PREVALENCE OF HEPATITIS B, C AND HIV INFECTIONS IN CHILDREN WITH SICKLE CELL ANAEMIA AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

By

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A Dissertation Submitted in Partial Fulfilment of the Requirements for the Degree of Master of Medicine (Paediatrics and Child Health) of Muhimbili University of Health and Allied Sciences.

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance a dissertation entitled **"PREVALENCE OF HEPATITIS B, C AND HIV INFECTIONS IN CHILDREN WITH SICKLE CELL ANAEMIA AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA"** in partial fulfillment of the requirements for the degree of Master of Medicine (Paediatrics and Child Health) of the Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, Kamaria Kassim, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

I dedicate this work to my parents, Mr and Mrs S. Kassim.

My dear sisters Zubeida and Afiya.

My dear brothers Ally and Nawaf.

My lovely Irfan and Saeed.

My sweet Nathania, Ashour, Afiya and Aaliyah.

Some other people who are very special in my heart who supported me all the way.

Summary

Background: Hepatitis B virus (HBV) accounts for a large portion of the disease burden worldwide with 350 million chronic carriers of the disease. Africa, with 12% of the world's population, carries approximately 18% of the global burden of HBV infection, with hepatocellular carcinoma and cirrhosis accounting for 2% of the continent's annual deaths. World Health Organization (WHO) estimates that about 170 million people, 3% of the world's population, are infected with hepatitis C virus (HCV) and are at risk of developing liver cirrhosis and/or liver cancer. Besides HBV, HCV infections, Sub-Saharan Africa is also affected by human immunodeficiency virus (HIV) infection. In 2007 the number of people living with HIV was estimated to be 1.4 million in Tanzania. The majority of children get infected with HIV perinatally. Acute severe anaemia necessitating blood transfusion is very frequent in Tanzania because of malaria and infections. Children with sickle cell anaemia (SCA) are at even a greater risk of frequent blood transfusions and consists mainly the use of packed RBCs. The viruses mentioned above can be transmitted from mother to child (intra-uterine, breast feeding), through horizontal transmission by contaminated blood. Part of the national blood transfusion services is to reduce transmission of infections. Donor blood is screened for Hepatitis B, HIV and syphilis. Data on the magnitude of HBV, HCV and HIV infections in children with SCA are limited.

Objectives: To determine the prevalence and factors associated with HBV, HCV and HIV among children with SCA aged between 6 months and 10 years in a tertiary referral hospital.

Materials and methods: This was a hospital based cross-sectional study that was carried out between November 2008 and March 2009 at Sickle Cell Disease (SCD) clinic at Muhimbili National Hospital in Dar es Salaam, Tanzania. All children with SCA aged between six months and ten years inclusive attending the SCD clinic who met the inclusion criteria during the study period were eligible to be enrolled in the study after getting informed consent. Data was collected using structured questionnaire which included patient history, physical examination and test results for HBV, HCV and HIV infection. The data were analyzed using EPI Info version 6.4 and the SPSS version 15.

Results: During the study period, 540 children with SCA were enrolled into the study. Of 540 children, 308 (57%) were males. Three hundred and seventy eight (70%) children were not vaccinated with hepatitis B vaccine. Seventy three point five percent of those vaccinated had protective anti-HB_s levels $\geq$10mIU/mL.

Of 540 children, three (0.6%) had HBV infection, two were female, one being below five years of age and two being above. Both had no hepatomegally, splenomegally was present in one and jaundice was also present in one child. Five (0.9%) had HCV infection, 3 were male, 2 female and all were above 5 years of age. Three children had received blood transfusions. Hepatomegally was present in one child. Splenomegally was also present in one child while jaundice was present in 2 children. There were no statistically significant differences between HCV infected and uninfected children in relation to socio-demographic, anthropometric measurements and clinical characteristics.

Twenty four (4.4%) children had HIV infections. Of these, 11 were males and 13 were female. Nineteen of 24 children were above five years of age. Fourteen children had received blood transfusions. Hepatomegally was present in 4 children, splenomegally in 3 and jaundice in 18. There were no statistically significant differences between HIV infected and uninfected children in relation to socio-demographic, anthropometric measurements.

Conclusions: The seroprevalence of HBV, HCV and HIV were found to be 0.6%, 0.9% and 4.4%, respectively, in children with SCA. Seventy percent of children with SCA were not immunized with Hepatitis B vaccine. In spite of having multiple blood transfusions, blood transfusion was not associated with HBV, HCV or HIV infections.

Recommendations: It is recommended that screening of donated blood for HBV and HIV should be continued to prevent risk of transmitting these infections via blood transfusions. Screening of HCV should be started.

There is a need for vaccinating those who were not vaccinated especially those who show no evidence of prior infection. A booster dose should be given to those who did not mount a response to vaccination.

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ABBREVIATIONS

Anti-HBsAg	antibody to Hepatitis B surface antigen
Anti-HBcAg	antibody to Hepatitis B core antigen
ELISA	Enzyme linked Immune Sorbent assay
Hb	Haemoglobin
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human immunodeficiency virus
HBsAg	Hepatitis B surface Antigen
IgM	Immunoglobulin M
SCD	Sickle cell disease
SCA	Sickle cell anaemia
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
WHO	World health organization

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1. INTRODUCTION AND LITERATURE REVIEW

1.1 Background

Sickle cell disease is a common genetic disorder. It is characterized by chronic haemolytic anaemia, aplastic, sequestration and vaso-occlusive crises. Sickle haemoglobin (HbS) results from substitution of a single amino acid namely valine for glutamic acid in the beta globin gene at chromosome number 11. The susceptibility of red cells to sickle correlates well with the concentration of HbS within the red cells. [1]The sickle cell allele is most common in areas where malaria is endemic, with sickle cell trait (the heterozygous state) affecting up to 30% of Africa's tropical populations. In the USA, 8% of the African-American population is heterozygous for the sickle cell gene (AS) while in Africa it ranges between 2-28%. [2] In Tanzania, the carrier frequency is 10-38%. [3]Sickle cell disease is more common in individuals of African and Caribbean descent, Middle Eastern and Mediterranean countries including Turkey, Greece and Italy, as well as India.[4] Sickle cell anaemia (SCA) is the homozygous state of the disease. In developing countries this condition is associated with high mortality, thought to be due to malaria and other co-morbid conditions. In contrast, survival of children with SCA in developed countries is relatively better.[2]

The clinical manifestations of the disease are quite variable. They include haemolytic, vaso-occlusive, sequestration and aplastic crises. The cause of anaemia in SCA includes hemolysis due to the rupture of the sickled red blood cells, which is a common finding in SCA. About one third of red blood cells (RBCs) undergo intravascular hemolysis, possibly due to loss of membrane filaments during oxygenation and deoxygenation. The remaining, two thirds of the RBC's are hemolyzed through erythrophagocytosis by macrophages. This process can be partially modified by crystallizable fragment (Fc) blockade, suggesting that the process is mediated by immune mechanisms.[5] The sickled RBCs have increased immunoglobulin G (IgG) on the cell surface. Vasoocclusive crisis is often triggered by infection. Levels of fibrinogen, fibronectin and D-dimer are elevated in these patients. [5] In Africa, malaria is one of the most common causes of anaemia and vaso-occlusive crisis in SCA.[5]However, other infections may also precipitate crisis and lead to anaemia.

An acute splenic sequestration crisis is a life-threatening complication of SCA. It occurs mainly in infants and young children aged less than 8 years, 30% of them are under the age of 5 years. [6, 7] This is rare in adults due to progressive splenic fibrosis as a result of repeated infarctions. However,

acute splenic sequestration crisis may also occur in patients who have not developed splenic fibrosis and in those with high levels of foetal haemoglobin (Hb-F). [8] The diagnosis is a clinical one, based on a sudden and massive enlargement of the spleen, which is often associated with a rapid fall in haemoglobin and haematocrit levels due to excessive pooling of blood in the spleen. [6, 9, 10]

Aplastic crisis can occur in different types of chronic haemolytic anaemias [11]. This brings the stopping of erythropoiesis followed by the sudden drop in haemoglobin concentration which leads to death due to peripheral circulatory failure. [11] Infection caused by Parvovirus B19 can also bring the aplastic crisis. This happens because the virus decreases the production of red blood cells (RBC) for about ten days, this leads to the sudden drop of haemoglobin levels. [11]

Factors that may precipitate the occurrences of different sickle cell crises are not fully understood. Infections, hypoxia, dehydration, acidosis, stress (such as major surgery), flu and cold are believed to play a significant role.

Blood transfusion in SCD and its risks

The consequences of anaemia may be potentially fatal. Very low haemoglobin or severe anaemia has been associated with severe morbidity and mortality. [12] The under fives mortality rate due to anaemia was found to be 14.3% in Kenya, 12.2%in Zaire and 11.2% in Sierra Leone. [13] Studies have reported that 60% of SCD patients require blood transfusion due to anaemia during their lifetime. [13] Most of the time, severe anaemia occurs acutely and blood transfusion is given as an emergency.

There are several risks associated with blood transfusion. It includes the transmission of viral related diseases such as Hepatitis B, C, human immunodeficiency virus (HIV).[14] and other blood borne pathogens. Other risks are transfusion reactions resulting from mismatched blood type, alloimmunization which happens when a person receives repeated blood transfusions and then develops antibodies to the donor blood. [15] In addition to the above other risks are heart failure, hemosiderosis, etc. Despite the stated risks associated with blood transfusion there is often inadequate supply of blood. The lack of blood is a risk for mortality. In order to improve blood supply adequacy and transfusion safety, in the year 2000 World Health Organization (WHO) recommended that resource-limited countries adopt comprehensive national policies for blood transfusion services. This was established in order to have adequate blood supply and carefully screen donated blood for hepatitis B, C and HIV so as to limit their transmission. [16] Tanzania

established the National blood transfusion service (NBTS) in 2004. Part of the national blood transfusion services is to reduce transmission of infections. There has been an increase of blood collection from 52,000 units in 2006 to 114,000 units in 2008. [17] In 2007, the number of whole blood units collected in Tanzania from NBTS was 109,471 units and the number of whole blood units collected per 1000 population was 2.7. [17] In 2008, the requirement of blood transfusion was 350,000 units per year.

The transmission of HBV and HCV infection through donated blood is fairly common in the developing world including the sub-Saharan Africa. The prevalence of HBV chronic carriage ranges between 3% and 22% in blood donors. [18] WHO estimates that about 50% of the blood supply in sub-Saharan Africa is screened for HBsAg and this low rate of screening could be due to lack of funds or lack of perceived utility. [19] The diagnostic techniques often used in identifying HBV infected donors through the detection of HBsAg are known to be reasonably reliable. [20] Circumstances which lead to have blood with HBV infection include collection of blood during the infectious window period following infection when tests used are unable to detect the infection, false negative test, error in sampling, testing and recording of test results. Also, blood collected from individuals with fluctuating or waning levels of HBsAg during later stages of HBV carriage. [20]

The prevalence of HBV and HIV among blood donors in Nigeria in 2003 was 1.3% and 1.1% respectively. [21] In 2006, the seroprevalence of HBV, HCV and HIV in Ethiopia among blood donors was found to be 25%, 13.3% and 11.7% respectively. [22] While the prevalence of HBV, HCV and HIV among blood donors in Dar es Salaam, Tanzania in a study done between April 2004 and May 2005 was 8.8%, 1.5% and 3.8% respectively. [23]

In 2004, when the NBTS started, the prevalence of HBV, HCV and HIV was 17%, 0.2% and 6.6% among the blood donors. [24] In 2008, the prevalence of HBV, HCV and HIV was lower among healthy blood donors in Tanzania, it was 6% and < 1% and 3.5%, respectively.[24] With these results we can see not only the reduction of HBV, HCV and HIV but also the adequacy of safe blood.

1.2 Epidemiology of Hepatitis

Hepatitis is an inflammation of the liver, most commonly caused by a viral infection. There are five main hepatitis viruses, namely hepatitis A, B, C, D and E. [25]

1.2.1 Hepatitis B virus

There are three main modes of transmission for Hepatitis B virus; via transfusion of blood and blood products, sexual contact, and perinatally from mother to fetus.[25]

HBV is a hepadnavirus, a 42 nm partially double stranded DNA virus, composed of a 27 nm nucleocapsid core (HBcAg), surrounded by an outer lipoprotein coat (also called envelope) containing the surface antigen (HBsAg). [26-28] The core particle is the one which surrounds the viral DNA and the enzyme DNA polymerase. [28] When the virus enters the host, it has to pass the immune system, so as to infect the liver.[28] The virus then attaches itself on the liver cell membrane which allows it to enter and transport itself to the liver cell (hepatocyte).[28] The core particle of the virus then releases its DNA contents and DNA polymerase into the nucleus of the hepatocyte. In the nucleus HBV DNA causes the hepatocyte to produce the surface proteins (HBs), the HBe protein, the core protein and the DNA polymerase. The DNA polymerase causes the hepatocyte to reproduce hepatitis B DNA from the messenger RNA.[28] Through the same process; versions of HBV are made by the hepatocyte. These stick together to form spheres and chains and give a ground glass appearance under the microscope. The surface proteins produced make them stick together. The copies of the virus are then released into the blood stream together with the excess surface antigen.[28] It is known that when reproducing, mistakes can be made in copying the DNA of the virus, resulting in different strains of hepatitis B. The incubation period is 6-25 weeks, and there are several histological and biochemical changes that occur after the infection with hepatitis B virus.[28] Persistent infections is known to display pronounced hepatotropism. [29]

Hepatitis B Surface proteins (HBsAg)

The outer coat which is made up of hepatitis B surface proteins is produced in many quantities, more than required by the virus to reproduce. They clump together to form rods and spherical paricles.[28] When these enter the blood stream in large numbers, they are detected easily. After the infection, it takes 1-6 weeks for the symptoms to occur, but the HBsAg occurs immediately after the infection.[28]

HBe Protein (HBeAg or 'e' antigen)

This is a peptide and it is detectable when the virus is replicating, and this is the time when the person is infected, and is highly infectious and consequently the risk of progressing into liver disease is also high. The function of this non-structural protein is not known.[28] It appears at the same time with HBsAg but disappears earlier than HBsAg. When it appears during chronic infection, it indicates that HBV is actively replicating and this may lad to liver disease.[28]

Antibodies to HBc (HBcAb, Anti-HBc).

These antibodies are the first to appear after the infection and they appear after 8 weeks post infection with HBV. The first classes to appear are the IgM and IgG. These antibodies to HBcAg do not neutralize the HBV. The presence of IgM HBcAb in serum indicates an acute phase of infection. While the presence of IgG HBcAb indicates a resolved case of HBV infection or a chronic infection.[28] This is used in determining whether the presence of HBsAb is due to vaccination or if there was a previous exposure to the live virus.

Antibodies to HBs protein (HBsAb)

These antibodies appear last. These antibodies can neutralize the HBV. These can also be induced by vaccination.[28] Eighty five percent of deaths associated with HBV infection are vaccine-preventable. HBV vaccine is effective if it is given before or immediately after exposure. [27] The WHO recommended that the hepatitis B vaccine should be included in the vaccinations which are given routinely. By giving the vaccine, chronic HBV infection can be prevented and this chronic HBV infection can lead to chronic liver disease later in life [27].

There are three different types of hepatitis B vaccines which are: plasma derived vaccines, recombinant DNA yeast-derived also known as mammalian cell-derived vaccines and the combination vaccines.

Plasma derived vaccines: these are derived from the plasma of HB_sAg-positive donors. They have a high purified formalin-inactivated and heat–inactivated alum-absorbed hepatitis B subvirion particle of HB_sAg which are free of detectable nucleic acid hence being non-infectious. [30] The reactions are generally insignificant and they may be only of mild pain or discomfort at the injection site. [29]

Recombinant DNA yeast derived vaccine: the S gene is cloned, isolated and inserted into an expression plasmid and introduced into S.cerevisiae (yeast) or mammalian cells (Chinese hamster ovary). The proteins are then expressed and assembled into the antigenic particles. [27] The epitopes that elicit the immune response are exposed on the surface of the artificial particles like in the natural HB_sAg particles.

Combination vaccines: the Hepatitis B vaccine can be given in combination with the Diphtheria Pertussis Tetanus (DPT). Other vaccines like Measles Mumps Rubella (MMR), Haemophillus influenza type b (Hib), Calmette-Guerin bacillus (BCG) and the Oral Polio Vaccine (OPV) can be given in the vaccination programmes. The combined hepatitis A and B vaccine has been introduced in some countries in Europe since 1997.

In Tanzania the Hepatitis B vaccine has been introduced in 2002. It is given in combination with DPT as DPT-Hb. The vaccine is administered by intramuscular injection in the anterolateral aspect of the right thigh of infants at the age of 4, 8 and 12 weeks of life. [31] The vaccine is a recombinant type.

The prevalence of HBV and its patterns of transmission vary throughout regions of the world, with about 45% of the world's population living in areas of high endemicity, defined as areas where 8% of the population has a positive test for the HBsAg (the main surface antigen of the HBV viral envelope). Another 43% of the world's population lives in areas of moderate endemicity (i.e. 2%-7% of the population is HBsAg positive). Only 12% of the world's population lives in areas of low endemicity (i.e. <2% of the population is HbsAg positive). Tanzania is among the countries with high endemicity. [32] In areas with high endemicity like Tanzania, where the lifetime risk of HBV infection is more than 60%, most infections occur at birth or during childhood and there is highest risk of chronic infection.

It is also estimated that 3-5% of all infants may develop chronic HBV infection in early childhood. [32]A previous study done in Turkey showed that the seroprevalence of HBV is 0.75% among transfusion dependent individuals i.e. Thalassemia and SCA. [33]

Africa, with 12% of the world's population, carries approximately 18% of the global burden of HBV infection, with hepatocellular carcinoma and cirrhosis accounting for 2% of the continent's annual deaths. [34] The prevalence of HBsAg was between 9% in South Africa and 20% in Zaire in adult population (kiire 1996). However, a study done by Prince et al in Liberia observed that the prevalence of HBV in children aged below 4 years to be 5%. Another study from the Gambia by

Whittle et al reported a prevalence of 86% of children had HBsAg from two villages which they conducted the study. Animashaun et al in Nigeria, showed that the prevalence of HB_sAg in transfused patients with sickle cell anaemia was 20%. In 1987 Hepatitis B surface carrier rates were 10% in the general population and 15% among pregnant women, and the seroprevalence of anti-HBs antibody in the general population was 60%. [35] The vertical transmission rate of hepatitis B among pregnant women and their newborn babies was found to be 11.8% in a study done in Tanzania. [36] In another study done in Tanzania by Matee et al the seroprevalence rate of transfusion associated HbsAg among blood donors was found to be 11%. [23]

For those who are newly infected and develop acute hepatitis, the average incubation period i.e. time from exposure to onset of jaundice is 90 days (range 60–150 days). [23, 37]

Chronic HBV infection is the presence of HBsAg in the serum 6 months following infection by HBV or the presence of HBsAg in a person who tests negative for IgM antibodies to hepatitis B core antigen. Patients with chronic HBV infection do not develop anti-HBs, and HBsAg typically persists for decades. HBeAg is usually present in the early phases of the illness. In 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. Approximately 0.5 percent of adults and a lower proportion of children, with chronic HBV infection will clear HBsAg and develop anti-HBs annually. [38-41] The diagnosis of HBV is by detection of HbsAg. HBsAg is the serologic hallmark of HBV infection. It can be detected by radioimmunoassays (RIA) or enzyme immunoassays (EIA). It appears in serum 1 to 10 weeks after an acute exposure to HBV, prior to the onset of hepatitis symptoms or elevation of serum alanine aminotransferase (ALT). [37] In patients who subsequently recover, HBsAg usually becomes undetectable in four to six months. If HBsAg occurs for more than six months, this shows that it is a chronic infection. It is estimated that less than 1% of immunocompetent adult patients with genuine acute hepatitis B progress to chronic infection. [42] After chronic HBV infection, the patient's immune system attempts to clear the HBV by destroying infected hepatocytes.

This leads to increasing circulatory blood levels of ALT. Most patients will clear HBeAg (and produce anti-HBe antibodies) and achieve a state of non-replicative infection, characterized by low or undetectable serum levels of HBV DNA (referred to as HBeAg-positive CHB) and normal ALT levels. High HBV DNA and ALT levels may persist in some anti-HBe-positive patients referred to as HBeAg-negative CHB because of the presence of an HBV variant that is unable to produce HBeAg i.e. HBeAg-negative variant, also called HBV precore stop codon mutant. Severe disease

progresses quickly with HBeAg-negative HBV; 60% of patients with this form of disease develop cirrhosis within 6 years. [43]

In the management of HBV, no specific treatment is available for patients with acute infection. There are studies that suggest the usage of interferon could affect the serologic profile of patients with CHB infection. [44] Diagnosis and prognosis of chronic HBV are determined by liver biopsy. Most patients who are chronic carriers usually have no or little inflammation as noted on their liver histology. For those with inflammation on liver histology, the degree of inflammation and the presence of cirrhosis or fibrosis indicate a worse prognosis. [45]

1.2.2 Hepatitis C Virus (HCV)

HCV is an enveloped RNA virus in the Flaviviridae family which appears to have a narrow host range and it is the only member of the Hepacivirus genus.[46] An important feature of the HCV is the relative mutability of its genome, which in turn is probably related to the high propensity (80%) of inducing chronic infection. HCV is clustered into several distinct genotypes which may be important in determining the severity of the disease and the response to treatment. [47] There are about 6 genotypes and more than 50 subtypes.[48] A positive single stranded RNA genome is contained by the virion. The viral genome encodes a large single polyprotein with one third of the N-terminal containing the structural proteins and the two thirds of the C-terminal containing the non-structural proteins.[48] The structural proteins of the HCV comprise of the core protein and two envelope glycoproteins, while the non-structural proteins, including helicase, proteases and RNA-dependent RNA polymerase. These perform the functions essential for the lifecycle of the virus.[48]

The polyprotein cleavage of the structural protein from the polyprotein is catalyzed by the host signal peptidase, while in the non-structural protein HCV-encoded proteases are required.[48]
The HCV enters the susceptible host through the blood, and then enters the hepatocyte through the surface molecule as the viral receptor.[49] The virus enters the cell and uncoats and releases the genome. After the genome is released, it begins replication.[50] The genome will serve as an example for the translation of the polyprotein. A complex is formed by the non-structural proteins which are processed and the genome, this will start the synthesis of the negative strand which will function as an example for the synthesis of the positive strand. This complex resides in the cytoplasm. The core interacts with the mature RNA intermediate replicate and envelope the proteins to assemble into the virion. Some of the non-structural proteins are used in the viral replication, but most of the replicative processes are yet to be defined.[48]

The immune response to any viral infection is by the macrophages and dendritic cells that present the viral proteins to the cytotoxic T cells, B cells and T helper cells.[48] During the viral infections, the B cells will produce antibodies that will clear the circulating virus and protect from the phagocytosed and proteolytically cleaved HCV proteins.
During activation of T cell receptor, the T helper cells specific for the HCV assist with the differentiation, activation, induction of B cells and stimulation of cytotoxic T cell which are virus

specific. This leads to lysis of cells which are infected by the virus. The cytotoxic T cells and the T helper cells, secrete cytokines which inhibit replication.[48]

The major route for HCV transmission is exposure and transfusion of infected blood and blood products, intravenous drug use (IDU), unsterile medical and dental procedures, and traditional medical and cosmetic procedures (e.g., scarification, tattoos) involving blood exposure. [50]
Transmission of HCV has been reported with all blood products including factor VIII, immunoglobulin D, and immunoglobulin infusions. The risk of infection is highest in children who received multiple transfusions or pooled blood products for their underlying disease.[51]
Most acutely infected patients are asymptomatic and have a clinically mild course; jaundice is present in fewer than 25%.As a result, periodic screening for infection may be warranted in patients who are at high risk for infection. [52]

World Health Organization (WHO) estimates that about 170 million people, 3% of the world's population, are infected with HCV and are at risk of developing liver cirrhosis and/or liver cancer. The prevalence of HCV infection in some countries in Africa, the Eastern Mediterranean, South-East Asia and the Western Pacific is high compared to some countries in North America and Europe. [53] The prevalence of HCV in Africa is 5.3% with the infected population to be around 31.9 million [53] and a concurrent HIV infection. The central African region has the highest estimated prevalence of 6%; West Africa has an estimated prevalence of 2.4%, and southern and east Africa with the lowest estimated prevalence of 1.6%. [54] In 1999 the prevalence of hepatitis C in Tanzania was found to be 0.7%. [55]

1.3 HIV

More than 40 million people are currently infected with HIV and over 25 million deaths have been attributed to the virus since the beginning of the epidemic. HIV belongs to Retroviridae family and is the cause of acquired immunodeficiency syndrome (AIDS).

The HIV virus can be divided into two types, HIV-1 and HIV-2. HIV-1 infects the CD4-expressing T cells. Primary HIV-1 infection occurs with a single variant. The rapid replication and turnover of HIV-1 and the high mutation rate of the viral reverse transcriptase result in high mutation frequencies that lead to the production of a population of genetically distinct but related variants called a quasispecies.[56] HIV-1 is currently widespread among humans, and its symptoms start to show within 5 years of infection, while HIV-2 is localized in Africa, and it takes longer for the symptoms to appear.[57]

The HIV virus targets the host immune system and it is a difficult pathogen for the body of the human to fight. The HIV has an affinity for the CD4+ T cells and monocytes. The glycoproteins of the virus are transmembrane protein gp41 and gp120. The gp120 is non-covalently linked to gp41 and these recognize the CD4 ligand of the host cells.[58] The conformational change occur within the gp120 and it is induced to expose the co-receptor binding site. The co receptors
bind a host chemokine receptor – either CXCR4 or CCR5.

The T-tropic particles recognize CXCR4, which is highly expressed in CD4+ T-cells, and induce the fusion of cells to create one large cell with many nuclei. When interacting between gp120 and the host's chemokine receptor, gp41 binds to a host herparan sulfate, triggering fusion of the host and viral membranes, and the entry of the capsid into the cytoplasm. [58]

The immunological response shows the B cell decline in number and function. The cytokine regulation is distorted which leads to the decrease in the CD4+ T cells, as a result of toxicity of the virus.[59]

There have been a lot of researches going on in combating the disease and antiretroviral drugs were discovered in inhibiting the viral replication, so as to give the host immune system a chance of recovering from infection. These drugs are a temporary solution because they do not address the

latent viral reservoirs.[59] The efficacy of the antiretroviral drugs is significantly increased if used as combination therapy.

Availability of accurate diagnostic tests can help in combating the spread through blood products. Currently there are simple, rapid, inexpensive tests, which can be performed in any remote area with just a drop of blood.[60] Such tests will benefit the developing and under-developed countries where infrastructure is poor and resources are limited, but will also be extremely helpful in developed countries in clinical settings such as emergency rooms where obtaining immediate results could be beneficial. Rapid detection can significantly decrease the transmission of HIV.[60]

AIDS cases have been reported throughout the world. Worldwide, the number of people estimated to be living with HIV is 38,217,530. Studies in Central Africa showed an annual incidence of 550-1000 cases per a million adults with a male to female ratio of 1:1. [59] A study done by Animashaun et al in Nigeria, reported that the prevalence of HIV among transfused patients with sickle cell anaemia was 3.8%. Another study done in Nigeria by Ogunrinde et al showed a prevalence of 1.8% (1 out of 55 patients) with HIV infection among patients with SCA who were transfused.[75]

In 2007 the number of people living with HIV is estimated to be 1.4 million in Tanzania. The prevalence was 6.2% in adults aged 15-49 years. Deaths due to AIDS in adults and children were estimated to be 96,000 in 2007.[60] The majority of children get infected with HIV perinatally.

2. Problem Statement

Children with SCA are likely to receive multiple blood transfusions, due to frequent episodes of anaemia experienced by most of them. For most developing countries, ensuring safer blood products has been a big challenge faced with satisfactory advancements only recently. In Tanzania, the National Blood Transfusion Centre was started in 2004 with sole responsibility of promoting safe blood transfusions. The set up has shown the effectiveness of the reduction of transfusing contaminated blood products to this particular group of children vulnerable to HIV and Hepatitis B and C; compared to the past.

There is no recent published data on the incidence of Hepatitis B and Hepatitis C among patients with sickle cell anemia. No study has been done in East Africa which shows the prevalence of hepatitis in children with sickle cell anaemia.

Indications for blood transfusion in patients with SCA depend on the history and clinical characteristics like severe pallor. In Tanzania, generally children develop anaemia because of malaria, infections and other conditions like severe acute malnutrition; thus with the presence of SCA, these children with SCA are even more vulnerable to blood transfusions and consists mainly the use of packed RBCs.

3. Rationale of the Study

This study was conducted in order to provide baseline prevalence rates of HBV, HCV and HIV among children with sickle cell anaemia.

The possibility of infection presents new pathological dynamics with direct implications in terms of how such cases can be successfully managed. Increased complexities experienced in managing this particular vulnerable group results into an emerging public health challenge in this era of safer blood and blood products.

Data from this study will help in planning public health strategies for screening and development of treatment/managements protocol for children with sickle cell anaemia.

Children with SCA need to have specific protocols for a comprehensive management. This data will augment the specific needs in terms of blood-borne infections.

4. OBJECTIVES

4.1 BROAD

To determine the prevalence and factors associated with HBV, HCV and HIV among SCA children aged between 6 months and 10 years in a tertiary hospital.

4.2 SPECIFIC OBJECTIVES:

1. To determine the prevalence of HBV, HCV and HIV among SCA children by age and sex
2. To assess the relationship between blood transfusion and HBV, HCV and HIV among sickle cell children aged between 6 months and 10 years of age

5. MATERIALS AND METHODOLOGY

5.1 Study design

This was a hospital-based cross-sectional study that was conducted between November 2008 and March 2009.

5.2 Study setting

The study was conducted at the Sickle Cell Disease clinic in Muhimbili National Hospital in Dar es Salaam, Tanzania. Muhimbili National Hospital is a referral and a teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS). There are 1,600 SCD patients enrolled at the SCD clinic with an average of 40 patients attending the clinic every week, usually on Thursday.

5.3 Study population

All children with SCA aged between six months and ten years inclusive attending the SCD clinic.

5.4 Inclusion criteria

Children

1. Aged between 6 months and 10 years inclusive
2. Who had been confirmed to be HbSS and documented in the file
3. Whose parents/guardians consented for the study

5.5 Exclusion criteria

Children

1. Aged less than 6 months and more than 10 years
2. Whose parents/guardians/caretakers refused to consent for the study

5.6 Sample size estimation

Sample size (n) was calculated using the following formula:

$n = Z^2 P (100-P) / E^2$

where Z= critical value 1.96 corresponding to 5% significant level

n=estimated sample size

E= margin of error 2.5%

P= the expected prevalence level, 7.1% based on a study by Kitundu et al. [61]

n=405

Thus, the minimum sample size was 405 children.

A total of 540 children were included in the study.

5.7 Sampling procedure

Convenient sampling procedure was used. All children who met the inclusion criteria were consecutively enrolled into the study until the sample size was reached. Children were enrolled every Thursday. The investigator was present at the clinic every Thursday for data and specimen collection.

5.8 Data collection procedure

Parents/guardians/caretakers with children who met the inclusion criteria were assessed and the information needed was recorded in the questionnaire designed for the purpose of the study (APPENDIX I).

Data collected included socio-demographic data, past medical history such as history of blood transfusion and history of Hepatitis B vaccination. A thorough physical examination was done to every child according to standard clinical methods (Hutchinson's clinical methods). Child's weight and length/height were measured.

Blood samples were collected from each child for laboratory investigations. All laboratory results were communicated to the attending clinician to facilitate accurate management of these children according to national protocols for the management of SCA patients.

5.8.1 Anthropometric measurements

Weight

Weight was taken using a solar cell SECA weighing scale (CMS weighing equipment, High Holborn, London, United Kingdom). Weight was taken to the nearest 100 gm. Calibration of the weighing scales to 0 was done before each session. For accuracy and consistency, the scales were standardized once weekly using a standard weight of 1 kg. Heavy clothes like coats and shoes were removed.

Length/height

Length/height was measured using locally made portable devices equipped with height gauges. Parents/guardians assisted in removing the child's shoes and gently laying the child in supine position on the length board. The assistant placed the child's head at 90° to the fixed head piece. The legs of the child were straightened at the knees by the investigator and ensured that the feet were at right angles (90°) to the sliding foot piece placed at the child's heels. The length was measured to the nearest 0.1cm. Children who were able to stand and those who were 24 months and

above, had their heights measured while the child stood upright on the fixed foot piece, looking straight forward at 90°. Height was recorded to the nearest 0.1 centimeter.

Using "Epi Nut" programme on the "Epi Info" statistical package version 6.4, weight for height Z score (WHZ) was calculated:

Z score was interpreted as follows:

Z between mean and <-1 SD = normal nutritional status

Z between -1 SD and <-3 SD = moderate wasting

Z -3 SD = severe wasting

And for height for age Z score (HAZ) was calculated:

Z between mean and <-1 SD = normal height

Z between -1 SD and <-3 SD = moderate stunting

Z -3 SD = severe stunting

Clinical assessment.

All children were clinically assessed for palmar pallor, jaundice, splenomegally and hepatomegally.

Immunization status.

It was determined by checking in the Reproductive and child health care (RCH) card number 1.

5.8.2 Laboratory investigations

Blood samples were collected from the anterior cubital fossa of each child using a sterile syringe and needle. This was done aseptically after disinfection of the skin area with a cotton swab soaked in 70% ethyl alcohol and left to dry. About 5 milliliters of venous blood was collected. These were dispensed into a 5 ml plain red top vacutainer tube (Becton Dickinson, NJ, USA) for Anti-HBs, HBsAg, Anti-HCV and HIV testing. The blood samples were put in a tray at room temperature until the end of the clinic and taken to the laboratory for analysis. At the laboratory the samples in plain red top were immediately centrifuged at 3000 revolutions per min for 5min in order to obtain sera. Anti-HBs, HBsAg, Anti-HCV and HIV testing were done at the Central Pathology Laboratory (CPL) at the Muhimbili National Hospital.

5.8.2.1 Anti-HB_s assay

Anti-HB_s was determined using a microparticle enzyme immunoassay technique (MEIA Ab) according to the manufacturer's instructions (AxSYM Abbott, Germany). This involved pipeting 200 µL of a sample and 100 µL of AxSYM AUSAB reagents (Abbott, Germany) by a sampling probe into various wells of a reaction vessel. The reaction vessel was immediately transferred into the processing centre. Sample and Recombinant Hepatitis B virus surface Antigen (rHBsAg) coated microplates were combined in one reaction vessel well.

When Anti-HB_s was present in the sample it bound to the coated microplates forming Ab-Ag complex in the reaction mixture. A portion of reaction mixture was transferred to the matrix cell.

The microparticles bound irreversibly to the glass fibre matrix. Hundred µL of the anti-biotin: alkaline phosphatase conjugate were dispensed into the matrix cells and bound with any microparticle bound Ag-Ab complex. The cell was washed to remove materials not bound to the microparticles. The substrate 4 Methylumbelliferyl phosphate was added, the alkaline phosphatase catalyses the removal of a phosphate group from the substrate yielding the fluorescent product, 4 Methylumbelliferone. The fluorescent product was measured by microparticle enzyme immunoassay technique (MEIA) optical assembly, using previously generated calibration curve. If the concentration of the sample was greater than or equal to 10 mIU/mL, the sample was considered reactive for anti-HB_s antibodies.

5.8.2.2 HB_sAg assay

HB_sAg was determined using a microparticle enzyme immunoassay technique (MEIA AxSYM HB_sAg) according to the manufacturer's instructions (AxSYM Abbott, Germany). This involved pipeting 200 µL of a sample and 100 µL of AxSYM HB_sAg (V2) reagents by a sampling probe into various wells of a reaction vessel. The reaction vessel was immediately transferred into the processing centre. Sample, anti-HB_s coated microplates and biotinylated anti- HB_s were combined in the reaction vessel (RV). When HB_sAg was present in the sample it bound to the Anti-HB_s coated microplates and biotinylated anti-HB forming Ab-Ag complex in the reaction mixture. A portion of reaction mixture was transferred to the matrix cell. The microparticles bound irreversibly

to the glass fibre matrix. The anti-biotin: alkaline phosphatase conjugate was dispensed into the matrix cells and bound with any microparticle bound Ag-Ab complex.

The cell was washed to remove materials not bound to the microparticles. The substrate 4 Methylumbelliferyl phosphate was added, the alkaline phosphatase catalyses the removal of a phosphate group from the substrate yielding the fluorescent product, 4 Methylumbelliferone. The fluorescent product was measured by microparticle enzyme immunoassay technique (MEIA) optical assembly, using previously generated calibration curve.

The presence or absence of Hb_sAg in the sample was determined by comparing the rate of formation of fluorescent product, in the test sample to a cut off rate determined from a previous AxSYM HB_sAg (V2) mean index calibrator rate. Samples with index greater than or equal to the cut off rate were considered reactive for HB_sAg.

5.8.2.3 Anti-HB_c IgM assay

Anti-HB_c IgM was determined using a microparticle enzyme immunoassay technique (MEIA core) according to the manufacturer's instructions (AxSYM Abbott, Germany). This involved pipeting 200 µL of a sample and 100 µL of AxSYM CORE-M reagents by a sampling probe, into various wells of a reaction vessel. The reaction vessel was immediately transferred into the processing centre. Antibody to Human IgM coated microplates were dispensed onto the matrix cell. The microparticles bound irreversibly to the glass fibre matrix. Sample diluted in the specimen diluent was dispensed onto the matrix cell. IgM that is present in the sample bound to the antibody to human IgM coated microparticles.

The matrix cell was washed to remove materials not bound to the microparticles. Hepatitis B virus core antigen (*E. coli*, recombinant) was added which bound to any Anti-HB_c present in the sample that had bound to the microparticles forming Ab-Ag complex. Antibody to Hepatitis B virus core antigen (Human) alkaline Phosphatase conjugate was dispensed into the matrix cells and bound with any microparticle bound Ag-Ab complex. The cell was washed to remove materials not bound to the microparticles. The substrate 4 Methylumbelliferyl phosphate was added. The alkaline phosphatase catalyses the removal of a phosphate group from the substrate yielding the fluorescent product, 4 Methylumbelliferone. The fluorescent product was measured by microparticle enzyme

6. Ethical clearance

The ethical clearance to conduct the study was obtained from the Higher Degree Research and Publication Committee of the Muhimbili University of Health and Allied Sciences, Dar es salaam, Tanzania.

6.1 Ethical considerations

A written informed consent to participate in the study and a separate consent for HIV testing were both obtained from the parents/guardians prior to enrolment in the study. The information was given during the education to the parents/guardian, so as to ensure that they had the information needed to make the informed choice of enrolling into the study. A thorough description of the aim of the study, the infectious agents that were screened, the potential benefits and risks, the blood collection procedures and assurance of confidentiality of any information given as well as the results of the tests. Children who were found to be HBV, HCV and HIV positive were referred to the general paediatrics clinics where they were cared according to standardized protocols and followed up and the caregivers were informed. All patients' information and test results were accessed by only authorized personnel to ensure confidentiality.

7. RESULTS

During the study period, 540 children with SCA were enrolled into the study. Table 1 summarizes baseline socio-demographic, anthropometric, clinical characteristics and hepatitis B vaccination status of the study population. Of the 540 children, 308 (57%) were males. The mean age was 81.6 months with ±30.432 SD.

About 70% of children reported not to be vaccinated with hepatitis B vaccine from the MCH card number 1, but for those vaccinated, 73.5% had protective anti-HB_s levels ≥10mIU/mL.

Anti-HBc IgM was negative for the whole group.

Table 1: The distribution of socio-demographic, anthropometric measurements, clinical characteristics, history of blood transfusion and history of vaccination of the study population (N=540).

Characteristics

		N	%
Sex	Males	308	57
	Females	232	43
Age	<5 years	133	24.6
	≥5years	407	75.4
Anthropometric Measurements			
Weight for height			
	Normal	358	66.3
	Moderate wasting	147	27.2
	Severe wasting	35	6.5
Height for age			
	Normal	231	42.8
	Moderate Stunting	216	40.0
	Severe stunting	93	17.2
Clinical characteristics			
Hepatomegally			
	Present	69	12.8
	absent	471	87.2
Splenomegally			
	Present	104	19.3
	absent	436	80.7
Jaundice			
	Present	249	46.1
	Absent	291	53.9
History of blood transfusion	Yes	270	50.0
	No	270	50.0
No. of blood transfusions received			
	0	270	50.0
	≤5	231	42.8
	>5	39	7.2
Hepatitis B vaccination			
DPT-Hb vaccine			
	Vaccinated	162	30.0
	Not vaccinated	378	70.0

Table 2: The prevalence of HBV, HCV and HIV among SCA children by age and sex (n=540)

			HBV %		
Variable	Category	n	positive	negative	*P value
Sex	Male	308	0.3	99.7	
	Female	232	0.9	99.1	0.580
Age	<5years	133	0.8	99.2	
	≥5years	407	0.5	99.5	0.573

			HCV %		
Variable	Category	n	positive	negative	*P value
Sex	Male	308	1.0	99.0	
	Female	232	0.9	99.1	1.000
Age	<5years	133	0.0	100.0	
	≥5years	407	1.2	98.8	0.340

			HIV %		
Variable	Category	n	positive	negative	*P value
Sex	Male	308	3.6	96.4	
	Female	232	5.6	94.4	0.294
Age	<5years	133	3.8	96.2	
	≥5years	407	4.7	95.3	0.811

*p-value for Fisher's Exact test

Of the 540 children, 3 (0.6%) had HBV infection. Two of them were female and one being male. One being under five years of age and the other two above five years of age. The prevalence of HCV infection in the study population was (0.9%) that is 5 children had HCV infection, 3 were male, 2 female and all were above 5 years of age. Twenty four (4.4%) children had HIV infections. Of these, 11 were males. Nineteen of 24 (79.2%) of the HIV infected children were above five years of age.

Table 3: Frequency distribution of HBV, HCV and HIV by blood transfusion among sickle cell children aged between 6 months and 10 years.

	HBV		
	Positive	**Negative**	*P value
	%	%	
No.of BT			
0	0.4	99.6	
≤5	0.9	99.1	
>5	0.0	100.0	0.674
		HCV	*P value
0	0.7	99.3	
≤5	1.3	98.7	
>5	0.0	100.0	0.665
		HIV	*P value
0	3.7	96.3	
≤5	4.8	95.2	
>5	7.7	92.3	0.503

p-value for Fisher's Exact test

Those children with HBV infection, two had received blood transfusions and the third had no history of transfusion. Three children out of five with HCV infection had received blood transfusion. Fourteen children out of 24 received blood transfusions among those with HIV infection.

There was no association between vaccination against HBV infection and hepatitis B infection in this study. It was found to be that of the three children with HBV infection, two (1.7%) were vaccinated. Both of them did not mount adequate immunity as the antibody levels were below 10mIU/mL (anti-HB_s levels <10mIU/mL).

8. DISCUSSION

The aim of this study was to determine the seroprevalence of hepatitis B, hepatitis C and HIV among children with sickle cell anaemia attending sickle cell disease clinic at Muhimbili National Hospital in Dar es Salaam, Tanzania. This is the first cross-sectional study on prevalence of HBV, HCV and HIV among children with sickle cell anaemia in Dar es Salaam, Tanzania.

Among the 540 studied children, 8 (1.5%) had hepatitis (HBV and HCV), which is approximately one out of 68 children with sickle cell anaemia.

The prevalence of HBV observed in this study is (0.6%), which is significantly lower than that observed by Nakai et al, in which they found the seroprevalence of HBV was 8% among healthy individuals in Myanmar.[62] The difference in the seroprevalence of this study from the Myanmar study could be due to different age groups which were studied, i.e.: in the former study, the age range was from 7-80 years, while in this study, the age was ranging from 6 months to 10 years. Secondly, the methods used were different, in this study the HBsAg was detected by microparticle enzyme immunoassay technique while in their study they used HBV-DNA by PCR.

All children with HBV in this study did not have hepatomegaly, this is in contrast with the study done by Nagu et al that reported a prevalence rate of hepatomegaly of 11.1% in adults who had hepatitis B virus. [63]This could be due to the fact that they studied patients who had co-infection with HIV and the study population was patients aged 18 years and above while in our study, the study population was between 6 months and 10 years. Jaundice was absent in two patients and present in one patient with HBV, this is different from the study done by Nagu et al [63]in which they found the jaundice in 11.1%, this could be due to the fact that in the latter study, they had patients who were HIV positive.

It is important to appreciate that the ELISA based results are confirmed with more sensitive technique such as HBV-DNA by PCR. [62]In the study done by Kitundu et al, it showed that the prevalence of HBV was 12% among children transfused with anti-HIV negative donor blood at the same hospital. [64] The lower prevalence in this study could probably be due to the fact that the Hepatitis B vaccination in Tanzania was started in 2002 and the study was done in 2000. The main objective of hepatitis B immunization is preventing the sequelae of acute hepatitis B which is

chronic hepatitis B infections which leads to chronic liver disease later in life. By preventing the CHB infection, the major reservoir for transmission of new infections is also reduced. [65]Even though the prevalence of hepatitis B found in this study is low, it is comparable with those findings by Telatela et al who found the overall prevalence of HBsAg was 1.2% among children infected with HIV [66]done on the same study setting. This could be due to true reflection of the seroprevalence of HBV in children.

The number of blood transfusions has no influence on risk of acquiring the HBV infection. As found in this study, two patients with HBV infection had blood transfusions less than 5 times, and one patient had no history of blood transfusion. These findings are different from the ones found by Al-Fawaz et al [67] where he found no patient with HBV among the Saudi children with SCA he studied. These findings could be due to the small sample size as he had only 55 children.

In the same study Al-Fawaz et al [67] found no vaccine failure among their patients who were vaccinated against HBV, this is in contrast with this study as we found two patients who were vaccinated but did not mount enough immunity and therefore acquiring the disease.
It is difficult to say that the patients did not mount immunity as the history of vaccination which was not taken did not include things like how many doses of vaccine were given. In a study done by Metodi [79] et al showed that 69.3% had antibodies within the protective ranges while in this study the ones within the protective ranges was 73.5%. There was no significant difference and this could be due to the fact that they were from the same study area and the study population was children in both groups.[79]

Regarding HCV, we had two females and three males; this is different from the study done by Telatela et al [66] in which they found the predominance in females. But this is difficult to conclude as our children who had HCV were only five among the studied population.

This study showed that the prevalence of HCV in the study population to be low (0.9%), this is the same as the study done by Vardas et al [68] who saw the prevalence of HCV among young blood donors in Namibia to be 0.9%. This could be due to the fact that both studies used the ELISA test which (according to the manufacture) had specificity of more than 99% and sensitivity of 99%. Another study done by Elsheikh et al [69] showed that the prevalence of HCV was found to be 0.6% among pregnant women, though this study showed the same low prevalence of HCV, but the socio-

demographic characteristics should be remembered as in this study of Elsheikh, pregnant mothers were studied while in this study, children with SCA were studied.

In another study done by Blankson, [70] it showed that the prevalence of HCV infection was 7.1% of those who were transfused. This high prevalence could be due to the fact that they studied admitted patients at their hospital who already had cirrhosis of the liver.

A study done by Biggar et al, [71] showed that the prevalence of HCV among transfused children with SCA was 3%. These results are the same in this study. This could be explained by the fact that the study setting and study population were the same.

Hepatomegaly was found in one (20%) child who had HCV infection which is in contrast with the study done by Abdulla et al, [72] in which they found hepatomegaly in 10% of their study population. This could be due to the fact that their study population did not only include adults but also only 13% had SCA, though in their study they had a strong association with blood transfusion.

Another study by Hussain et al [73] showed the presence of hepatomegaly in 98.7% of their patients who had HCV infection, this is in contrast with this study which showed that only one patient with HCV had hepatomegaly. In the same study the prevalence of HCV was 41.7% which was much higher than the one found in this study, these results could be due to the donor blood being screened during the window period, thus transfusing patients with infected blood.

In a study done by Torres et al, [74] showed that the patients who had more than 10 transfusions had a high prevalence of HCV compared to those with less than ten transfusions. This is quite the opposite from our study which showed that those with transfusions less than 5 times are the ones with HCV infection. These differences could be due to the fact that they studied individuals before and after the serologic screening was started. While in this study it was not established when exactly they got the transfusions, whether before or after the implementation of safe blood transfusion services. They also found the high prevalence among those who were tested using HCV RNA which is a more sensitive method compared to the one we used which is by detecting anti-HCV antibody.

Prevalence of HIV in this study was 4.4% which is high compared to the study done by Ogunrinde et al [75] in Nigeria, in which they found the prevalence to be very low of 1.8%. This could be due to the small sample size of 55 they had compared to our sample size. A study done by Animashaun et al in Nigeria showed that the prevalence of HIV in transfused patients with SCA was 3.1% in children aged 5-14 years, this is a little bit less than what was seen in this study and this could be explained by the fact that they had a small sample size but the tests used are the same.

In a study by Ampofo et al, [76] the prevalence of HIV was 3.8% among blood donors in Ghana. This is low compared to this study and this could be due to the fact that they tested for HBsAg before someone donates blood, and if found positive the person does not donate blood. Therefore, the ones tested for HIV were already negative for HBV infection. Therefore, in this study there were no patients who had HBC infection.

In another study done by Diagne et al in Senegal, [77] showed that the prevalence of HIV among transfused patients with SCA was 0%, this could be explained by the fact that in Senegal they have a relatively low prevalence of HIV in the general population. The prevalence of HIV in Senegal is 1% in the general population. [77]
Prevalence of HIV was found to be 11.3% among patients with SCD in Congo. [78] Splenomegaly was found to be 30% and hepatomegaly 44.6%. This is higher than the one found in this study which is 12.5% and 16.7% respectively. This can be explained by the fact that in the Congo study, they had a small sample size thus, having large numbers with splenomegaly and hepatomegaly.

One of the strengths of this study is that this is the first study which describes the prevalence of transfusable transmissible viral infections (HBV, HCV and HIV) among children with SCA in Tanzania. Together with this, the clinical characteristics were also seen among this study group together with the immunity mounted as there was no study before which showed how this cohort group responded to vaccination.

Study limitations

1. This was a hospital based study, thus the prevalence observed does not reflect the true prevalence of HBV, HCV and HIV in the population.

2. The detection of HCV was based on the finding of IgG antibody against the virus in the blood, instead of using a more reliable method of HCV RNA.

8.0 CONCLUSION

In conclusion, the seroprevalence of HBV, HCV and HIV were found to be 0.6%, 0.9% and 4.4%, respectively, in children with SCA. History of multiple blood transfusions was not associated with HBV, HCV or HIV infections.

9.0 RECOMMENDATIONS.

It is recommended that screening of donated blood for HBV and HIV should be continued to prevent risk of transmitting these infections via blood transfusion. Screening for HCV should be started.

There is a need for vaccinating those who were not vaccinated especially those who showed no evidence of prior infection. A booster dose should be given to those who did not mount a response to vaccination.

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