Shandi University

Faculty of graduate studies and scientific research

Frequency of viral hepatitis (B &C) Among Homeless populations in Omdurman region- Sudan

A athesis Submitted in partial fulfillment for the requirement of MSC degree in Medical laboratory science(Microbiology)

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August 2018

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Dedication

To my mother soul …..

To my father memory…..

To my friends indeed…….

Acknowledgment

Thanks to Allah for giving me strength to conduct this thesis, and appreciation to our professor Dr Leila, who saved no effort to guide and support. Great fortress of knowledge and humanity is submitted as basement for Shandi University, and members of Medical Laboratory Science College, microbiology sector colonies our souls and thoughts to its horizon. Thanks to every subject who involved in this study and not intentionally missed mentioned.

Abstract

Back ground:Viral hepatitis B (HBV) and C (HCV) are a major health concern worldwide, with 170 million people chronically infected and at risk of liver cancer, cirrhosis or liver failure. Since no vaccination is available against HCV, it is important to understand how to prevent future infection. Homeless where at high risk ,since they were at poor hygiene and mal nutrition and human low level of the education. This study aimed to determine the frequency of HBV &HCV and there are risk factors among homeless community.

Methods : Under hygienic conditions and considering labeling 5 ml of blood was withdrawn from ninety seven (97) individuals, blood allowed to clot , serum separated . Both of HBV and HCV immunoglobulins were measured using ELISA technique with semi-automation analyzer . Detected via enzyme-immunoassay based on a sandwich principle.

Result**s:** Infected individuals with HBV were (39.2%) and negative result were among (60.8%). While HCV positive result among (3.1%) and negative result were among (96.9%).

Conclusions: results confirms the hypothesis that the frequency of HBV infection in the homeless population is significantly highers thi s corresponds with the higher incidence of these disease in recent years not only in the Omdurman region-(Sudan) but also in worldwide .but in the cases of the HCV no significant variation.

الملخص

يعتبر التهاب الكبد الفيروسي بى(HBV)) و سى(HCV) من الشواغل الصحية الرئيسية في جميع أنحاء العالم ، حيث يوجد170 مليون حالة التهاب الكبد وبائى مزمن ويواجهون الإصابة بسرطان الكبد أو تليف الكبد أو فشل الكبد. بما أنه لا يوجد تطعيم متوفر ضد HCV ، فمن المهم فهم كيفية منع العدوى في المستقبل. وتشمل طريقة انتقال العدوي عن طريق تعاطي المخدرات بواسطة حقن (الوريد) ، ومنتجات الدم ، والوشم ، وبدرجة أقل ، الجماع الجنسي. يعتبر المتشردون اكثر عرضة لخطر لإصابة بالتهاب الكبد الوبائي بى و سى و ذلك بسبب البيئة والسلوكيات المرتبطة بالمجتمعات المتشردة مثل سوءالنظافة وسوء التغذية و تعاطي المخدرات بواسطة حقن (الوريد). تهدف هذه الدراسة لتحديد مدى انتشار فيروس التهاب الكبد الوبائي بي وفيروس التهاب الكبد الوبائي سي وخطورته بين مجتمع المتشردين .

منهجية هذه الدراسه تم سحب 5 مل من الدم تحت ظروف صحية من سبعة وتسعين (97) من الأفراد المتشردين ،ويترك الدم في انابيب معلمه حتي يتخثر ،ويتم فصل المصل عن طريق جهاز الطرد المركزي. تم فحص كل من HBV و HCV عن طريق مقايسة الامتصاص المناعي المرتبط بالإنزيم [ELISA] مع جهاز شبه اوتوماتيكي BTS350 ألمانيا الصنع وطقم ELISA صنع في المملكة المتحدة. تم الفحص عن ذلك عن طريق enzyme - immunoassay على أساس مبدأ ساندويتش.

النتيجة الأشخاص المصابون بلتهاب الكبد وبائى بي 38 (39 .2%)وكانت النتيجة السلبي 59(60.8%). بينما كانت النتيجة الإيجابية لفيروس HCV بين 3 (3.1%) وكانت النتيجة السلبية بين 94 (96.9%).

الاستنتاج: تؤكد نتائجنا على فرضية أن انتشار العدوى بفيروس الالتهاب الكبدي الوبائي بي في عدد الأشخاص الذين لا مأوى لهم أعلى بشكل كبير من عموم السكان ؛ تتوافق مع ارتفاع نسبة الإصابة بهذا المرض في السنوات الأخيرة ليس فقط في منطقة أم درمان - (السودان) ولكن أيضًا في جميع أنحاء العالم ، ولكن في حالات HCV لا يوجد اختلاف كبير.

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Abbreviation

Abbreviation	Refer to
CCCDNA	covalently closed circular DNA
DNA	Deoxyribonucleic Acid
ELISA	enzyme linked immunosorbent assay
ER	Endoplasmic reticulum
GSHV	ground squirrel hepatitis virus
H AART	highly active antiretroviral therapy
HAV	Hepatitis A virus
HB c Ag	Hepatitis B core antigen
HB e Ag	HB e antigen
HB s Ag	Hepatitis B surface antigen
HB x Ag	Hepatitis B x antigen
HBc Ag	Hepatitis B core Antigen
HBIG	Hepatitis B immunoglobulin
HBs Ag	Hepatitis B surface Antigen
HBV	Hepatitis B virus
HCC	hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HEV	Hepatitis E virus
HIV	Human Immunodeficiency virus
IDU	Injection Drug Use
IG	Immunoglobulin
Kb	Kilo base

Nm	**Nanometer**
NS2	**Non -Structural protein 2**
ORFs	**open reading frames**
Pol/RT	**Polymerase/ Reverse transcriptase**
rcDNA	**relaxedcircular dinucleotide acid**
RNA	**Rib nucleotide acid**
SPSS	**package of social science package of social science**
STI	**Sexually Transmitted Infection**
USA	**United State American**
UV	**Ultra violet irradiation**
VHA	**Veterans Health Administration**
WHV	**Woodchuck Hepatitis Virus**

1. Introduction

Hepatitis: is defined inflammation of the liver and subsequent hepatocellular damage caused by bacteria infective, drugs, toxin or viral infections **(***Armstrong 2000).*

Acute viral hepatitis is a systemic infection affecting the liver predominantly. Almost all the cases of acute viral hepatitis are caused by one of five viral agents: Hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus and hepatitis E virus (HEV). Hepatitis may occur with limited or no symptoms, but often leads to jaundice, anorexia and malaise. Clinically classified the hepatitis in two form acute and chronic; hepatitis is acute when it lasts less than 6 months and chronic when it persists longer. Hepatitis A virus and HEV are acquired by consuming food and water contaminated by the virus (excreted in-patient's stool) by way of the fecal-oral. HBV, HCV are contagious by blood and blood products, also may be transmitted by sexual contact. Vaccine for hepatitis A and B is available, but no vaccine is available for hepatitis C or E. Viral hepatitis infection has been reported to be present throughout the year, but some particular months are associated with higher incidences in most of the countries around the world. The exact reasons why hepatitis infection cases present in one season more than other are not completely understand. However, several researchers have suggested that the climatic and behavioral factors such as, summer travel to endemic area, swimming habits of the population in hot months, increase in sexual contact, tattoo, poor hygiene and environmental sanitation and food habits (feco-oral transmission of viral hepatitis) may play a significant role in the seasonal appearance of diseases (*Chamberlain et al 2003*)

Other viruses causes hepatitis such as Epstein Barr virus (the cause of infection mononucleosis) ,cytomegalovirus Yellow fever vires infect the liver but also infect other sites in the body and therefore are not exclusively (*Warren 2016*)

The Word Heath origination estimation that more than 500 million people all around the world are chronically infected with HBV or HCV and approximately 1million people die each year (about 2.7% all death) from causes related to viral hepatitis's and liver disease. (*World Health 2009*).

An estimated 100 million people worldwide are homeless(.*UN Press briefing,2012*) Although methodological difficulties exist in counting homeless people definitions of homelessness vary, these estimates help to quantify the number of homeless people (*Chamberlain etal 2003*). Health problems in homeless populations have been previously reported (*Geddes et al 2011*). Mortality rates are four times higher than in the general population (*Nordentoft 2003*). Morbidity is substantially increased in homeless populations, who have higher prevalence's of mental disorders(*Nielsen 2011*). And infectious diseases than do general populations (*Hwang 2001*), which, being modifiable, could be targeted by health interventions to reduce the frequency of adverse outcomes. Infections in homeless people can lead to community infections and are associated with malnutrition (*Barry,et al 1986*) long periods of homelessness (*Zolopa,1994*), and high use of medical services (*Salit, 1998*).Because absolute numbers of homeless people are high in some countries, improvements in care could have pronounced effects on public health. A wide range of estimates for the prevalence of infectious diseases in homeless people have been reported, particularly for tuberculosis, hepatitis Band C virus, and HIV. (*Raoult etal 2001*)

Homelessness is a community issue: One of the biggest effects of homelessness is the breakdown of community life itself. When a large number of people survives day-to-day and lives with the isolation, fear, and shame that accompanies

homelessness, the very foundations of our communities are tested. Communities are affected by homelessness in a number of ways:

The moral dimension we are all morally affected by homelessness as we share public space with fellow citizens living in substandard conditions that affect their physical health, mental health, and spirit. Some of us justify our inaction by claiming that "they brought it on themselves" or that "people choose to be homeless" without understanding the issues that have contributed to the current crisis.

Social cohesion: Evidence is growing those societies in which large inequities exist in the distribution of income and resources are unhealthy for all members. Large-scale inequality is associated with a breakdown of social cohesion that leads to increased fear and uncertainty for everyone. Healthy communities are communities in which all members can share in wealth and opportunity.

Social inclusion Growing homelessness creates divisions within the community as an "us vs. them" mentality develops. If a family is left homeless due to a flood, fire or other sudden tragedy, communities will often rally around to provide aid. In those same community individuals living on the streets because of tragedies that are less immediate, but no less severe, often suffer from shame, stigma and isolation.

Social harmony: Conflicts over the use of public and community spaces increase when there are large numbers of people without access to their own "private" space. These conflicts can bring to the surface deeply rooted issues linked to negative perceptions about members of society who are poor, vulnerable or marginalized (*lkinWison etal 2009*).

1.2 Study hypothesis:

Homeless individuals are related to hepatitis viruses B and C, which are related to habitual activities such as alcoholic addiction, injection drug using and sexual contacts.

1.3 Problems statement:

Not allowing to public service (health care providers, educational welfare and organizing forces) entering the homeless community by its own members. Sexually active homeless individuals are working at marginal jobs, which can increase the potential of HBV and HCV out of their community.

Homeless individuals who were not having hepatitis viruses, in the future the probability to gain the viruses if they would follow their folks

1.4. Rationale

Sudan has remote areas suffering from war, hunger, instability of living style due to many reasons thus homeless population appear in community.

Homeless population as marginal group of residence, live in status not by their choice but how the manage to survive puts them in at zone of risk.Homeless were at high risk since they were malnourished and practice bad habits ,they always bind to illegal situations, which consistent with outcome of health issues, such as drug abuse, illegal sex, open social areas and live in term of no consequences matter, and that what make infectious disorders take place. Hepatitis B and C are related to all these kinds of behaviors and living status. So this study aimed to point an angle toward homeless through HBV and HCV to set a protocol of awareness and protection beside treatment in order to diminish harmless.

1.5 Objectives

1.5.1 General objectives

To detect immunoglobulin of hepatitis (B &C virus) among homeless population in Omdurman region- Sudan

1.5.2 Specific objectives

1. To detect frequency of viral hepatitis B among homeless
2. To detect frequency of viral hepatitis C among homeless
3. Association infection with duration of being homeless
4. To correlate Frequency of infection according to age, gender and education
5. To find out which type of hepatitis is more frequent among homeless population

2. Literature review

2.1. Hepatitis B virus:

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem. Affecting millions of people throughout the world (*Ganem 2001, Robinsin 1995*& *Mahoney 1999*)

More than 2000million people alive today have been infected with HBV at some time in their lives. Of these, about 350million remain infected chronically and become carriers of the virus. (,*Mahoney 1999, Ganem, 2001*)Three quarters of the world's population live in areas where high levels infection is. Every year there over 4 million acute clinical cases of HBV , and about 25%of carriers ,1million people a year ,die from chronic active hepatitis, cirrhosis or primary liver cancer . (*World Health Organization ,2001*)Hepatitis B has also been called type B , Serum Hepatitis , homologous serum jaundice.(*Robinsin -1995*& *Mahoney 1999*)

2.1.1 Causes of the disease:

Hepatitis B is caused by the hepatitis B virus (HBV), an enveloped virus containing a partially double stranded circular DNA genome, and classified within the family hepadnavirus. The immune system is than activated to produce a specific reaction to combat and possibly eradicate the infectious agent. As consequence of pathological damage, the liver becomes inflamed.

HBV may also cause of up to 80% of all cases of hepatocellular carcinoma worldwide second only to tobacco among known carcinogen (*Hollinger 2001*&*Gitlin 1997*)

2.1.2 HBV spreading:

One should not judge by appearance; most infected people look perfectly healthy and have no symptoms of disease, yet may be highly infectious.

HBV is transmitted through percutaneous or parenteral contact with infected blood, body fluids and by sexual inter course. (*Ganem -2001*& *Mahoney 1999*)

HBV is able to remain on any surface it comes in to contact with for about week, e g table tops ,razor blades blood stains ,with losing infectivity(Hollinger 2001& *Robinsin 1995*) .

HBV does not cross the skin or the mucous membrane barrier .some break in this barrier, which can be minimal and insignificant, is required for transmission .(*Robinsin 1995*)

HBV is a large virus and does not cross the placenta, hence it cannot infect the fetus unless there have been breaks in the maternal fetal barrier ,e.g. via amniocentesis .still ,pregnant who are infected with HBV can transmit their disease to their babies at birth if not vaccinated at birth ,many of these babies develop lifelong HBV infection ,and many develop liver failure ,or liver cancer later in life .(*Mahoney etal 1999*)

Sexual intercourse with multiple partners or with persons who have multiple partners can be dangerous hepatitis B is the only sexually transmitted infection for which there is a protective vaccine (*Mahoney etal 1999*)

All persons who are hepatitis B surface antigen positive are potentially infection. The many millions of people around the world who become HBV carriers are constant source of new infections for those who have never contracted. (Robinsin 1995)

Blood is infective many weeks before the onset of the first symptoms and throughout the disease .The infectivity of chronically infected individuals varies

form highly infectious (HBVeAg) positive to often sparingly infectious(anti-HBe positive).

Susceptible to infection of the HBV :

Susceptible are general .Only people who have been vaccinated successfully or those who have developed anti HBs antibodies after HBV Infection are immune to HBV infection.

Persons with congenital or acquired immunodeficiency including HIV infection, and those with immunosuppression including those lymph proliferative disease, and patients treated with immunosuppressive drugs including steroids and by maintenance hemodialysis are more likely to develop persistent infection with HBV.

Following acute HBV infection, the risk of developing chronic infection varies inversely with age. Chronic HBV infection occurs among about 90% of infants infected at birth, 25-50% of children infected at 1-5years of age and about 1-5%of persons infected as older children and adults' .chronic HBV infection is also com Mahoney FJ mon in persons with immunodeficiency (*Ganem 2001, Hollinger 2001, Mahoney 1999*)

2.1.3 Prevalence of chronic of HBV in world:

- The world can be divided in to the three areas where the prevalence of chronic HBV infection is high (>8%) intermediate (2-8%), and low (<2%)

High endemicity areas include south-east Asia Pacific Basin(excluding Japan Australia and New Zealand), Sub-Saharan Africa, Amazon Basin, parts of the Middle East ,the central Asian Republics, and some countries in eastern Europe .In these areas about 70to90%

Of the population becomes HBV-infected before the age of 40 and 20% 0f people are HBV carries. (*Hollinger 2001*)

In countries such as China Senegal, Thailand, infection rates are very high infants and continue through early childhood .At stage, the prevalence of HBsAg in serum may exceed 25%. In other countries such as Panama, Papua New Guinea Solomon Islands, Green land and in population such as Alaskan Indians, infection rates in infants are relatively low and increase rapidly during early childhood.(*Hollinger 2001*)

Low endemicity areas include North America Western and Northern Europe Australia, and parts of South America. The carries rate here is less than 2% of the population is infected with HBV. (*Hollinger 2001*)

The rest of the world falls into the intermediate range of HBV prevalence, with 2-8% of a given population being HBV carriers.

2.1.4 Contagious of HBV:

The most important mode of HBV transmission globally is perinatal, from the mother to her newborn baby. If a pregnant woman is an HBV carrier. And also HBeAg positive her newborn baby has a 90% likelihood to infected and become carriers of these children, 25% will die later from chronic liver diseases or liver cancer (*Hollinger 2001*).

Another important mode of transmission is from child to child during early life from blood contact. (*Gitlin 1997*)

All patients with acute hepatitis B are HBeAg positive .and therefore highly infectious and careless contact with their blood or body fluids can lead to HBV infection.

HBeAg –positive specimens contain high concentration of infectious visions and HBV DNA, in contrast to anti HBeAg positive samples, in which the number of hepatitis B various is substantially reduces.

No treatment for the acute disease :

There is no specific treatment for acute viral hepatitis B. (*Mahoney 1999*)

Hepatitis B is viral disease, and as such, antibiotics are of no value in the treatment of infection.

The use of adrenococorticosteroids in the management of acute, uncomplicated hepatitis B is not indicated because they have effect on the resolution of the underlying disease process, and may increase the rate of relapse. Early treatment of acute hepatitis B With steroid may result in the development of persistent infection. Corticosteroid therapy is only to be used in patients with chronic active hepatitis who are symptomatic, HBsAg negative, and who have severe histologic lesions in liver biopsies. (*Thoelen 1999*)

The therapeutic effectiveness of the course and prognosis of acute hepatitis B is no known. (*Mahoney 1999*)

Hemodialysis, exchange transfusions, cross- perfection, and immunoglobulin (IG) containing high titers anti HBs(HBIG) do not favorably the course of fulminant hepatitis.

Therapy for acute hepatitis B should be supportive and aimed at maintaining comfort and adequate nutritional balance. (*Hollinger 2001*)

Specific antiviral drugs such as lamivudine, a second generation nucleoside analogue, are available, and other are under development, but these drugs have not been evaluated for treatment acute hepatitis B.

2.1.5 Hepatitis B virus life cycle:

The hepatitis B virus, a hepadnavirus ,is a42nm partially double stranded DNA virus ,compsed of a27nm nucleocapsid core (HBcAg),surrounded by an outer lipoprotein coat (also called envelope) containing the surface antigen (HMsAg). (*Ganem 2001, Gitlin 1997, Mahoney 1999, Robinsin 1995 , Robinson 1994*)

The family of hepadnaviruses comprises member recover from a variety of animal species, including the woodchuck hepatitis virus (WHV), the ground squirrel hepatitis virus (GSHV), and theduck HBV.

Common features of all of these viruses are enveloped virions containing 3to 3.3kb of relaxed circular ,partially duplex DNA and virion –associated DNA-dependent polymerases that can repair the gap in the virion DNA template and have reverse transcriptase activities. Hepadnaviruses show narrow host ranges, growing only in species close to the natural host, like gibbons ,African green monkeys, rhesus monkeys, and woolly momnkey.(*Robinson WS 1994,. Hollinger 2001, Robinsin, 1995*)

Hepatocytes infected in vivo by hepadnaviruses produce an excess of no infection viral lipoprotein particles composed of envelope proteins. Persistent infection display pronounced hepato tropism. (*Hollinger 2001*)

Mammalian hepadonaviruses fail to propagate in cell culture .(, *Robinsin 1995, Mahoney 1999, Robinson.1994*)

Intracellular HBV is non-cytopathic and cause little or no damage to the cell, (*Ganem 2001, Robinsin. 1995,*)

The HBV virion binds to a receptor at the surface of the hepatocyte. (*Ganem \ 2oo1*).

A number of candidate receptor have been identified, including the transferrin receptor, the a sialoglycoprotien receptor molecule and human liver endonexin the mechanism of HBsAg binding to a specific receptor to enter cells has not been established yet.

Viral nucleocapsids enter the cell and reach the nucleus, where the viral genome is delivered. (*Ganem 2oo1, Hollinger 2001*) In the nucleus second strand DNA synthesis is completed and the gap in both strands repaired tor yield covalently closed circular (ccc)supercoiled DNA molecule that serves as a template for

transcription of four viral RNAs that are 3.5, 2.4, 2.1 and 0,7 kb long.(*Nielsen etal 2011, Raoult 2001 , Crisis*:*2003, Amanda etal 2017*)

These transcripts are polyadenlated and transported to the cytoplasm, where they are translated in to the viral nucleocapsid and precore antigen (C, pre-C), polymerase (P)envelope L(large), M(medium),S(small), and transcriptional trans activating proteins (X). (*Ganem 2001, Robinsin 2001, Mahoney 1999, chisari 1997*).

The envelope proteins insert themselves as integral membrane proteins in to lipid membrane of the endoplasmic reticulum(ER).

The 3.5 kb species, spanning the entire genome and termed pregenomic RNA (pgRNA), is packaged together with HBV polymerase and a proteins kinase in to core particle where it serves as a template for reverse transcription of negative-strand DNA. The RNA to DNA conversion takes place inside the particles. (*Ganem 2001, Mahoney 1999*).

The new, mature, viral nucleocapside can then follow two different intercellular pathway ,one of which leads to the formation and secretion of new virions, whereas the other leads to amplification of the viral genome inside the cell nucleus.(*Ganem 2001, Mahoney 1999*)

In the virion assembly pathway, the nucleocapasids reach the ER, where they associate with the envelope proteins and bud in to the lumen of the ER, from which they are secreted via the Golgi apparatus out of the cell. (*Ganem 2001, Mahoney 1999*).

In the genome amplification pathway, the nucleocapsids deliver their genome to amplify the intranuclear pool of covalently closed circular DNA (cccDNA). (*Ganem 2001, Mahoney 1999*)

The precore polypeptide is transported in to the ER lumen, where its amino –and carboxy-termini are trimmed and the resultant protein in secreted as precore antigen (eAg).

The x protein contributes to the efficiency of HBV replication by interacting with different transcription factors, and is capable of stimulating both cell proliferation and cell death. (*Ganem 2001, Mahoney 1999*)

The HBV polymerase is a multifunction enzyme. The products of the P gene are involved in multiple function of the viral life cycle, including a priming activity to initiate minus-strand DNA synthesis, a polymerase activity, which synthesizes DNA by using either RNA or DNA Templates, a nuclease activity which degrades the RNA strand of RNA-DNA hybrids, and nucleocapsids .(Nielsen 2011, Raoult 2001 , Crisis :2003) Nuclear localization signals on the polymerase mediate the transport of covalently linked viral genome through the nuclear pore. (*Robinsin 1995*)

2.1.6 Morphology of HBV:

They are three morphological forms. (*Tassopoulos*-1997)

The most abundant are small, spherical, noninfectious particles, containing HBsAg that measure 17 to 25 nm in diameter.

Tubular, filamentous forms of various lengths, but with a diameter comparable to that of the small particles, are also observed. They also contain HBsAg polypeptides. (*Tassopoulos-1997, Thoelen-1999*0)

The third morphological form , the42nm hepatitis B virion ,is a complex ,spherical, double shelled particle that consists of an outer envelope containing host –derived lipid sand S gene polypeptides ,the large(L) ,middle(M) and small (S) surface also known as pre-S1, preS2, and HBsAg. With the sphere is an electron dense inner core or nucleocapsid with a diameter of 27nm.The nucleocapside contains core

proteins HBcAg, a 3.2 kb circular partially double stranded DNA genome ,an endogenous DNA polymerase (reverse transcriptase) enzyme and protein kinase activity. (*Hollinger2001, Robinsin -1995 , Mahoney 1999*)

2.1.7 Genome and proteins:

HBV virion DNA is relaxed circular, partially duplex molecule of 3.2 kb, whose circularity is maintained by 5 cohesive end . (*Hollinger 2001, Robinsin -1995*)

The positions of the 5 end of both strands map to the regions of short (11 nucleotides) direct repeats (DRs) in viral DNA. The 5 end of the minus strand DNA maps within the repeat termed DR1 ,while plus strand DNA begins with DR2.These repeat are involved in priming the synthesis of their respective DNA strands. (*chisari1997*)

The viral minus stand is unit length and has protein covalently linked to 5 end.

The viral plus strand is less than unit length and has a capped oligoribonucleotide at its 5 end. The single strand region or gap is of fixed polarity but variable lengh . (*Robinsin1995*)

A virion- associated polymerase can repair this gap and genome fully duplex genome .

Negative strand DNA is the template for the synthesis of the viral m RNA transcripts. HBV DNA has a very compact coding organization with four partially over lapping open reading frames (ORFs) that are translated in to seven known protein. Noncoding regions are not present.

Four separate viral promoters have been identified, driving expression of

a\ genome P and pre-C and C RNAs b\ L protein m RNA c\M and S protein m RNA and d\ X protein. They are referred to as the genome, pre-S1, S, and X promoters, respectively.

Two major classes of transcripts exist: genome and sub genome. The sub genomic RNAs function exclusively as messenger RNAs (mRNAs) for translation of envelope and X protein. The genomic RNAs are bifurcation, serving as both templates for viral DNA synthesis and as messages for ORF pre-C, C and P translation. (*Mahoney 1999, chisari 1997*)

ORF P encodes the viral polymerase and the terminal protein found on minus strand DNA. ORF C encodes the structural protein of the nucleocapsid and the HBeAg, and ORF S/encodes the viral surface glycoproteins. The product of ORF X is poorly understood regulatory protein that enhance the expression of heterologous and homologous cellular genes in trans. (*Robinsin 1995,Chisari 1997*)

Classic HBsAg, which contain the S domain only, is also called the S- protein (24KD). Two other proteins share the C-terminal S domain, but differ by length and structure of their N-terminal (pre S) extensions. The large L protein (39KD) contains pre S1 and the medium M protein (31KD) contains the pre-S2 and the S region only. HBsAg is the most abundant of the S-related antigen. The Land M proteins are expressed at levels of about 5-15 %and 1-2%compared with S protein. (*Robinsin 1995*)

The glycosylation of the s domain gives rise to tow isoforms of each protein. In addition, the M protein contains an N-linked oligosaccharide on its pre-S2 specific domain, and the l protein carries amyristic acid group in amide linkage to amino terminal glycine reside. While the function of M protein is still obscure, l proteins play a role in viral assembly and infectivity. (*Robinsin 1995*)

The three envelope glycoproteins are no distributed uniformly among the various HBV particle types. Sub viral 22nm particles are composed predominantly of S proteins, with variable amounts of M proteins and few or not L proteins. Virus

particle are enriched for L proteins. L proteins carry the receptor recognition domain, which allows efficient binding to cell surface receptors.

Two in-forme are code present in O RF Classic HBsAg (21KD) is product of initiation from the more internal start Condon, while initiation at the upstream produce a C-related protein that is not incorporated into virions but instead is independently secreted from cells accumulating in serum as an immunologically distinct antigen known as HBsAg (16-18KD). The function of HBsAg is still unknown. (*Robinsin 1995*)

HBsAg is the most conserved polypeptide among the mammalian hepadnaviruses with 63% homology between HBV and GSHV an92% between GSHV and WHV-core proteyns spontaneously assemble in to forms resembling core particles.

The polymerase protein is a DNA-dependent DNA polymerase, a reverse transcriptase, a RNAse H, AND it binds to 5end of HBV DNA, acting thus as a primer for reverse transcription of the pregenome, an RNA intermediated , to from negative strand DNA. (AfarinRahimi 2010) Furthermore, it plays important roles in the encapsidation of the viral pregenomic RNA. The polymerase protein is quite immunogenic during both acute and chronic infection. (*Chisari, 1997*)

QRF X encodes the protein X (17KD), a Tran's activator for the viral core and S promoters. The X protein is the least-conserved protein among hepadnaviruses with only 33% amino acid homology between GSHV and HBV and 71% between the rodent viruses. (*Chisari, 1997*)

2.1.8 Stability:

The stability of HBV does not coincide with that of HBsAg (*Hollinger 2001*)

Exposure to ether, acid (2.4 for at least 6h), and heat (98c for 1min; 60c for 10h) does not destroy immunogenicity, however, inactivation may be incomplete under these conditions if the concentration of virus excessively high. (Hollinger 2001)

Antigenicity and probably infectivity are destroyed after exposure of HBsAg to 0.25%sodium hypochlorite for 3min. (*Hollinger 2001*)

Infectivity is lost after autoclaving at 121c for 20 min or dry heat treatment at 160c for 1h. (*Hollinger 2001*, *Robinsin 1995*)

HBV is inactivated by exposure to sodium hypochlorite (500mg free chlorine per liter) for 10 min, 2% aqueous glutaraldehyde at room temperature for 5min ,heat treatment at 98c for 2min ,sporicidin (Ash DENTSPLY, York, PA)(pH 7.9), formaldehyde at 18.5 g/l (5%formalin In water),70% isoproylalcohol ,80%,ethyl alcohol at 11c for 2min,Wascodyne(a iodophor disinfectant, American Sterilizer Co, Erie, PA) diluted 1;213, or combined Beta-propriolactone and UV irradiation.

HBV retains infectivity when stored at 30c to 32c for at least 6 months and when frozen at-15c for 15 years. HBV present in blood can with stand drying on a surface for at least weak. (*Hollinger* 2001, *Robinsin 1995*)

2.1.9 Transmission:

The three main modes of transmission :

Via blood: the observation that needle- stick injuries can transmit the virus indicates that only very s mall amounts of blood are necessary. HBV infection is especially prevalent in addicts who use intravenous drugs. (*Hollinger 2001*)

During sexual intercourse: the is natural route of transmission HBV (found in semen and vaginal fluids.

Prenatally form mother to newborn: there is important natural route. Trans placental transmission, if it occurs, is rare. There is no evidence that transmission of HBV occurs during breast feeding. (*World Health Organization 2009*)

2.1.10 Risk groups:

Here is a list of groups of people who are at risk of contracting HBV. (*Hollinger 2001, Robinsin 1995*.)

Infant born to infected mother .

Young children in day care or residential setting with other children in endemic areas .

Sexual/household contacts of infected persons.

Heath care workers.

Patients and employees in hemodialysis centers.

Injection drug users sharing unsterile needles .

People sharing unsterile medical or dental equipment.

People providing or receiving acupuncture and/or tattooing with unsterile medical devices.

Persons living regions or travelling to regions with endemic hepatitis B.

Sexually active heterosexual.

Men who have sex with men.

Frequent and routine exposure to blood or serum is the common denominator of health care occupational exposure, surgeons, dentists, oral surgeons, pathologists, operating room and emergency room staff, and clinical laboratory workers who handle blood are at the highest risk (*Robinsin 1995*).

2.1.11 Pathogenesis and immunity:

After entering the blood, the virus infects hepatocytes, and viral antigens are display on the surface of the cells. Cyto-toxic T cells mediate an immune attack against the viral antigens, and inflammation and necrosis occur, immune attack against viral antigens on infected hepatocytes is mediated by cytotoxic T cells. The pathogenesis of hepatitis B is probably the result of this cell-mediated immune injury, because HBV itself does not cause a cytopathic effect. Antigen-antibody complexes cause some of the early symptoms (e. g, arthralgia, arthritis and uricaria) and some of the complication in chronic hepatitis (e.g, glomerulonephritis, cryoglobulinemia and vacuities). (*World Health Organization 2009*)

About 5% of adult patient with HBV infection become chronic carriers. In contrast, 90% of infected newborns become chronic carriers. A chronic carrier is someone who has HBsAg persisting in their blood for 6 months or longer .(*UN Press briefing 2005*) The main determinant of whether a person clears the infection or become a chronic carrier is adequacy of the cytotoxic T-cell response. HBV DNA exists primarily as an episome in the nucleus of persistently infected cell; a small number of copies of HBV DNA are integrated into cell DNA. (*World Health Organization 2009*)

2.1.12 HBV and hepatocellular carcinoma (HCC):

Number of patients with chronic hepatitis will develop hepatocellular carcinoma. (*Hollinger 2001*) Persons at increased risk of developing HCC include adult male and chronic hepatitis B patient with cirrhosis develop HCC. On the other hand, between 60 and 90%af HCC patients have underlying cirrhosis. (*Hollinger -2001, Robinson etal 2005*)

The incidence of HCC varies with geography, race, age and sex .HCC is responsible for 90% of the primary malignant tumors of the liver observed in adults. Worldwide, it is the seventh most frequent cancer in males and ninth most common in females. Liver cancer is the cause of more than500, 000 deaths annually throughout the world, with a male: female's ratio 4:1. The frequency of HCC follows the same general geographic distribution pattern as that of persistent HBV infection. The age distribution of patients with clinically recognized tumors suggests that these tumors appear after mean duration of about 35 years of HBV infection. (*Hollinger- 2001*, *Robinsin 1995*)

Patients who develop HCC as a result of malignant transformation of hepatocytes have a mean5-years survival rate 25-60%.(*World Health Organization 2009*) This variation depends on the size of tumor, its testability, and the presence or absence of `alph fetoprotein (A F P) .Non respectable tumors have a mean survival rate of 5 months for AFP-positive tumors and 10- 5 months for AFP –negative tumors. (*Hollinger2001*)

When serum Alph fetoprotein (AFP) followed serially in HBsAg carriers rises significantly above the patient's own baseline (>100mg/ml), HCC can often be detected by liver scanning or ultrasound procedures at a stage when the tumor can be cured by surgical resection.(*Afarin-2010*) this suggests that HBsAg carries should have regular serial serum AFP determinations and ultrasound examinations (at 6 months intervals for those above 40 years). Both these tests are recommended to be repeated regularly for all HBsAg carriers with cirrhosis. (*Robinsin 1995*)

HBV causes 60-80% of the world's primary liver cancer, and primary cancer is one of the three most common causes of cancer deaths in males in east and South east Asia, the pacific basin, and sub-Saharan Africa.

Primary liver cancer is the eighth most common cancer in the world. (*Afarin-2010*) Up to 80% of liver cancers are due to HBV. When HCC presents clinically, the disease is fatal. (*Robinsin -1995*)

2.1.13 Extra hepatic manifestations of hepatitis B:

Extra hepatic manifestations of hepatitis B are seen in 10-20%of patients as

-transient serum sickness-like syndrome (symptoms, fever, skin rash ,polyarthritis, and jaundice by a few days to 4weekes. (*Robinsin -1995*, *Wilkins- 2001*, *Robinsin -1995 ,Thornton*)

Immune complexes (e,g, surface antigen-antibody)are important in the pathogenesis of other disease syndromes characterized by severe damage of blood vessels. (*Robinsin 1995*)

-acute necrotizing vacuities. (poly arteritis nodosa) (*Robinsin -1995,Wilkins 2001,Obinsin 1995*)

High fever, anemia, leukocytosis, arthralgia, arthritis, renal disease, Hyperion, heart disease gastrointestinal disease skin manifestations, neurologic disorder. Highly variable disease with mortality rate of40%within 3years unless treated.

-Membranous glomerulonephritis. (*Robinsin 1995*, Wilkins *2001*, *Nsin -1995***)**

Is present in both adults and children .remission of nephropathy occur in85to 90% of cases over a period of 9 years and is associated with clearance of HBeAg from serum.

-popular acrodermatitis of childhood. (Gianotti-crosti syndrome) (*Robinsin -1995* and *Wilkins- 2001***)**

Disease is relatively to childhood. Skin lesions, lentil, flat, erythematous, and popular eruptions localized to the face and extremities, last 15 to days. The disease is accompanied by generalized lymphadenopathy hepatomegaly, and acute anicteric hepatitis B of ayw subtype.

2.1.14 Laboratory diagnosis:

The two most important serologic tests for the diagnosis of early hepatitis B are the tests for HBsAg and for IgM antibody to the core antigen. Both appear in the serum early in the disease, HBsAg appears during the incubation period and is detectable in most patients during the prodrome and acute disease. It falls to undetectable levels during convalescence in most cases; their prolonged presences (at least 6 months) indicate the carrier state and the risk of chronic hepatitis and hepatic carcinoma. HBV is not detectable in the choric carrier state. Note that HBsAb is, in fact, being mode but is not detectable in the laboratory test because it is bound to the large amount of HBsAg present in the blood. HBsAg is also being mode during the acute disease but is similarly undetectable because it is bound in antigen-antibody complexes. The window phase is period of several weeks when HBsAg has disappeared. At this time, the HBcAb is always positive and can used to make the diagnosis. HBcAg is present in those with acute infection and chronic infection. The IgM from of HBcAg is present during acute infection and disappears approximately 6 months after infection.

HBeAg arise during the incubation period and is present during prodrome and eayly acute disease and in certain chronic carriers.

DNA polymerase activity is detectable during the incubation period and early in the disease,The detection of viral DNA (viral load) in the serum is strong evidence that infectious virions are present. Reduction of the viral load in patients with chronic hepatitis B is used to monitor the success of drug therapy. (*World Health Organization, 2009*)

2.1.15 Treatment:

No antiviral therapy is typically used in acute hepatitis B. (*World Health Organization2009*)

For chronic hepatitis B, entecavir (Barclude) or tenofovir (Viread) are the drugs of choice. They are nucleoside analogues that inhibit the reverse transcriptase of HBV. Interferon in the form of peginterferon alfa-2a (pegasys)is also used. Other nucleoside analogues such as lamivudine (Epivir-HBV), adefovir (hepsera), and telbivudine (Tyzka) are used less frequently.

There drugs reduce hepatic inflammation and lower the viral load of HBV in patients which chronic active hepatitis.

Neither interferon nor the nucleoside analogues cure the HBV infection .in most patients when the drug is stopped, HBV replication resumes.

Patients co infected with HBV and HIV should be prescribed highly active antiretroviral therapy (H AART) with caution because recovery of cell-mediated immunity can result in an exacerbation of hepatitis (immune reconstitution syndrome, IRIS). Consideration should be given to treat the HBV infection prior to starting HAAR. (*World Health Organization*, *2009*)

2.1.16 Prevention:

Prevention involves the use of either the **vaccine** or **hyper immune globulin** or both.

Vaccine against hepatitis B has been available since 1982. (*Robinsin-1995*.)

The vaccine, active immunization (e.g. Recombivax) contains HBsAg produced in yeast by recombinant DNA techniques. The vaccine is highly effective in preventing hepatitis Band has few side effects. The seroconversion rate is approximately 95% in healthy adults. It is indicated for people who are frequently expose to blood or blood products, such as certain heath care personal (e.g.

medical students, surgeons, and dentists),patients receiving multiple transfusions or dialysis ,patients with frequent sexually transmitted disease, and abusers of illicit intravenous drugs .Travelers who plan along stay in areas of endemic infection. (*Armstrong-2OOO*)

At present, booster does after the initial three-doe regimens are not recommended. However, if antibody titers have declined in immunized patient who are at high risk .such as dialysis patients, than booster dose should be considered.

Widespread immunization with the HBV vaccine has significantly reduced the incidence of hepatocellular carcinoma in children. A vaccine called Twinrix that contains both HBsAg and inactivated HAV provides protection against both hepatitis B and hepatitis A. (*Armstrong-2000*)

Hepatitis B immune globulin (HBIG)

Passive immunization, contain a high titer of HBsAb. It is used to provide immediate .passive protection to individuals known to exposed to HBsAg-positive blood (e. g after an accidental needle-stick injury).

The recommendation regarding to medical students, the needle-stick injuries form a patients with HBsAg –positive blood, is that both the vaccine and HBIG be given (as separate sites) this true even if the patriot's blood is HBcAb positive.(*Armstrong-2000*)

Both the vaccine and HBIG should also be given to a newborn whose mother is HBsAg –positive. This regimen is very effective in reducing the carriers the infection rate of newborns whose mother is HBsAg-positive. This regimen is very effective in reducing the infection rate of newborns whose mothers are chronic carries. (**passive-active** immunization, in which both immediate and long-term protection are provided) . (*Armstrong-2000*)

All blood for transfusion should be screened for HBsAg .

No one with history of hepatitis (of any type) should donate blood, because non-A-non-B viruses may be present. Screening of high- risk population to identification and treatment of carriers will reduce transmission.

2.2 Hepatitis C Virus:

The estimated global prevalence of HCV infection is 2.2%, corresponding to about 130000000 HCV-positive persons worldwide (. Because many countries lack data, this estimate is based on weighted averages for regions rather than individual countries. Region-specific estimates range from < 1.0% in Northern Europe to > 2.9% in Northern Africa. The lowest prevalence (0.01%-0.1%) has been reported from countries in the United Kingdom and Scandinavia; the highest prevalence (15%-20%) has been reported from Egypt (*Shepard -2005*, *Frank -2000*). An estimated 27% of cirrhosis and 25% of HCC worldwide occur in HCV-infected people (*Perz 2006*). There are both geographic and temporal differences in the patterns of HCV infection (*Alter 2000*), as vastly different countries, including the United States, Australia, Turkey, Spain, Italy, and Japan, belong to regions of the world with similar overall average prevalence of HCV infection (1.0%-1.9%), but have different patterns of age-specific prevalence. In the United States, prevalence is highest among persons 30-49 years old, who account for two-thirds of all infections, and lower than average among persons less than 20 and greater than 50 years old (*Alter -1994*, *Armstrong -2006*). This pattern indicates that most HCV transmission occurred in the last 20-40 years, and primarily among young adults, a pattern similar to that observed in Australia (*Law 2003*). In the United States (*Alter 2002*, *Recommit. 1998*) and Australia (Dore 2003) the greatest variations in prevalence occur among persons with different risk factors for infection. . The highest HCV prevalence in the world occurs in Egypt, where the prevalence of infection increases steadily with age, and high rates of infection are observed

among persons in all age groups (*Perz -2006, Abdel- 2000*). This pattern indicates an increased risk in the distant past followed by an ongoing high risk for acquiring HCV infection, although there are regional differences in average overall prevalence (*Perz 2006 , Medhat2000*). Determining the incidence of HCV infection (i.e., the rate of newly acquired infections) is difficult because most acute infections are asymptomatic, available assays do not distinguish acute from chronic or resolved infection, and most countries do not systematically collect data on cases of acute disease. Even in countries with well-established surveillance systems, acute disease reporting systems underestimate the incidence of HCV infection (*Hagan 2002, Spada -2001*). For several countries, mathematical models have been used to infer trends in incidence, which rely on the assumption that current age-specific prevalence reflects the cumulative risk of acquiring infection. In the United States, trends in HCV incidence were modeled using age-specific incidence from reported cases of acute disease (*Alter -1999*) and age-specific prevalence from a cross-sectional national survey (*Alter -1999*). This model showed a large increase in the incidence of newly acquired HCV infections from the late 1960s to the early 1980s (Medhat -2000). The estimated annual incidence was low (18 per 100000) before 1965, increased steadily through 1980, and remained high (130 per 100000) through 1989, corresponding to an average of 240000 infections per year in the 1980s. Since 1989, the incidence of reported cases of hepatitis C has declined by more than 80% (*Medhat -1997*), consistent with the finding that the national seroprevalence of infection remained unchanged between 1988 and 2002 (*Armstrong -2006*). The rate of new HCV infections also declined in Italy in the 1990s according to reported cases of acute disease (*Spada 2001*). In both the United States and Italy, most newly acquired infections are in young adults (30-35 years old) (*Medhat -1997, Prati -1997*). A model of HCV burden in France, which employed death rates from hepatocellular carcinoma in

addition to cross-sectional seroprevalence studies to estimate past incidence, showed a trend similar to that of the United States with increasing incidence through the 1980s (*Deuffic -1999*), whereas an alternative approach to modeling disease burden in Australia showed a steady increase in new HCV infections in that country from 1961-2001 (*Law etal -2003*).

2.2.1 Hepatitis C virus life cycle:

HCV belongs the Flaviviridae, a large family of enveloped, single-stranded RNA viruses which is organized into the genera Hepacivirus, Flavivirus, Pestivirus and Pegivirus (*Choumet-2013*), and that includes many viruses transmitted by arthropods and is a growing matter of health concern (*Choumet-2015*). The HCV life cycle is only partly understood; difficulties in establishing an in vitro model of replication and the complex network of cell surface molecules used to mediate viral entry have delayed comprehension of various molecular mechanisms (*Maggi 2015*). The HCV virion circulates in the bloodstream either as a free particle or surrounded by host low-density lipoproteins (*Andre-2013*) attaches onto the target cell membrane by sequential binding of various receptor molecules, and enters into the cell by a clathrin-mediated endocytosis process. Disruption of the viral capsid in the endocytic compartment releases the 9.6-kb single-stranded RNA genome of positive polarity into the cytoplasm. The RNA genome is then directly translated at the rough endoplasmic reticulum (ER) in a single polyprotein precursor of about 3000 amino acid residues that is eventually cleaved by cellular and viral proteases into ten mature products (*Andre etal -2013*). These proteins, enlisted in the order they are encoded, include the structural core and envelope glycoproteins E1 and E2, and the following nonstructural proteins: p7 viroporin and nonstructural protein 2 (NS2) that participate in virus assembly and release; NS3 and NS4A, the protease complex that is actively targeted by the protease inhibitor class of DAAs;

NS4B, a membrane-associated protein that mediates virus–host interactions; NS5A, a zinc-binding and proline-rich hydrophilic phosphoprotein involved in HCV RNA replication and targeted by NS5A inhibitor DAAs; and NS5B, the RNA-dependent RNA polymerase targeted by nucleoside and non-nucleoside polymerase inhibitor DAAs. New virions are assembled in an ER-derived compartment and released by exocytosis following a Golgi-dependent secretory pathway. Along this process, the virus undergoes maturation and becomes surrounded by endogenous lipoproteins that, as described below, are believed to help immune escape (64-65). Binding to host lipoproteins and envelopes without clearly discernible surface features confer to HCV virions low buoyant density and a broad size range (40–80 nm diameter). (*Maggi-2015*)

2.2.2 Transmission:

Humans are the reservoir for HCV it is transmitted primarily via blood. At present, injection drug use accounts for almost all new HCV infections. Transmission from to child during birth is another very common mode of transmission. Transmission via blood transfusion rarely occurs because donated blood containing antibody to HCV is discarded. Transmission via needle stick injury occurs, but risk is lower than for HBV. Sexual transmission is are uncommon ,and there no evidence for transmission across the placenta or during breast feeding. (*Warren-2016*)

2.2.3 Pathogenesis and immunity:

HCV infects hepatocytes primarily, but there is no evidence for virus-induced cyto pathic effect on the liver cells.

Rather, death of the hepatocytes is probably caused by immune attack by cytotoxic T cell ,HCV infection strongly predispose and to hepatocellular carcinoma,but

there is no evidence for an oncogene in the viral genome or for insertion of acopy of the viral genome into the DNA of the cancer cell.

Antibodies aginast HCV are made,but approximately 75% of patients are chronically infected and continue to produce virus for at least 1 year.(Note that the rate of the chronic carriage of HCV is the much higher than the rate of the chronic carriage of the HBV) .

Chronic active hepatitis and cirrhosis occur in approximately 10% of these patient for the patient who clear the infection, it is not known whether reinfection occur or whether there is lifelong immunity. (*Warren-2016*)

2.2.4 Laboratory Diagnosis:

HCV infection is diagnosed by detecting antibodies to HCV is an enzyme-linked immune sorbent assay (ELISA). The antigen in the assay is a recombinant protein formed from three immunologically stable HCV proteins and does not include the highly variable envelope protein. The test dose not distinguishes between IgM and IgG and dose not distinguish between an acute, chronic infection .or resolved infections.

If the result of the ELISA antibody test is positive, a polymerase chain reaction-based test that detected Of the viral RNA (viral load) in the serum.

Treatment of acute hepatitis C with peg interferon alfa significantly decreases the number of patients who become chronic carriers.

The treatment of the chronic hepatitis C is a combination of drugs from three classes: RNA polymerase inhibitors, NS5A inhibitors, and protease inhibitors.

These drugs are dminstreated orally which is an improvement over the drugs in previous regimens that often included pegylated interferon –alfa which is an improvement over the drugs in previous regimens that often included pegylated

interferon-alpha which is administered parenterally and has significant adverse . (*Warren* 2016)

2.2.5 Prevention:

There is no vaccine and hperimmune globulins are not available.Pooled immune serum globulins are not useful for postexposure prophylaxis following needle-stick injury; only monitoring is recommended.

Blood found to contain antibody is discarded – a procedure that has prevted virtually all cases of transfusion –acquired HCV infection since 1994, when screening of individuals born in the united states between 1945 and 1965 for HCV antibody is recommended because they have a high rate of infectio. (*Warren*2016)

2.3 Surveillance and control:

2.3.1 Hepatitis B and c disease surveillance procedures should include :

Monitoring disease incidence .

Determination of sources of infection and mode of transmission by epidemiological investigation .

Detection of outbreak.

Spread containment .

Identification of contacts of case-patients for postexposure prophylaxis (*Robinsin 1995*).

2.3.2 Hepatitis B and C disease control measures should include:

Immunization (Hepatitis B), the most effective and cost-saving means of prevention.

Education of high risk groups and health care personnel to reduce the risk of contracting the virus and to reduce the chances for transmission to others, as well as to promote acceptance of vaccination schemes.

Screening of blood and blood products to reduce the chance that the blood supply system may contain pathogens live HBV and HCV. (*Robinsin 1995*)

2.4 Homeless:

Chronically homeless individual refers to an individual with a disability who has been continuously homeless for one year or more or has experienced at least four episodes of homelessness in the last three years where the combined length of time homeless in those occasions is at least 12 months (*Hershow etal 1998*). Homelessness became a major social issue in the 1980's; however, it has changed from being dominated by "skid row male alcoholics" but now includes "women, children, and the mentally disabled. Poor health and long-term homelessness are significantly interrelated (Shepard -2005). The number of individuals in US experiencing chronic homelessness declined by 18 percent, or over 19,000 people, between 2010 and 2017. Just fewer than 87,000 individuals experiencing homelessness on a particular night in January 2017 had chronic patterns of homelessness. Nearly seven in ten individuals experiencing chronic homelessness were staying outdoors, in abandoned buildings, or other locations not suitable for human habitation rather than staying in shelters, reflecting the high degree of vulnerability of this population. In 2017, there were nearly 94,000 more permanent supportive housing (PSH) beds dedicated to people with chronic patterns of homelessness than there were in 2010 (*thoelen,1999*). The state that health can be improved by improving housing, which decreases exposure to infections, environmental elements, and violence . Extended exposure to weather, violence, infections, and drugs, along with restricted access to ongoing health care drastically increases both acute and chronic health issues, along with premature mortality (*Frank,2000*).

2.4.1 Risk factors for homeless:

The impact of being homeless on the life course of people who experience homelessness has been poorly understood, partly because longitudinal data on homeless populations have been sparse and have been limited to specific subgroups of the homeless population, such as those who are severely mentally ill (*Perz2006*& *Alter2000*). Substance abuse ranks high among factors that distinguish homeless people from those who have never been homeless (*Alter -1988,Armstrong -2006*& *Law -2001*). Family experiences, such as out-of-home placement during childhood (*Alter 2002* &*Dore 2003*), parental instability (*Abdel-Aziz -2003*), poor) and inadequate family support during adulthood (*Law 2003Alter 2002& Abdel-Aziz 2003*), are another domain that has distinguished homeless people from stably housed people. Finally, opportunity differences, such as educational achievement have distinguished homeless people from never homeless people (*Alter -1994*& *Law -2001*).

2.4.2 Homeless and viral hepatitis (B & C):

Hepatitis B is spread when body fluids—such as semen or blood—from a person infected with the Hepatitis B virus enter the body of someone who is not infected. The Hepatitis B virus is 50–100 times more infectious than HIV and is easily transmitted during sexual activity. Hepatitis B also can be spread through sharing needles, syringes, or other equipment used to inject drugs. • Hepatitis C is spread through contact with the blood of an infected person, primarily through sharing needles, syringes, or other injection drug equipment (*Hagan -2002*).

2.5 Previous studies:

Many studies have been interested in HBV and HCV infections and roots of transmission. Injection drug use is the primary mode of transmission for HCV and HBV infection in the developed world. In one study conducted in USA, seroprevalence of HCV and HBV infection among long-term injection drug users were 85% for HCV and 77.4% for HBV and 64.7%, 49.8%, among those who had injected for 1 year or less. (World Health Organization Executive Board (2009). Interestingly, of age). In another study conducted in Australia using arrest data found evidence of higher arrest rates for drug possession and use during the Australian fall and winter (April through July) and seasonality of illicit drug has been reported to be higher in winter than in summer among the USA teens (12–17 years lower rates during the Australian spring (November and December). (*Robert 2005*). Additionally, a recent longitudinal study of cocaine and cocaine metabolites in wastewater a clear seasonal difference indicative of human seasonal cocaine use patterns (*Mari etal 2009*). Travel history and sexual activity, which is supposed to be higher in summer, may give us explanation regarding to the summer seasonal peak of acute viral hepatitis. In a study conducted in UK found that the higher sexual activity and unsafe sex coinciding with the summer vacation. Data relating to sexually transmitted infections and attendances for human immunodeficiency virus tests similarly show an increase in the months following Christmas and in late summer (*Wellings 1999*).

Finally it gets attention, homeless group of people, not only in human mercy thing, but also due to its bind to many local issues; most of them tend to health sectors. Street population experiences have a strong intersection with drug users and sex workers, representing a vulnerable population that mostly has poor access to health services .(*Fazel 2014*). Locally In Sudan, there is no data on homeless situation established to be reference. But globally studies estimated 100 million people

worldwide are homeless (-*UN Press briefing 2012*). In high-income countries, country-specific data suggest that more than 650 000 individuals in the USA (Sermons MW. Homelessness) and around 380 000 in the UK are homeless at any one time (Crisis:2003). Although most live in sheltered accommodation—like emergency hostels, bed and breakfasts, squats, or other temporary accommodation—a 2011 US report (Sermons MW. Homelessness) has estimated that almost 40% of homeless people are unsheltered, and thus roughly 250 000 individuals live on the streets, more than 120 000 of whom are in the New York City and Los Angeles metropolitan areas (Sermons MW. Homelessness). Although methodological difficulties exist in counting homeless people and definitions of homelessness vary, these estimates help to quantify the number of homeless people (*Chamberlain 2oo3*).

Health problems in homeless populations have been previously reported (*Geddes etal 2011* &*Hwang 2001*-). Brazilian study conducted among marginal population with high risk of sexually transmitted infection, including hepatitis B to investigate it's epidemiology in homeless persons lodged in a public shelter in Goiania, Central Brazil. From August 2014 to June 2015, 353 individuals were interviewed and tested for markers of HBV infection. Over all HBV prevalence was 21.8%. Older individuals (> 50 years), blacks, and homosexuals or bisexuals showed increased exposure to HBV, other factor contributed in increasing the risk of HBV infection was recycling of waste materials including needles (*Hwang 2001*). Another Brazilian study concerned about viral hepatitis caused by Hepatitis C virus among homeless men, it mentioned that homeless men considered highly vulnerable to acquisition of the hepatitis C virus (HCV) compared to the general population in Brazil. 481 men aged over 18 years were investigated for HCV markers. The prevalence of HCV exposure was 2.5% and was associated with age, absence of family life, injection drug use, number of sexual partners, and history of

sexually transmitted infections (STI) beside multiple risk behaviors among participants, such as alcohol (78.9%), cocaine (37.1%) and/or crack use (53.1%), inconsistent condom use (82.6%) and injection drug use was reported by 8.7% of participants (Priscilla 2017). An Iranian study aimed of this to characterize hepatitis C virus (HCV) epidemiology in Iran and estimate the pooled mean HCV antibody prevalence in different risk populations. Drug users, homeless, prisoners and sex workers were sorted as intermediate risk exposure to HCV infection; it showed that they were 6.2% having HCV in comparison to other groups of HCV risk exposure (*Sarwat 2018*). American Veterans (people who served in war) Health Administration (VHA) is the largest provider of hepatitis C virus (HCV) care nationally and provides health care to >200 000 homeless veterans each year. Data warehouse and HCV clinical case registry of homeless and non-homeless veterans to evaluate engagement cascade of HCV among both groups in 2015. Among 242740 homeless veterans in care and 5424712 non-homeless, homeless were more likely to be diagnosed with chronic hepatitis C infection in compare with non-homeless group, as they more likely received antiviral therapy (*Amanda etal 2017*). An Iranian study among homeless assessed the prevalence of HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections and co-infections among injecting drug users in Tehran. 899 of injected drug users (861 male and 38 female) was recruited, HIV also detected, the prevalence of HIV was 10.7%, HCV infection was 34.5%, and past or current HBV infection was 50.7%. Infection with all three viruses was seen in 6.5% of participants. HIV/HCV, HIV/HBV, and HBV/HCV co-infections were seen in 8.7%, 7.8%, and 21.0% of participants, respectively. The rate of HCV infection among HIV-positive cases was significantly higher than in HIV-negative injected drug users (80.6% vs. 28.7%, $p < 0.0001$). There was no significant association between these infections and co-infections with gender and source of sampling (*Afarin etal 2010*).

3. Material and Methods

3-1Study design

Descriptive cross sectional study.

3.1.2 Study area

Khartoum state-homeless areas

3.1.3 Study population

Homeless individuals and families in Khartoum state-Omdurman region.

3.1.4 Inclusion criteria

Homeless individual with no permanent residency were enrolled in this study.

3.1.5 Ethical consideration

This study was approved by the ethical committee of Shandi University- faculty of graduate. Local authority and population of homeless campus agreed to be part of this study.

3.1.6 Data collection

Direct well-constructed questionnaire was used to obtain data for enrolled subjects, contained age, gender, education status, duration of living in the campus and drug and alcohol usage. According to them they did not tested for hepatitis B or C before.

3.1.7 Sampling

3.1.7.1 Sample Size

They are 97 homeless they are 48 male and 49 Female.

3.1.7.2 Sample Collection

Under hygienic conditions and considering labeling 5 ml of blood then let the blood allowed clotting formation, serum separated by means of centrifugation and kept frozen till time of laboratory analysis.

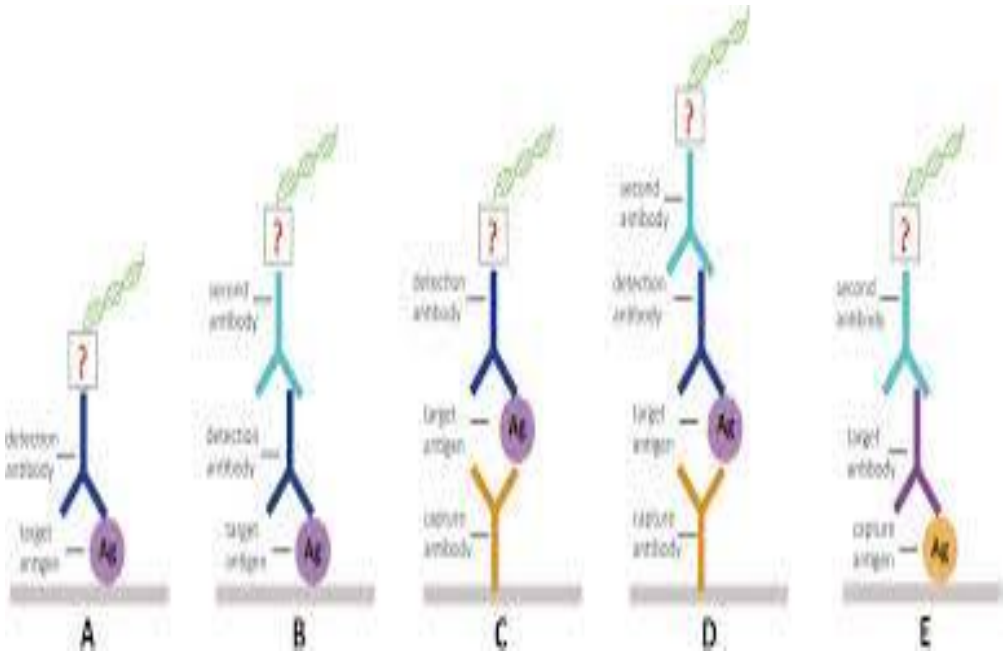
3.2 Methodology:

3.2.1 Consumable

Consumable	Manufacturer
Syringes	Shandong- China
Plane containers	Mingbo MS LAB-China
Cotton	Sudan
Doctor aid (plaster)	Egypt
Tourniquet	Shandong- China
Alcohol	Germany
Gloves	Malaysia
Instrument	Germany
ELISA kit	UK

3.2.2 Measurement step:

Laboratory measurement was conducted in Aljaily Khalid Musa medical laboratory- Omdurman. Both HBV and HCV were assessed by means of enzyme linked immunosorbent assay (ELISA) with semi-automatic analyzer BTS350-Germany and viral ELISA kit trade mark Fortress-UK.



Methodology of antibody working through ELISA

3-2-3 Data analysis:

Data when collected and analysis performed was analyzed with statistical package of social science (SPSS) program version 21.

4 -Results

This cross sectional study conducted among homeless group population in Omdurman region-Khartoum, they were living in campus and shelters, it was an open community to deal through with drug, alcohol and prostitution. Subjects involved in this study were volunteered to participate to be tested for various laboratory investigations including viral hepatitis B and C. They were 49(51%) females and 48 (49%) males as in figure 4-1.

Infected individuals with HBV were 38 (39.2%) and negative result were among 59 (60.8%). While HCV positive result among 3 (3.1%).

Considering educational status, they were sorted to 3 groups, non-educational group included 23% of them, primary school group contained 35% and high school school group with 42% of them as in figure(4-2).

Considering age, they were divided to more than 40 Years old (31%) and less than 40 years (69%) as in figure (4-3)

Considering period of being homeless, they were sorted to less than 10 years at homeless state, they were 29% and more than 10 years of homeless state, they were 71% as in figure.(4-4)

Investigation of hepatitis B gave results sorted according to age groups, as less than 40 years old group has 23 subjects (34.3%) positive results for HBV infection and negative results among 44 (65.7%). And more than 40 years group has positive results among 15 (50%) and negative results among the other 15 (50%), and there was no significant difference obtained according to positive results among groups of age in table(4-1). While groups according to gender, among males 19 (39.6%) with positive results of HBV and 29 (60.4%) with negative results, while females; 19 (38.8%) were positive for HBV and 30 (61.2%) were negative results and no significant different obtained between gender- positive result in table (4-2).

Educational status and results of HBV infection showed positive results among non-educated group 10 (45.5%), primary schooled 15 (44.1%) and high schooled population with 13 (32.5%), with no significant difference in table(4-3). While duration of being homeless and exposed to drug usage, individuals were grouped to < 10 years HBV positive results among 12 () 42.9% and >10 years positive HBV among 26 (37.7%) giving significant difference as p value was 0.034 as in table(4-4).

Sub-groups of homeless, for infection with HCV, did not give significant difference, as positive results of HCV were among 3 (3.1%), one of them was male and 2 were females, all were under 40 years old, one was non-educated and the rest were high schooled, one was under 10 years of duration as homeless and drug user, and the rest were above 10 years of time, as in table(4-5, 4-6,4 -7 and 4-8).

Figures

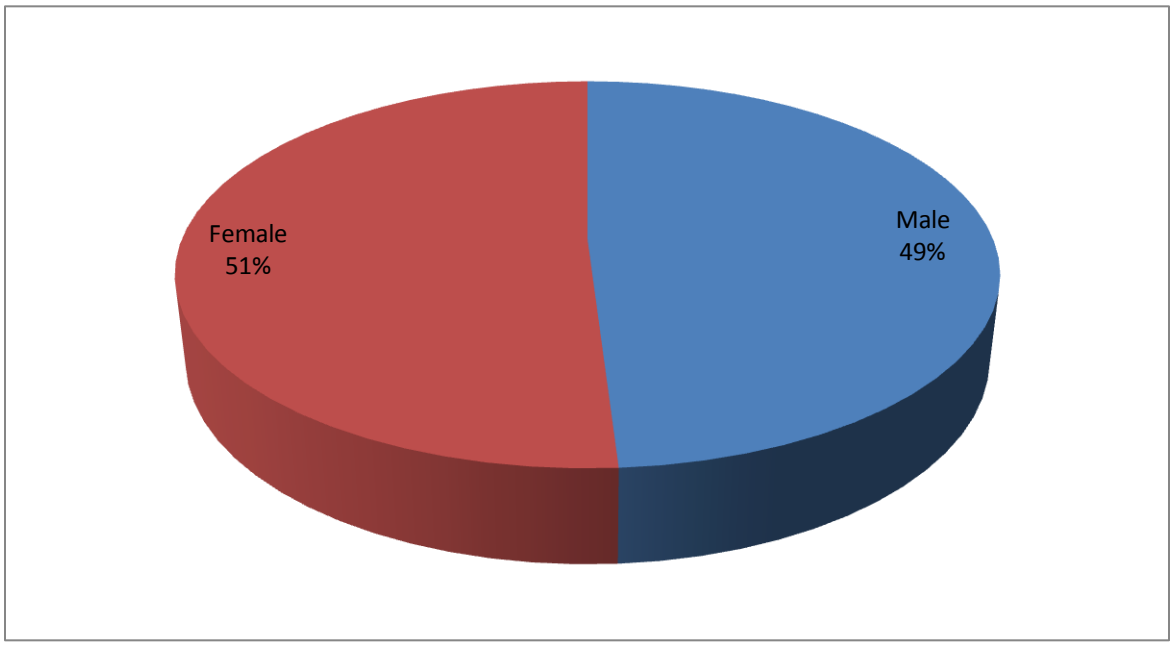


Figure (4-1) Distribution of study population according to gender

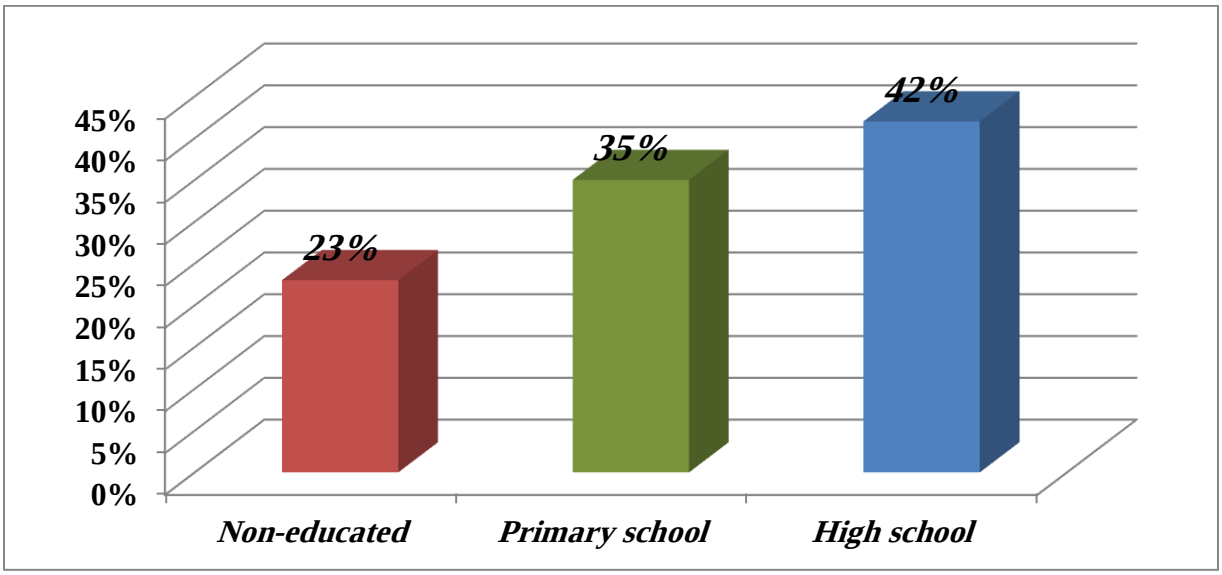


Figure (4-2) Distribution of study population according to education level

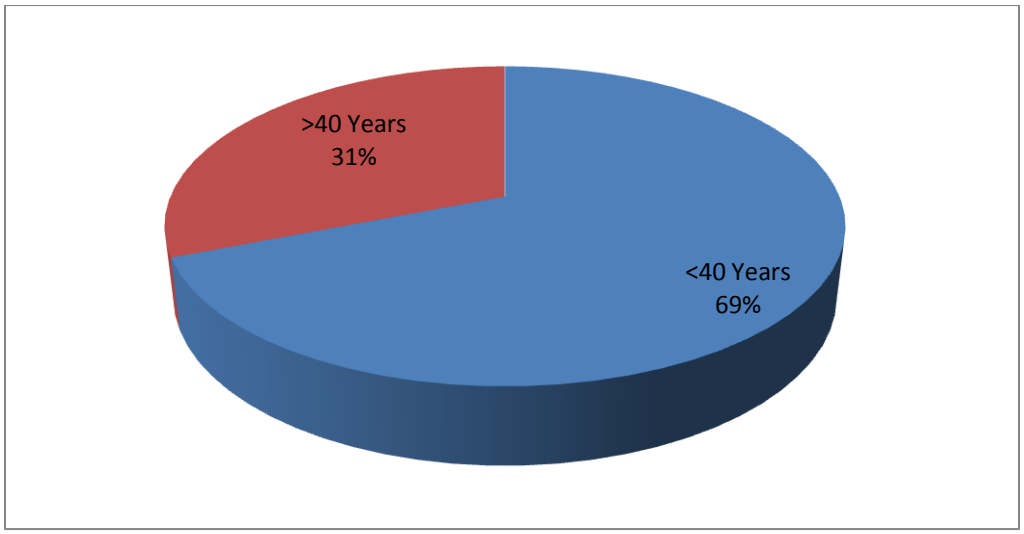


Figure (4-3) Distribution of study population according to age group

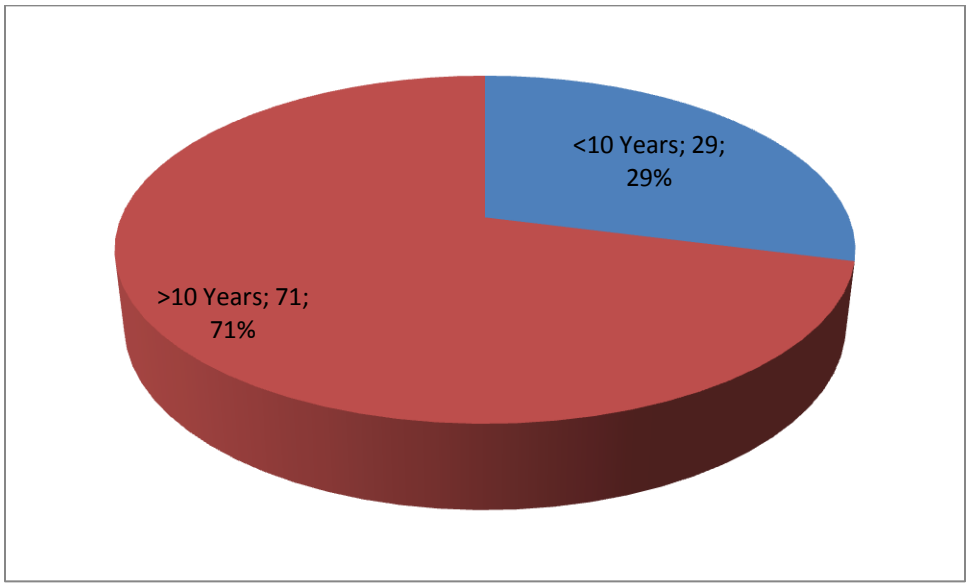


Figure (4-4) Groups of homeless according to duration of homeless living status

Tables

Table (4-1) Association between HBV and age

Variable	Result		Total	P value
	Positive	Negative		
Age				0.109
<40 Years	23 (34.3%)	44 (65.7%)	67 (100.0%)	
>40 years	15 (50.0%)	15 (50.0%)	30 (100.0%)	

Significant difference p value <0.05.

Table (4-2) Association between HBV and gender

Variable gender	Result		Total	P value
	Positive	Negative		
Male	19 (39.6%)	29 (60.4%)	48 (100.0%)	0.550
female	19 (38.8%)	30 (61.2%)	49 (100.0%)	

Significant difference p value <0.05.

Table (4-3) Association between HBV and education

Variable education	Result		Total	P value
	Positive	Negative		
Non-educated	10 (45.5%)	12 (54.5%)	22 (100.0%)	0.453
Primary school	15 (44.1%)	19 (55.9%)	34 (100.0%)	
High school	13 (32%)	27 (68%)	41 (100.0%)	

Significant difference p value <0.05

Table (4-4) Association between HBV and duration of being homeless

Variable education	Result		Total	P value
	Positive	Negative		
<10 Years	12 (42.9%)	16 (57.1%)	28 (100.0%)	0.034
>10 Years	26 (37.7%)	43 (62.3%)	69 (100.0%)	

Significant difference p value <0.05.

Table (4-5) Association between HCV and age

Variable	Result		Total	P value
	Positive	Negative		
Age				0.352
<40 Years	**3 (4.5%)**	**64 (95.5%)**	**67 (100.0%)**	
>40 years	**0 (0.0%)**	**30(100.0%)**	**30 (100.0%)**	

Significant difference p value <0.05.

Table (4-6) Association between HCV and education

Variable	Result		Total	P value
	Positive	Negative		
Non-educated	**1 (4.5%)**	**21 (95.5%)**	**22 (100.0%)**	**0.426**
Primary school	**0 (0.0%)**	**34 (100.0%)**	**34 (100.0%)**	
High school	**2**	**39**	**41**	

Significant difference p value <0.05.

Table (4-7) Association between HCV and Duration of being homeless

Variable	Result		Total	P value
	Positive	Negative		
Male	1 (2.1%)	47 (97.9%)	48 (100.0%)	0.508
Female	2 (4.1%)	47 (95.9%)	49 (100.0%)	

Significant difference p value <0.05.

Table (4-8) Association between HCV and gender

Variable	Result		Total	P value
	Positive	Negative		
<10 Years	1 (3.6%)	27 (96.4%)	28 (100.0%)	0.645
>10 Years	2 (2.9%)	67 (97.1%)	69 (100.0%)	

Significant difference p. value <0.05.

5-1-Discussion

This study was carried In Khartoum state in Jabrona west Omdurman in period (may 2018-to-august-2018) .Homeless populations were targeted to be checked for many medical concerns including viral hepatitis B and C, they lived in shelters, exposed to all means of causatives of hepatitis and other infections, they were drug users, sex worker with open community without moral barriers, they were in families and individuals living status. HBV and HCV inspection conducted among 97 individuals, 38 (41.8%) were positive for HBV Ag, 19 (50%) of they were females and 19 (50%) were males, and 3 (3.3%) were HCV Ag positive 1 (33.3%) was female and 2 (66.7%). This partially agrees with an Iranian study, concerned about homeless males only, they were drug users and the prevalence of HBV was low than HCV, as they were 0.98% and 31.3% respectively. (*Amin etal 1999*) And also partial agreement with an American study revealed that both HBV and HCV were prevalent among homeless, with 43% and 72% respectively. (*Judith - 2012*)

Our populations were sorted to sub-groups according to age, gender, education and duration of being homeless which was duration of using drugs as well. For age they were group of under 40 years old (<40), which contained 67 individuals and group of more than 40 years old (>40) contained 31 individuals. HBV infection <40 years included 23 (34.3%) positive and 44 (65.7%) negative, > 40 years were 30, 15 (50%) of them were positive for HBV and other 50% were negative. This is in agreement with Brazilian study among homeless individuals, it revealed how a marginalized population with high risk of sexually transmissible infections (STI), including hepatitis B. From August 2014 to June 2015, 353 individuals were interviewed and tested for markers of HBV infection. Overall HBV prevalence was 21.8%. For age groups, between 18-30years positive results among 10.8%, while

older individuals (> 50 years), blacks, and homosexuals or bisexuals showed increased exposure to HBV (*Paulie -2017*).

Gender distribution, males were 48, out of them 19 (39.6%) were positive for HBV and 29 (60.3%) were negative for HBV and females were 49 out of them 19 (38.8%) were positive and 30 (61.2%) were negative for HBV, this in disagreement with study found that HBV infection was more among male than females, as 25% and 14.8% respectively (*Malew etal 2017*). Education groups, non-educated were 22, 10 (45.5%) of them were HBV +ve and 12 (55.5%) were –ve for HBV, primary educated group contained 34 subjects, 15 (44.1%) were +ve for HBV and 19 (55.9%) were –ve HBV, and high schooled group were 40 individuals, 13 (32.5%) were +ve HBV and 27 (67.5%) –ve HBV, this in agreement of a Chinese study concerned about knowledge and risk of HBV infection, but it didn't involve homeless, rural residents as they had low education level, It showed that HBV existence no matter what they were educated (*higuSi-2017*).

Infection with hepatitis C virus in this study showed low prevalence, as it was among only 3%, one of them was female under 40 years old, no-educated and the two were > 40years old, high schooled, one female and one male. This in agreement of study among homeless, it revealed that increased infection was among adults than younger subjects.

Homeless people are defined as "those who do not have customary and regular access to a conventional dwelling or residence (*Rossi-1987*). The homeless populations that have been studied have varied greatly depending on the country and type of study. Studies have been done in shelters, emergency medicine departments (*Monsuez -1993*), and in the street by social workers or the welfare services. Homeless people are predominantly male (60–95%) with children and adolescents being frequently reported in several countries such as the USA, but

only rarely in others. Other groups of people at an increased risk of becoming homeless are refugees and illegal immigrants (.*Monsuez 1999*) Homelessness is a major problem in both developing and wealthy countries. Today at least half a million Americans are homeless (-*Hwang -1998*&*Brickner -1986*). Comparable numbers of people were estimated to be homeless in England in 1988 (*Brickner -1990*) and in France in 1996 (*Chauvin etal 1997*& *Chauvin etal 1998*). Homeless people are predisposed to infections because of their poor physical state and lack of hygiene; hence outbreaks of contagious diseases are more prevalent in the homeless (*Gutierrez 1998*). Sharing of equipment used for injecting drug use causes substantial disease burden. Transmission via contaminated injection paraphernalia of blood-borne viruses, including HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV), is a leading contributor to morbidity and mortality as a consequence of injecting drug use (*Degenhardt etal 2o13*). Quantification of the size of the population of people who inject drugs, their demographic characteristics, and the extent of their exposure to risk behaviors and environments is essential to enable effective health policy planning (*ECDC, EMCDDA 2011*, *Close* 2010 & *Altice etal -2005*)) even the treatment of homeless people is a therapeutic challenge because they are often unable to pay for their treatment and adherence is often poor. In addition, access to health care may be limited by mental illness, transport problems, self-neglect, and fear of institutions (*Crane etal 2001*).

Hepatitis C is found worldwide. The most affected regions are WHO Eastern Mediterranean and European Regions, with the prevalence of 2.3% and 1.5% respectively. Prevalence of HCV infection in other WHO regions varies from 0.5% to 1.0%. Depending on the country, hepatitis C virus infection can be concentrated in certain populations (for example, among people who inject drugs) and/or in general populations. There are multile strains (or genotypes) of the HCV virus and their distribution varies by region. (*world health organization 2017*). The highest

sexual risks for HCV infection appear to be having sex with multiple partners and traumatic sex that results in blood exchange (*Hershow 1998*) Research regarding HCV transmission in relation to other documented risk behaviors; such as non-injection drug use (e.g., inhaled cocaine, and methamphetamine) (*Hagan 2001*) is advancing. Alcohol abusers have also been found to be at increased risk in some studies in which no other risk factors existed (*Rosman-1996*) However, other studies found alcohol users to be at greater risk only in the presence of injection drug use (*Schiff-1999*). Injected drug use and blood-borne diseases, homeless people are at high risk for blood-borne infections since they are common users of intravenous drugs (*Clarke-2013*).). High-risk behavior also predisposes homeless people to acquiring HBV infection (*Roy-1999*).

5-2-Conclusion:

From the result and finding obtained from this study, we can conclude the following .There are high frequency of HBsAg(38%) and law frequency of HCV (3%). The groups of infected with HBsAg sorted in two groups according to the duration, more than 10 years and less than 10 years , when the two groups compered to each other significant difference was presented (the more than 10 years more frequency of infection of the HBsAg)at p.volue 0.034m.

5-3-Recommendations:

Call to stop the war and the spread of peace on the level of Sudan, and at the level of the world, which reduces displacement and leads to stability, which leads to the reduction of the homeless and thus reduce the spread of diseases.

International and local humanitarian organizations should help the homeless to provide hepatitis B vaccines before infection, Hepatitis B immunoglobulin for acute infections and vaccination of newborn babies.

The Government must develop stable programs that include fixed housing, health care, job creation so as to increase income and thus reduce bad habits such as drug and alcohol trade, unrestricted sex.

The Health awareness of the seriousness of diseases and the causes of their spread and vulnerability.

Checkup of home workers to control the spread of diseases among the rest of society.

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Appendix (I)

جامعة شندى

كلية المختبرات الطبية

اقرار بالموافق

الاسم ... . العمر .....

العنوان .....

اوافق بمحض ارادتى بالمشاركة فى البحث العلمى المتعلقة بدراسة انتشار مرض الكبد الوبائى بين اللا ماؤى لهم فى منطقة جبرونا غرب امدرمان وذلك باعطاء الباحث 5سى من دمى بعد ان شرح لى بانه لا يترتب علي اى اذى جسدى او نفسى و اعلم المشاركة فى هذا البحث لن تؤثر باى حال من الاحوال فى حالتى الرهانة كما انه يحق لى بدون ابداء اسباب الانسحاب من هذا البحث فى اى مرحلة من المراحل

اعداد الطالبة\عائشة محمد خير

البحث باشراف

د\ ليلى محمد احمد

التوقيع:.....

التاريخ.....

Appendix (I)

Shandi University

Faculty of medical laboratory science

Questionnaire:

Name: …….

Age: ……

Gender: ……..

Duration of homeless: ……..

Drug Injection:……..

Appearance of Jaundices: ……

Other disease: ……

Appendix (III)

BTS-350analyzer(Biosystem trade mark)

Appendix (IV)

Fortr55555ess ELISA kit-UK

Glossary

Amino acids the basic units of proteins, each amino acid has NH-C(R)-COOH structure, with variable R group. There are altogether 20 types of naturally occurring amino acids.

Antibody a protein molecule formed by immune system which reacts specifically with antigen that induced its synthesis. All antibodies are immune globulins.

Antigen; any substance which can elicit in a vertebrate host the formation of specific antibodies or the generation of a specific population of lymphocytes reactive with the substance. Antigen may be protein or carbohydrate ,lipid or nucleic acid, or contain elements of all or any of these as well organic or inorganic chemical groups attached to protein or other macromolecule. Whether amaterial is an antigen in a particular host depends on whether the material is foreign to the host and also on the genetic makeup of the host, as well as the dose and physical state of the antigen. (Churchill's Illustrated1999)

Arthralgia joint pain with objective findings of heat, redness, tenderness to touch, loss of motion, or swelling .(World health organization 2017)

B - Cells also known as B lymphocytes. A class of white blood cells which carry out humeral immune response. They mature in the bone marrow. (World health organization 2017)

Bilirubin is the chief pigment of bile, formed mainly from the breakdown of hemoglobin. After formation it is transported in the plasma to the liver to be then excreted in the bile. Elevation of bile in the blood (>30mg/l) causes jaundice(Walton J 1994)

-Carcinoma a malignant epithelial tumor**.** This is the most frequent form of cancer.

-Carrier is a person who has HBV (HCV, HDV) in his or her blood for longer than 6 months even if all systems have disappeared. Because the virus is present in the blood, it can be transmitted to others. The HBV carrier can be recognized by a specific blood test.

-Cirrhosis a chronic disease of liver characterized by nodular regulation of hepatocytes and diffuses fibrosis. It is caused by parenchymal necrosis followed

By nodular proliferation of the surviving hepatocytes, The regenerating nodules and accompanying fibrosis interfere with blood flow through the liver and result in portal hypertension, hepatic insufficiency, jaundice and ascites.

-Cytopathic that kills the cells.

-Cytoplasm the protoplasm of the cell which is outside of the nucleus. It consist of ta continuous aqueous solution and the organelles and inclusions suspended in it. It is the site of most of the chemical activities of the cell.

-Endemic prevalent continuously in some degree in community or region (Walton J 1994).

-Endoplasmic reticulum a network or system of folded membranes and interconnecting tubules distributed within the cytoplasm of eukaryotic cells. The membranes form enclosed or semi enclosed spaces. The endoplasmic reticulum functions in storage and transport and as a point of attachment of ribosomes during protein synthesis.

Enzyme any protein catalyst, i, e, sustenance which accelerate chemical reaction without itself being used up in the process. Many enzymes are specific to the substance on which they can act, called substrate. Enzymes are present in all living matters and are involved in all the metabolic processes up on which life depends.

-epidemic an outbreak of disease such that for limited period a significantly greater number of persons in community or region suffer form it than in normally the case. Thus an epidemic is a temporary increase in prevalence. Its extent and

duration are determined by the interaction of such variables as the nature and infectivity of the causal agent, its mode of transmission and the degree of preexisting and newly acquired immunity. (Walton J 1994)

- Epitope also known as antigen determinant. Localized region on the surface of an antigen which antibody molecules can identify and bind. -fulminant describes pathological conditions that develop suddenly and are of great severer. (Churchill's Illustrated1999)

-genome the total genetic information present in a cell, In diploid cell, the genetic information contained in one chromosome set. (Churchill's Illustrated1999)

-Hepadnavirus family of single stranded DNA viruses of which hepatitis B virus (HBV) and woodchuck hepatitis virus (WHV) are members.

-**Hepatocytes** are liver cells. (Churchill's Illustrated1999)

-Icterus see jaundice

-IgG antibodies IgG is the most abundant of the circulating antibodies .It readily crosses the walls of blood vessels and enters tissue fluids. IgG also crosses the placenta and confers passive immunity from the mother to the fetus IgG protects against bacteria, viruses, and toxins circulating in the blood and lymph.

IgM antibodies IgM are the circulating antibodies to appear in response to an antigen. However, their concentration in the blood declines rapidly. This is diagnostically useful, because the presence of IgM usually indicates a current infection by the pathogen causing its formation. IgM consists of five Y-shaped monomers arranged in a pentamer structure. The numerous antigens –binding sites make it very effective in agglutinating antigens. IgM is too large to cross the placenta and hence does not confer maternal immunity.

-Immune globulin(IG) is sterile preparation of concentrated antibodies (immune globulins) recovered from pooled human plasma processed by cold ethanol fractionation .Only plasma that has tested negative for a) hepatitisB surface

antigen(HBsAg) b)antibodies to human immunodeficiency virus (HIV),and c)antibody to hepatitis C virus (HCV) is used to manufacture IG. IG is administered to protect against certain diseases through passive transfer of antibody, labeled respectively IgM, IgG, IgA, IgE and IgD.

-Immune system our body's natural defiance system, involving antibodies and a class of white blood cells called lymphocytes.

-incidence the number of cases of a disease, abnormality, accident, arising in defined population during stated prior, expressed as a proportion ,such as x cases per1000 persons per year. (Churchill's Illustrated1999)

-**Interferon** a protein produced in organisms infected by viruses, and effective at protecting those organisms from other virus infections. Interferons exert virus-nonspecific but host-specific antiviral activity by inducing the transcription of cellular genes coding for antiviral proteins that selectively inhibit the synthesis of viral DNA and proteins. Interferons also have immunoregulatory function. Production of interferon can be stimulated by viral infection, especially by the presence of double stranded RNA, by intracellular parasites, by protozoa, and by bacteria and bacterial products .Interferons have been divided into three distinct types (alpha, beta & game) associated with specific producer cell and functions, but all animal cells are capable of producing interferons, and certain producer cells (leukocytes and fibroblasts) produce more than one type (both alpha & Bata).

-Jaundice is a yellow discoloration of the skin and mucous membranes due to excess of bilirubin in blood, also known as icterus **.**

-Lymphoproliferrative aneoplastic or systemic tumor like proliferation of lymphocytes, as in lymphoid leukemia, malignant lymphomas, or in waldenstroms macroglobulinemia.

-**Major histocompatibility complex (MHC)** originally defined as the genetic locus coding for those cell surface antigens presenting the major barrier to transplantation between individuals of the same species.

Now known to be a cluster of genes on human chromosome 6 or mouse chromosome 17 that encodes the MCH molecules. These are the MHC class 1molecules or proteins that present peptides generated in cytosol to CD8 T cells, and the MHC class11 molecules or proteins that present peptides degraded in cellular vesicles toCD4 T cells, The MHC also encodes proteins involved in antigen processing and host defense . The MCH is the most polymorphic gene cluster in the human genome, having large numbers of alleles at several different loci. Because this MHC proteins are often called major histocompatibility antigens.

-**Myalgia pain** in the muscles.

-**Nucleotide** molecule formed from the combination of one nitrogenous base (purine or pyrimidine), a sugar (ribose or deoxyriose) and phosphate group. It hydrolysis product of nucleic acid. (Churchill's Illustrated1999)

-**Nucleus** a membrane –bound compartment in eukaryotic cell which contains the genetic material and the nucleoli.

The nucleus represents the control center of the cell. Nuclei divide by mitosis, or meiosis.

-**Plasma** the liquid matrix in which the blood cells and proteins are suspended in. It contains an extensive variety of solutes dissolved in water .Water accounts for about 90% of blood plasma.

-**Plasmid** a small, circular DNA molecule. Separate from the bacterial chromosome, capable of independent replication.

-**Polymerase** an enzyme which catalyzes the replication of DNA (DNA polymerase) or RNA (RNA polymerase).

Prevalence is the number of instances of infections or persons ill, or of any other event such as accidents, in a specified population, with any without distinction between new and old cases.

-Promoter region of DNA Usually occurring upstream from a gene coding region and acting as a controlling element in the expression of that gene. It serves as a recognition signal for an RNA polymerase and marks the site of imitation of transcription.

-prophylaxis is the prevention of disease, or the preventive treatment of a re current disorder (Walton J 1994)

-protein is large molecule made up of many amino acids chemically linked together by amide linkages, biologically important as enzymes structural protein and connective tissue.

- **Serum** is the clear, slightly yellow fluid which separates from blood when it clots. In composition it resembles blood plasma, but with fibrinogen removed, sera containing antibodies and antitoxins against infection and toxins of various kinds (antisera) have been used extensively various disease.(Walton J 1994)

T-cells are also known as T-lymphocytes. White blood cells which function in cell-mediated response. They originate from stem cells in bone marrow but mature in the thymus.

-**Titer** a measure of the concentration or activity of an active substance. **Transcription** the process by which a strand of RNA is synthesized with its sequence specified by a complementary strand of DNA, which acts as a template. The enzymes involved are called DNA-complementary strand of DNA polymerase.

-Translation the process of forming a specific protein having its amino acid sequence determined by the condones of messenger RNA. Ribosomes and transferRNA are necessary for translation. **(**Churchill's Illustrated1999)

-**Tumor** alump due to uncontrolled cell division, may be benign or malignant. Malignant tusmour cause cancer. Tumours are able to spread to other parts of body (metastasize) and begin secondary growths at these other sites.

-**Vaccine** an antigenic preparation used to produce active immunity to a disease to prevent or ameliorate the effects of infection with the natural or 'wild' organism. Vaccines may be living, attenuated strains of viruses or bacteria which give rise to inapparernt to trivial infections. Vaccines may also be killed or inactivated organisms or purified products derived from them. Formalin-inactivated toxins are used as vaccines against diphtheria and tetanus. Synthetically or genetically engineered antigens are currently being developed for use as vaccines. Some vaccines are effective by mouth, but most have to be given parenterally. (Churchill's Illustrated1999& Walton J 1994)

-**Vaccinee** person receiving a vaccine.

-**Virion** a structurally complete virus, a viral particle. (Churchill's Illustrated1999)

-**Virus** any of a number of small, obligatory intracellular parasites with a single types of nucleic acid, either DNA or RNA and no cell wall. The nucleic acid is enclosed in a structure called a capsid, which is composed of repeating protein subunits called capsomeres, which or without a lipid envelope. The complete infectious virus particle, called a virion, must rely on the metabolism of the cell it infects. Viruses are morphologically heterogeneous, occurring as spherical, filamentous, polyhedral, or pleomorphic particles. They are classified by the host infected, the type of nucleic acid, and the symmetry of the capsid, the presence or absence of an envelope. (Churchill's Illustrated1999)