference Laboratory (NPHRL) for testing. Disease control officers are also supposed to conduct frequent record reviews of the consulting room registers to identify suspected cases which they may not have been notified of and to take the necessary steps in investigating such cases. Based on the responses of the disease control officers, surveillance of yellow fever in the region was fairly good according to the former Director General of WHO, Margaret Chan there is the need to practice enhanced surveillance to be able to identify all suspected yellow fever cases using the surveillance case definition and to forestall future outbreaks ("full-text," n.d.).

When clinicians are well sensitized on the need to report all suspected yellow fever cases based on the surveillance case definition, there would be an increase in number of suspected cases reported. However, this surge in reporting of suspected cases should not be hampered by lack of

reporting tools such as notification forms or case based forms. The PHU of facilities and the DHMA should therefore make available at all times these reporting tools. Finally, sensitized clinicians being able to identify fever with jaundice cases would invariably lead to the desired increase in suspected yellow fever cases reported.

Eighteen of the 21 District Disease Control Officers of the 21 operational districts of the Greater Accra Region were interviewed to assess the surveillance systems run and how they facilitate the detection and reporting of suspected yellow fever cases. All disease control officers interviewed said they had reporting tools i.e. Yellow Fever Case Based Forms, Weekly and Monthly IDSR Forms and 66.7% said they had case notification forms. All disease control officers said they conducted record reviews. 55.6% said they had identified fever with jaundice cases within the last 6 months but out of these, only 27.8% said they had investigated all such cases; 16.7% said they had investigated some and some were lost to follow up. All officers interviewed also said they had adequate transportation for sending samples to the NPHRL and none did batch processing of samples. Though clinicians complained that feedback for samples sent was very poor, 77.8% of disease control officers reported that they gave feedback to clinicians whenever available.

5.7 Proposed method of control

Most studies advocate enhance surveillance as a means of detecting cases and forestalling future outbreaks of yellow fever. According to Oyewele et al (2011), the four strategies proposed for the prevention and control yellow fever are:

1) improving on routine immunization coverages

2) enhanced surveillance

3) prevention of outbreaks and

4) prompt response to outbreaks

According to studies done by Tomori et al, all countries that are at risk are required to establish a *"continued and sensitive surveillance system for early detection of YF cases as a prerequisite for institution of rapid response to contain any potential outbreak. Laboratories with capability for differential diagnosis are also essential because of the difficulties in distinguishing YF from other diseases with similar symptoms such as hepatitis, malaria, typhoid fever and other febrile jaundice"* (Tomori, 2002).

5.8 Limitations of the study

Due to limitations of time and funds, a convenient sampling of clinicians had been done from the facilities classified as government, quasi government and private. Hence it may not be possible to generalize the study to all clinicians in the region since those who participated in the study were selected by convenient sampling. A more meticulous way of sampling would have been to obtain a list of clinicians working in these categories of facilities and the number of clinicians interviewed divided proportionally. Then the clinicians to be interviewed selected randomly from these proportions.

Secondly, factors associated with self-reporting studies such as accuracy of recall and personal bias may affect the study. It may be difficult for some of the clinicians to remember the number

of fever with jaundice cases they may have seen in recent times and how many were investigated during their practice this was however minimized by use of one year recall period.

Thirdly, limited information on background characteristics of study participants were collected. Due to limited time frame of the study, health service related characteristics deemed directly affecting detection and reporting of suspected yellow fever cases were considered. Further studies could explore more background characteristics to determine which factors would be directly affect detection of suspected yellow fever cases.

Finally, some questionnaires were completed in the presence of research assistants whiles others were completed by clinicians alone. This can cause social desirability, information and selection biases and also uncontrolled confounder effect.

5.9 Need for further studies

According to Margaret Chan, the Director General of WHO, the recent confirmation of yellow fever in the capital cities of Angola and the Democratic Republic of the Congo (DRC) has raised grave concerns about urban outbreaks of yellow fever. The demography and land use patterns in West Africa have generated ideal conditions for explosive outbreaks of urban yellow fever. Individuals who have migrated from rural areas, and people working in mines and on construction sites, can now easily carry the virus into urban areas with low herd immunity and dense populations. These factors coupled with heavy infestations of mosquitoes adapted to urban life, and weak infrastructures that make mosquito control almost impossible for effective vector

control. Lax migratory procedures and air travel around the world further complicates the response activities.

"The world has had a safe, low-cost yellow fever vaccine that confers long-duration immunity since 1937. WHO has robust preparedness and response mechanisms in place, including an international coordinating group that oversees the emergency release of vaccines, but the key question is whether they will be sufficient to control the outbreaks quickly and prevent further international spread." ("full-text," n.d.)

More work needs to be done in individual member states to determine why there is a resurgence of this erstwhile dormant disease. Issues like gaps in surveillance systems and why index of suspicion for a disease with many fairly common differentials such as malaria, anaemia, typhoid fever, hepatitis etc. is so low, should be addressed. This study seeks to identify gaps in the surveillance system which does not encourage detection and subsequent reporting of suspected yellow fever cases in the Greater Accra Region.

CHAPTER SIX

6.1 Conclusion

Although clinicians in the Greater Accra Region see a lot of fever with jaundice cases in their consulting rooms, which is the surveillance case definition for a suspected yellow fever case, this does not translate to the number of suspected cases reported. From this study, even though about 57% of clinicians have been sensitized and have reporting tools, the index of suspicion is very low due to the low prevalence of the disease. In addition, only 10% of cases that fit the suspected yellow fever case definition seen get reported and investigated and the main reasons for non-reporting are that clinicians do not suspect yellow fever cases (53.2%) or are unaware of the reporting system (25.2%).

6.2 Recommendations

Based on the results of the study the following recommendations are made;

- District Health Directorates should further sensitize clinicians on the application of the surveillance case definition for yellow fever and the need to report all such cases
- The Public Health Unit should make case notification forms readily available and accessible in all consulting rooms and wards
- Every report submitted by a doctor should be acknowledged by the Public Health Unit and a feedback provided on actions taken and the results
- Clinicians should be sensitized more through workshops, continual education and even through social media on the need to adhere to and apply the WHO surveillance case definition for a suspected yellow fever case in the identification of suspected yellow fever cases.

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APPENDICES

INFORMED CONSENT FORM

FACTORS ASSOCIATED WITH DETECTION AND REPORTING OF SUSPECTED YELLOW FEVER CASES IN THE GREATER ACCRA REGION

Institutional Affiliation:

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

Telephone Number: 0303970990

Personal Introduction:

My name is Magdalene Norkai Sayah, a student of the Epidemiology Department of the School of Public Health, University of Ghana.

I am conducting a study on"Factors Associated with Detection and Reporting of Yellow Fever Cases in the Greater Accra Region". Two research assistants are helping me carry out this study.

General information about the study

This is a research study undertaken as a requirement in the University of Ghana, School of Public Health, in pursuance of a Masters degree in Public Health. This study therefore is intended to find out which factors affect the detection and subsequent reporting of yellow fever cases in the region. The study would therefore explain the general Yellow Fever surveillance performance indicators as reported in the Greater Accra Region.

We will ask you questions about how and why you suspect a case to be Yellow Fever and the case or otherwise of reporting.

Possible Risks and Discomforts

The study will not involve any risk even though there may be some discomfort in answering some of the questions. You are free to ignore any question you are not comfortable with.

Possible Benefits

A copy of the dissertation would be submitted to the Disease Surveillance Department of the Public Health Division of the Ghana Health Service. Issues raised in this study would help address gaps in the identification of suspected cases and the reporting channels thereby strengthening the whole surveillance system in the region. Additionally, it can form a basis for a national policies for the whole disease surveillance system in Ghana as a whole.

Voluntary Participation and Right to Refuse

Your participation in this study is voluntary. During the filling of the questionnaire, you can choose to ignore any question that you are uncomfortable with and also at liberty to withdraw from the study at any time. However, we will encourage you to participate and complete the questions since your opinions are invaluable to us.

Confidentiality

Your name and identity are not needed for the study. All the information you give will be treated with strict confidentiality. All the information and the data will be stored in a locked cabinet.

Access will be limited to only me and my research supervisor. Electronic data would be password protected. I assure you that your name shall not appear or be mentioned in any report that might come out from this study.

Contact for Additional Information

If you have further questions, you may contact:

Magdalene Norkai Sayah

Department of Epidemiology and Disease Control,

School of Public Health, College of Health Sciences

University of Ghana

P. O. Box LG 73, Legon

Mobile: 0268989969, 0275787979

Email: mnsayah@st.ug.edu.gh

Your rights as a Participant

If you have any questions about your rights as a participant in this study, you can contact the Administrator of the GHS Ethical Review Committee at the following address:

Madam Hannah Frimpong

GHS-Ethical Review Committee

Research and Development Division

Ghana Health Service

P. O. Box MB 190

Accra

Office: 0302 681 109

Mobile: 024 451 6482

E mail: Hannah.Frimpong@ghsmail.org

Volunteer Agreement

I _____, declare that the above document describing the purpose, procedures as well as risks and benefits of the research titled "Factors Associated with Detection and Reporting of Suspected Yellow Fever Cases in the Greater Accra Region" has been thoroughly explained to me in English language. I have been given the opportunity to ask any questions about the research and answered to my satisfaction. I hereby voluntarily agree to participate as a subject in this study.

_____ ____/____/_____

Signature of Participant Date

Interviewer's statement

I, _____, certify that the nature and purpose, the potential benefits and possible risks associated with participating in the study have been explained to the above individual in the English language. The participant has freely agreed to participate in the study.

_____ _____/____/_____

Signature of person who obtained consent Date

Questionnaire:

- Assessing use of surveillance case definition by clinicians for notification and Surveillance Officers for investigation of suspected yellow fever cases

Questions

For clinicians

1. Do you have surveillance case definition posters in your consulting room?

   ☐ Yes ☐ No

2. Do you have case notification forms in your consulting room?

   ☐ Yes ☐ No

3. Approximately how many case notification forms do send to the Public Health Unit in a month? ☐ None ☐ 1 – 3 ☐ 4 – 6 ☐ 7 – 9 ☐ 10 and above

4. How many case notifications do you send for suspected yellow fever?

   ☐ None ☐ 1 – 3 ☐ 4 – 6

   ☐ 7 – 9 ☐ 10 and above

5. On the average, how many fever with jaundice cases do you see in your consulting room in a month? ☐ None ☐ 1 – 3 ☐ 4 – 6

   ☐ 7 – 9 ☐ 10 and above

6. Reasons for non-notification

   ☐ Heavy workload ☐ Unaware of the reporting procedure ☐ Lack of sensitization

   ☐ Poor feedback ☐ Lack of confidence in the reporting system

For Disease Control/Surveillance Officers

1. Have you provided case definition posters for the consulting rooms?

   ☐ Yes ☐ No

2. Do you receive case notifications from clinicians?

   ☐ Yes ☐ No

3. How often do you do record review of the consulting room registers?

   ☐ Daily ☐ Twice a week ☐ Weekly

   ☐ Fortnightly ☐ Monthly ☐ Quarterly

4. Do you sign in the registers after reviewing the records?

   ☐ Yes ☐ No

5. How many fever with jaundice cases have you identified in the last 6 months?

   ☐ None ☐ 1 – 3 ☐ 4 – 6

   ☐ 7 – 9 ☐ 10 and above

6. How many have you investigated? ☐ All ☐ Some ☐ None

7. If not all, why?

- Determining the availability and accessibility of reporting tools for yellow fever

No.	Question	Yes	No	Comment
1.	Do you have case notification forms?			
2.	Do you have yellow fever case based forms?			
3.	Do you have CD1 forms?			
4.	Do you have CD2 forms?			
5.	Do you have line listing forms?			
6	Do you have a table for monitoring timeliness and completeness?			
7.	Do you have access to DHMIMS II?			
8.	Do you have access to the internet?			

- Evaluating processes involved in investigating suspected yellow fever cases

1. How do you obtain blood samples from patients for investigation? ----------

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2. Do you always fill a case based form for sample taken?

☐Yes ☐No

3. How many copies of case based forms do you fill for a sample?

☐None ☐1 ☐2 ☐3

4. Do you keep a copy of the case based form?

☐Yes ☐No

5. In filling the case based form, do you probe for vaccination status?

☐Yes ☐No

6. How long do you keep the sample before sending to the next level? Within

☐a day ☐3 days ☐1 week ☐2 weeks ☐a month

7. Do you do batch processing of samples?

☐Yes ☐No Comment_____

8. Do you maintain the cold chain in storing and transporting samples?

☐Yes ☐No

9. What sample do you send for testing?

☐Whole blood ☐Serum

10. How do you package sample before sending to the next level? ----------

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11. What means of transportation do you use in sending samples to the next level?

☐ Official transport ☐ Private transport ☐ Public transport

12. Do you receive feedback for samples sent for testing?

☐ Yes ☐ No Comment_____

13. Do you give back to the clinician who notified/requested for the test?

☐ Yes ☐ No

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

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MyRef. GHS/RDD/ERC/Admin/App/559
Your Ref. No.

Magdalene Norkai Sayah
University of Ghana
School of Public Health
Accra

Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of the Study Protocol.

GHS-ERC Number	**GHS-ERC: 43/12/16**
Title	Factors Associated with Detection and Reporting of Suspected Yellow Fever Cases in the Greater Accra Region
Date	8th June, 2017
Date	7th June, 2018
GHS-ERC Decision	**Approved**

This approval requires the **following from the Principal Investigator**

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report **after completion** of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

Note that any modification of the study without ERC approval of the amendment is invalid.

GHS-ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....

DR. CYNTHIA BANNERMAN
(GHS-ERC CHAIRPERSON)
Director, Research & Development Division, Ghana Health Service, Accra