

**SEROPREVALENCE OF HEPATITIS B INFECTION IN CHILDREN
LESS THAN FIVE YEARS OF AGE AT THE UNIVERSITY TEACHING
HOSPITALS - CHILDREN'S HOSPITAL AND KAMWALA HEALTH
CENTRE IN THE VACCINATION ERA IN LUSAKA, ZAMBIA**

BY

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**A dissertation submitted to the University of Zambia in partial fulfilment of the
requirements for the award of Master of Medicine in Paediatrics and Child Health**

THE UNIVERSITY OF ZAMBIA

LUSAKA

2019

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DECLARATION

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ABSTRACT

HBV infection is a serious infection affecting the liver and causes significant morbidity and mortality in sub-Saharan Africa. While most patients with chronic hepatitis B virus infection are asymptomatic, the infection acquired during infancy or childhood accounts for a disproportionately large share of worldwide morbidity and mortality. The prevalence of hepatitis B virus infection in Africa is between five to ten percent in the adult population. The seroprevalence of this infection in Zambian children after the introduction of the hepatitis B vaccine is not known.

This was a cross sectional study done in children below the age of five years. Three hundred and forty children from University Teaching Hospitals – Children’s Hospital and Kamwala Health Centre in Lusaka were enrolled for the study. Information about immunisation against hepatitis B virus and medical history was collected. The children’s parents or guardians who were willing to be tested were also tested for hepatitis B virus infection.

Three hundred and forty children and eleven guardians were sampled for this study. One hundred and seventy-one (51.8 percent) were male children. The mean age was 13.2 months (SD = 16.07). There were 181 (53.2 percent) children who were fully vaccinated against HBV while 35 (10.3 percent) were partially vaccinated and 96 (28.2 percent) were less than six weeks old hence had not yet received any hepatitis B vaccine. Immunisation status against hepatitis B of the remaining 28 (8.2 percent) was unknown. The prevalence of HBsAg positivity among children less than five years old was 1.5 percent. Three (60 percent) of those positive for hepatitis B were above three years. Factors such as sex, household income, hepatitis B vaccination status and history of blood transfusions were not associated with HBsAg positivity. However, the following factors were independently associated with HBV infection; maternal HIV infection, maternal HBV infection, child’s HIV infection and the child’s age. Age was an important factor independently associated with hepatitis B virus infection. For every increase of one month in child age, the odds for positive HBsAg increased by an average six percent (OR = 1.06, 95% CI = 1.01 – 1.11, P-value = 0.03).

The seroprevalence of HBsAg was 1.5 percent. There was no association between hepatitis B vaccination status and hepatitis B surface antigen positivity. There was an association between maternal HIV status and HBsAg positivity. There was also a non –significant association between maternal hepatitis B status and HBsAg positivity. Hepatitis B vaccine has had an impact on the prevalence of hepatitis B though this study did not show that association, however larger studies are needed to demonstrate this association.

Key words: hepatitis B, vaccination era, Children’s Hospital-UTH, Kamwala Health Centre

DEDICATION

I dedicate this work to my beautiful daughters Nambwela and Walusungu: After enduring many nights and days of mummy's absence, you understood and waited for me patiently, love you my girls. My mum for her encouraging words and her prayers for my success, am forever grateful. My sisters in law who helped me with our daughters' school errands during this period. Finally, but not the least, my husband Dr. Tebuho Mateele for being so understanding and supportive throughout the hard times, I wouldn't have done it without his unwavering support.

ACKNOWLEDGEMENTS

This research would not have been possible without the support of the Tropical, Gastroenterology and Nutrition (TROPGAN) group at University Teaching Hospital where the samples were tested for hepatitis B surface antigen.

I would like to thank my supervisors Dr E M Mpabalwani, Dr B Amadi and Professor P Kelly for their guidance. I am also indebted to Dr V. Mulenga and other senior doctors at the Children's Hospital for their invaluable help. Thank you for your patience and for allowing me to disturb your work at any time.

I would like to thank my hard working assistants who assisted me in data and blood sample collection, Sr Josephine Chisha, a nurse at the University Teaching Hospitals - Children's Hospital and Sr Mubanga Mvula a nurse at Kamwala Health Centre. Am grateful to Mutinta Muchimba from TROPGAN laboratory at UTH for testing the blood samples.

I acknowledge all the faculty in the Children's Hospital as well as some of my colleagues for their input. Last but not the least, a special thanks to all the study participants without whom this study would not have been possible.

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ABBREVIATIONS AND ACRONYMS

| | |
|----------|--|
| Ab | Antibody |
| Anti-HBs | Antibodies against hepatitis B surface antigen |
| Anti-HBc | Antibodies against hepatitis B core antigen |
| Anti-HBe | Antibodies against hepatitis B e antigen |
| BCG | Bacille Calmette Guerin |
| CDC | Centre for Disease Control |
| CLD | Chronic Liver Disease |
| DPT | Diphtheria, pertussis, tetanus vaccine |
| EDTA | Ethylenediaminetetra acetic acid |
| EPI | Expanded Programme on Immunisations |
| ERES | Excellence in Research and Science |
| HBcAg | Hepatitis B core Antigen |
| HBeAg | Hepatitis B e Antigen |
| HBsAg | Hepatitis B surface Antigen |
| HBIG | Hepatitis B Immunoglobulins |
| HBV | Hepatitis B Virus |
| HBV DNA | Hepatitis B Virus Deoxyribonucleic Acid |
| HCC | Hepatocellular Carcinoma |
| MTCT | Mother To Child Transmission |
| TROPGAN | Tropical Gastroenterology and Nutrition |
| UTH | University Teaching Hospital |
| WHO | World Health Organization |
| ZDHS | Zambia Demographic Health Survey |

CHAPTER ONE: INTRODUCTION

1.1 Background

Hepatitis B infection is a potentially life-threatening liver infection caused by the Hepatitis B Virus (HBV). HBV infection remains a global public health problem despite the availability of a cheap and effective vaccine.¹ The infection can cause chronic infection and puts infected persons at high risk of death from cirrhosis and hepatocellular carcinoma (HCC).^{2,3} The likelihood that infection with the HBV becomes chronic depends upon the age at which a person becomes infected. Children less than six years of age who become infected with the HBV are at higher risk of developing chronic infection.^{4,5}

In the absence of post exposure prophylaxis:

- If mother is positive for HBsAg and HBeAg, 70 to 90 percent of infants become infected of which 90 percent of infected infants become chronically infected.⁵
- If mother is positive for HBsAg only, ten percent of infants become infected of which 90 percent of infected infants become chronically infected.⁵

Of the adults who are chronically infected with hepatitis B infection 20 to 30 percent will develop cirrhosis and/or HCC.⁵ Chronic infections acquired during infancy or childhood account for a disproportionately large share of worldwide morbidity and mortality.⁶ Many studies have suggested that HBV transmission in Africa occurs predominantly in childhood, by the horizontal rather than the perinatal route.⁷

In the pre vaccination era in the 1990s, 500 children with general paediatric conditions at the University Teaching Hospital (UTH), Lusaka, Zambia were studied. A seroprevalence for HBsAg of 2.5 percent was found at that time.⁸ According to the World Health Organisation,

(WHO) vaccination has reduced the rate of chronic HBV infection to less than one percent among immunised children.⁹ The prevalence of hepatitis B among immunised and unimmunised children against hepatitis B at the university teaching hospitals and Kamwala health centre in Lusaka is not known.

1.2 Statement of the problem

HBV infection is a serious infection affecting the liver and causes significant morbidity and mortality in Sub-Saharan Africa, yet there is no routine screening for HBV infection in most African countries including Zambia, except in blood donors. While most patients with HBV infection are asymptomatic, this infection can lead to liver failure, liver cirrhosis, hepatocellular carcinoma and death.¹⁰ The first dose of hepatitis B vaccine in Zambia is given at six weeks and not at birth as recommended by WHO.¹¹ The prevalence of hepatitis B in the general paediatric population after the introduction of hepatitis B vaccine in Zambia is not known. Therefore, knowledge of the prevalence of HBV infection from the two institutions would improve care and reduce on morbidity and mortality from HBV infection in children.

1.3 Study justification

Currently the prevalence of HBV infection in children in Zambia is not known and yet most people including children who are infected are asymptomatic for HBV infection. This study aimed at determining the seroprevalence of HBV infection in children with various non-surgical conditions presenting to University Teaching Hospitals and Kamwala Health Centre, Lusaka Zambia.

The patients whose HBsAg statuses are known can be counselled and/or treated appropriately to minimise sequelae such as chronic liver disease or eliminate it all together.

Epidemiologic data about hepatitis B infection in children in Zambia are needed to guide health policy for hepatitis B screening and optimize therapy. Establishing the prevalence not only add to the existing body of knowledge but also would aid clinicians and policy makers in serving the paediatric population better. The findings also gave some insight on the impact of HBV vaccine.

1.4 Research Question

What is the seroprevalence of HBV infection in children under the age of five years at the University Teaching Hospitals –Children’s Hospital and Kamwala Health Center in Lusaka after the introduction of the HBV vaccine?

1.5 Objectives

1.5.1 Main Objective

To ascertain the prevalence of hepatitis B surface antigen (HBsAg) among children under the age of five years at University Teaching Hospitals (UTHs)-Children’s Hospital and Kamwala Health Centre in Lusaka.

1.5.2 Specific Objective

1. To determine the percentage of children presenting to the two institutions who are fully vaccinated against HBV.
2. To compare the prevalence of hepatitis B between children who are fully vaccinated and those who are not, in Lusaka.
3. To identify some of the risk factors for HBV among children.
4. To determine the association between children’s HBsAg status and their parents/guardians.

1.6 Organization of Dissertation

The study is divided into preliminaries and chapters. The preliminaries include: The title page, copyright, declaration, approval, abstract, acknowledgement, table of contents and lists of tables, figures, appendices, abbreviations. The chapters which are included are as follows:

Chapter 1 describes the background, statement of the problem, study justification, objectives and specific objectives. Chapter 2 deals with literature review, explains the prevalence, associated risks of hepatitis B infection and hepatitis B vaccination in infants. Chapter 3 provides the study conceptual framework, research methodology, ethical consideration and limitations. Chapter 4 states the results of the study with figures and tables to interpret the data collected. Chapter 5 discusses the study findings comparing them with local, regional and international literature and Chapter 6 summarises the study findings and recommendations.

CHAPTER TWO: LITERATURE REVIEW

2.1 Nomenclature and markers of HBV infection

HBV is a deoxyribonucleic acid (DNA) virus classified in the virus family Hepadnaviridae. Humans are the only known natural host. HBV enters the liver via the bloodstream, and replication occurs only in liver tissue.⁶ The description of the markers of HBV infection and their significance is shown in Table 1 below.

Table 1: Markers of HBV infection and their significance

| Marker | Description | Significance |
|-------------------------------------|---|--|
| Hepatitis B Virus (HBV) | The 42 nm, double-shelled particle, that consists of a 7 nm thick outer shell and a 27 nm inner core which contains a small, circular, partially double-stranded DNA molecule. It's a complete infectious virion. | A virus which primarily causes inflammation of the liver. The HBV can be transmitted in several ways including blood transfusion, needle sticks, body piercing and tattooing using unsterile instruments, dialysis, sexual and in utero or during childbirth from mother to child. |
| Hepatitis B surface antigen (HBsAg) | Also called envelope antigen. It's a complex antigenic determinant found on the surface of HBV and it's a 22 nm particle and tubular. Formerly designated Australia (Au) antigen or hepatitis-associated antigen (HAA). | The presence of HBsAg indicates that the person is infected and infectious. It can be detected in serum during acute or chronic HBV infection. HBsAg is the antigen used to make hepatitis B vaccine. |
| Hepatitis B core antigen (HBcAg) | The antigen specifically associated with the 27 nm core of HBV. | A protein marker found on the core of the HBV. Does not circulate in the blood but is found only in liver cells infected by HBV. |
| Hepatitis B e antigen (HBeAg) | The antigenic determinant that is closely associated with the nucleocapsid of HBV. It also circulates as a soluble protein in serum. | The presence indicates that the virus is replicating, and the infected person has high levels of HBV. Can be found in serum during acute and/or chronic HBV infection. |

| | | |
|--------------------------------|---|--|
| Antibodies to HBsAg (Anti-HBs) | Specific antibodies that are produced in response to HBsAg. | Anti-HBs positivity generally is interpreted as indicating recovery and immunity from HBV infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B virus. |
| HBeAg (anti-HBc) | Specific antibodies that are produced in response to HBeAg | Anti-HBc (immunoglobulin M) positivity indicates recent infection with HBV (≤ 6 months). Its presence indicates acute infection. |
| HBeAg (anti-HBe) | Specific antibodies that are produced in response to HBeAg | Anti-Hbe positivity is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV. |

Source-Hollinger FB, Liang TJ (2001) & Centres for Disease Control (2016).^{12,47}

2.1.1 Clinical course of HBV infection

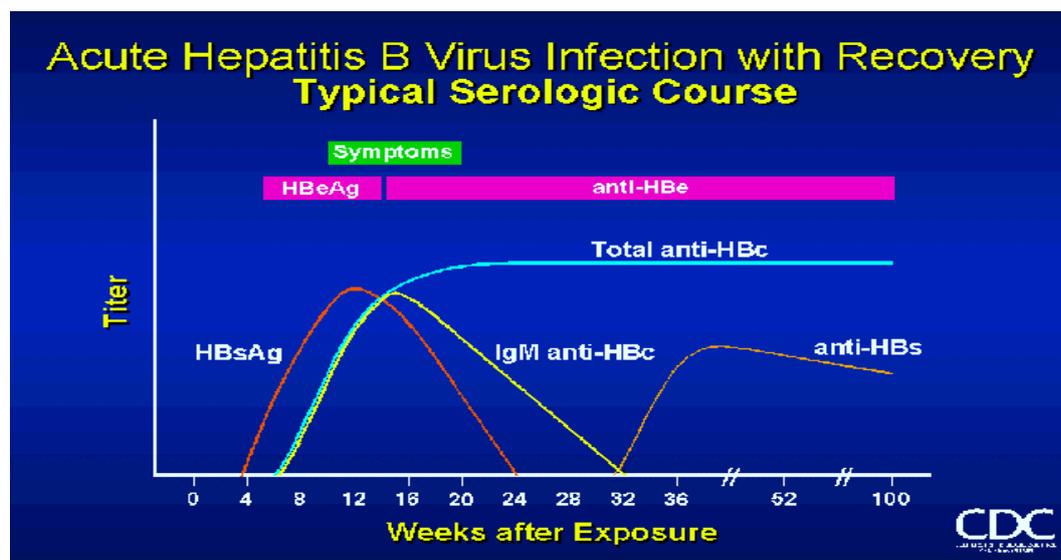


Figure 1: Acute hepatitis B infection- Typical serologic course

Source-<http://www.microbiologybook.org/virol/hepatitis-disease2.htm>.¹³ & CDC

The first serologic markers to become detectable in persons with acute HBV infection are HBsAg and antibodies to hepatitis B core antigen. In the first 6 to 12 months after infection, immunoglobulin M antibodies to hepatitis B core antigen become undetectable. Total antibodies to hepatitis B core antigen persist for life and are found in persons with chronic

infection as well as those who recover from infection as seen in Figure 1. In persons who recover from HBV infection, HBsAg is eliminated from the blood, and antibody to hepatitis B surface antigen (anti-HBs) develops during convalescence as shown in Figure 1. The presence of anti-HBs indicates immunity to HBV infection. Most persons who recover from natural infection (resolved infection) will be positive for both anti-HBs and antibodies to hepatitis B core antigen, but anti-HBs becomes undetectable in some over time.⁶

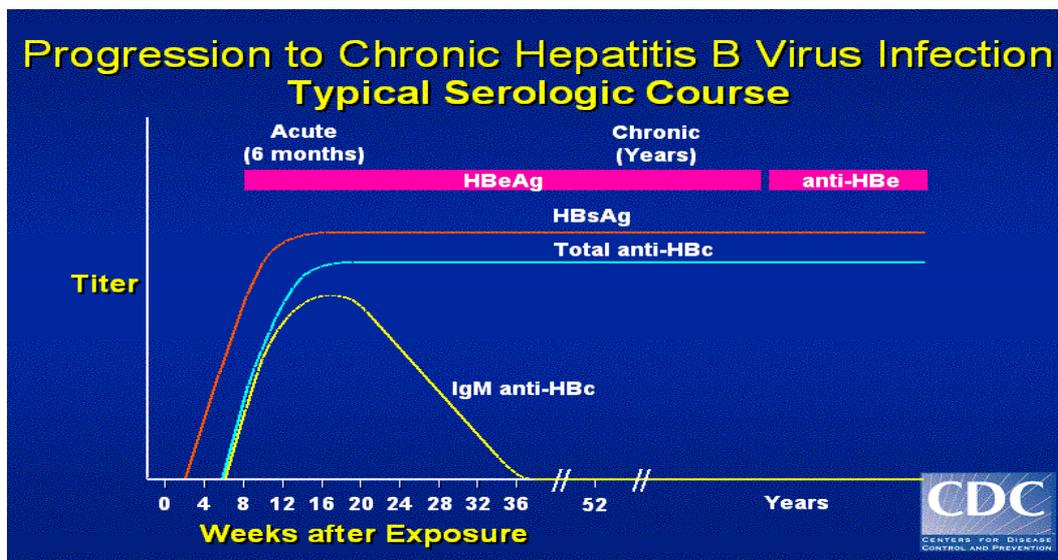


Figure 2: Chronic hepatitis B infection-typical serologic course

Source- <http://www.microbiologybook.org/virol/hepatitis-disease2.htm>.¹³ & CDC

Chronic HBV infection is defined as either the presence of HBsAg in the serum for at least 6 months or the presence of HBsAg in a person who tests negative for immunoglobulin M antibodies to hepatitis B core antigen. Unlike persons who recover from acute HBV infection, persons with chronic HBV infection do not develop anti-HBs, and HBsAg typically persists for decades as shown in Figure 2. HBeAg, a marker of high viral replication activity which correlates with greater infectivity is also usually present in the early phases of illness.⁶ For many persons with chronic infection, HBeAg becomes undetectable at some point (usually a decade or more) after the acute infection; this change usually indicates a decrease in viral

replication. ⁶ Most children with chronic HBV infection are asymptomatic and do not generally, require treatment. These children are, however, at increased risk for severe complications later in life, including advanced liver disease and Hepatocellular Carcinoma (HCC).¹⁰

2.2 Epidemiology of Hepatitis B virus – Global, Regional & Local

An estimated 248 million people have chronic HBV infection globally. The prevalence globally is distributed as shown in Figure 3.¹⁴



Figure 3: World map - Prevalence of Hepatitis B Surface Antigen -2014

Source: CDC; Health information for international travel, (2014).¹⁴

High rates of chronic infections are found in the Amazon and the southern parts of eastern and central Europe. In the Middle East and the Indian subcontinent, an estimated two to five percent of the general population is chronically infected. Less than one percent of the population in Western Europe and North America is chronically infected.¹⁵ However, the prevalence is highest in East Asia and sub-Saharan Africa, where between five to ten percent of the general population is chronically infected.¹⁶ There are approximately 50 million chronic carriers of

HBV in Africa, with a 25 percent mortality risk.⁷ In Nigeria the prevalence was 11.5 percent in children and 14 percent in adults between 2000 and 2013.¹⁷ This was comparable to South Africa where prior to the introduction of the hepatitis B vaccine into the South African Expanded Programme of Immunisation (EPI) in 1995, prevalence rates of this disease was upto 15 percent in the adult population.¹⁸ In The Gambia, rates of chronic HBV among 9-year-old children was 10 percent before the introduction of the HBV vaccine. It reduced to 0.6 percent after introduction of the HBV vaccine series.¹⁹ Zambia, is among the countries with the highest prevalence of HBV infection with a prevalence of more than eight percent in the adult population.¹⁴

2.2.1 Distribution of HBV genotypes

There are 10 known genotypes of HBV. The distribution of HBV genotypes is different geographically. Genotype A is found mainly in Northern and Western Europe, North America, and Africa. Genotypes B and C, with many sub genotypes being prevalent in Asia. Except for sub genotype B1, B2, C1, and C2, which are reported to be distribute commonly in the Chinese mainland, the other sub genotypes of genotype B and C are distributed commonly in Southeast Asian countries. Genotype D and the C/D recombinant are concentrated in Northwest China, where most of the residents are migrants from Central Asia. Genotype E is the most prevalent genotype in Eastern and Central Africa, and sporadically found in Colombia and Northern India. Genotypes F and H are prevalent in the Amerindian population and in Central America, respectively. Recently, the newly designated genotype I has been characterized using phylogenetic analysis, which was identified in Vietnam, Laos and Canada, and seems localized in Southeast Asia.^{20,21} Accurate classification of HBV genotypes and sub genotypes is important since HBV genotypes are related to the course of the infection, responses to antiviral treatment regimens, and clinical outcomes.²¹

2.3 HBV infection in some special populations

2.3.1 HIV/HBV co-infection in Lusaka

Approximately 3 million human immunodeficiency virus (HIV)-infected individuals in sub-Saharan Africa are chronically co-infected with HBV.²² HIV/HBV co-infection is associated with increased incidence of serum aminotransferase elevations, delayed CD4+ count recovery, and increased mortality during ART compared with HIV Alone.^{23,24} Another potential complication of HIV/HBV co-infection is renal dysfunction. HBV mono infection causes various forms of kidney disease. Among HIV infected Zambian adults, HBV co-infection was associated with increased odds of baseline estimated glomerular filtration rate <50 mL/minute/1.73 m², the threshold at which tenofovir/emtricitabine use is discouraged by the WHO's HIV treatment guideline.^{20,25} HIV and hepatitis B coinfection is common among patients initiating ART at the University Teaching Hospital with a prevalence of 9.9 percent in HIV infected adults.²⁶ In urban Zambia, those screened for HBV from 2011 to 2014, approximately 10 percent of paediatric HIV infected patients had chronic HBV infection.²⁷ Meanwhile in 2015 HBV infection in HIV infected children seen at the Paediatric Center of Excellence (PCOE) at UTH was at 5.9 percent.²⁸

2.3.2 HBsAg in paediatric patients with sickle cell disease at UTH

The seroprevalence of HBsAg and HBsAb at the then UTH in patients with Sickle Cell Anaemia (SCA) in 1992 was 5.8 percent and 24.7 percent respectively. There was no significant difference between SCA patients who had received blood transfusions and those with no history of receiving blood transfusion.⁸ Later, in 2014 the prevalence of HBsAg amongst SCA patients at UTH dropped to 2.2 percent and its prevalence was not associated with the number of blood transfusions. There was a non-significant association between HBV prevalence and increase in age as well as sexual activity.²⁹

2.3.3 HBsAg in pregnant women in Zambia

The overall prevalence of HBsAg in pregnant women in Lusaka was 6.5 percent in the nineteen nineties, and HBeAg was present in 16.1 percent of those positive for HBsAg.³⁰ Antibody positive rate (HBsAb and/or HBcAb) was 51.3 percent in randomly selected HBsAg negative samples.

HBsAg positivity rate varied between 3.3 percent and 13.6 percent in each study sites. Prevalence for both HBsAg and antibodies to HBV were significantly higher in rural areas (district hospitals) than in urban areas (urban health centres in Lusaka). This data showed that although HBV is endemic in Zambia, the prevalence varies from region to region.³⁰ Zambia National Blood Transfusion Services (ZNBTS) records a prevalence of 8-10 percent of HBsAg across the country among its blood donors who are aged 16-64 years old and the majority of these are of child bearing age.³¹ A percentage of 8.5 percent for HBsAg among adults at UTH and 4 percent among children was recorded in 2015 according to data from the virology laboratory at UTH, Lusaka.³²

2.4 Hepatitis B vaccination in children

The success story of the Western Pacific region points to the power of birth dose vaccination against HBV MTCT in high-burden countries. Rates of chronic HBV infection were estimated to be greater than 8% in many countries in this region in the 1990.¹⁹ In African and Asian women, it has been shown that seroconversion to HBsAg negative does not fully protect newborns from HBV mother to child (MTC) transmission, when maternal HBV DNA loads exceed 5 Log₁₀ I.U/ml, regardless of the women's origin or HBV genotype.³³ The three dose vaccine series in Zambia typically begins at six weeks of age and provides little protection against HBV MTC transmission.¹⁹ Providing a first dose of HBV vaccine at birth as is done for BCG and oral polio vaccine in most African countries may be an important step in reducing

HBV MTC transmission.²³ Administration of HBV vaccine and immunoglobulin (HBIG) within 12 hours of life, the standard-of-care for HBV exposed infants in the United States and other developed nations, reduces the rate of HBV MTC transmission by 85–95 percent.¹⁹ HBIG is not available in many developing nations because of cost and storage issues. However, there is evidence to suggest that the efficacy of HBV vaccine alone approaches that of HBV vaccine plus HBIG when a three-dose series is initiated at birth.¹⁹

This may greatly contribute to reducing morbidity and mortality from hepatitis B as there is still limited access to diagnosis and treatment of hepatitis B in many resource constrained settings, and many people are diagnosed only when they already have advanced liver disease or HCC which progresses rapidly, and since treatment options are limited, the outcome is generally poor. In low-income settings, most people with HCC die within months of diagnosis.²³

However, many studies have suggested that HBV transmission in Africa occurs predominantly in childhood, by the horizontal rather than the vertical route. The exact mode of transmission is uncertain but probably involves percutaneous infection through saliva or traces of blood, as well as through unsterile needles, tribal scarification, and other possible vehicles.³⁴ Compared with adult HBsAg carriers in the Far East, those in Africa have a low rate of HBeAg positivity, which may account for the low rates of vertical infection. It is also possible that African infants are less susceptible to vertical HBV infection compared with their Asian counterparts.³⁴ Alternatively, it may be that African infants are indeed infected with HBV at birth but, for genetically determined reasons, have persistently negative tests for a number of years until the virus is reactivated. In view of the high HBV carrier rates in the general population, universal immunisation of all infants is recommended.³⁴ There has been a decline in the prevalence of

occult HBV infection in post-vaccination era in Africa, although the disease burden remains significant in the HIV co-infected population.³⁵

WHO recommends that all infants receive the hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. The birth dose should be followed by three or four doses to complete the primary series. In most cases, one of the following two options is considered appropriate:

- a three-dose schedule of hepatitis B vaccine, with the first dose (monovalent) being given at birth and the second and third (monovalent or combined vaccine) given at the same time as the first and third doses of diphtheria, pertussis and tetanus – (DTP) vaccine;
- or
- a four-dose, where a monovalent birth dose is followed by three monovalent or combined vaccine doses, usually given with other routine infant vaccines.³⁶

The complete vaccine series induces protective antibody levels in more than 95 percent of infants, children and young adults. Protection lasts at least 20 years and is probably lifelong. Thus, WHO does not recommend booster vaccination for persons who have completed the three-dose vaccination schedule. However, envelope antigenic variants may have a selective advantage over wild type under immune selection pressure, as observed in some cases after hepatitis B immune globulin (HBIG) treatment or HBV vaccination.³⁷

Hepatitis B vaccine was introduced in the national Expanded Programme on Immunisation (EPI) in Zambia in 2005 as part of the pentavalent combination given in three doses beginning at the age of six weeks. The pentavalent combination includes vaccines against diphtheria, pertussis, tetanus, hepatitis B and haemophilus influenza type B (DPT-HepB-Hib).¹¹

The map below shows children aged 12 to 23 months who received all basic vaccinations in Zambia. (2013-2014). The following are percentage coverage for each province.

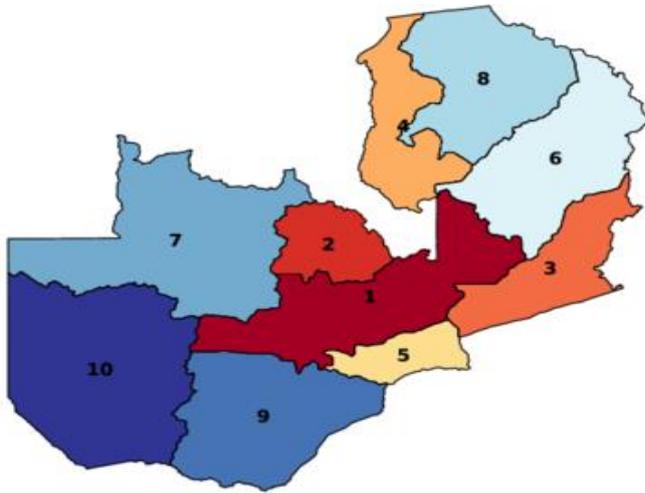


Figure 4: Pentavalent vaccination coverage in Zambia (2013-2014)

| | | | | | |
|---------------|-----|----------------|-----|-------------|-----|
| 1. Central | 66% | 5.Lusaka | 72% | 8. Northern | 72% |
| 2. Copperbelt | 81% | 6.Muchinga | 61% | 9. Southern | 69% |
| 3. Eastern | 64% | 7.NorthWestern | 63% | 10.Western | 64% |
| 4. Luapula | 60% | | | | |

Source -Zambia Demographic Healthy Survey (ZDHS) (2015).³⁸

Full vaccination coverage against hepatitis B in children in Lusaka averaged 82.3 percent.³⁸

A study to determine whether horizontal transmission of the hepatitis B virus contributes to the high prevalence of infection with this virus in an endemic region was done.³⁹ Residents of five villages in Zambia were tested for hepatitis B serologic markers. The prevalence of hepatitis B was determined by testing samples from 620 residents. By examining paired serum samples from 79 children and 80 adults, it was determined that new infections occurred during the five years of this study in at least 14 children (18 percent) (aged 4 to17 years) and ten adults (12 percent) (aged 23 to 65 years).These 24 new infections were distributed among 20 households and were not associated with active HBV infections in the mother or, in most cases, other family members.³⁹

Vaccine failures due to HBV variants with mutations in the small surface protein (S) gene (S mutants) have occurred in perinatally exposed infants who received hepatitis B vaccine or HBIG appropriately and who have concentrations of anti-HBs that are usually protective. There has been concern that these HBV variants, which are sometimes resistant to the neutralizing effect of anti-HBs, could threaten the effectiveness of hepatitis B immunisation programmes and that immunisation may accelerate the formation of HBV variants.⁶ Despite these concerns, there are several reasons to believe that hepatitis B vaccination will continue to reduce disease burden.⁶ Several factors have been associated with nonresponse to hepatitis B vaccine. These include vaccine factors (e.g., dose, schedule, injection site). Host factors such as older age (40 years and older), male sex, obesity, smoking, and chronic illness have been independently associated with nonresponse to hepatitis B vaccine.¹⁴

In Zambia the pentavalent vaccine is given to children at 6, 10 and 14 weeks of age.¹¹ Hepatitis B screening in pregnant women is not routinely done in Zambia and the neonates born of these women may be exposed to HBV, yet do not receive the vaccine or HBIG at birth as per WHO recommendation.

CHAPTER THREE: METHODOLOGY

3.1 Study design

This was a cross sectional study conducted in children below the age of five years.

3.2 Study sites

University Teaching Hospitals –Children’s Hospital, a tertiary hospital and Kamwala Health Centre, a primary health centre in Lusaka, Zambia. The two institutions in Lusaka were chosen because the University Teaching Hospitals receives patients with different social economic statuses and from all corners of Lusaka and surrounding areas as well from all over the country requiring specialist attention. While Kamwala Health Centre on the other hand is likely to receive children who are not very ill, and its location enables it to serve those with low and medium income status. The point of entry for both institutions was the outpatient department and the wards for UTHs-Children’s Hospital, those who met the criteria were enrolled.

3.3 Target population

Children below the age of five years.

3.4 The study population

The study population comprised of children from birth to five years of age seeking medical attention from UTHs-Children’s Hospital and Kamwala Health Centre with non-surgical conditions. Consent to test the guardians/parents who came with these children for HBsAg was sought. However, children whose parents/guardians declined to be tested for HBsAg and yet

consented to have their children participate in the study, were also enrolled. Testing the guardians to these children would show if there is any association between a child's HBsAg positivity and his or her parents/guardians status.

3.5 Eligibility

3.5.1 Inclusion criteria

Children below the age of five years old.

Children whose parents/guardians will give consent.

3.5.2 Exclusion criteria

Non-residents of Lusaka.

3.6 Description of variables

3.6.1 Dependent variables

3.6.1.1 Primary outcome (1) Positive HBsAg

3.6.1.2 Secondary outcomes (1) Percentage of children who have received all three doses

of hepatitis B vaccine.

(2) Distribution of HBsAg positivity in children at Children's

Hospital and Kamwala Health centre in Lusaka.

3.6.2 Independent variables

- (1) Maternal Hepatitis B status
- (2) Age
- (3) Maternal HIV status
- (4) Transfusion history
- (5) Parental/guardian Education
- (6) Economic status
- (7) Religion
- (8) Race

3.7 Sampling method

A convenient sampling method was used. Children who met the criteria were enrolled and included in the study until the sample size was met/exceeded.

3.8 Sample size calculation

The following prevalence formula was used to calculate the sample size

$$N=Z^2 \{P (1-P)/ (D^2)\}$$

Where N=sample required

Z=Z statistics=1.96(95 percent CI)

P=expected prevalence of 0.08 (assuming the prevalence is 8%)

D=acceptable accuracy range= 0.03

$$N=\frac{(1.96)^2 \times 0.08(1-0.08)}{(0.03)^2} = 315.$$

Therefore the minimum sample size was 315 children.

3.9 Study procedures

3.9.1 Patient screening, study enrolment and collection of socio-demographic and medical information

The purpose of the study and the procedures involved were explained in the language the guardian understands. Children who met the criteria and whose guardians/parents gave written consent to have them participate in the study were enrolled. Informed written consent (appendix 2) was obtained from the participants guardians/parents. Their hepatitis B immunisation status was among the medical history collected.

Guardians/parents of children presenting to the 2 institutions were requested to be tested. Permission to test guardians/parents who came with these children was sought and those who consented to be part of the study were also tested for HBsAg. Informed written consent was obtained for recruitment of both by signing both section A and B of the consent form. However, the children of those guardians/parents who were not willing to be tested but gave consent for their children to participate, were recruited and only signed section A of the consent form.

The participants' socio-demographic and medical information was obtained using the structured questionnaire (appendix 3). Personal information that may identify the participant was not included in the data collection tool. The only identity for each participant was the study number. The phone numbers of parents/guardians were collected for the easy of communication of the results. These numbers were recorded in two separate diaries, one at each study site, which was kept by the researcher and her two assistants. The phone numbers were needed to facilitate the communication of results. Once the results were ready, only the principle researcher and her supervisors had access to the results. One study number was given to each pair with parent/guardian sample being labelled with an M, F or G for mother, father or any other guardian respectively. The results were communicated biweekly to the participants

so that those who were found positive for the virus could be referred appropriately for further follow up and treatment.

3.9.2 Laboratory procedures and data collection

Two millilitres of blood was drawn from the dorsal aspect of hand or cubital fossa using a sterile disposable needle and syringe. The blood was put in an EDTA bottle and transported to the Tropical, Gastroenterology and Nutrition (TROPGAN) laboratory in the Department of Internal Medicine at the UTHs, where they were analysed for HBsAg.

Participants who tested positive had their samples tested for other markers of HBV infection and these included HBeAg and HBcAb as part of the assessment to determine who needed treatment.

The adults i.e. parents /Guardians who tested positive for HBsAg were contacted and linked to infectious disease specialists under the infectious disease unit in internal medicine at UTH for further management.

The children who were found positive for HBsAg were managed just like any other child who has HBV infection under infectious disease unit at the University Teaching Hospitals-Children's hospital.

3.10 Data management and analysis

The plan included sorting data and performing quality control checks by pretesting the research instruments and research procedures, checking at the end of each day whether the questionnaires were filled in completely and consistently during the data analysis stage.

Data was entered, stored using Epi data Version 3.1 software and analyzed using SPSS Version 21.0. Chi square test was used to determine the association between, vaccination status, parental/guardian hepatitis B status and Hepatitis B infection. The data has been presented using tables, graphs and pie charts for easy communication.

3.11 Ethical consideration

The study endeavoured to adhere to the ethical standards of the Excellence in Research and Science (ERES) converge International Review Board (IRB) and the Helsinki declaration. Ethical approval was sought from ERES. Permission to carry out the study was sought from the Lusaka District Health Office and permission was granted. The purpose and procedures of the study were fully explained, and a written informed consent was obtained from all the parents/guardians. It was emphasized that participation in the study was purely voluntary and that participants were free to withdraw from the study at any point without affecting their child's right to treatment or care. They were also be assured that no harm will be done to them or their child/children during the study or afterwards. The researcher observed respect when interacting with parents/guardians. Study aim and objectives of the study were explained to guardians/parents. After which they were given an opportunity to ask questions, allow them time to think and make informed decision before obtaining informed consent. Personal information that may identify the participant was not included in the data collection tool. The only identity for each participant was the study number.

3.11.1 Benefits to participants

HBsAg test is not part of the routine tests except in blood donors and most patients are not aware of their Hepatitis B status. Participants had the opportunity to know their Hepatitis B

status. The participants who were positive had an opportunity to be treated. An infectious disease specialist was consulted on all patients who tested positive for HBsAg. Those who were found positive were referred appropriately for care and possible treatment as appropriate treatment following detection may cure, reverse or delay further liver damage.⁴⁰

3.11.2 Risks to participants

Discomfort of venepuncture and possible psychological trauma. Venepuncture may be associated with pain, bleeding or infection. These were minimised by use of a topical analgesia and skilful aseptic blood collection techniques. The research team was responsible for any research related injuries.

3.12 Limitations

- i. The study was done from 2 health facilities in Lusaka urban thus the results may not reflect the provincial or indeed the national picture on the prevalence of HBV infection in under 5 children in Lusaka, Zambia.
- ii. This being a hospital based study, it was unable to give the true prevalence of the hepatitis B virus in children.
- iii. The other viral markers for hepatitis B infection were not done during this study hence the study was unable to determine if the hepatitis B infection was due to acute or chronic HBV infection.
- iv. This study was under powered due to low numbers of positive outcomes and thus could not confidently identify the risk factors associated with hepatitis B virus infection.

CHAPTER FOUR: RESULTS

4.1 Baseline characteristics of participants

A total number of 340 children and 11 guardians were recruited for this study. The youngest child was a neonate about 16 hours old who presented with neonatal sepsis and the oldest was a five year old admitted with pneumonia. There were seven samples that had an invalid laboratory results for HBsAg. The distribution of participants between the two institutions was as shown in Figure 5 below.

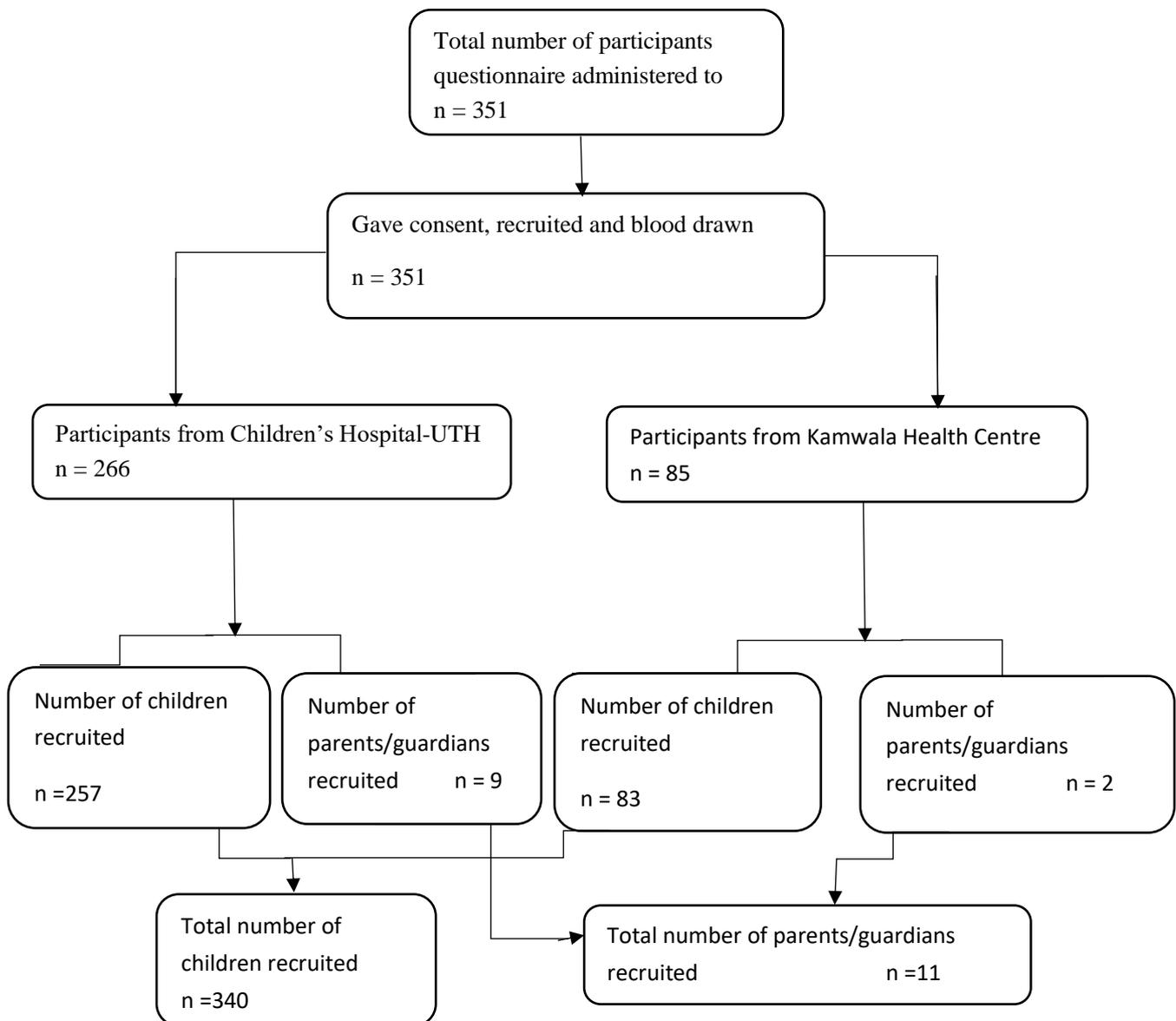


Figure 5: Summary of findings - Flow chart of study procedures

Three-quarters of the children recruited, 257/340 (75.6 percent), were from the UTH while 83/340 (24.4 percent) were from Kamwala health centre (Figure 5). This distribution proportion difference in patient source site was statistically significant ($P < 0.001$). The mean age was 13.2 months ($SD = 16.07$). There were slightly more male children, 176/340 (51.8 percent), than female children, 164/340 (48.2 percent), however, this difference was not statistically significant ($P = 0.52$). Slightly over half of the guardians, 190/340 (55.9 percent), had a monthly income between K1, 000.00 and K5, 000.00, while about one-third, 113/340 (33.2 percent) earned less than K1, 000.00 monthly (Figure 6). Almost two-thirds of the children, 214/340 (62.9 percent), had never had a blood test for hepatitis B while only about one-thirds, 120/340 (35.3 percent) had the blood test. This difference in proportion was significant ($P < 0.001$). There were 5/340 (1.5 percent) children with a positive hepatitis B surface antigen result, 7/340 were invalid and 328/340 (96.5 percent) had a negative result (Table 3). Thus, the prevalence of HBsAg among the children was 1.5 percent. of participants

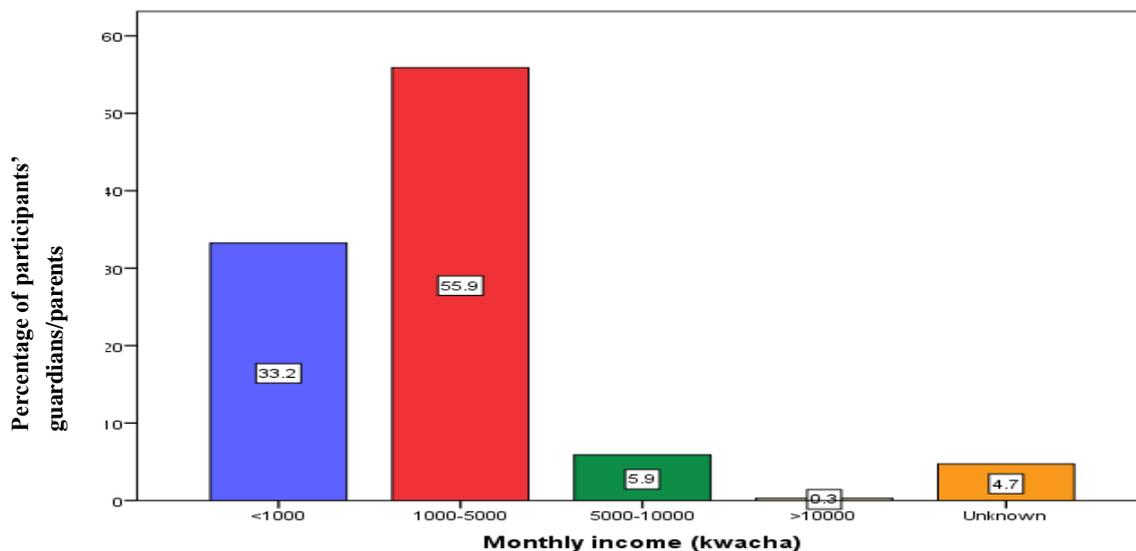


Figure 6: Guardian's monthly income distribution

There were 181/340 (53.2 percent) children who were fully vaccinated against HBV and 35/340 (10.3 percent) partially vaccinated. There were 225/340 (66.2 percent) children who had ever tested for HIV and 101/340 (29.7 percent) who had never had the HIV test. The proportional difference between children who had ever had the HIV test and who had never was significant ($P < 0.001$). There were 6/340 (1.8 percent) children with HIV positive status. There were 14/340 (4.1 percent) children with a history of a blood transfusion, while a greater majority 281/340 (82.6 percent) had no history of blood transfusion and 45/340 (13.2 percent) were unknown. There were 211/340 (62.1 percent) mothers with negative HIV status, 85/340 (25 percent) with positive status, and status was unknown for 44/340 (12.9 percent). There were 7/340 (1.5 percent) mothers/guardians who knew their HBV status. Out of 11 guardians five (36 percent) mothers tested positive for HBsAg. Of the five mothers who were positive, three of their children were also positive for HBsAg. One neonate exposed to HBV was negative for HBV infection while the other neonate exposed to both HIV and HBV was also negative for HBV infection. Both neonates had not received any vaccination against HBV at the time of recruitment.

4.2 Descriptive characteristics of participants

Table 2: Descriptive characteristics of study participants (n = 340)

| Variable | Frequency | Percent |
|---|------------------|----------------|
| Study site | | |
| UTH-Children's Hospital | 257 | 75.6 |
| Kamwala | 83 | 24.4 |
| Sex | | |
| Female | 164 | 48.2 |
| Male | 176 | 51.8 |
| Guardian's Monthly income | | |
| <1000 | 113 | 33.2 |
| 1000-5000 | 190 | 55.9 |
| 5000-10000 | 20 | 5.9 |
| >10000 | 1 | 0.3 |
| Unknown | 16 | 4.7 |
| Hepatitis B Surface antigen | | |
| Positive | 5 | 1.5 |
| Negative | 328 | 96.5 |
| Invalid | 7 | 2.0 |
| HBV vaccination status | | |
| Unknown | 28 | 8.2 |
| Partial immunised | 35 | 10.3 |
| Fully immunised | 181 | 53.2 |
| N/A | 96 | 28.2 |
| Child ever had HIV test | | |
| Yes | 225 | 66.2 |
| No | 101 | 29.7 |
| Unknown | 14 | 4.1 |
| Child's HIV result | | |
| Positive | 6 | 1.8 |
| Negative | 199 | 58.5 |
| Unknown | 135 | 39.7 |
| Child received blood transfusion | | |
| Yes | 14 | 4.1 |
| No | 281 | 82.6 |
| Unknown | 45 | 13.2 |
| Maternal HIV status | | |
| Unknown | 44 | 12.9 |
| Positive | 85 | 25 |
| Negative | 211 | 62.1 |
| Maternal/guardian HBV status | | |
| Unknown | 329 | 96.7 |
| Positive | 5 | 1 |
| Negative | 6 | 2.4 |
| Age (months) (mean, SD) | 13.2, 16.07 | |

Table 3: Characteristics of HBsAg positive children

| Age (months) | HBV vaccination | HIV status | Maternal HBV status | History of Blood transfusion |
|---------------------|------------------------|-------------------|----------------------------|-------------------------------------|
| 24 | Fully vaccinated | Negative | Positive | No |
| 42 | Fully vaccinated | Negative | Positive | Yes |
| 45 | Fully vaccinated | Positive | Negative | No |
| 25 | Partially vaccinated | positive | positive | No |
| 49 | Unknown | Negative | unknown | No |

4.3 Bivariate Analysis of study variables

Table 4 below shows bivariate analysis results for the association with HBV status in children.

At 5 percent significance level, the following variables were associated with HBV infection:

- a) Childs HIV status ($P < 0.001$)
- b) Maternal HIV status ($P = 0.03$)
- c) Maternal hepatitis B status ($P < 0.01$)
- d) Age of child ($P = 0.01$)

Factors such as sex, household income, hepatitis B vaccination status and history of blood transfusions were not associated with hepatitis B surface antigen positivity.

Table 4: Bivariate analysis for the association with HBV status

| Variable | Invalid Result | | HBsAg Negative | | HBsAg Positive | | P-value |
|-------------------------------------|----------------|--|----------------|-------|----------------|--------|---------|
| | N | | N | % | N | % | |
| Study site | | | | | | | |
| UTH | 7 | | 245 | 75.0% | 5 | 100.0% | 0.63 |
| Kamwala | 0 | | 83 | 25.0% | 0 | 0.0% | |
| Sex | | | | | | | |
| Female | 2 | | 123 | 37.5% | 2 | 40% | 0.91 |
| Male | 5 | | 205 | 62.5% | 3 | 60% | |
| Guardians monthly Income | | | | | | | |
| <1000 | 0 | | 113 | 34.5% | 2 | 40.0% | 0.96 |
| 1000-5000 | 7 | | 178 | 54.3% | 3 | 60.0% | |
| 5000-10000 | 0 | | 14 | 4.3% | 0 | 0.0% | |
| >10000 | 0 | | 11 | 3.4% | 0 | 0.0% | |
| Unknown | 0 | | 12 | 3.7% | 0 | 0.0% | |
| Ever tested for Hepatitis B | | | | | | | |
| No | 7 | | 274 | 83.5% | 5 | 100.0% | 0.64 |
| Yes | 0 | | 42 | 12.8% | 0 | 0.0% | |
| Unknown | 0 | | 12 | 3.7% | 0 | 0.0% | |
| HBV vaccination | | | | | | | |
| Unknown | 4 | | 23 | 7.0% | 1 | 20.0% | 0.59 |
| Partially vaccinated | 2 | | 32 | 9.8% | 1 | 20.0% | |
| Fully vaccinated | 1 | | 177 | 53.9% | 3 | 60.0% | |
| N/A | 0 | | 96 | 29.3% | 0 | | |
| Child HIV status | | | | | | | |
| Positive | 0 | | 4 | 1.2% | 2 | 40.0% | <0.001 |
| Negative | 0 | | 196 | 59.8% | 3 | 60.0% | |
| Unknown | 7 | | 128 | 39.0% | 0 | 0.0 | |
| Maternal HIV status | | | | | | | |
| Unknown | 3 | | 236 | 71.9% | 1 | 20.0% | 0.03 |
| Positive | 0 | | 85 | 25.9% | 3 | 60.0% | |
| Negative | 4 | | 7 | 2.1% | 1 | 20.0% | |
| History of Blood Transfusion | | | | | | | |
| Yes | 0 | | 14 | 4.3% | 1 | 20.0% | 0.09 |
| No | 7 | | 301 | 91.7% | 4 | 80.0% | |
| Unknown | 0 | | 13 | 3.9% | 0 | 0.0% | |
| Guardian HBV status | | | | | | | |
| Unknown | 7 | | 317 | 96.6% | 1 | 20.0%/ | <0.01 |
| Positive | 0 | | 5 | 1.5% | 3 | 60.0% | |
| Negative | 0 | | 6 | 1.8% | 1 | 20.0% | |
| Age | | | | | | | |
| mean (SD) | | | 17.9 (15.97) | | 36.9 (20.09) | | 0.01 |

4.4 Logistic regression Analysis

The backward logistic regression analysis showed that age of the child was an important factor independently associated with child HBV status. For every increase of one month in child age, the odds for positive HBV status increased by an average six percent (OR = 1.06, 95% CI = 1.01 – 1.11, P-value = 0.03).

4.5 Hepatitis B vaccination status of participants

A total of 181 (53.2 percent) children were fully vaccinated against HBV according to the Zambian guidelines while 32(9.4percent) had received two of the required three doses of the hepatitis B vaccine and three (0.9 percent) children received only one dose of the vaccine. The remaining 96 (28.2 percent) were six weeks old or younger and they had not yet received their first hepatitis B vaccine. Five children were positive for HBsAg, giving a seroprevalence of 1.5 percent. Three (60 percent) of those positive for HBsAg were above 40 months and two were around 24 months old. 3 /5 (60 percent) of HBsAg positive were fully vaccinated.

CHAPTER FIVE: DISCUSSION

5.1 Prevalence of HBV, pre and post introduction of HBV vaccine in the region

The prevalence of hepatitis B infection at Children's Hospital and Kamwala health centre was found to be 1.5 percent. A total of three of the five children who had a positive hepatitis B surface antigen were fully vaccinated, one did not receive any hepatitis B vaccine and the immunisation status was not known for the other one. One of the mothers to the participants who had a positive HBsAg was positive for HBsAg and she knew her status prior to the study, however, the status of the child was not known prior to the study.

The low prevalence in hepatitis B can be attributed to the hepatitis B vaccine that was introduced in Zambia in 2005 though there was no association shown in this study due to the low number of positive results. The vaccine in spite of the first dose being given at six weeks and not at birth as recommended by the WHO, though effective, there may be a few children who may slip through this six week period as seen in this study where we had three children who were fully vaccinated against hepatitis B coming with HBV Infection. It can be seen from this study that the seroprevalence of HBV infection in children at the University Teaching Hospitals has declined to 1.5 percent compared to 2.5 percent in the pre vaccination era.⁸ There has also been a decline in the prevalence of HBV infection in children with sickle cell disease at UTH – Children's Hospital from 5.8 percent.⁸ to 2.2 percent.²⁹ A similar trend was seen in HIV infected children at UTHs -paediatric centre of excellence where the prevalence of HBV infection was found to be 5.9percent.²⁸from 6.2 percent in hospitalised children with HIV.⁴¹ The decline in the prevalence of HBV infection in these special paediatric populations can partly be attributed to the hepatitis B vaccine. However, this was not the case in South

Africa where 28 percent of infants born to HIV positive mothers with chronic HBV infection had some evidence of HBV infection by the twelfth month of life. Which seems high and suggests that increased attention is warranted regarding peripartum and infant HBV transmission.²³

However, many studies have suggested that HBV transmission in Africa occurs predominantly in childhood, by the horizontal rather than the vertical route. The exact mode of transmission is uncertain but probably involves percutaneous infection through saliva or traces of blood, as well as through unsterile needles, tribal scarification, and other possible vehicles.³⁴ Compared with adult HBsAg carriers in the Far East, those in Africa have a low rate of HBeAg positivity, which may account for the relatively low rates of vertical infection.⁷ The younger a child is at the time of HBV infection the more likely they are to develop chronic HBV infection and its complications,⁹ hence the need to prevent children from acquiring the infection by vaccinating them early.

The seroprevalence of hepatitis B infection of 1.5 percent found in this study was not significantly different from the estimated figure of less than one percent in immunised children by WHO.⁹ However, larger studies with bigger sample sizes are required to know the true prevalence of hepatitis B virus infection in children below the age of five years in Lusaka.

The results obtained from this study are comparable to other results found in the region in the paediatric population after the introduction of the hepatitis B vaccine. For instance, in Tanzania the hepatitis B vaccine was introduced in 2002, about three years earlier than Zambia. The pre vaccination prevalence of HBV infection in that country was 11.2 percent

but declined to 1.7 percent post vaccination in children.⁴² In this study, three (60 percent) of the children who had a positive HBsAg were fully vaccinated while one (20 percent) had received one dose of the hepatitis B vaccine and the vaccination status for the other one (20 percent) was not known. A study done in Kenya after the introduction of the hepatitis B vaccine found none of the children vaccinated against HBV had the infection.⁴³

A significant impact of the hepatitis B vaccine has been seen in Taiwan where the introduction of the vaccine in 1984 saw the drastic decline in morbidity and mortality from hepatitis B virus related hepatocellular carcinoma.^{44,45} Taiwan like Zambia does not screen its pregnant women routinely for hepatitis B virus infection and neonates only get their first hepatitis B vaccine at six weeks at which time it may be too late to prevent not only vertical but also horizontal transmission of the virus. It has been noted in developed countries that vaccinating neonates at birth can reduce the prevalence to near zero.⁴⁶

The prevalence of HBV infection among blood donors in Zambia was at eight to ten percent.³¹ Majority of these blood donors are of child bearing age (16-64 years) and yet there is no routine screening of pregnant women for HBV infection. It is therefore important to vaccinate children against HBV at birth if this reduction in prevalence of HBV infection is to be sustained. Some developed countries have shown that giving the birth dose of hepatitis B vaccine reduces the prevalence to near zero,⁴⁶ though in this study the association between hepatitis B vaccination status and hepatitis B virus infection was not shown as the study was underpowered by the small number of HBsAg positivity.

Factors such as sex, household income and history of blood transfusions were also not associated with HBsAg positivity. However, the following factors were independently associated with HBV infection; maternal HIV infection, maternal HBV infection, child's HIV infection and the child's age. Age was an important factor independently associated with hepatitis B virus infection. For every increase of one month in the child's age, the odds for positive HBsAg increased by an average six percent (OR = 1.06, 95% CI = 1.01 – 1.11, P-value = 0.03).

CHAPTER SIX: CONCLUSION

6.1 Conclusion

The seroprevalence of hepatitis B at Children's Hospital – University Teaching Hospital and Kamwala Health Centre is 1.5 percent. This low prevalence can be associated with the introduction of the hepatitis B vaccine which was introduced in Zambia in 2005. However, our small study did not demonstrate this thus the need to do a larger study to demonstrate the association and better understand the risk factors for HBV infection in children.

It is important to note that three (60 percent) of the children who were positive for HBsAg were fully vaccinated against hepatitis B in accordance with the Zambian schedule. Though the seroprevalence found in this study is close to the estimated prevalence of less than one percent in vaccinated children by WHO, there may be a few children who may slip through the six week gap before the first vaccine is given, however larger studies are needed to know the true prevalence of Hepatitis B infection in Lusaka and Zambia after the introduction of the hepatitis B vaccine.

Timely HBV birth dose vaccination is one of the key interventions identified by the WHO in its Global Health Sector Strategy on Viral Hepatitis, with the target coverage rate of 90 percent by 2030 with the goal of eliminating viral hepatitis by the year 2030.¹⁹

6.2 Recommendations

- i. To introduce the birth dose of hepatitis B vaccine in Zambia considering the high morbidity associated with the disease.
- ii. To carry out large studies with larger sample sizes to better identify the risks associated with the HBV infection in children under the age of five years.
- iii. To screen all pregnant women for hepatitis B virus infection.

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APPENDICES

APPENDIX 1.1



The University of Zambia

Directorate of Research and Graduate Studies

PARENTS/GUARDIANS INFORMATION SHEET - ENGLISH

STUDY TITLE

SEROPREVALENCE OF HEPATITIS B INFECTION IN CHILDREN LESS THAN FIVE YEARS OF AGE AT THE UNIVERSITY TEACHING HOSPITALS-CHILDREN'S HOSPITAL AND KAMWALA HEALTH CENTER IN THE VACCINATION ERA IN LUSAKA, ZAMBIA

My name is Jane Goma, am doing my masters in Paediatrics and Child Health at the University of Zambia (UNZA). I will be doing a research on hepatitis B virus (HBV) infection in children.

What is known about hepatitis B infection is that;

Most people do not experience any symptoms during the acute infection phase. At least 7 out of 10 patients have hepatitis without yellowing of eyes. Most children with chronic Hepatitis B infection (persistent hepatitis B infection for more than 6 months) have no signs and do not generally require treatment. These children are, however, at increased risk for severe

complications later in life, including advanced liver disease, cancer of the liver and do require close monitoring.

Chronic hepatitis B infection is the leading cause of liver cancer in Asia and Africa, where the virus is endemic and transmission from mother to child is common.

It is not possible, just on examination, to tell the difference between hepatitis B from hepatitis caused by other viral agents and, hence, laboratory confirmation of the diagnosis is essential.

Several manifestations not involving the liver are associated with chronic hepatitis B infection, many with significant morbidity and mortality.

The likelihood that infection with the virus becomes chronic depends upon the age at which a person becomes infected. Children less than 6 years of age who become infected with the hepatitis B virus are the most likely to develop chronic infections. Hence the need to screen the children below 6 years of age for the infection.

80–90% of infants infected during the first year of life develop chronic infections;

30–50% of children infected before the age of 6 years develop chronic infections.

An individual may acquire hepatitis B infection through direct contact with infected bodily fluids such as infected blood or in the womb a child may get infected from an infected mother.

Benefits of this study to participants

Participants will have the opportunity to know their hepatitis B status. This test is not part of the routine test and most patients are not aware of their hepatitis B status. Those who will be found positive will be referred appropriately for appropriate care. Early initiation of treatment

to those who need treatment significantly reduces the risks of liver cirrhosis or liver cancer although it does not completely eliminate the risk.

Risks to participants

The test requires collection of blood from the vein which may be associated with bleeding and infection. The procedure of collecting blood is also associated with pain at the puncture site but this will be minimised by use of topical analgesic cream. Bleeding and infection will be minimised by use of skilful aseptic blood collection techniques.

In the unlikely event that any adverse event arises from the procedure, all reasonable measures such as, applying pressure in an event of a bleed or giving the participant appropriate antibiotics should an infection occur, will be taken in accordance with the standard medical practice to mitigate adverse results. The research team will be responsible for any research related injuries.

What is being requested from you?

You are kindly requested to participate in the above study. For the study to be a success, 2ml of blood is required from your child and you if you are willing to participate. If you don't wish to be tested, your child is still eligible to participate in the study. Your participation is voluntary, should you withdraw from the study at any time, it will not affect the care your child will receive.

You are free not to respond to questions which you feel are uncomfortable.

You will remain anonymous, your only identification is the study number, only the researcher and her three supervisors will have access to your result.

After the study there will very little blood that will remain and this will be disposed of by the laboratory.

Your participation will be highly appreciated.

For any concerns or questions kindly contact.

Dr Jane Goma

or

The Chairperson

The University Teaching Hospitals

ERES CONVERGE IRB

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APPENDIX 1.2



The University of Zambia

Directorate of Research and Graduate Studies

MAKOLO / OTSOGOLERA NKHANI YOLINGALIRA- NYANJA

PHUNZIRO

PHUNZIRO PA HEPATIS B KUCHITA M'BANA PAKATI PA ZAKA ZISANU KU UNIVESITI YOPHUNZITSA NTCHITO-CHIPATALA CHA A ANA NA CHIPATALA CHA KAMWALA MZIMU WA ZAMALIZA KU LUSAKA, ZAMBIA

Dzina langa ndine Jane Goma, ndi kuphunzira masters mu chikhalidwe cha ana

ku Universiti of Zambia (UNZA). Ndidzachita kafukufuku pa matenda a chiwindi cha hepatitis B (HBV).

Chimene chimadziwika pa matenda a hepatitis B ndicho;

Anthu ambiri samakhala ndi zizindikiro pa nthawi yoopsa ya matenda. Odwala asanu ndi awiri mwa khumi alionse ali ndi chiwindi cha hepatitis popanda maso a chikasu. Ana ambiri omwe ali ndi matenda opatsirana a Hepatitis B (matenda opatsirana ndi chiwindi chakumtunda B kwa miyezi isanu ndi umodzi) alibe zizindikiro ndipo samafuna chithandizo. Ana awa ali ndi chiopsezo chowonjezeka cha mavuto akuluakulu m'moyo, kuphatikizapo matenda a chiwindi, khansa ya chiwindi ndipo amafunika kuyang'anitsitsa.

Matenda a chiwindi ndi omwe amachititsa khansa ya chiwindi ku Asia ndi Africa, kumene kachilombo ka doyo kamayambira ndipo kufalitsa kwa amayi kupita kwa mwana ndi kofala.

Sizingatheke, pokhapokha ngati atayesedwa, kuti adziwe kusiyana pakati pa chiwindi cha mtundu wa B kuchokera ku chiwindi cha chiwindi chomwe chimayambitsa, motero, umboni wa labotori wokhudzana ndi matendawa ndi wofunikira.

Mawonetseredwe angapo osagwirizanitsa chiwindi ndi odwala matenda opatsirana ndi chiwindi cha chiwindi, omwe ambiri ali ndi matenda aakulu komanso amfa

Mwinamwake kuti kachilombo ka hepatitis B kamakhala kochepe kumadalira zaka zomwe munthu ali ndi kachilombo ka hepatitis B. Ana osakwana zaka zisanu ndi chimodzi omwe amapezeka ndi kachilombo ka hepatitis B ndi omwe amakhala ndi matenda aakulu. Choncho kufunika kusindikiza ana osapitirira zaka 6 kuti adziwe matendawa.

- 80-90% ya ana omwe ali ndi kachilombo ka chiwindi m'chaka choyamba cha moyo amakhala ndi matenda akuluakulu;
- 30-50% mwa ana omwe ali ndi kachilomboka asanakwanitse zaka zisanu ndi chimodzi (6) amakhala ndi matenda akuluakulu.

Munthu akhoza kutenga matenda a hepatitis B kudzera mwachindunji ndi madzi omwe ali ndi kachilombo ka HIV kapena m'mimba mwana angatenge kachilombo ka mayi.

Phindu la phunziroli kwa ophunzira

Ophunzira adzapeza mwayi wodziwa chikhalidwe chawo cha hepatitis B. Mayesowa sali mbali ya kuyesedwa kwachizoloŵezi ndipo ambiri odwala sakudziwa kuti ali ndi chiwindi cha chiwindi. Amene adzalandire chithandizo adzatumiziridwa moyenera kuti azisamalidwa bwino. Kuyambira koyambirira kwa chithandizo cha mankhwala kwa omwe akusowa chithandizo kumachepetsa kwambiri kuopsa kwa chiwindi cha chiwindi kapena khansara ya chiwindi ngakhale kuti sikunga chotseretu chiopsezo chonse.

APPENDIX 2

2.1 CONSENT FORM

PART A.

Ias the parent/guardian of the child named.....aged....., agree to have my child participate in the study on seroprevalence of hepatitis B among children presenting to University Teaching Hospitals – Childrens hospital or Kamwala Health Centre. I understand that the study will involve the drawing of two millilitres of blood. I also understand that the Procedure which is the drawing of blood from the above child will be performed by adequately trained and experienced medical staff. It has further been explained to me that the above procedure presents some risks and minimal pain to the child. In the unlikely event that any adverse event arises from the procedure, I understand that all reasonable measures will be taken in accordance with the standard medical practice to mitigate adverse results and that any injuries arising from the study will be the responsibility of the research team.it has also been explained to me that my refusal to have my child participate in the study will not affect the care my child will receive.

PARENT/GUARDIAN

WITNESS

Signature.....

Signature.....

Date.....

Date.....

Relationship to child.....

Name and designation.....

Thumb Print

PART B.

I

..... aged.....as the guardian/parent of the child named.....aged....., agree to participate in the study on seroprevalence of hepatitis B among children presenting to University Teaching Hospital or Kamwala Health Centre. I understand that the study will involve the drawing of two millilitres of blood from me. I also understand that the Procedure which is the drawing of blood from me will be performed by adequately trained and experienced medical staff. It has further been explained to me that the above procedure presents some risks and minimal pain. In the unlikely event that any adverse event arises from the procedure, I understand that all reasonable measures will be taken in accordance with the standard medical practice to mitigate adverse results and that any research related injuries will be the responsibility of the research team. It has also been explained to me that my refusal to participate in the study will not affect the care my child will receive.

PARENT/GUARDIAN

WITNESS

Signature.....

Signature.....

Date.....

Date.....

Name and designation.....

Thumb Print

APPENDIX 3

SEROPREVALENCE OF HEPATITIS B DATA COLLECTION TOOL

Study id

Date of interview DD MM YY YY

Interviewer.....

Study site (tick one) UTHs OPD
 Ward

Kamwala

Date of birth.....

Place of birth.....

Age.....

local clinic.....

Gender (please tick)

F

M

Residence

Race.....

Monthly income (guardian)

<K1000

1000-5000

5000-10 000

>10 000

Religion Christian

Islam

Atheist

Others (specify)

Has the child ever had a blood test for hepatitis B?

Yes

No

If yes, what was the result?

Positive

Negative

HBV Immunisation status, tick for each vaccine

unknown/no evidence

not vaccinated

Has the child ever had an HIV test before?

Yes

No

If yes, what was the result?

Positive

Negative

Has your child ever been transfused before?

Yes

No

Maternal HIV status

unknown

Positive

Negative

Parental /guardian HBV status

unknown

Positive

Negative

Provisional diagnosis on presentation

Researcher's / Assistant researcher's signature

APPENDIX 4
FOR LABORATORY USE ONLY

TICK AS APPROPRIATE

| TEST | POSITIVE | NEGATIVE |
|-----------------------------|----------|----------|
| HEPATITIS B SURFACE ANTIGEN | | |

Lab technicians' signature _____.

PARENTS/GUARDIANS RESULT

TICK APPROPRIATELY

DONE M F G NOT DONE

| TEST | | |
|-----------------------------|--|--|
| HEPATITIS B SURFACE ANTIGEN | | |

Lab technicians' signature _____.