KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

A PARAMETRIC MODEL FOR ESTIMATING FORCE OF INFECTION FOR HEPATITIS B-CASE STUDY KOMFO ANOKYE TEACHING HOSPITAL

By

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APPLIED STATISTICS

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Declaration

I hereby declare that this submission is my own work towards the award of the Msc. Applied Statistics degree and that,to the best of my knowledge,it contains no material previously published by another person nor that which had been accepted for the award of any other degree of the university,except where due acknowledgment had been made in the text.

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Dedication

This study is dedicated to my children Nana Kwame Opoku, Mame Asiedua and Nana Duako.

Abstract

Serological data are increasingly being used in monitoring the transmission of infectious deseases.

The aim of this study is to estimate the age-dependent force infection for patients showing symptoms of hepatitis B virus (HBV). A secondary data was obtained from the serology department at the Komfo Anokye Teaching Hospital (KATH,January 2013June 2016).

A total of 18,528 blood donors and people coming to the serology department to test for antigen in the blood voluntarily.

Linear and quadratic age-dependent logits models was suitable for the mean prevalence of HBV, with a significant negative linear and positive quadratic effect respectively. From the results, the prevalence increase from a lower age to age 40 decrease at a higher ages and the estimated force of infection (FOI) is higher at lower ages decreasing to age 26 and increases to age 52. In conclusion, the prevalence of HBV is higher at age 40 and the FOI is lower at 26 but higher at ages 2 and 52.

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List of Abbreviations

Eg . . . . . Example

HBV . . . . . Hepatitis B Virus

GSS . . . . . GHANA STATISTICAL SERVICE

HIV . . . . . HUMAN IMMUNODEFICIENCY VIRUS

WHO . . . . . WORLD HEALTH ORGANISATION

CI . . . . . CONFIDENCE INTERVAL

RR . . . . . RISK RATIO

DNA . . . . . DEOXYBONUCLEIC ACID

FOI . . . . . FORCE OF INFECTION

AJOL . . . . . AFRICAN JOURNAL ONLINE

KATH . . . . . KOMFO ANOKYE TEACHING HOSPITAL

GLM . . . . . GENERAL LINEAR MODEL

AIC . . . . . AKAIKE'S INFORMATION CRITERION

CDC . . . . . CENTERS FOR DISEASES CONTROL AND PREVENTION

Chapter 1

INTRODUCTION

1.1 Background of Study

Hepatitis B is contagious liver infection caused by the virus (HBV), known as a 42nanometer, partially double strand DNA virus. The short term illness occurs within the first six months after the person is exposed to HBV. It can be chronic depending on the person's age at the time of infection. Most individuals affected by the constant hepatitis infection are not mindful until they have side effects of cirrhosis or a sort of liver cancer, hepatocellular carcinoma (HCC) numerous a long time afterward. HBV is 50 to 100 times more transmissible than HIV (Yami et al., 2011).

The global epidemic of HBV public health problem is among the leading causes of preventable death worldwide. It is estimated that about 2 billion individuals across the world have been infected by the hepatitis B virus (HBV) with approximately 350 million chronic carriers across the globe (WHO, 2000; Zukerman, 1996).

Between 500,000 and 1.2 million people die every year from acute or chronic hepatitis B (Lavanchy, 2004). The prevalence of chronic HBV infection has been constantly viable. It ranges 10 percent in some Asian and Western Pacific countries and under 0.5 percent in the United State and Northern European countries (Custer et al., 2004).

In the United States between 50,000 and 100,000 people are affected with HBV each year even though a high effective vaccine is available. (Moradpour and Wands, 1995). Asia and Africa have been considered as areas where there is high prevalence of

heptitis B, World Health Organisation (WHO) has projected that the prevalence of HBV infection in Africa ranges between 5% - 10% (WHO, 2015a).

Asia and Africa carry this infection with up to 58 million and 130 million chronic carriers respectively .

Hepatitis B virus is endemic to sub-sahara Africa, the rate varies between 5% and 19% between different African countries (Custer et al., 2004). In these countries wide spread of infection may occur in infancy and childhood (WHO, 2015b).

In Sub-sahara Africa the prevalence of HBV ranges between 3 percent and 22 percent in blood donors. Currently not more than 50 percent of blood supplied in sub-sahara Africa is screen for HBsAg (Allain et al., 2003). Most countries in Africa have high HBV prevalence with the exception of Tunisia and Morocco which has intermediate endemicity (Andre, 2000).

A study in Gambia, shows no infant below the age of six months was found to be infected with HBV, but infants between the ages of two and four years from one village had a prevalence of HBsAg 17.6% (Whittle et al., 1983). These studies showed that, African mothers had a low risk of transmitting the virus to their children prenatally and that children were being infected after the age of one year, indicating that the major mode of HBV transmission was horizontal.

A study conducted in Saudi Arabia on age-specific prevalence on children aged 110 years found the highest prevalence of HBsAg positivity (9.7%) among 1-year old children (Al-faleh et al., 1992). World Health Organization (WHO) projected that the prevalence of HBV infection in Africa ranges between 5%-10% (WHO, 2015a).

Also, a study conducted in Ethiopia (Taye et al., 2014), determine a prevalence of 22.3% in HBV infection in chronics hepatitis patients. In addition to this, a study

conducted by (Schweitzer et al., 2015) estimated the prevalence of of chronic HBV infection in Ghana at 12.92%.

1.2 Problem Statement

Hepatitis B virus infection is a serious public health disease in sub-Saharan Africa and about 600,000 were dying worldwide from the virus, (Shepard et al., 2006). The prevalence of HBV infection in Ghana is likely high due to lack of public awareness, knowledge and under reporting. An understanding of the prevalence of chronic hepatitis B infection in Ghana is necessary for effective public health efforts. Although HBV is classified as ”disease of priority”, there is an incessant increase in detection of new cases worldwide. The force of infection that helps to measure the transmission of the infection within a population is an important epidemic logical parameter.

It has been studied that the force of infection is high but as to where the transmission rate is high within the age range is also unknown in many of the studies. This is so because no comprehensive population based survey of chronic hepatitis B infection has been conducted and due to this, the high prevalence within the ages is unknown. In this study, the problem is to identify the extent to which the age-specific prevalence of HBV and age-specific transmission occurs.

1.3 Objective of the study

The main objectives of this thesis are outlined as follows;

- to study the prevalence of HBV infection in and around Kumasi Metropolis.
- to model the prevalence of HBV infection as a function of age using parametric models.
- to estimate the force of infection from the prevalence model obtained.

1.4 Justification

The disease has been tremendously studied worldwide but many individual in Ghana have little knowledge of it. Some people becomes aware of having the infection only when it's severe. Understanding the rate of the infection and its prevalence will provide grounds for policy makers to formulate policies to check the spread of the HBV virus which can have a negative effect on the economy. It is important for the study to be carried out since the growth of every economy depends on its human resources.

1.5 Methodology

The statistical model adopted for the data are the parametric model which are formulated as linear and quadratic of age. A formal request was made to obtain secondary data on those who tested for the HBV infection in Komfo Anokye Teaching Hospital (KATH) and data was collected on the basis of the total number who tested positive within a specified age range. The test was conducted on the basis of sick patients coming to the serology department to test for the antigen in blood voluntarily. The statistical software used in this study is the Rstudio-0.99.903.

1.6 Limitation of study

This study is limited to only the Ashanti Region of Ghana. The results cannot be generalized because data from many hospitals were not considered. This study is limited to only the past four (4) years that is, before 2017 and cannot focus on previous years.

1.7 Organisation of study

The study is classified under five chapters.

Chapter 1: Introduction This covers the background of study, the statement of the problem, objectives, methodology, justification and limitations.

Chapter 2: Literature Review Examines the relevant literature where various views from different authors are reviewed.

Chapter 3: Methodology. Concentrates on the methodology of the project. *Chapter 4: Data Analysis and Discussions* Focuses on the data, interpretation, analysis and research findings.

Chapter 5: Conclusion and Recommendations The project will be appraised, concluded and recommendations made on ameliorating the study.

Chapter 2

LITERATURE REVIEW

2.1 Introduction

This chapter examines the various literatures related to the topics under consideration in order to disclose critical facts and general findings which have already been identified by previous researchers and numerous studies. It focuses on published books, papers, journal, reports, articles and views on the subject matter.

2.2 Hepatitis B viral infection (HBV)

Hepatitis B virus (HBV) infections causes substantial morbidity and mortality despite being preventable and also treatable. Most viral hepatitis death in 2015 were due to chronic liver disease. As global trend for tuberculosis and HIV decline, hepatitis B increased. An estimate of about 257 million people have the chronic HBV infection (WHO, 2017). When the guide lines for its prevention and management are not followed it leads to personal and economic burden.

2.2.1 Acute Hepatitis B

Hepatitis B is said to be acute when is short live, it may not need treatment instead may be recommended to the affected to rest and take some fluid while the antibodies fight the infection. When transmission in adults, usually through sexual contacts or contaminated needles, the infection usually resolved with the exception of person having HIV

virus.

2.2.2 Chronic Hepatitis B

Chronic hepatitis B is one of the most common persistent viral infections in humans. The age of the patient at the period of infection has an influence on it developing into chronic infection. Chronic HBV infection is defined as HBsAg positivity for more than six months.

Almost 90% of new born babies with the infection through birth are likely to be chronic carries if not vaccinated at birth. The mortality of this disease and its attribution to hepatitis infection is well known. More than 887,000 HBV-related deaths are approximated to occur yearly (WHO, 2015a) and 73% of all liver cancer mortalities worldwide are as a result of hepatitis viruses (Ott et al., 2012).

Person with chronic infection may often be asymptomatic and may not be aware that they are infected, however they are capable of transferring the virus unto an uninfected person. The chronic Hepatitis B affects the liver which results in the malfunctioning of the liver.

It is a chronic infection and can caused cirrhosis, liver failure ,liver cancer and death. It can be fatal if not treated (Gourley et al., 2008).

2.3 Persons at Risk

The group of people who are at risk of contracting HBV includes persons born in geographic regions that have HBsAg prevalence of at least 2% infacts born to infected mothers, household contacts of persons who have chronic HBV infection. Also sexually active person who are not in long-term, mutually monogamous relationships (for example, more than one sex partner during previous 6 months) in as much the same way men who have sex with men, health-care and public safety workers are at risk for occupational exposure to blood or blood-contaminated body fluids. In

addition residents and staff of facilities for developmentally disabled persons, person who have chronic liver disease, hemodialysis patients and travelers to countries that have intermediate or high prevalence of HBV infection.

2.4 Potentials for chronic infection

Among newly infected, unimmunization persons, chronic infection occurs in about 90% of infants, between a quarter and half of children agaed 1-5 years and about 10% of older children and adults.

2.5 Mode of Transmission of Hepatitis B

Hepatitis B virus is transmitted through contact with infectious blood semen, and other body fluids. Primarily through birth to an infected mother, sexual contact with an infected person, sharing of contaminated needles, syringes, or other injection-drug equipment less commonly through contact with infectious blood through medical procedures (CDC, 2009).

2.6 Signs and Symptoms of HBV infection

Most people are asymptomatic during the period of acute infection. However, some people have acute illness with symptoms that persist for several weeks, including jaundice, abdnominal pain, nausea, dark urine, tiredness, loss of appetite and vomiting. Less than 1% of patients with HBV infection may develop acute liver failure which may result in death (WHO, 2015a). In chronic HBV patients, HBV can progress to hepatitis disease such as liver cirrhosis or liver cancer. Over 90% of healthy people who may contract HBV will recuperate normally from the acute infection within the maiden year (WHO, 2015a).

2.7 Treatment for Hepatitis B

Treatment for hepatitis B is used to managed the effects of the infection but not to cure, WHO suggests the administration of tenofovir or entecavir, to patient with HBV infection due to the high effectiveness in preventing viral replication. Compared with other drugs,these drugs hardly develop drug resistance and have few side effects. Although the treatment does not cure HBV infection, it inhabits the viral replication. Because of this, the therapy should be taken throughout a person's life. Treatment using interferon injections is highly utilized in developed countries than developing countries due to high cost. Diagnosis of HBV is detected when a person is in progressive stage of the liver disease. Liver cancer develops quickly as treatment option are little and the consequence in general is mostly poor. Patients with liver cancer die shortly after detection in poor resource settings.

In developed nations, surgery and chemotherapy utilization extends life expectancy for some years. Liver transplantation in developed nation is done from time in patient with cirrhotic liver conditions (WHO, 2015a).

2.8 Empirical Bayesian Hierarchical Model on Age

Ott et al. (2012) considered the empirical Bayesian hierarchical model on aged specific prevalence and endemicity based on the observed to estimate global epidemiology on hepatitis virus infection. The main objective of the research was to estimate age, sex and region specific prevalence of chronic HBV infection. Studies reporting HBV infection was conducted and worldwide sero-prevalence data was collected over a 27-year period which was between the periods of 1980 – 2007.

The researchers observed that from 1990 – 2005 the prevalence of chronic HBV infection declines in most regions, which was particularly evident in central Sub-

Sahara African, tropical and Central Latin America, south east Asia and central Europe. Although there was a decrease in prevalence, the absolute number of HBsAg positive increase from 233 million in 1990 to 240 million in 2005. Age specific prevalence varies in different geographical region with Sub-Sahara Africa having the highest endemicity and below 2% in regions in such as tropical and central Latin America and Western Europe.

Asians showed distinct pattern with lower intermediate in south Asia but up to 8.6% HBsAg in south east Asia. It was concluded that the decline in the HBV infection prevalence was related to expanded immunization and data are therefore needed in national levels to estimate disease burden and guide health vaccine policy.

2.9 Sero-prevalence of Hepatitis B Infection During Pregnancy and Risk of Perinatal Transmission.

Dwivedi et al. (2011) conducted a research on seroprevalence of hepatitis B infection during pregnancy and risk of perinatal transmission.The research were investigating the seroprevalence of hepatitis B surface antigen (HBsAg) in pregnant women and possible risk factors for perinatal hepatitis B virus (HBV) transmission.

Out of the 4,000 women studied, 37 (0.9%) tested positive for HBsAg. Of these 37 women, 6 (16%) present with acute hepatitis and 31 (84%) were asymptomatic. The highest HBsAg positive rate was seen in the age group of 21-25 years (1.15%) followed by 26-30 years (0.86%).

Assessment of risk factor revealed history of tattooing in 29 of 37 (78.4%) women. HBeAg was positive in 21 of 37 (56.8%) women. Of the 16 HBeAg negative women, 5 were positive for HBV DNA nor anti-HBeAg. Vertical transmission was seen in 65% of

babies born to mothers who were positive for HBeAg and HBV DNA. In contrast, it was only 9.1% for babies born to mothers who were negative for both HBeAg and HBV DNA. Of the 25 babies delivered vaginally, 15 (60%) developed vertical transmission. None of the four babies delivered by cesarean section had evidence of vertical transmission.

In conclusion, sero-prevalence of HBsAg in antenatal women was found to be 0.9%. HBe – antigen and HBV DNA. A positivity was associated with a higher chance of vertical transmission.

2.10 Frequency of Hepatitis B Reactivation in Rheumatoid Arthritis Patient

A research conducted by Fukuda et al. (2016) on the frequency of hepatitis B reactivation in rheumatoid arthritis patients in Japan. Their aim is to study the incidence and risk factors of HBV reactivation. Just over 1,040 patients who are above 18 years were included for analysis; 959 of those patients were diagnosed with RA.

A majority of patients with RA were treated with methotrexate (MTX), and almost one-third used a biologic —73% of which were tumor necrosis factor inhibitors (TNFis).

Investigators detected HBV DNA in 35 patient-32 with RA and 3 with other rheumatic diseases. Positivity > 2.1 log copies/mL was seen in 10 patients (8 with RA, 2 with other rheumatic diseases). Researchers calculated HBV reactivation frequency to be 1.93 per 100 person-years and found that quantitative positivity (defined as ≥ 2.1log copies/ml) was 0.55 per 100 person-year.

Patients with negative HBsAb had higher incidence rates of reactivation than patients with negative HBsAb or positive antibodies.

Poisson regression analyses found that risk ratio (RR) of a low HBsAb titer was 2.8 (95%) confidence interval [CI],(1.3 – 6.8) below the median (71.4) and 3.1 (95% Cl, 1.4-6.4) below the cut-off (titer < 10.0).

Age > 69 years increased patient's RR for HBV reactivation to 3.3 (95% Cl, 1.58.4), while patients treated with MTX had lower risk ratios especially compared to those treated with prednisolone (RR:0.4; 95% Cl, 0.2-0.7 vs RR:2.2; 95% Cl, 1.04.6, respectively). The interval between the start of patient's immunosuppressant drug regimen and HBV reactvation was between 3 and 183 months (mean: 66.2 months, median:66 months; interquatile range [IQR]:60).The conclusion of the research stated that although a low HBsAb titer has been considered a candidate risk factor for HBV reactivation, we had no direct evidence to support this idea, however, results show that low HBSAb titers at baseline were significant risk factors for HBV reactivation.

2.11 Natural History of Chronic Hepatitis B: Special emphasis on disease progression and prognostic factors

Fattovich et al. (2008) embarked on a research on the natural history of chronic hepatitis B virus (HBV) infection and disease. They review the natural history of chronic hepatitis B with emphasis on the rates of disease progression and factors influencing the course of the liver disease. Chronic hepatitis B is characterized by an early replicative phase (HBeAg positive chronic hepatitis) and a late low or non-replication phase with HBeAg seroconversion and liver disease remission (inactive carrier state).

Most patients become inactive carriers after spontaneous HBeAg seroconversion with good prognosis, but progression to HBeAg negative chronic hepatitis due to HBV variants not expressing HBeAg occurs at a rate of 1-3 per 100 person years following HBeAg seroconversion. The incidence of cirrhosis appears to be about 2-fold higher in HBeAg negative compared to HBeAg positive chronic hepatitis.

In the cirrhotic patient the 5-year cumulative risk of developing hepatocelllular carcinoma is 17% in East Asia and 10% in the western Europe and the United States and the 5-year liver related death rate is 15% in Europe and 14% in East Asia. There is a growing understanding of viral, host and environmental factors influencing disease progression, which ultimately could improve the management of chronic hepatitis B.

2.12 Evolution of the Global Burden of Viral Infections from unsafe Medical Injection

Pepin et al. (2014) evaluated the burden of viral infection from unsafe medical injections. A mass action model was updated, to recalculate the number of injection-related HIV, HCV and HBV infections acquired in 2000 and provide estimates for 2010. Data about the annual number of unsafe injections were updated. HIV prevalence in various regions in 2000 and 2010 were calculated from UNAIDS data.

Their findings was that despite a 13% population growth, there was a reduction of respectively 87% and 83% in the absolute numbers of HIV and HCV infections transmitted through injections. For HBV, the reduction was more marked (91%) due to the additional impact of vaccination.

While injections related cases had accounted for 4.6%-9.1% of newly acquired HIV infections in 2000,this proportion decreased to 0.7%-1.3% in 2010, when unsafe

injections caused between 16,939 and 33,877 HIV infections, between 157,592 and 315,120 HCV infections, and 1,679,745 HBV infections.

In conclusion substantial progress was made in reducing the burden of HIV, HCV and HBV infection transmitted through injections. In some regions, their elimination might become a reasonable public health goal.

2.13 Modelling the Force of Infection for Hepatitis A in an Urban Population

Ximenes et al. (2014) model the force of the infection for hepatitis A in urban population. The study is to identify the transmission pattern of hepatitis A (HA) infection based on a primary dataset from the Brazilian National Hepatitis Survey in a prevaccination context.

The seroprevalence data from 7,062 individuals aged 5-69 years from all the Brazilian macro-regions were included. The researchers built up three models; fully homogeneous mixing model, with constant contact pattern; the higher assortative model and the higher assortative model with the additional component accounting for contacts with infected food and water. Curves of prevalence, force of infection (FOI) and the number of new infection with 99% confidence intervals (CIs) were compared between the intermediate.

They observed that anti- HAV IgG seroprevalence was 68.8% (95% CI, 64%-72.5%) and 33.7% (95% CI, 32.4%-35.1%) for the intermediate and low endemicity areas, respectively, according to the field data analysis. The models showed that a higher force of infection was identified in the 10-19 year-old age cohort (9,000 infected individuals per year per 100,000 susceptible persons) in the intermediate endemicity area, whereas a higher force of infection occurred in the 15-29 year-old age cohort (

6,000 infected individuals per year per 100,000 susceptible persons) for the other macro-region.

In conclusion the findings support the shift of Brazil toward intermediate and low endemicity levels with the shift of the risk of infection to older age groups. These estimates of HA force of infection stratified by age and endemicity levels are useful information to characterized the pre-vaccination scenario in Brazil.

2.14 Sero-prevalence of Hepatitis B Virus Infection

A study was carried by Nadeem et al. (2016) with the aim of evaluating the seroprevalence of hepatitis B surface antigen (HBsAg) and IgG antibodies to hepatitis core antigen in Balochitan Province of Pakistan. A cross-sectional, population-based study. Place and time of the study: The study was conducted from 1st January 2004 to 31st December, 2008.

A total of 15,260 subjects were enrolled; 11,900 (78%) agreed to undergo screening. Fresh serum samples were tested for the presence of hepatitis B surface antigen and IgG antibodies to hepatitis B core antigen.

Result: HBsAg was detected in 1166 (9.8%) while anti-HBc IgG was found in 117(10.0%). HBsAg positivity was seen in 875(12.7%) males and 291(5.8%) females.

Conclusions: It is utmost important to educate the public, to take proper measures to control the spread of infection and vaccination in order to interrupt transmission of this threatening public health problem in Balochistan province of Pakistan.

Bignal et al. (2017) undertook a study to estimate the seroprevalence of HBV infection in Cameroon. The objective is to have a better knowledge of hepatitis B virus(HBV) infection prevalence at the national level and help to implement pertinent strategies to address HBV related burden. Electronic database, including PubMed/MEDLINE, African Journal Online (AJOL), Science Direct, WHO-Afro Library, WHO-IRIS, African

Index Medicus, National Institute of Statistics and National AIDS control Committee, Cameroon; regardless of language from 1st January 2000 to 30th September 2016. This was completed with a manual search of references of relevant papers. Risk of bias in methodology of studies was measured using the Newcastle-Ottawa Scale.

Results: Out of 511 retrieved papers, 44 studies with a total of 105,603 individuals were finally included. The overall pooled seroprevalence was 11.2% (95% CI: 9.7% to 12.8%) with high heterogeneity between studies (I2=97.9%). Egger's test showed no publication bias (p = 0.167). A sensitivity analysis excluding individuals at high risk of HBV infection and after adjustment using trim and fill method showed a pooled seroprevalence of 10.6% (95% CI: 8.6% to 12.6%) among 100,501 individuals (general population, blood donors and pregnant women). Sources of heterogeneity included geographical regions across country and setting (rural 13.3% vs born before 0.7%). Sex, site, timing of data collection, HBV screening tools and methodological quality of studies were not sources of heterogeneity.

Conclusion: The seroprevalence of HBV infection in Cameroon is high. Effective strategies to interrupt the transmission of HBV are the transmission of HBV are urgently required. Specific attention is needed for rural settings, certain regions and people born before the implementation of the HBV universal immunisation programme in Cameroon in 2005.

Kolou et al. (2017) study the high prevalence of HBV infection in the age group of 20-39 years old individuals in Lome, a cross-sectional study from 2009-2011. The aim of the study is to access the prevalence of HBV infection at CHU of Lome.

The total of 1,200 individual were tested for HBsAg carriage at the immunology laboratory at lome for the study using AXSYM HBsAg (Abbot Diagnostics, Chicago, USA). The patients were grouped in the following age groups; 0-9 years, 10-29 years,3039 years, 40-49 years and ≥ 50 years.

Bio-data such as gender,age and clinical indications of participates were carefully documented.

RESULTS

A p-value of less than 0.05 was used to indicate statistical significance. There were no statistical difference between female and male. A higher number of individuals in the group of 20-29 years and 30-39 years were observed as compared to the other age groups suggested a drive for one to go for screening could be influenced by some factors according to clinical indication.

A number of 229 individuals who turned positive after screening corresponds to a prevalence of 19.08%. the prevalence of the infected male individual (25.00%) was higher than infected females (14.80%).

CONCLUSION

Finding presented will be a valuable to epidemiologist and national health workers in the prevention and treatment of HBV infection and recommended systematic screening of HBV in Togo and other countries in the Sub-Sahara Africa to bring to light the epidemiology of HBV in the region.

In another study (Jian et al., 2017) in estimating age-related incidence of HBsAg seroclearance in chronic hepatitis B virus infections of china by using a dynamic compartment model. The study was base on three national serosurvey data of hepatitis B, on age-and-time-dependent discrete model and use the method of non-linear least squares to estimate the age specific annual rate of HBsAg seroclearance. The study found that HBsAg seroclearance in chronic infection in aged 1-59 years occurred at an averaged annual rate of 1.80% (95% CI 1,54-2.06%) from 1993 to 2016. The HBsAg seroclearance occurred predominantly in early childhood, 20-29 and 3539 years aged groups.

The model estimated that HBsAg seroclearance resulted in 23.8% of the decrease of total HBsAg prevalence for population aged 1-59 years in 2006 and prevented 9.30% of HBV related death (about 0.25 million people).

The participants in the survey were local residents living in 160 disease surveillance points in 31 province in China.

Frempong et al. (2018) model the force of infection for hepatitis B among heterogeneous group at Komfo Anokye Teaching Hospital(KATH).

The aim of the study is to estimate the age-dependent force of infection from hepatitis B virus (HBV) for sick patients showing symptoms, blood donor and people coming to the serology department to test for the antigen in the blood voluntary.

A total number of 18,528 patients were involved in the study which was a secondary data obtained from the serology department at Komfo Anokye Teaching Hospital (KATH), (KATH January, 2013 – June, 2016). Linear and Quadratic age-dependent beta regression models were fitted to the prevalence of HBV.

The result from the estimated quadratic model was suitable for the mean prevalence of HBV, with a significant positive linear and negative quadratic age effects respectively. The prevalence increased from lower age to age 38 and decrease at higher ages.The estimated force of infection for the heterogeneous group is higher at lower ages; decrease at age 38 and increase to age 64.

In conclusion, the prevalence is high at age 38 and transmission rate is lower at age 38 but higher at age 11 and 64.

In much the same way, (Carvalho et al., 2017), study prevalence, risk factors and hepatitis B immunization helping fill the gap of hepatitis B epidemiology among homeless people in Goiania in central Brazil. The purpose of the survey was to investigate the prevalence, risk factor and HBV immunization status among homeless people being served in public shelter.

A total number of 353 homeless individual above the age of 18 were used for the study from August 2014 to June 2015. Using a Poisson regression model, Individuals were interviewed and listed for markers of HBV infection, 81.3% were male and 20.4% were married.

The overall HBV prevalence was21.8% (95% CI; 17.82-26.4) and 19.5% (95%CI: 15.75-26.4) showed a serological profile of previous HBV vaccination older individual (<50 years), black and homosexual or bisexuals showed increase exposure to HBV. There is no difference between the properties of vaccinated and the un-vaccinated homeless regarding sex, ethnicity and years of education ($p < 0.05$).

Statistically, significant difference were observed in the proposition of the of individuals exposed to HBV, considering the following variables: age, sleeping on the street and sexual intercourse with the people living with people living with HIV/AIDS ($p<0.05$).

Nwoegahay et al. (2016) investigated the prevalence of hepatitis B virus infection among blood donors at the Yaounde military hospital ,Cameroon .The aim is to determine the seroprevalence of Hepatitis B virus infection among voluntary donors. A cross sectional study was conducted on 313 volunteers whose donated blood were tested for Hepatitis B surface antigen using rapid chromatographic immunoassay and ELISA. The result show a prevalence of 11.2% from the study the prevalence of HBV infection could be high among blood donors hence it demand screening of donated blood prior transfusion. Joanah Ikobah also study the prevalence of hepatitis B virus infection in Nigeria before vaccines was introduced into the national program on immunization schedule (Ikobah et al., 2016).

The objective was to determine the seroprevalence and predictor of the viral hepatitis B in Nigerian children aged 11-19 years.

A total of 749 children from six secondary school in a community was used in the study. Blood samples were obtained for qualitative detection of HBsAg using rapid

chromatographic, immunoassays with test kits, having sensitivity, specificity and accuracy of > 99%, 97% and 98.5% respectively.

Analysis of the data was performed by using SPSS version 20.2. Binary logistic regression analysis was used to control co-founders. Nine out of the 749 students screen were positive for HBsAg with an overall prevalence of 1.2%. The sex specific prevalence was 0.8% for males and 1.8% females.

Age was the predictor of hepatitis B infection. In conclusion, though the prevalence was low the introduction of vaccine is justifiable in view of public health importance of the infection.

In investigating whether some patients with HIV infection have HBV , S. K. Mustapha and J. B. Jibrim conduct this study in HIV patient in Nigeria. Two hundred recruited HIV infected individuals were screen for HBsAg using ELISA at the Federal medical centre, Gombe, Nigeria (Mustapha and Jibrin, 2004).

The purpose was to determine the seroprevalence of HBsAg in patients with HIV infection. The chi-square test was used to assess the significance of the difference among the group a p-value of 0.05 was considered as significant.

An overall prevalence rate of 26.5% which is higher ($p<0.001$) the 10.4% recorded among non-HIV infected individuals. The study supports the prevalence rate of HBV co-infection in HIV-infected patients compare to non-HIV infected population.

In much the same way Kheini and Makvandi investigated the prevalence of hepatitis B surface antigen (HBsAg) in pregnant women. The aim is to determine the prevalence of hepatitis B surface antigen(HBsAg) and its influential factors in pregnant women (Kheini and Makvandi, 2015).

The aim is to determine the prevalence of hepatitis B surface antigen(HBaAg) and its influence factors in pregnant women. Medical records of 850 pregnant women referred to healthcare centre of Dehloran, Iran in 2011-2012. Description statistics, t-test and fisher's exact test were performed by using spss version 16.0. The prevalence

of the positive HBsAg results was 0.59% though low among the pregnant women HBV screening during pregnancy is highly recommended.

In study of barbers on their knowledge, attitude and practices on HB virus. Three hundred eighty-five barbers from sukkur district, Sindh were interviewed and blood samples were collected and tested for HBsAg, the aim was to ensuing workers safety in the occupation. Approval for the study was obtained from Ethnics review committee of the Aga Khan University and analysed using SPSS version 19. The prevalence of HBV among barbers was lower compared to the available national figures among the general population (Abbasi et al., 2014).

Chapter 3

METHODOLOGY

3.1 Introduction

The study selected Komfo Anokye Teaching Hospital for the research though it considered all the main hospital in the country. This section is to provide detailed methods and information about the study area and research design, sampling procedure, data collection procedure and analysis. The statistical package to be used is the RStudio-
0.99.903.

3.2 Data Collection Procedure

Ethical approval was obtained from Komfo Anokye Teaching Hospital (KATH) for the release of the data. Data is screened for completeness and validity. The interest lies in modeling the proportion of those who tested positive as a function of the ages of individuals who were diagnosed. The complete data is entered into excel for

processing and analysis. Statistical analysis is performed using the parametric model in the R statistical software, after which a model is derived. Mathematical calculation is used in deriving the force of infection. The data to be used in conducting the study was obtained from the KOMFO ANOKYE TEACHING HOSPITAL (KATH) which
is located in the vibrant and culturally rich city of Kumasi in the Ashanti region and is the second largest teaching hospital in Ghana and hence the only tertiary health institution. It is the main referral hospital in the Ashanti and Brong-Ahafo region of Ghana.

A secondary data was obtained from the virology and serology unit under blood transfusion department at KATH. The data collected spanned over a four (4) year period (2013-2016). Data consist of 18,528 patients out of which 2,568 tested positive to HBV. Each patient has information on age, diagnosis and outcome of diagnosis.

3.3 Categorical data

These are variables that place individuals literally in categories and cannot be quantified in a meaningful way. Examples like hepatitis B, rubella, occupation, gender etc. Analysis of categorial data involve use of data tables. A two-way present categorical table by counting the number of observations that falls into each group of the variable.

3.4 General Linear Model (GLM)

General linear models was introduced by Nelder and Wedderburn (1972). It is an extention of traditional linear model which allow the population mean to depend on a linear predictor through a non-linear function. It also allow the response probability to be a member of an exponential family distribution. There are two issues to

consider: 1. The distribution of the response. 2. The model (link function) that relate the mean response to the explanatory variable.

3.5 The Structure of the GLMs

The GLM consist of three components;

1. Random Component:Usually a family of exponential distribution.
2. Systematic component: are linearly
3. Link function:transforms the expectation of the response variable

3.6 General Linear Model for Binary Data

Many response variable are binary which has success and failure outcomes represented

by 1 and 0 respectively. let $p(y = 1) = \pi$ *and* $p(y = 0) = 1 - \pi$

$$f(y;\pi) = \pi^{y}(1-\pi)^{(1-y)} = (1-\pi)\left[\frac{\pi}{(1-\pi)}\right]^{y} = (1-\pi)exp\left(y\log\left(\frac{\pi}{1-\pi}\right)\right) \tag{3.1}$$

The natural parameter $\log(\frac{\pi}{1-\pi})$ is the log odds of the response 1, the logit of π. The mean

$$E(y) = p(y = 1) = \pi(x)$$

and the variance of y is

$$var(y) = \pi(x)[1 - \pi(x)]$$

The linear probability model of a binary is given by $\pi(x) = \alpha + \beta(x)$.

It is a GLM with binomial random component and identity link function. The linear probability model has a structure defect, since probabilities falls between 0 and 1 but the linear functions takes values over the whole real line.

It has $\pi(x) < 1$ and $\pi(x) > 1$ for large or small values, difficulty often occurs filling this model because during the filling process π(x) falls outside the $[0,1]$ range of x

values.

Binary data result form a nonlinear relationship between π(x) and x. A fixed change in x often has less impact when π(x) is near 0 or 1 than when π(x) is near 0.5 In practice, non linear relationship between π(x) and x are often monotonic with π(x) increasing continuously or π(x) decreasing continuously as x increases. The curve with this shape has the model formula, (logistic regression model)

$$\pi(x) = \frac{exp(\alpha + \beta x)}{1 + exp(\alpha + \beta x)} \tag{3.2}$$

As $x \to \inf \pi(x)$ decreasing to 0 where β determines whether π(x) is increasing or decreasing as x increases. The rate of climb or descent increases as βincrease as $\beta \to$ 0 the curve flattens to horizontal, straight line.

Finding the link function for which logistic regression is a GLM. The odds,

$$\frac{\pi(x)}{1 - \pi(x)} = exp(\alpha + \beta x)$$

The log odds has the linear relationship

$$log\left(\frac{\pi(x)}{1 - \pi(x)}\right) = \alpha + \beta(x)$$

The appropriate link is the log odds transformation, the logit-logistic regression models are GLMs with binomial random component and logit link function. The logit is the natural parameter of the binomial distribution and the logit link is its canonical link.

Whereas π(x) must fall is the $(0,1)$ range, the logit can be any real number.

The real numbers are also the range for linear predictors (such as α+β x) that form the systematic component of a GLM. Exponential both sides of (3.1) shows that the odds are an exponential function of x. This provides a basic interpretation for the magnitude

of ./;

The odds increase multiplicatively βe^{β} for every 1-unit increasing in x.

Since it has a curve rather than a linear appearance, then logistics regression function implies that the rate of change in π(x) per unit change in x varies.

Calculating $\frac{\partial \pi(x)}{\partial(x)}$ using (3.5) yield a complex function of the parameters at x, but it simplifiers to the form $\beta\pi[(1-\pi(x))]$.

Another property of logistic regression relates to situation in which the explanatory variable x rather than the response variable Y is random. This occur with retrospective sampling designs, such as case-control biomedical studies.

For samples of subjects having Y_1 (cases) and association if the distribution of x values differ between cases and controls.

In retrospective studies, one can estimate odds ratios, models can be filled to estimate effects on case-control studies. let T indicate whether a subject is sampled (Yes=1,No=0). Let $p_1 = p(t = 1/y = 1)$ denoted the probability of sampling a control. Even though the condition distribution of Y given $X = x$ is not sampled we need a model for $p(y = 1/z = 1,x)$, assuming that $p(y = 1/x)$ follows the logistics model.

By Bayes theorem,

$$p(y = 1/T = 1, x) = \frac{p(T = 1/y = 1, x)p(y = 1/x)}{\sum_0^1 p(t = 1/y = j, x)p(y = j/x)} \quad (3.3)$$

Suppose that $p(t = 1/y,x) = p(T = 1/y)$ for $y = 0$ and 1, the sampling probabilities do not depend on x. with case-control studies one cannot estimate B in other binary models. Unlike the odds ratio, the effect for the conditional distribution of X given x. This is an important advantage of the logit link and is a major reason why logit models have surpassed other models in popularity in biomedical studies.

3.7 The Logit Model

Y_i = 1 HBV+

$\lfloor 0$ HBV-

$$Y_i = Bin(1,\pi(a_i)) \tag{3.4}$$

Where (a_i) is the probability of subject i having infection right before age group a_i

$$\pi(a_i) = 1 - g(a_1). \tag{3.5}$$

Where $g(a_i)$ is the probability Consider a seroprevalence

$$f(Y_i,\pi(a_i)) = \pi(a_i)^{Y_i}(1 - \pi(a_i))^{1-Y_i} \tag{3.6}$$

under logit link assumption

$$\pi(a_i) = \frac{e^{\beta_0+\beta_i a_i}}{1 - \beta_0 + \beta_i a_i} \tag{3.7}$$

$$\pi(a_i) = \frac{e^{\beta_0+\beta_1 a_i+\beta_2 a_i^2}}{1 + e^{\beta_0+\beta_1 a_i+\beta_2 a_i^2}} \tag{3.8}$$

The complimentary log-log link function was also considered.

Force of infection is defined as:

$$l(a_i) = \frac{\pi'(a_i)}{1 - \pi'(a_i)} \tag{3.9}$$

3.8 Parameter Estimation

In carrying out parametric estimation under GLM models the following iterative methods can be used to establish the parameter.

- Newton-Raphson method
- Fisher Scoring algorithm
- Iterative reweighted least squares method.

Newton-Raphson method.

Given a function f(x) and its derivation f(x), we can use the Newton-Raphson updating equation;

$$X_n + 1 = X_n - \frac{f(X_n)}{f'(X_n)}, n = 0, 1, .. \tag{3.10}$$

Fisher Scoring algorithm Specifically, given an initial estimate β, the algorithm update equation for Fisher Scoring is;

$$\beta^{new} = \beta + [E(-\frac{\delta^2 I}{\delta\beta\delta\beta^T})]^{-1}\frac{\delta I}{\delta\beta} \tag{3.11}$$

Iterative Reweighted Least Squares method in GLM, if we let z* be an n-vector with the i^{th} component given by;

$$Z*_i = (Y_i - \mu_i)g'(\mu_i) + X_i^T\beta \tag{3.12}$$

The force of infection or hazard rate is defined as;

$$l(a) = \frac{\pi(a_1)'}{1 - \pi(a_i)} \tag{3.13}$$

Let $g(a_i)$ be the probability that an individual is susceptible at age a_i.

$$\pi(a_i) = 1 - g(a_i) \tag{3.14}$$

Consider a seroprevalence sample of size *n* where a_i is the age of the i^{th} subject with a binary variable Y_i the pdf is;

$$f(Y_i,\pi(a)) = \pi(a)^{Y_i}(1 - \pi(a))^{1-Y_i} \tag{3.15}$$

The log-likelihood is given as;

$$L = \sum_{i=1}^{n}(Y_i ln[\pi(a)] + (1 - Y_i) ln[1 - \pi(a)]) \tag{3.16}$$

for logit assumption,the probability of an individual getting infected of HBV by age a is given as

$$\pi_a = \frac{e^{\beta_a}}{1 + e^{\beta_a}} \tag{3.17}$$

using the logit function and a linear predictor;

$$g[\pi(a)] = \eta(a) \rightarrow \pi(a) = g^{-1}[\eta(a)] \tag{3.18}$$

Force of infection

$$l(a) = \eta^{0(}a)\delta[\eta(a)] \tag{3.19}$$

3.9 Inference of Logistic Regression

Models with a single predictor

$$logit[\pi(x)] = \pi + \beta x$$

significance tests focus on $H_0 : \beta = 0$, the hypothesis of independence. The Wald test uses the log likehood at $\hat{\beta}$, with test statistic$z = \frac{B}{SE}$ or its square , under , Z^2 is asymptotically x^2

The likelihood-ratio test uses twice the difference between the maximized log likellihood at β and at $\beta = 0$ and also has an asymptotic x^2, null distribution.

The score test uses the log likelihood at B=0 through the derivative of the log likelihood at that point. The test statistics compares the sufficient statistics for β to its null expected value, suitably standardized $[N(0,1)$ or $x^2]$.

For large samples, the likelihood-ratio test is preferred over the Wald. It uses more information, since it incorporates the log likelihood at H_0 as well as at β.

When $|\beta|$ is relatively large, the Wald test is not as powerful as the likelihood-ratio test and can even show aberrant beavior and problem.

Confidence intervals are more informative than tests. An interval for B results from inverting a test of $H_0 : \beta = \beta_0$. The interval is the set of β_0 for which the chi-squared test statistic is no greater than $X^2,(\alpha) = Z_\alpha^2/2$.

For the Wald approach, this means $[(\beta - \beta_0)/SE]^2 < Z_\alpha^2/2$ the interval is

$$\beta \pm Z_\alpha/2(SE)$$

For summarizing the relationship, other characteristics may have greater important than β, such as π(x) at various x values. For fixed $X = X_0$

$$Logit[\pi(\hat{x}_0)] = \hat{\alpha} + \beta\hat{x}_0 \quad (3.20)$$

has larger sample SE given by the estimate squared root of

$$var(\hat{\alpha} + \beta\hat{X}_0) = var(\alpha) + x^2var(\hat{\beta}) + 2x_0cov(\hat{\beta}) + 2x_0cov(\alpha,\hat{\beta}) \quad (3.21)$$

A 95% confidence interval for $logit[\pi(x_)0]is(\alpha+\beta x_0)\pm 1.96SE.$ Goodness of fit:Ungroup and Groupes data.

In practice, there is no guarantee that a certain logistics regression model fits the data well. For any type of binary data, one way to detect lack of fit uses a likelihoodratio test to compare the model to more complex ones. A more complex model might contain a nonlinear effect, such as a quadratic term. Models with multiple predictors would consider interaction. If mmore complex models do not fit better, this provides some assurance that the model chosen is reasonable.

This is simpliest when the explanatory variables are solely categorical. At each setting of x, one can multiply the estimate probabilities of the two outcomes by the number of subjects at that setting to obtain estimated expected frequencies for $y = 0$ and $y = 1$. These are fitted values, the test of the model compares the observed counts and fitted values using a pearson x^2 or likelihood ratio G^2 statistic.

For a fixed number of settings as the fitted counts increased,X^2 and G^2 have limiting chi-squared null distributions. The degrees of freedom, called the residual for the model, subtract the number of parameters in the saturated model.

Goodness of fit as a likelihood-rate Test:

The likelihood-ratio statistic $-2(L_0 - L_1)$ test whether certain model parameters are zero by comparing the log likelihood L_1 for testing M_0 given that M_1 holds, by $G^2(M_0/M_1)$.

The goodness-of-fit statistic $G^2(M)$ is a special case in which $M_0 = M$ and M_1 is the saturated model. In testing whether M fits, we test whether all parameters in the saturated model but not in M equal zero. The asymptotic df is the difference in the number of parameter in the two models, which is the binomial modelled minus the number of parameters in M.

Chapter 4

ANALYSIS

4.1 Introduction

This section deals with the analysis of seroprevalence data collected from Komfo Anokye Teaching Hospital. The first part of the analysis focus on the charts of the exploration data with age. Parametric models are fitted to select the best model in the determination of the force of infection of the HBV as a function of age.

4.2 Exploratory data analysis

The analysis examined the age of persons in the infected group, the proportion of the infected compare to the total number of patients tested for the infection in the year. A secondary data obtained from the serology department of the Komfo Anokye

Teaching Hospital (KATH January 2013 – June 2016). A total of 18,528 samples of serum was obtained with about 13.89% (2,574) being HBV^+ with a mean age of 46 years.

Table 4.1 shows that patients infected with HBV virus increase from age group (12 – 14) to age group (30-34). It then declined from age group (35 – 39) to age 60. Out of 1,104 teenagers diagnose, 161 (14.58%) were found to be HBV positive, with age group (40-44) being the highest group infected at 19.1 percent.

Table 4.1: AGE GROUP AND DIAGNOSED OF PATIENTS

AGE GROUP	HBV^+	HBV^-	TOTAL
12-14	25	219	244
15-19	136	724	860
20-24	220	1,440	1,660
25-29	403	2,831	3,234
30-34	442	2,860	3,302
35-39	396	1,801	2,197
40-44	287	1,215	1,502
45-49	235	1,076	1,311
50-54	158	1,032,	1,184
55-59	114	722	836
60^+	164	2,034	2,198
TOTAL	2,572	15,954	18,528

Seroprevalence of Hepatitis B

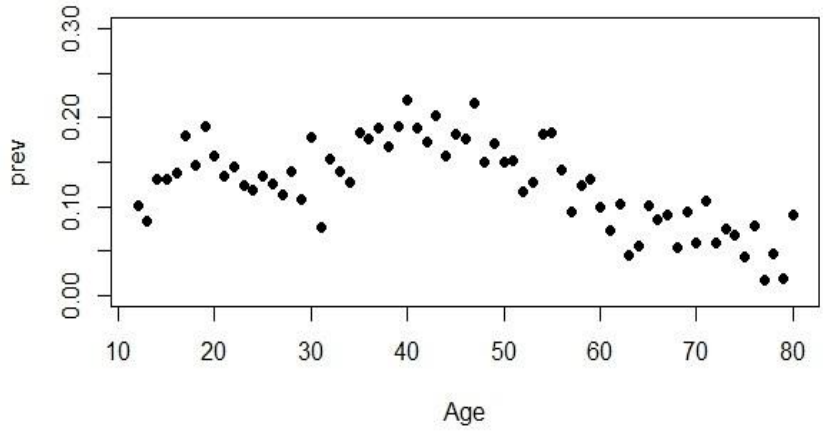

Figure 4.1: Age-Specific Prevalence of HBV

Figure 4.1 shows the sero-prevalence of HBV at single year age level class. The prevalence increase from age 12 years to about 40 years and decline steadly to age 60 years.

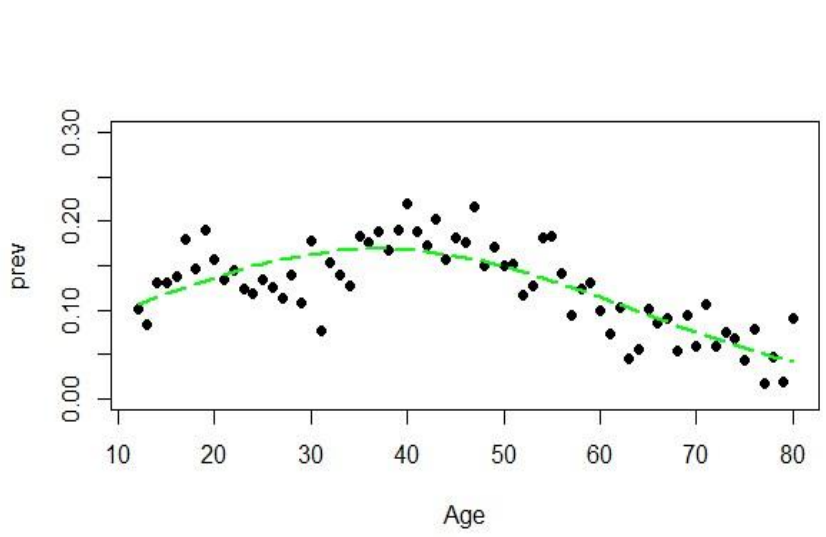

Figure 4.2: The lowess curve on prevalence

The steady growth at different single age in Figure 4.2 represent the prevalence increase to its peak about age 39 and decline as indicated by the lowess curve.

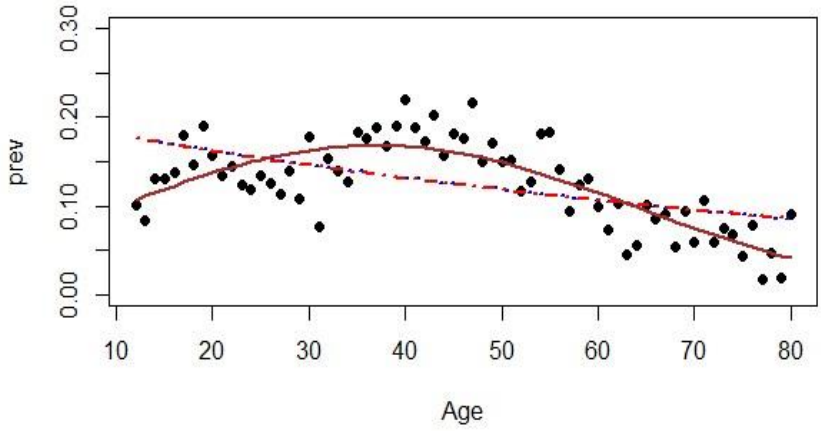

Figure 4.3: Linear and Quadratic Logit Models on HBV

Figure 4.3 show the linear and quadratic age dependent models for the prevalence using a single year age under the logit assumptions. The quadratic model depict a concave shape and the linear model represent a negative slope

4.3 Parametric models

Two parametric models were fitted with logit and complimentary log link function to determine the best model for the estimation of the force of infection.

Table 4.2: Linear Model with Logit Function

Co-effients	Estimate	Standard Error	Z-value	P-vaue
Intercept	-1.3984	0.1122	-12.442	<0.001
Age	-0.01225	0.0024	-5.104	<0.001

From Table 4.2, age is significant to the logit of infection of HBV. This is formulated as:

$$g(age) = -1.39848 - 0.01225(Age)$$

Table 4.3: Linear Model with Complmentary log-log link

Co-efficents	Estimation	Standard Error	Z-value	value

Intercept	-1.51059	0.80036	-1.887	0.0591
Age	-0.01129	0.01731	-0.652	<0.5141

Table 4.3 shows the complimentary log-log link with age not significant to the function assumption

$$g(age) = -1.1059 - 0.01129(Age)$$

Table 4.4: Quadratic model with logit link function

Co-efficients	Estimate	Standard Error	Z-value	P-value
Intercept	-2.745984	0.191	-14.377	<0.001
Age	0.0620880	0.0095	6.536	<0.001
Age-square	-0.0008403	0.00011	-7.639	<0.001

Table 4.4 shows both co-efficient are significant under the logit function assumption.

$g(age) = -2.745984 + 0.0620880(Age) - 0.0008403(Age^2)$ (4.1) Table 4.5: Quadratic model with Complimentary log-log link function

Co-efficients	Estimate	Standard Error	Z-value	P-value
Intercept	-2.7755040	0.19 1	-14.531	0.155
Age	0.0588064	0.0095	6.190	0.543
Age^2	-0.0007956	0.00011	-7.233	0.462

In Table 4.5, none of the co-efficient were significant under the complimentary log-log link function assumption.

$$g(age) = -2.7755040 + 0.0588064(Age) - 0.0007956(Age^2)$$

Table 4.6: Goodness of Fit

Model	AIC
Linear Logit link	22.567
Quadratic Logit link	21.587
Linear Log-log	24.667
Quadratic Log-log	24.662

Akaike's information criterion (AIC) was used for choosing between competing statistical models such that the model with the least AIC is chosen as the model best model. From Table 4.6, the model with the least value of AIC is the quadratic logit link model with AIC of 21.587. From the selected model the prevalnce

$$\pi = g(\mu^{-1}) = -2.745984 + 0.0620880(Age) - 0.0008403(Age^2)$$

$$FOI = \frac{\pi}{1-\pi} \tag{4.2}$$

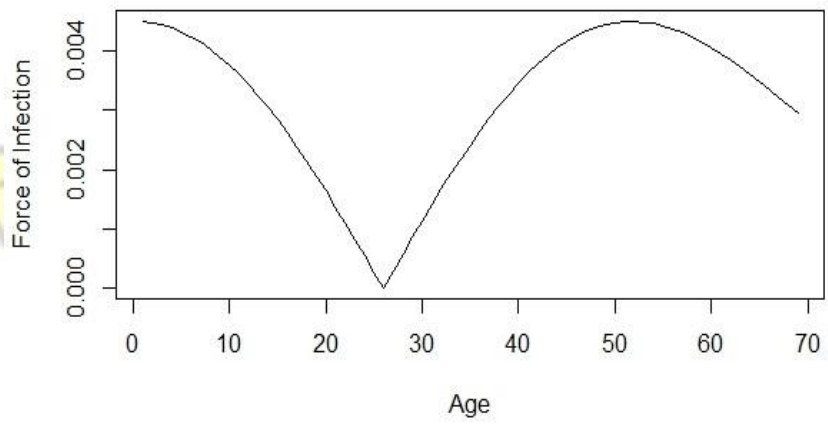

Figure 4.4: Estimated Force of Infection

The estimated quadratic model was used to estimate the force of infection (FOI). Figure 4.4 shows the estimated FOI decrease exponentially from age 2 to about age 26. The FOI increase from age 26 to age 52 and decrease afterwards.

Chapter 5

CONCLUSION AND RECOMMENDATION

5.1 Findings from the study

The data use for the study consist of three variable: Age, +HBV and -HBV. The total number of patients for the study is 18,528 out of which 2,574 tested positive for HBV and 15,954 not infected with the virus.

Two models: the linear and quadratic logit models and linear and quadratic complementary log was used to select the best fitted model. From the AIC values from table 4.5 shows that the linear and quadratic logit model was the best fitted model.

From study, the prevalence increase from a lower age to age 40 and decrease at higher ages, the estimated force of infection foe heterogeneous group is higher at lower ages decreasing to age 26 and increasing to age 52. In conclusion, the prevalence is higher at the age 40 and the FOI is lower at 26 but higher at ages 2 and 52.

5.2 Recommendation

Recommendation, This study was carried out in one of the teaching hospitals in Ghana and does not represent the general view of the Ghanaian people. I recommend a further study to estimate the age-specific force of infection in Ghana and the sub region.

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