KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY,

KUMASI

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF CLINICAL MICROBIOLOGY

PREVALENCE OF HEPATITIS B AND C VIRAL INFECTIONS AMONG CHILDREN AND ADULTS PRESENTING WITH HEPATIC DISEASE AT KOMFO ANOKYE TEACHING HOSPITAL

A THESIS SUBMITTED TO THE DEPARTMENT OF CLINICAL MICROBIOLOGY,

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FULFILMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF SCIENCE

IN CLINICAL MICROBIOLOGY

BY

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DECLARATION

I hereby declare that this submission is my own work towards the MSc (Clinical Microbiology) and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University, except where due acknowledgement has been made in the text .

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ABSTRACT

Background: Viral hepatitis may be the cause of infection among children and adults presenting with hepatic disease. The present study sought to establish the prevalence of Hepatitis B and C viral infections among children and adults presenting with hepatic disease at Komfo Anokye Teaching Hospital (KATH). **Methods:** A cross section of 155 patients were recruited from November 2015 to April 2016. Blood samples were collected for the determination of HBsAg and anti-HCV antibodies. Socio-demographic data and clinical information were also collected using structured questionnaires. The HBV profile of HBsAg-positive participants was then determined. The data was analyzed using Microsoft Excel spread sheet and GraphPad Prism. **Results:** Of the 155 patients recruited, 71 were HBsAg positive, 18 were anti-HCV positive and 4 were both HBV/HCV coinfected. Among the 71 HBsAg positive patients, the prevalence of chronic hepatitis was 66.20%. This was followed by liver cirrhosis, HCC and acute liver failure with a prevalence of 32.39%, 16.90% and 2.82% respectively. In addition to this, among the 18 anti-HCV positive patients, the prevalence of chronic hepatitis was 50%, followed by liver cirrhosis (38.89%), HCC (11.11%) and acute liver failure (11.11%). With the HBV/HCV coinfected patients, the prevalence of chronic hepatitis was 3.37%. This was followed by both liver cirrhosis and HCC with a prevalence of 1.12% each. **Conclusion:** Hepatic diseases were associated with HBV and HCV infections with the most prevalent being chronic hepatitis. Information about the transmission, prevention and awareness of hepatic diseases should be strengthened by giving health education.

KNUST

TABLE OF CONTENT

CONTENT

KNUST
W J SANE NO
BADWENNI

LIST OF TABLES

KNUST

LIST OF FIGURES

KNUST

LIST OF ABBREVIATIONS

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HBsAg: Hepatitis B Surface Antigen

HBsAb: Hepatitis B Surface Antibodies

HBeAg: Hepatitis B „e" Antigen

HBeAb: Hepatitis B „e" Antibodies

HBcAb: Hepatitis B Core Antibodies

HBcAg: Hepatitis B Core Antigen

Anti-HBs: anti-Hepatitis B surface Antigen

Anti-HBe: anti-Hepatitis B „e" Antigen

Anti-HBc: anti-Hepatitis B core Antigen

Anti-HCV: Hepatitis C Antibodies

HCC: Hepatocellular carcinoma

IgM: Immunoglobulin M

DNA: Deoxyribonucleic acid

RNA: Ribonucleic acid

NS: Non-structural

NCR: Non-coding region

HIV: Human immunodeficiency virus

EIA: Enzyme immunoassay

RIBA: Recombinant immunoblot assay

ALT: Alanine Aminotranferase

KNUST

AST: Aspartate Aminotranferase

rpm: Revolution per minute IVD:

Intravenous drug

PCR: Polymerase Chain Reaction

RT-PCR: Reverse Transcriptase Polymerase Chain Reaction

GIT: Gastrointestinal Tract

KATH: Komfo Anokye Teaching Hospital

CHRPE: Committee on Human Research, Publication and Ethics

KNUST: Kwame Nkrumah University of Science and Technology

WHO: World Health Organization

E: Envelope

UGIB: Upper Gastrointestinal Bleeding

CDC: Centre for Disease Control and Prevention

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CHAPTER ONE

1.0 BACKGROUND

Viral hepatitis prevails all over the world and is a key global public health issue. It is the inflammation of the liver resulting in hepatic diseases such as liver cirrhosis, hepatocellular carcinoma (HCC) and acute liver failure. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most common viral causes of hepatic diseases universally (Xing *et al.,* 2003). HBV causes hepatitis of altering severity and remains in 95% of children and 10% of adult patients (Muhammad *et al.,* 2007).HBV and HCV both share a common mode of transmission through parenteral, sexual and perinatal means. However, HBV is 50 to 100 times more transmissible than HIV (Geberemicheal *et al.,*2013; Yami *et al.,* 2011). It is projected that over 2 billion people globally have been infected with HBV (Trepo *et al.,* 2014). Of these, over 240 million are chronically infected and stand the chance of developing hepatic diseases which may result in death (WHO, 2015a). The issue of HBV infection is topmost in the developing world, especially in sub-Saharan Africa and Asia. World Health Organization (WHO) projected that the prevalence of HBV infection in Africa ranges between 5-10% (WHO, 2015a). WHO also estimated that about 130 - 150 million people globally are chronically infected with hepatitis C infection (WHO, 2015b).

Hepatitis B and C infections initially begin from acute infection and progress to chronic infection. A study conducted by Mboto *et al.,* (2005) on HCC in Gambia reported a prevalence of 38.5% and 7.7% in patients with HBV and HCV infections respectively. Similarly, a study carried out by Chin‟ombe *et al.,* (2009) in Zimbabwe, observed a prevalence of 48.3% and 20% in patients with HBV and HCV infections respectively. In this same study, Chin‟ombe *et al.,*

(2009) reported a prevalence of 8% in HBV/HCV coinfection. Furthermore, a study conducted in Ethiopia by Taye *et al.,* (2014) determined a prevalence of 22.3% and 3.6% in HBV and HCV infections respectively in chronic hepatitis patients. In this same study, Taye *et al.*, (2014) determined a prevalence of 4.8% for HBV/HCV coinfection. The prevalence of HCV reported in USA among patients with HCC increased from 0.07% in 1996 to 1.3% in 2006. In that same study, that of cirrhosis increased from 9% in 1996 to 18.5% in 2006 (Kanwal *et al.,* 2012). In Ghana, a study conducted by Blankson *et al.,* (2005) observed a prevalence of 42.9% and 7.1% in HBV and HCV respectively in cirrhotic patients. In addition to this, a study conducted by Schweitzer *et al*., (2015) estimated the prevalence of chronic HBV infection in Ghana at 12.92 %. Hepatic diseases as a result of HBV and HCV infection have been observed to increase over the years especially in developing countries which pose a serious health threat. Therefore, the present study sought to determine the trends with regards to the prevalence of hepatitis B and C viral infections among children and adults presenting with hepatic disease at Komfo Anokye Teaching Hospital (KATH).

1. 1 PROBLEM STATEMENT

Chronic HBV and HCV infections are the principal sources of hepatic diseases such as HCC, which is one of the most widespread cancers in developing nations and the third cause of cancerassociated mortality worldwide (Jemal *et al.,* 2012). In Africa, about 100 million individuals are projected to be infected with HBV and or HCV, whereas resource-rich countries report 23 million HBV and or HCV-infected subjects (Blachier *et al.*, 2013). Developed countries have less prevalence of hepatic diseases as opposed to developing countries due to implementation of highly effective antivirals and HBV vaccine campaigns (Thursz *et al.*, 2012).

1.2 JUSTIFICATION

Hepatic diseases are serious conditions with increased morbidity and mortality rates globally. Thus, WHO is calling for enhancement in interventions for the inhibition, maintenance, and control of viral hepatitis which may result in hepatic diseases worldwide (WHO-Secretariat, 2010). Viral hepatitis is endemic in sub-Saharan Africa including Ghana. There is limited literature on patients with Hepatitis B and C viral infections presenting with hepatic diseases in Ghana and Africa. It is therefore necessary to undertake this study to increase awareness of these viruses which would inform better alternatives for diagnosis and management of viral hepatic diseases in Ghana.

1.3 MAIN OBJECTIVE

- To determine the prevalence of hepatitis B and C viral infections among children and adults presenting with hepatic disease.

1.4 SPECIFIC OBJECTIVES

- To determine the seroprevalence of hepatitis B and C viral infections among patients presenting with hepatic disease.
- To determine the association between hepatitis B and C viral infections and the clinical information of patients presenting with hepatic disease..
- To determine the HBV profile of participants positive for HBsAg.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 HEPATITIS B VIRAL INFECTION

Hepatitis B virus (HBV) is a major cause of liver disease morbidity and mortality worldwide, affecting more than 2 billion people, responsible for more than 240 million cases of chronic hepatitis and greater than 780,000 deaths per year (Trepo *et al.*, 2014; WHO, 2015a).

2.1.1 Structure/ Description of HBV

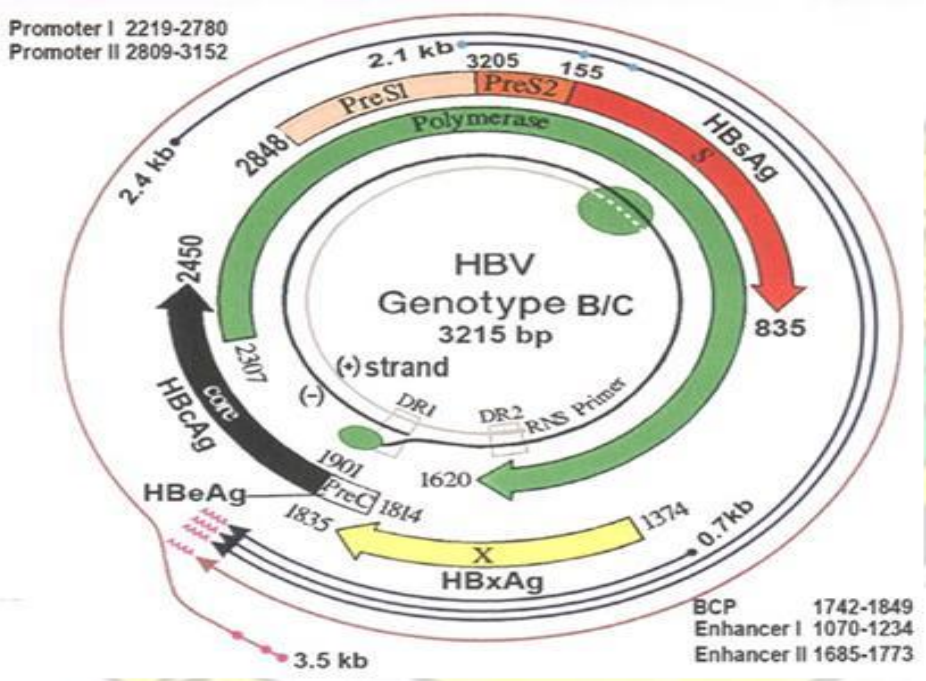

Figure 1.Genomic structure organization of HBV (Zhang & Cao, 2011)

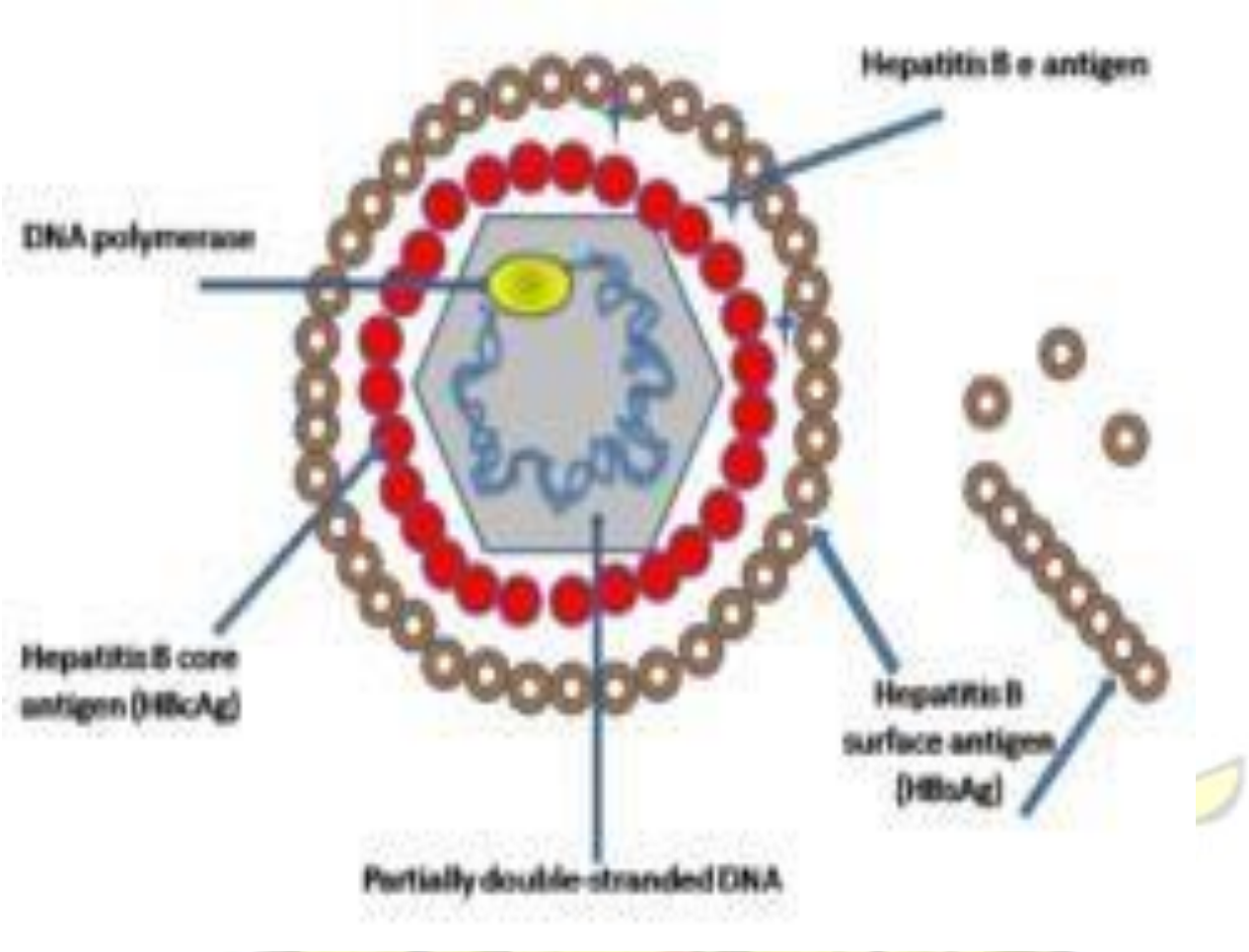

Figure 2. Structure of nuclear genome of Dane particle. (Nuclear genome of the Dane particle .In Wikipedia. Retrieved on 23rd July,2016).

HBV is a DNA virus with important traits similar to that of retroviruses (Ganem *et al.*, 2001). It is in the family Hepadnaviridae. HBV can be categorized into eight genotypes, A to H based on sequence similarity. Each of the genotype has a varying geographic allocation. Three kinds of viral particles can be found in the serum by electron microscopy. The spheres and filaments consist of hepatitis B surface antigen (HBsAg) and lipids (Gavilanes *et al.*, 1982). The virion of HBV has a round, double structure 42 nm in diameter of a lipid envelope consisting of HBsAg

that surrounds an inner nucleocapsid composed of hepatitis B core antigen (HBcAg) complexed with virally encoded polymerase and the viral DNA genome (Gerlich & Robinson, 1980).

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2.1.2 Pathogenesis of HBV Infection

HBV is spread primarily by skin contact, blood and other body fluids. Diseases resulting from HBV infection include chronic hepatitis, hepatic failure, liver cirrhosis and HCC. The age of the patient at the period of infection is inversely proportional to the chances of developing into chronic infection.

Approximately 90% of newborns with the infection through birth become chronic carriers, except when they are vaccinated at birth. The danger of chronic HBV infection decreases to 30% of children infected within the ages 1 and 4 years (Hyams, 1995). After HBV infection, majority of the patients either develop immunity (87–90%) and clear the infection or become chronic carriers. A small percentage develop liver disease or develop chronic active hepatitis with a high risk of HCC, liver cirrhosis or both (Goldstein *et al.*, 2002). The mortality of these diseases and their attribution to hepatitis infection is well known. More than 780,000 HBV-related deaths were approximated to occur yearly (WHO, 2015a) and 73% of all liver cancer mortalities worldwide are as a result of hepatitis viruses (Ott *et al.*, 2011).

2.1.3 Epidemiology of HBV Infection

The most frequent cause of hepatitis is HBV. Close to 240 million people are chronically infected (WHO, 2015a) and over 780000 deaths occur every year as a result of acute liver failure, liver cirrhosis and hepatocellular carcinoma (Sagnelli *et al.*, 2012; Sagnelli, Sagnelli *et al.*, 2014). HBV is transmitted perinatal to newborn babies, by parenteral route or by unprotected

sex. The transmission of HBV infection varies greatly from one geographical region to another. The prevalence of HBsAg chronic carriers determines the degree of endemicity. The prevalence of < 2% is classified as low endemicity , between 2% - 7% is classified as intermediate and > 8% is classified as high in different countries (Ott *et al.,* 2012) . In Ghana, the prevalence of HBsAg ranges between 8–15% in urban areas and some parts of rural areas; this suggests that the disease is endemic (Nkrumah *et al.,* 2011; Dongdem *et al.,* 2012; Sarkodie *et al.,* 2001). In nations with a high occurrence of HBsAg chronic carriers, HBV infection is usually transferred perinatal or during early childhood (WHO, 2015a). HBV infection in nations with a low occurrence is normally acquired during adulthood via skin or sexual transmission (Lavanchy, 2004).

2.1.4 Prevalence of HBV and HCV Hepatic Diseases in Ghana and Africa

There have been several reports of over 8% chronic HBV infection with an increased risk for progressive hepatic disease in sub-Saharan Africa (Howell *et al.,* 2014). Hepatocellular carcinoma is the commonest cancer among males and third most common among females (Howell *et al.,* 2014).

Ghana is part of the areas of the world with a high (>8%) prevalence of chronic HBV infection (Howell *et al.,* 2014). Schweitzer *et al*., (2015) for instance, after assessing the global burden of hepatitis B in 2013, reported the prevalence of chronic hepatitis B virus infection in Ghana at 12.92 % (Schweitzer *et al.,* 2015).

In other parts of Africa, a prevalence of 38.5% and 7.7% were recorded in HCC patients with HBV and HCV infection respectively in Gambia. In a similar study conducted by Chin"ombe *et al.,* (2009) in Zimbabwe, a prevalence of 48.3% and 20% was detected in patients with HBV

and HCV infections respectively. In this same study, Chin‟ombe *et al.,* (2009) observed a prevalence of 8% in HBV/HCV coinfection. Furthermore, a study conducted in Ethiopia by Taye *et al.,* (2014) determined a prevalence of 22.3% and 3.6% in HBV and HCV infections respectively in chronic hepatitis patients. In this same study, Taye *et al.,* (2014) determined a prevalence of 4.8% for HBV/HCV coinfection.

2.1.5 Signs and Symptoms of HBV Infection

Most people are asymptomatic during the period of acute infection. However, some people have acute illness with symptoms that persists for several weeks, including jaundice, abdominal pain, nausea, cola-like urine, tiredness and vomiting. Less than 1% of patients with HBV infection may develop acute liver failure which may result in death (WHO, 2015a).

In chronic HBV patients, HBV can progress to hepatic diseases such as liver cirrhosis or liver cancer. Over 90% of healthy people who may contract HBV will recuperate normally from the acute infection within the maiden year (WHO, 2015a).

2.1.6 Diagnosis of HBV Infection

Laboratory identification of hepatitis B infection concentrates on revealing HBsAg. HBsAg is the main clinical marker depicting acute or chronic infection and occurrence as well as endemicity of HBV infection (Shepard *et al.,* 2006). WHO suggests that all blood donations are examined for HBV and make sure blood is safe to prevent unintentional transmission to people who receive blood products (WHO, 2015a).

The presence of HBsAg and immunoglobulin M (IgM) antibody to the core antigen describes acute infection. During the primary stage of HBV infection, patients are also seropositive for

HBeAg. Active replication of HBV is indicated by the presence of HBeAg. It also suggests high infectivity in blood and body fluids. HBV Chronic infection is diagnosed by the persistence of HBsAg for at least 6 months. Continuance of HBsAg in patient‟s blood is the main indicator of acquiring hepatic diseases such liver cirrhosis and HCC (WHO, 2015a).

2.1.7 Treatment of HBV Infection

WHO suggests the administration of tenofovir or entecavir, in patient with HBV infection due to the high effectiveness in preventing viral replication. Compared with other drugs, these drugs hardly develop drug resistance and have few side effects. Although the treatment does not cure HBV infection, it inhibits the viral replication. Because of this, the therapy should be taken throughout a person‟s life. Treatment using interferon injections is highly utilized in developed countries than developing countries due to high cost. Even up till now, diagnosis of HBV is detected when a person is in progressive stage of the liver disease. Liver cancer develops quickly as treatment options are little and the consequence in general is mostly poor. Patients with liver cancer die shortly after detection in poor resource settings. In developed nations, surgery and chemotherapy utilization extends life expectancy for some years. Liver transplantation in developed nations is done from time to time in patient with cirrhotic liver conditions (WHO, 2015a) .

2.1.8 Prevention of HBV Infection

Vaccination with hepatitis B vaccine is the backbone of HBV prevention. After, the complete

HBV vaccine intake, individuals develop protective antibody against HBV. Immunity may be lifelong or can last up till 20 years (WHO, 2015a). However, a booster dose should be given to immunocompromised patients, based on serological response (Plotkin *et al*., 2011).

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2.2 HEPATITIS C VIRAL INFECTION

Hepatitis C is the second most prominent viral infection globally after hepatitis B and its importance is associated with the occurrence of hepatic diseases (Craxi *et al.,* 2008) . About 130 – 150 million people universally are chronically infected with hepatitis C infection (WHO, 2015b) and about 500000 people die every year of hepatitis C-associated liver infections (Lozano *et al.,* 2012).

2.2.1 Structure / Description of HCV

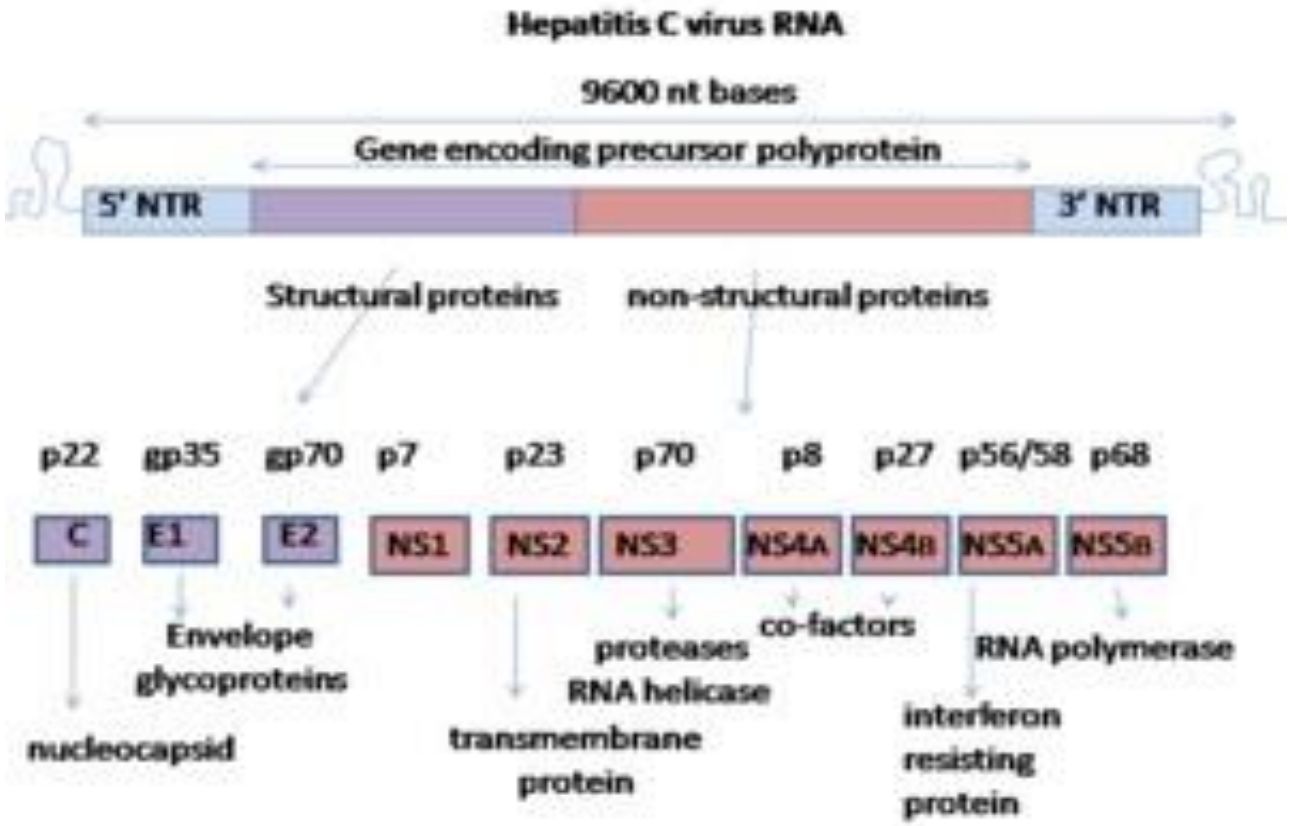

Figure 3. Summary of HCVgenomic organization. (Genomic organization of HCV. In Wikipedia. Retrieved on 23rd July, 2016).

HCV is an RNA virus in the genus Hepacivirus and the family Flaviviridae. The genome of HCV is made up of a single-stranded RNA of positive polarity. The genome sequence codes for a lengthy polyprotein (Simmonds, 1995) which is processed co-translationally and posttranslationally to produce several structural proteins and non-structural proteins (Lindenbach *et al.,* 2001). E1 and E2 envelope proteins are the outward surface of the viral particles responsible for viral entry into the host cell.

2.2.2 Transmission of HCV Infection

The mode of spread of HCV include: blood (Xia *et al.,* 2008); intravenous (IV) drug use (Tohme, 2010); sexual transmission (Jafari *et al.,* 2010); skin piercings (Lam *et.al.,* 2010) and through birth (Owusu-Ofori *et al.*, 2005) . The report of HCV in IV drug users in developed nations is about 80% while little is known about the rate of related risk associations in Africa (Simonsen *et al.,* 1999). On the other hand , Madhava *et al.* observed drug use to be a rare mode of HCV spread in Africa (Madhava *et al.,* 2002). While there are important differences among nations, WHO predicts 18% of injections in sub-Saharan Africa are due to reuse of needles and syringes (Gibb *et al.,* 2000). Transmission through birth is minimal but important in areas of dual-infection with HIV (Alter, 2007).

2.2.3 Pathogenesis of HCV Infection

HCV enters a host through blood, parenteral and sexual intercourse (Alter, 1997). The virus then moves into the liver cells using the viral receptor (Pileri *et al.*, 1998). After entry, the virus releases its genetic material to initiate replication. The viral genome is transcribed and then translated into polyprotein. The processed nonstructural proteins then develop a complex with the genome and begin formation of the negative strand, which in turn operates as the model for positive strand synthesis. The RNA replicative intermediate grows and interacts with the core and envelope proteins to convene into a virion (Liang *et al.*, 2000).

2.2.4 Epidemiology of HCV Infection

Hepatitis C infection is currently a worldwide public health issue and is prevalent in almost every part of the globe (Global Burden Of Hepatitis C Working Group, 2004; Ray, 2002). It is still one of the main causes of viral hepatitis and is a significant cause of terminal liver disease.

Acute HCV infection is normally symptomless, coincidentally known during regular examination. Majority of information are reliant on HCV seroprevalence studies indicating the occurrence of existent HCV in the blood.

The approximated prevalence of positive HCV infection was 169.7 (2.9%) million worldwide in 2002. Since hepatic disease is seen in about 75% of anti-HCV patients, it is valued that the occurrence of chronic hepatitis C is about 2.2% (127 million) (Ray, 2002). HCV infection can also be classified as high, intermediate or low when the occurrence is >3.5, 1.5–3.5 % and <1.5 % respectively (Hanafiah *et al.,* 2013).

HCV is more prevalent in some nations in sub-Saharan Africa and Asia. Egypt observed the maximum seroprevalence of 13.9% in healthy general population and this is lower than that reported in western nations (Chemaitelly *et al.,* 2013; Lehman & Wilson, 2009b; Shepard *et al.,* 2005).

2.2.5 Signs and Symptoms of HCV Infection

The incubation time for HCV is between 2 weeks to 6 months. After preliminary infection, 80% of people become symptomless. Those with acute symptoms may exhibit jaundice, fever, nausea, tiredness, vomiting, anorexia, abdominal pain, cola-like urine, grey-coloured faeces and arthritis (WHO, 2015b).

2.2.6 Diagnosis of HCV Infection

Diagnostic tests for HCV have developed evidently within the past decade (Carithers *et al.,* 2000). The two diagnostic tests for HCV are serological assay and molecular assay. Enzyme immunoassay (EIA) is used as a preliminary test whereas Recombinant Immunoblot Assay (RIBA) is used as a definitive diagnosis.

Over the years, there have been improvements with greater sensitivity in HCV diagnostic test kits (Gretch, 1997). Molecular test such as reverse-transcription PCR (RT- PCR) are highly sensitive for verifying the diagnosis of HCV infection, and for assessing the effectiveness to antiviral therapy through HCV viral load monitoring (Gretch, 1997). Absence of quantifiable HCV viral load is now the criteria for successful treatment (Carithers *et al.,* 2000).

2.2.7 Treatment of HCV Infection

It is advised to initiate treatment in patients with chronic HCV infection (Kim & Saab, 2005). Therapy is endorsed especially for patients at risk of liver cirrhosis (Ghany *et al.,* 2009) with raised serum ALT levels who satisfy the following conditions (Sandeep & Dhawan, 2012): patients more than 18 years, who are positive for anti- HCV antibody and with corrected liver conditions such as ascites. The current drugs for treatment is a combination treatment of Sofosbuvir and Ledipasvir (Chhatwal *et al.,* 2015).

2.2.8 Prevention of HCV Infection

Principal preventive actions against the transmission of HCV include: screening blood, increasing awareness through counseling services and application of infection-control practices.

Secondary preventive actions include recognition and testing of individuals at risk of HCV infection (Centers for Disease Control and Prevention, 1998).

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CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 STUDY SITE

The study was carried out at the Gastrointestinal Tract (GIT) clinic of the departments of Child Health, Medicine, Family Medicine and Serology unit of Komfo Anokye Teaching Hospital (KATH), Kumasi after securing ethical approval from the Committee on Human Research, Publication and Ethics (CHRPE) of KNUST and KATH.

3.2 STUDY SUBJECTS

This cross sectional study was carried out from November 2015 to April 2016.Criteria for recruiting subjects included children ≥ 3 months of age and all adult who were suspected of hepatic conditions evidenced by raised AST and/or ALT. Patients who did not give consent were excluded. In all, 155 patients were recruited for the study.

3.3 DATA COLLECTION

Recruitment of subjects was done during the clinic visit days of the study subjects. On such days the previous medical history of the subject were assessed to identify patients who qualified for the study. The study rationale and objectives were explained to the patients or guardians and written informed consent was obtained from them once subjects were identified. For parents who were illiterates, it was explained to them in their local parlance (Twi). Structured questionnaires were used to retrieve clinical profiles, laboratory parameters and socio-demographic characteristics of patients and their clinical information.

3.4 BLOOD SAMPLE COLLECTION AND PROCESSING

Three (3) millilitres of venous blood was collected following standard operating procedures and transferred into a serum separator tube. The blood was permitted to clot and the serum separated afterwards by centrifuging it at 3000 revolution per minute (rpm) for 5 minutes and was aliquoted into a cryovile. The samples were then stored at -20° C.

3.5 SEROLOGICAL DETECTION OF VIRAL HEPATITIS

The serum was analysed for the detection of HBsAg using Abon HBsAg Test Strip (Abon Biopharm Co. Ltd, Hangzbou, China), anti HCV antibodies using HCV Rapid Test Strip (Abon Biopharm Co. Ltd, Hangzbou, China) and HBV Profile using Abon HBV Combo (Abon Biopharm Co. Ltd, Hangzbou, China).

3.6 PRINCIPLES OF THE PROCEDURE

3.6.1 HBsAg Test

Abon HBsAg Test Strip is a qualitative immunoassay for identifying HBsAg.

The membrane within the test strip is pre-coated with anti-HBsAg antibodies. On testing, the serum or plasma specimen binds to the pre-coated anti-HBsAg antibody. The mixture ascends the membrane chromatographically by capillary action. It reacts with anti-HBsAg antibodies to form a coloured line. The formation of coloured line signifies a positive result, while its absence tells a negative result. The appearance of a coloured line denotes that the right amount of volume of specimen has been added .The test strip was immersed into the serum and then removed after 8-10 seconds and strip laid flat on a clean surface. The outcome was then read after 15 minutes.

3.6.2 Anti-HCV antibodies

Abon HCV Rapid Test Strip is a qualitative immunoassay for identification of antibody to HCV. The membrane within test strip is pre-coated with HCV antigen. During the test, the specimen binds to the pre-coated HCV antigen. The mixture moves upwards on the membrane by capillary

action to bind with the HCV antigen to form a coloured line. The formation of a coloured line shows a positive result, whereas its absence also denotes a negative result. A coloured band will constantly appear in the control line area to act as a control. If this does not appear then the test is invalid. The test strip was immersed into the test sample and was removed after 8-10 seconds. The strip was laid on a clean surface. The result was then read after 15 minutes.

3.7. HBV PROFILE

3.7.1 HBsAg and HBeAg

HBV profile is a qualitative test for detection of HBsAg and HBeAg in serum or plasma. The membrane in the test cassette is pre-coated with anti-HBsAg or anti-HBeAg antibodies. During the test, the specimen reacts with the pre-coated anti-HBsAg or anti-HBeAg antibodies. The mixture moves upward on the membrane chromatographically by capillary action to react with anti-HBsAg or anti-HBeAg antibodies on the membrane to form a coloured line. The appearance of the coloured line denotes a positive result while its absence signifies a negative result.

3.7.2 HBsAb

The test is a qualitative, lateral flow immunoassay for the identification of HBsAb. The membrane in the strip is pre-coated with HBsAg. During test, the serum or plasma specimen binds to the pre-coated HBsAg. The mixture moves upward on the membrane chromatographically by capillary action to bind the pre-coated HBsAg and to form a coloured line. The formation of the coloured line denotes a positive result, while its absence signifies a negative result.

3.7.3 HBeAb and HBcAb

The test is immunoassay grounded on the principle of competitive binding. On testing, the mixture ascends the membrane chromatographically by capillary action. The membrane in the strip is pre-coated with HBeAg or HBcAg. On testing, anti-HBe antibody or anti-HBc antibody, if present in the specimen will compete with particle coated anti-HBe antibody or anti-HBc antibody for less amount of HBeAg or HBcAg on the membrane, and no band will appear in the test line region, signifying a positive result. A visible coloured line will form in the test line region if there is no anti-HBe antibody or anti-HBc antibody in the specimen because all the antibody coated particles will be captured by the antigen coated in the test line region. To serve as a control, a coloured line will always form in the control line region indicating that right amount of the specimen has been added.

The test cassette was put on a leveled surface which was clean. Three drops of serum or plasma were added to each specimen well and delayed for the red line(s) to be seen. After 15 minutes, the results were determined.

3.8 STATISTICAL ANALYSIS

Data was entered and analyzed in Microsoft Excel spread sheet and GraphPad prism. Descriptive analysis was performed and the results were expressed as means and percentages. Chi square test was used to determine association within categorical variables. $P < 0.05$ was considered to be significantly associated.

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CHAPTER FOUR

4.0 RESULTS

A total of 155 patients with hepatic disease, aged 4 months to 79 years was recruited for the study. Questionnaires were designed to capture their socio-demographic characteristics and clinical information. Table 1 summarizes the socio-demographic characteristics of the patients. Seventy-two patients representing 46.45% were within the age category 18-45 years and 59.35% were males. Forty-four patients were children and 111 were adults. Among the adult patients, 88 were married, 21 were single and 2 were widowed. Forty-three patients representing 27.74% had junior high school (JHS) background and 37 (representing 23.87%) had no formal education. Concerning the occupational status of the patients, 56.13% were employed and 43.87% were unemployed.

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Table 1: Socio-Demographics of Study Subjects

Characteristics		Frequency(n)	Percentage (%)
Age Group	<18 years	44	28.39
	18-45 years	72	46.45
	>45 years	39	25.16
Gender	Male	92	59.35
	Female	63	40.65
Religion	Christian	116	74.84
	Muslim	31	20
	Others	8	5.16
Marital Status	Single	65	41.94
	Married	88	56.77
	Widowed	2	1.29
Current residence	Urban	50	32.26
	Rural	105	67.74
Level of Education	Preschool	11	7.1
	Primary	30	19.35
	JHS	43	27.74
	SHS	19	12.26
	Tertiary	15	9.68
	No formal education	37	23.87
Occupational status	Employed	87	56.13

Unemployed	68	43.87

Out of 155 patients, 71 were positive for HBsAg, 18 were positive for anti-HCV and 4 were positive for HBV/HCV coinfection. Table 2 summarizes the prevalence of hepatic diseases in HBV and HCV positive patients. The most prevalent hepatic diseases among HBV, HCV and HBV/HCV coinfected positive patients were chronic hepatitis followed by liver cirrhosis, HCC and then acute liver failure.

Table 2: Prevalence of Hepatic diseases among patients positive for HBV and HCV infections

Hepatic Disease	HBV	HCV	HBV/HCV
Chronic hepatitis	47(66.20%)	9(50%)	3(3.37%)
Liver Cirrhosis	23(32.39%)	7(38.89%)	1(1.12%)
HCC	12(16.90%)	2(11.11%)	1(1.12%)
Acute liver failure	2(2.82%)	2(11.11%)	0

Among the 71 HBsAg positive patients, 48 (67.61%) fell between the age category 18-45 years. The age categories between < 18 years and 18-45 years were significantly associated ($P < 0.0001$). Of the 71 HBsAg positive patients, 46 (64.79%) were males while 25(35.21%) were females. Fifty-one out of the 71 HBsAg positive patients representing 71.83% were married while 19 (26.76%) were single. Only 1 patient was widowed. Married and single patients were significantly associated ($P < 0.0001$). Forty-eight patients (67.61%) were employed and 23

(32.39%) were unemployed. Employed and unemployed patients were significantly associated (P = 0.0001). (Table 3)

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Table 3a: Prevalence of HBsAg in relation to Socio-demographic characteristics

Variable		HBsAg n=71
Age	<18 years	4(5.63%)
	18-45 years	48(67.61%)
	>45 years	19(26.76%)
Gender	Male	46(64.79%)
	Female	25(35.21%)
Marital Status	Single	19(26.76%)
	Married	51(71.83%)
	Widowed	1(1.41%)
Current residence	Urban	25(35.21%)
	Rural	46(64.79%)
Religion	Christian	51(71.83%)
	Muslim	15(21.13%)
	*Others	5(7.04%)
Level of Education	Preschool	1(1.41%)

	Primary	12(16.90%)
	JHS	24(33.80%)
	SHS or Higher	22(30.99%)
	No formal education	12(16.90%)
Occupational Status	Employed	48(67.61%)
	Unemployed	23(32.39%)

*Others = Traditionalist and Pagan

Table 3b :Comparison of socio-demographic characteristics among the HBsAg positive patients

Characteristic			P-value
Age	<18 years	18-45 years	
	4	48	<0.0001
Gender	Male	Female	
	46	25	0.0002
Marital Status	Single	Married	
	19	51	<0.0001
Occupational Status	Employed	Unemployed	
	48	23	0.0001

Among the 18 anti-HCV infected patients, 8(44.44%) were within the age category 18-45 years, 7 (38.89%) were > 45 years and 3 were < 18 years. The age categories < 18 years and 18-45 years was statistically significant (P = 0.0376). Of the 18 anti-HCV infected patients, 10(55.56%) were males and 8(44.44%) were females. Eleven patients representing 61.11% were married while 6(33.33%) were single. Only 1 patient was widowed. Married and single patients were also significantly associated (P = 0.0376). Concerning occupational status, 12 patients

(66.67%) were employed while 6(33.33%) were unemployed.

Table 4a: Prevalence of anti-HCV in relation to Socio-demographic characteristics

Variable		HCV n=18
Age	<18 years	3(16.67)
	18-45 years	8(44.44)
	>45 years	7(38.89)
Gender	Male	10(55.56)
	Female	8(44.44)
Marital Status	Single	6(33.33)
	Married	11(61.11)
	Widowed	1(5.56)
Current residence	Urban	5(27.78)
	Rural	13(72.22)
Religion	Christian	12(66.67)
	Muslim	4(22.22)
	*Others	2(11.11)
Level of Education	Preschool	1(5.56)
	Primary	4(22.22)
	JHS	3(16.67)
	SHS or Higher	5(27.78)
	No formal edu.	5(27.78)
Occupational Status	Employed	12(66.67)
	Unemployed	6(33.33)

*Others = Traditionalist and Pagan

Table 4b: Comparison of socio-demographic characteristics among the anti-HCV positive patients

Characteristic			P-value
Age	<18 years	18-45 years	
	3	8	0.0376
Gender	Male	Female	
	10	8	0.2879
Marital Status	Single	Married	
	6	11	0.0376
Occupational Status	Employed	Unemployed	
	12	6	0.0213

Among the clinical information for Hepatitis B and C positive patients, the most prevalent signs and symptoms were jaundice, followed by hepatomegaly, ascites, abdominal distension and abdominal pain as outlined in Table 5.

Table 5: Clinical Information of Study Subjects in relation to HBsAg and antiHCV positive patients

Characteristics		Frequency(%)	HBV Pos.	HCV Pos.
Jaundice		89(57.42)	35	11
Hepatomegaly		86(55.48)	33	11
Ascites		69(44.52)	32	11
Abdominal distension		61(39.35)	32	9
Abdominal pain		58(37.42)	30	6
Pedal edema		48(30.97)	24	8
Splenomegaly		36(23.23)	11	3
Hepatic Encephalopathy		19(12.26)	15	4
UGIB		21(13.55)	12	1
Alcohol consumption	Yes	37(23.87)	19	6
	No	80(51.61)	51	10
	NA	38(24.52)	1	2
Hospitalization	Yes	24(15.48)	10	5
	No	131(84.52)	61	13
IV Drug use	Yes	112(72.26)	53	15
	No	43(27.74)	18	3
Dental procedure	Yes	16(10.32)	9	2
	No	139(89.68)	62	16
Tatoo/Piercing	Yes	22(14.19)	14	2
	No	133(85.81)	57	16
Multiple Sexual Partner	Yes	34(21.94)	21	4
	No	80(51.61)	48	11
	NA	41(26.45)	2	3
History of Blood Transfusion	Yes	46(29.68)	15	5
	No	109(70.32)	56	13
History of Surgery	Yes	20(12.90)	9	4

	No	135(87.10)	62	14

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The profile for Hepatitis B positive patients was determined. Table 6 summarizes the Hepatitis B profile. Seventy one patients (100%) were positive for HBsAg. Of these, 7 (9.86%) were positive for HBeAg, 44 (61.97%) were positive for HBeAb and 68 (95.77%) were positive for HBcAb.

Table 6: HBV Profile of Participants positive for HBsAg

Parameter	Status	
	Pos. (%)	Neg. (%)
HBsAg	71(100)	0(0)
HBsAb	0(0)	71(100)
HBeAg	7(9.86)	
HBeAb	44(61.97)	64(90.14)
		27(38.03)
HBcAb	68(95.77)	3(4.23)

N=71

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CHAPTER FIVE

5.0 DISCUSSION

HBV and HCV infections are serious public health problems which affect approximately 2 billion and 130 - 170 million people across the globe respectively (Shepard *et al.,* 2005; Trepo *et al.,* 2014). Data on the prevalence of hepatitis viruses among patients presenting with hepatic disease in Ghana is very limited. This cross-sectional study was aimed at determining the prevalence of HBV and HCV infections among children and adults presenting with hepatic disease at KATH from November, 2015 to April, 2016.

In this study, the prevalence of chronic hepatitis in HBsAg positive patients was much higher than that reported in Accra by Schweitzer *et al.,* (2015) and in Ethiopia by Taye *et al.,* (2014). However, the prevalence of liver cirrhosis in our study was lower than that reported by Blankson *et al.,* (2005). More so, the prevalence of HCC was lower than that observed by Mboto *et al.,* (2005).These differences in prevalence could be due to the life style of the study subjects and the local endemicity of the study area.

The current study reported a higher prevalence of chronic hepatitis in anti-HCV positive patients compared to that accounted for by Taye *et al.,* (2014). Again, the current study observed a higher prevalence of liver cirrhosis in HCV patients and this was higher than that reported by Blankson

et al., (2005) in Ghana and Kanwal *et al.,* (2012) in the US. In addition to this, the prevalence of HCC in the study was higher than that observed by Mboto *et al.,* (2005) and Kanwal *et al.,* (2012). In contrast to the prevalence of HCC reported in the study, Chin‟ombe *et al.,* (2009) observed a higher prevalence than our report. These differences in prevalence could be due to the geographical location and living conditions of study subjects.

The prevalence of HBV/HCV coinfection among chronic hepatitis patients in the current study was in agreement with that conducted by Taye *et al.,* (2014). The prevalence of HBV/HCV coinfection in the study may suggest that the two viruses are endemic in Ghana and share a common mode of transmission with increased risk of developing into hepatic diseases.

Only 4 patients less than 18 years had HBV infection. However, the high number of patients who had HBV infection were between the age categories of 18-45 years and this could be due to an active sexual life (Hou *et al.,* 2005). Males recorded a high number of HBV infection than females. This may be due to the possibility of continual infection due to behaviours such as IV drug use and high risk sexual activities than females who may be briefly infected and develop anti-HBs (Khosravani *et al.,* 2012). Concerning marital status, married patients recorded a higher number of HBV infection. This implies that the mode of transmission is more likely to be transmitted through sexual intercourse (Hou *et al.,* 2005). These findings were similar to that of HCV infections with the exception of gender.

Among the clinical information presented for HBV infection, jaundice was the most prevalent symptom (Ochwoto *et al.,* 2016), followed by hepatomegaly, ascites, abdominal distension and

abdominal pain. These findings were similar to that of HCV infection. Patients who may present with these symptoms may suggest possible HBV and HCV infections.

Among the patients with chronic hepatitis, 39 were males and 25 were females. The reasons accounting for a high number of males than females with hepatic diseases are because males and females livers are innately dissimilar. Majority of the differences develop during puberty when male livers are exposed to regular explosions of growth hormone. This propels male livers to express various genes than female livers. In addition to this, when sex-specific genes were mapped, close associations were related to inflammatory pathways. Several sex-specific genes were overexpressed and others underexpressed in males with chronic hepatitis. Thus the liver was incapable of maintaining normal metabolic function and cancer emerged in a substantial number of the organisms (Rogers, 2008).

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CHAPTER SIX

6.0 CONCLUSION, RECOMMENDATIONS AND LIMITATION

6.1 CONCLUSION

Viral hepatitis is a major global public health issue. HBV and HCV infections are the most common viral causes of hepatic diseases. The study describes the prevalence of hepatitis B and C viral infections among children and adults presenting with hepatic disease at KATH. Of the 155 patients recruited, 71 were HBsAg positive, 18 were anti-HCV positive and 4 were both HBV/HCV coinfected. Among the 71 HBsAg positive patients in the current study, the prevalence of chronic hepatitis was 66.20%. This was followed by liver cirrhosis, HCC and acute liver failure with a prevalence of 32.39%, 16.90% and 2.82% respectively. In addition to this, among the 18 anti-HCV positive patients, the prevalence of chronic hepatitis was 50%, followed by liver cirrhosis (38.89%), HCC (11.11%) and acute liver failure (11.11%). Out of the HBV/HCV coinfected patients, the prevalence of chronic hepatitis was 3.37%. This was followed by both liver cirrhosis and HCC with a prevalence of 1.12%.

6.2 RECOMMENDATIONS

Information about the prevention, transmission and awareness of viral hepatic diseases should be strengthened by giving health education through the television, radio, newspapers, internet and

any means possible. Also, further studies should be conducted using a larger sample size. In addition to this, more sensitive and specific diagnostic tools like ELISA and PCR should be used in diagnoses of viral hepatitis.

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6.3 LIMITATION

Rapid test strip used in the study is less sensitive and less specific than other diagnostic tools such as ELISA and PCR.

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APPENDIX

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF CLINICAL MICROBIOLOGY

QUESTIONNAIRE ON PREVALENCE OF HEPATITIS B AND C VIRAL INFECTIONS AMONG CHILDREN AND ADULTS PRESENTING WITH HEPATIC DISEASE.

Dear Respondent,

I am a final year master‟s student from Kwame Nkrumah University of Science and Technology, Department of Clinical Microbiology, conducting a research on the topic "prevalence of hepatitis b and c viral infections among children and adults presenting with hepatic disease". The purpose of the research is to acquire knowledge of these viruses which would inform better alternatives for diagnosis and management of acute liver failure and hepatic encephalopathy cases in Ghana. We kindly ask you to answer this questionnaire as part of our academic exercise. We guarantee that information provided would be kept confidential and this is only for academic purposes.

Inclusion Criteria: All patients ≥ 3 months of age suspected of hepatic conditions evidenced by raised AST and/or ALT.

SECTION A

SOCIO-DEMOGRAPHICS OF PARTICIPANT

1. Age: …….

2. Sex a. Male [ ] b. Female [ ]

3. Religion a. Christian [ ] b. Muslim [ ] c. Traditional believer [ ] Other(s), specify……...

4. Level of education a. No formal education [ ] b. Nursrey /Kindergarten [ ] c. Primary [ ] d. JHS [ ] Other(s), specify……..

5. Marital status: a. Married [ ] b. Single [ ] c. Divorced [ ] d. Widowed [ ]

6. Current residence a. Urban [ ] b. Rural [ ]

7. Who do you live with? a. Father and Mother [ ] b. Father [ ] c. Mother [ ] d. Guardian [ ] Other(s), specify……..

8. What is the occupational status of your parents/guardian?

a. Employed [ ] b. Unemployed [ ] c. Other(s), specify……..

9. What is your source of drinking water? a. Well b. Pipe borne c. Others, Specify……..

10. Do you rear animals? a. Yes [ ] b. No [ ]

If Yes which one(s)? a. Swine b. Sheep c. Goats d. Others, Specify……

11. Do you consume pork? a. Yes [ ] b. No [ ]

If Yes, which part(s) do you consume? a. Head b. Intestines c. Leg d. Others, Specify……

12. Do you drink alcoholic beverages? a. Yes [ ] b. No [ ]. If Yes, which type(s)? a. Beer b. Wine c. Hard liquor d. Others, specify……..

13. Do you have multiple sexual partners? a. Yes [ ] b. No [ ]

14. Do you have a tattoo/ body piercing? a. Yes [ ] b. No [ ]

Medical History

15. Have you had any blood transfusion before? a. Yes [ ] b. No [ ]

16. Have you had surgery or any invasive procedure before? a. Yes [ ] b. No [ ]

17. Have you ever undergone a dental procedure? Yes [ ] b. No [ ]

18. Have you ever been hospitalized? Yes [ ] b. No [ ]

Drug History

19. Are you presently under certain medication? a. Yes [ ] b. No [ ] , If Yes, please list

i. ……. a. Therapeutic b. Overdose

ii. ……. a. Therapeutic b. Overdose

iii. ……. a. Therapeutic b. Overdose

iv. ……. a. Therapeutic b. Overdose

v. ……. a. Therapeutic b. Overdose

SECTION B

CLINCAL INFORMATION ON PARTICIPANT

Current Clinical Presentation

20. Is there the presence of jaundice? a. Yes [ ] b. No [ ] c. Not Known [ ], If Yes,

Date…….. & Time……

21. Is there the presence of fever? a. Yes [ ] b. No [ ] c. Not Known [ ] 22. Is there the presence of hepatomegaly? a. Yes [ ] b. No [ ] c. Not Known [ ]

If Yes, size …….

23. Is there the presence of splenomegaly? a. Yes [ ] b. No [ ] c. Not Known [ ]

If Yes, size …….

24. Is there the presence of ascites? a. Yes [ ] b. No [ ] c. Not Known [ ]

25. Is there the presence of pedal edema? a. Yes [ ] b. No [ ] c. Not Known [ ]

26. Is the patient experiencing abdominal discomfort? a. Yes [ ] b. No [ ] c. Not Known [ ]

27. Is there the presence of subclinical, occult or minimal confusion/disorientation? a. Yes [ ] b. No [ ] c. Not Known [ ]

28. Other clinical presentations ……

Encephalopathy

29. Is there the presence of encephalopathy? a. Yes [ ] b. No [ ] c. Not Known [ ],

If Yes, Date…….. & Time……

30. What is jaundice-to-encephalopathy interval? ……

31. What is the Hepatic encephalopathy clinical stage?

a. Stage I [ ] b .Stage II [ ] c. Stage III [ ] d. Stage IV [ ]

Cerebral edema

32. Is there the presence of life threatening coma with cerebral edema?

a. Yes [ ] b. No [ ] c. Not Known [ ]

33. Is there the presence of pupillary changes?

a. Yes [ ] b. No [ ] c. Not Known [ ], If Yes

Left Eye	Right Eye
Size	
Reaction	

34. Is there the presence of neurogenic hyperventilation?

a. Yes [ ] b. No [ ] c. Not Known [ ]

Coagulopathy

35. Is there the presence of upper gastrointestinal bleeding?

a. Yes [ ] b. No [ ]. If Yes, what was the presentation? Malaena / Haematimesis

36. Is there the presence of bleeding in other parts of the body? a. Yes [ ] b. No [ ]

Current Vital Signs

37. Temperature .....

38. Blood pressure ……..

39. Respiratory rate …….

40. Heart rate (Pulse) ……..

Infection

41. Is there the presence of meningitis/encephalitis?

a. Yes [ ] b. No [ ] c. Not Known [ ]

42. Is there the presence of septicaemia/bacteraemia?

a. Yes [ ] b. No [ ] c. Not Known [ ]

Blood Culture Results

43. What is the blood culture result of the patient? a. NBG b. BG c. Not Known [ ]

If bacterial growth is present, which organism(s) was/were isolated? …….

Other Precipitating Factors

44. Is there the presence of dehydration?

a. Yes [ ] b. No [ ] c. Not Known [ ]

45. Form of Clinical Management of Jaundice

a. Supportive b. Therapeutic

If Therapeutic, which drug(s) was/were used? ……

Clinical Outcome

46. Status of Patient: a. Discharged b. Dead

If Discharged, Date …… & Time …….

47. Hepatitis Clinic

Viral Hepatitis	Results
Hepatitis A	
Hepatitis B	
Hepatitis C	
Hepatitis D	
Hepatitis E	

48. Haematological profile

FBC	
Hb	
WBC	
NEUT	
LYMPH	
PLT	

INR	
APTT	
PT	

KNUST

49. Biochemical profile

Liver Function Test

AST	
ALT	
ALP	
GGT	
DB	
TB	

Electrolyte	
Na^+	
K^+	
Cl^-	

Renal (Kidney) Function Test

Urea …….

Creatinine …….

Bun to Creat Ratio …….

KNUST