
TURKISH REPUBLIC OF NORTH CYPRUS
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# PREVALENCE OF HEPATITIS B SURFACE ANTIGEN (HBSAG) IN NORTHERN CYPRUS FROM JANUARY 2017 TO DECEMBER 2018

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**Thesis Approval**

## STATEMENT (DECLARATION)

Hereby I declare that this thesis study is my own study, I had no unethical behavior in all stages from planning of the thesis until writing thereof, I obtained all the information in this thesis in academic and ethical rules, I provided reference to all of the information and comments which could not be obtained by this thesis study and took these references into the reference list and had no behavior of breeching patent rights and copyright infringement during the study and writing of this thesis.

Wrya Raouf Mahmood Mahmood

Signature 

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## Dedication

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## Abbreviations and Symbols List

| | |
|---|---|
| Aa | Australian aborigines |
| ADV | Adefovir |
| AFP | Alfa Fetoprotein |
| ALT | Alanine aminotransferase |
| Anti-HAV | antibody against hepatitis A virus |
| Anti-HBc | antibody against hepatitis B core antigen |
| Anti-HBc IgM | antibody against hepatitis B core Immunoglobulin M |
| Anti-HBc IgG | antibody against hepatitis B core Immunoglobulin G |
| Anti-HBe | antibody against hepatitis B e antigen |
| Anti-HBs | antibody against hepatitis B surface antigen |
| AST | Aspartate aminotransferase |
| cccDNA | covalently circular closed DNA |
| CLMIA | Chemiluminescent microparticle Immunoassays |
| CMV | Cytomegalovirus |
| DNA | Deoxyribo Nucleic Acid |
| dsDNA | double stranded DNA |
| EBV | Epstein-Barr Virus |
| ECLIA | Electro Chemiluminescence Immunoassays |
| EIA | Enzyme Immunoassays |
| ETV | Entecavir |
| FTC | Emtricitabine |
| HAV | Hepatitis A Virus |
| HBV | Hepatitis B Virus |
| HBV DNA | Hepatitis B Virus Deoxyribo Nucleic Acid |
| HBcAg | hepatitis B core antigen |
| HBeAg | hepatitis B e antigen |
| HBsAg | hepatitis B surface antigen |
| HCV | Hepatitis C Virus |
| HCC | Hepato cellular carcinoma |
| HDV | Hepatitis D Virus |
| HEV | Hepatitis E Virus |
| HSV | Herpes Simplex Virus |
| IFNs | Interferons |
| IFN-α | Interferon-alpha |
| IEM | Immune Electron Microscope |
| MEIA | Microparticle Enzyme Immunoassays |
| NAs | Nucleos(t)ide Analogue |
| NEU | Near East University |
| NEUH | Near East University Hospital |
| ORF | Open Reading Frame |
| PCR | Polymerase Chain Reaction |

| | |
|---|---|
| PEGylated IFN-α | Pegylated Interferon-alpha |
| RDTs | Rapid Diagnostic Tests |
| RIA | Radioimmuno Assay |
| RNA | Ribo Nucleic Acid |
| TBV | Telbivudine |
| TDF | Tenofovir |
| TEM | Transmission Electron Microscope |
| TRNC | Turkish Republic of Northern Cyprus |
| TTV | Transfusion Transmitted Virus |
| WHO | World Health Organization |
| 3TC | Lamivudine |

# 1. Türkçe Özet

Hepatit B virusu(HBV), bilinen en küçük, zarflı DNA virüsleri olan,Hepadnaviridae ailesinde yer alan, sadece insan ve şempazeleri infekte eden, primer olarak Karaciğerde çoğlan, karaciğer sirozu, hepatoselüler karsinom ve karaciğer yetmezliğine neden olan hepatotrop bir virüstür. Dünya genelinde 350 milyon kişinin Hepatit HBV ile kronik olarak enfekte olduğu tahmin edilmektedir. Dünya nüfusunun tahmini %5 'i inaktif taşıyıcıdır ve sağlıklı olarak yaşamlarını sürdürmektedirler. Amacımız Kuzey Kıbrıs'ta Hepatit B yüzey antijeninin (HBsAg) yaygınlığını ve virüs hakkında demografi bilgileri belirlemektir. Denekler sivil Kıbrıslılar, Kıbrıs Adasında yaşayan Türkler, Kan bağışçıları, Askerler, Turistler, Kıbrıs'ta iş veya eğitim için gelen yabancı insanlardı. Örnekleme dönemi Ocak 2017'den Aralık 2018'e kadar iki yıl. (23.980) serum örnekler Ocak 2017 ve Aralık 2018 arasında enzime bağlı immünosorbent testi (ELISA) ile geriye dönük olarak değerlendirildi.HBV enfeksiyonu ile ilgili demografik veriler de bilgisayar veritabanından alındı. HBsAg sero testleri, (314) hasta / tüm hastadan (% 1.3) pozitif, (15.344) erkek (% 64.0) ve (8636) kadın (% 36.0) pozitif sonuç verdi. (314) HBsAg seropozitif sonucu elde ettik, bunların 195'i (% 62.1) erkek ve (119) kadın% 37.9 idi. Pozitif deneklerin yaşları (0) ile (94) arasında idi. Ortalama yaş 34,92 ± 16,59 idi. Bu sonuçlar, Kuzey Kıbrıs'ta küresel olarak HBsAg'ın düşük endemisitede olduğunu ve% 2'den daha az olduğunu göstermiştir. 2006'da% 2,46'dan çalışmamızda % 1,3'e düştü. Sonuç olarak HBsAg için Aşılama Programı ile yüksek korunma sonucu ortaya çıkan çalışma sonuçları. Kuzey Kıbrıs toplumu HBV ile ilgili olarak, izleme, tarama, aşılama ve kontrol etmenin önemi konusunda farkındadırlar.

**Anahtar Kelimeler: Prevalans, Hepatit B, HBsAg, Kuzey Kıbrıs, HBV, KKTC**

## 2. English Abstract

Hepatitis B virus (HBV), the smallest, enveloped DNA virus belong to the family of Hepadnaviridae, it infects only humans and chimps. A Hepatotropic virus, which, as a primer prefers to replicates within liver cells and causes liver cirrhosis, hepatocellular carcinoma. It is estimated that 350 million people worldwide are chronically infected with the Hepatitis B virus (HBV). Our aim is to determine the prevalence of Hepatitis B surface antigen (HBsAg) and demographic information about the virus in Northern Cyprus. Subjects were civilian Cypriots, Turks living in Cyprus, Blood donors, Soldiers, Tourists, foreign people coming to Cyprus for work or education. The sampling period is two years from January 2017 to December 2018. (23.980) serum samples were retrospectively evaluated between January 2017 and December 2018 by enzyme-linked immunosorbent assay (ELISA). Demographic data on HBV infection were also taken from the computer database. HBsAg sero tests gave positive results from (314) patients / all patients (1.3%), (15.344) men (64.0%) and (8636) women (36.0%). We obtained (314) HBsAg seropositive results, of which 195 (62.1%) were men and (119) women were 37.9%. The ages of the positive subjects were between (0) and (94). The average age was 34.92 ± 16.59. These results have shown that HBsAg has a low endemicity and is less than 2% globally in Northern Cyprus. In conclusion results of the study caused by high prevention through Vaccination Program for HBsAg. Cyprus community is aware of monitoring, screening, vaccination and controlling of the HBV.

**Key Words: Prevalence, Hepatitis B, HBsAg, Northern Cyprus, HBV, KKTC**

# 3. Introduction and Aim

Hepatitis B is an inflammation of the liver caused by the Hepatitis B Virus, infection occurs through parenteral means, such as exposure to infectious blood or body fluids and perinatal infection. Distribution and prevalence of the virus that causes a dangerous disease in human body is more common nowadays, a virus that causes inflammation, cirrhosis, cancer of liver, day by day it would be more risky and dangerous to Public Health Problem and Medical issue around world, one type of virus among a group of agents which they would be identified as hepatitis virus. Hepatitis is responsible for high morbidity and mortality around the world, (WHO) as an international organization appending on their data estimated (328 million) people chronically infected with hepatitis viruses while (257 million) of them were living with HBV and (71 million) of them were living with HCV, also with (1.34 million) deaths by Hepatitis in 2015.( World Health Organization, 2017) Due to these data investigation on prevalence of hepatitis viruses in Northern Cyprus have a really important effect and true way to control and prevention of hepatitis disease with its states that will appear on the infected Human and those appeared burden on infected individual, general and the country. The aim of this study was to estimating, detecting incidence and prevalence of hepatitis B virus (HBsAg) in north of Cyprus Island among community of the Island and those people who living in there regardless with their multiple factors such as education, work, migration, military or others.

## 3.1 Hepatitis viruses target the Liver a large organ in the human body:

Hepatitis is a general term included the prefix of (hepat-) related to (liver) from Greek language with suffix (-itis) which is giving meaning of (disease or inflammation of). (Achord et al., 2002) Therefore together (hepatitis) is liver disease or inflammation of the liver (Brooks et al., 2013), the big organ in human body (Slonczewski et al., 2009; Achord et al., 2002) also is a systemic disease primarily liver including. (Brooks et al., 2013) several viruses are causing hepatitis, five medically important viruses are identified as (hepatitis Viruses) due to their main site infection in body that is the liver, there are hepatitis A, B, C, D and E agents viruses and with other viruses such as hepatitis G, Transfusion Transmitted Virus TTV, Cytomegalovirus CMV, Epstein-Barr Virus EBV, rubella virus, yellow fever virus and Herpes Simplex Virus HSV (Slonczewski et al., 2009; Brooks et al., 2013; Levinson, 2012; Achord et al., 2002**)** For infection of hepatitis men and women are equally susceptible, also hepatitis more often appear in lower socioeconomic populations than other population around the world. (Achord et al., 2002)

For the first time viral hepatitis described by Dr. Hippocrates of kos in approximately 500 BC (Güler, 2016), Hepatitis may cause acute and chronic infection depending viral agents of hepatitis and may cause Liver Cirrhosis, Hepatocellular carcinoma HCC, Cancer and death in some situations of some Hepatitis agents in Chronic Phase of the infection. (Brooks et al., 2013; Achord et al., 2002) In infected person with hepatitis viruses they have some of these clinical characterized without regarding types of hepatitis;

- Jaundice or icterus, eyes turn to yellow,
- Fever (sometimes more than 38˚C) (100.4˚F), (Terrault et al., 2018)
- Nausea,
- Vomiting to dehydration,
- Anorexia,
- Pale fece,
- Dark urine, (Brooks et al., 2013; Levinson, 2012; Achord et al., 2002)
- Liver enlargement (Schumann, 2014)

We can summarize hepatitis infection in a person to these stages:

1- New infection or acute phase
2- Chronic infection or chronic phase after six month, usually
3- Mortality, life threatening stage and/or
4- Co-infection or Superinfection (in some situations)

### 3.2. Hepatitis Coinfection:

Hepatitis Virus can be cause co-infection between one agent of itself group, (Hepatitis Viruses) with HIV or Tuberculosis such as HBV/HIV co-infection, HCV/HIV co-infection, HDV/HIV co-infection (Terrault et al., 2018) and HBV/TB co-infection while in 2015 according to (WHO) data, they estimated 36.7 million people infected with HIV and they are living with the disease that 2.7 million of them had HBV infection and 2.3 million of them had HCV (World Health Organization, 2017; World Health Organization, 2015). However there is co-infection between two agents or viruses of hepatitis like HBV/HCV and HBV/HDV co-infection.

### 3.3. Fifteen years challenge against Hepatitis Virus

Comparing with other disease, death by hepatitis day by day is increasing, globally recording data from 2000 to 2015 show us death or mortality caused by AIDS/HIV, Tuberculosis TB and malaria decreased from

this range time in contrast hepatitis mortality increased from 1.10 million death cases to 1.34 million deaths in range of (2000 to 2015), there is 15 years challenge, the chart in figure of (3.3), in reduction mortality of those worldwide diseases (Tuberculosis (TB), AIDS, Hepatitis, Malaria) by prevention treatment and vaccination, that HIV mortality As infectious agent of AIDS disease from 2000 was 1.46 million deaths then decreased to 1.06 million deaths in 2015. Tuberculosis from 1.67 million in 2000 decreased to 1.37 million in 2015, Malaria in 2000 from 0.86 million decreased to 0.44 million deaths around world in 2015. While hepatitis from 1.10 million increased to 1.34 million around world in 2015. (World Health Organization, 2017)

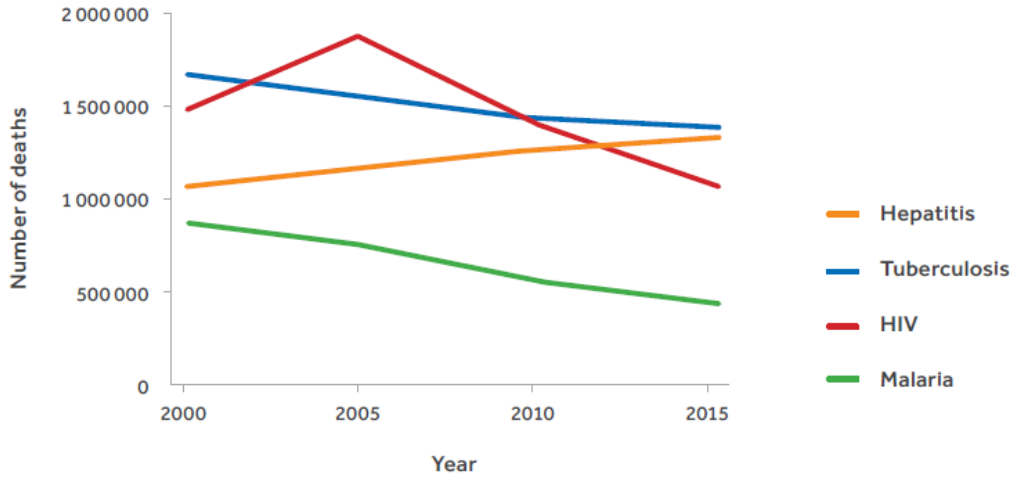


**Figure of (3.3):** Fifteen years of challenge against Hepatitis disease and Tuberculosis, AIDS with Malaria around world since 2000 to 2015 in prevention and treatment of them. As appeared Hepatitis increased during this time range from 1.10 million increased to 1.34 million. (Belong WHO 2015)

## 3.4. Hepatitis in North of Cyprus:

Globally (WHO) divided world upon several regions to describe and publish their data according to these regions. One of them is Eastern Mediterranean Region which North of Cyprus is a part of this region. Incidence of HBV in the region in 2015 was 21 million people and HCV Infection was 15 million.(World Health Organization, 2017)

While studies on that issue in North Cyprus with population of 300,000 people and with the people who came to North of Cyprus to live, work or study since 2010 until 2014 was 339 people infected with HBV and HCV infection was 31 people.(Güler et al., 2018; Güler, 2016) it means the prevalence of Hepatitis in Northern Cyprus is in low.(Güvenir et al., 2019)

# 4. General Information

## 4.1. Hepatitis A Virus:

Type A of the Hepatitis Viruses (HAV) Causes disease of Hepatitis A.

It was discovered and recognized at end of WWII that two unknown types of hepatitis in different times cause infections and illness, then that time called incubation period and those types called short incubation Hepatitis, and long incubation Hepatitis or infectious and serum. After more research on them in 1973 short incubation Hepatitis infections known as hepatitis A virus (Patlak et al., 2000) and serum long incubation hepatitis known as hepatitis B virus.(Achord et al., 2002) HAV is a member of picornavirus family, naked, a linear positive-sense, polymerase negative, single-stranded RNA genome, non-enveloped cubic symmetry ico-sahedral nucleocapsid. HAV in size is 27 to 32-nm, with genome size of 7.5 kb. It has only one serotype and its genome is *Hepatovirus*. (Slonczewski et al., 2009; Brooks et al., 2013; Levinson, 2012; Achord et al., 2002) HAV is stable against acid of stomach and heat at 60˚C (140˚F) for 60 minutes, acid (pH 1.0) for 2 hours.

### 4.1.1 Transmission:

The human is only natural host for HAV.(Achord et al., 2002) HAV is spreading and transmitting from person to another by facial-oral route, due to HAV appears in feces also can transmit by eating raw undercooked shellfish which collected from contaminated water, meaning contaminated food and water.(Slonczewski et al., 2009; World Health Organization, 2017)
HAV because it has low level of viremia and an early viremic stage, is rarely transmitted through blood. (Slonczewski et al., 2009)
HAV is not oncogenic infection. (Brooks et al., 2013)

### 4.1.2 Pathogenesis:

After entry of HAV to the body via food, replicates in gastrointestinal tract (intestinal endothelium) and spread through blood stream to liver, infects and replicates in hepatocytes, after infecting cells cytotoxic T cells attack cells and cause only acute infection not happened chronic infection. (Slonczewski et al., 2009; Levinson, 2012; Achord et al., 2002)

### 4.1.3 Symptoms:

While HAV invade the liver of the patient may become

- Jaundice
- Nausea
- Vomiting
- Fever (Slonczewski et al., 2009; Levinson, 2012)
- Diarrhoea
- Fatigue
- Urine turns to dark brown
- Pale faeces and
- Increasing level of ALT

Incubation period for HAV is (3-4weeks) and its immune response is (IgM) antibody. (Levinson, 2012)

### 4.1.4 Diagnosis:

HAV can be detected in Liver, bile, stool and blood during acute phase of infection (Brooks et al., 2013) the most important test to diagnosis is serologically detecting (IgM) antibody anti–HAV from serum of the patient. (Levinson, 2012) within 3-6 months. After onset of the disease anti-HAV (IgG) appears. Enzyme linked immunosorbent assay is the choice method to measure HAV Abs. (Brooks et al., 2013)

### 4.1.5 Treatment:

Till now no specific antiviral drugs are available to treating HAV infection, only due to self-immunity usually the disease resolves after few months. (Slonczewski et al., 2009; Levinson, 2012; Achord et al., 2002)

### 4.1.6 Prevention:

The disease can be prevented by using vaccine against HAV, there an inactivated hepatitis A vaccine which called HepA Vaccine (Slonczewski et al., 2009) that it is effective, safe and recommended to use, especially specific persons who have more risk than others, including:

- Drug users People Who Inject Drugs (PWID)
- Homosexual men
- International travellers (Brooks et al., 2013; World Health Organization, 2017)
- Children between ages of 2-18 years(Levinson, 2012), and
- Military personnel (Achord et al., 2002).

### 4.1.7 Prevalence:

HAV is widespread around world, crowded conditions, lack of pure water (Brooks et al., 2013) with poor sanitation and hygiene such as eating with dirty hands increase spread of HAV, its incidence estimated in 2015 approximately to 11000 deaths that equal to 0.8% of mortality of viral hepatitis. (World Health Organization, 2017) While in 2016 decreased to 7134 deaths that equal to 0.5% of mortality of viral hepatitis.(WHO 2019)

### 4.1.8 Coinfection:

There is no coinfection between Hepatitis A Virus and other types of Hepatitis Viruses or other infection.

### 4.1.9 Specific group with high risk: (WHO 2019/ Brooks et al., 2013)

- Poor sanitation
- Lack of safe water
- Travelers to high endemic countries
- Persons who inject drugs (PWIDs)
- Homosexual men
- Health care workers (HCWs)

## 4.2. Hepatitis C Virus:

Another type of hepatitis viruses is Hepatitis C Virus (HCV), which can cause diseases of Hepatitis C. (Slonczewski et al., 2009)
After both hepatitis A and B were identified in 1989, HCV was identified too. (Achord et al., 2002 World Health Organization, 2016)
HCV is a member of flaviviridae family, (Slonczewski et al., 2009) small, enveloped, positive-sense single-stranded RNA genome, (World Health Organization, 2016) spherical symmetrical with no polymerase in virion. HCV in size is 60 nm with genome size of 9.4kb. It has at least six major genotypes with multiple sub-genotypes based on gene differences, (Levinson, 2012) genotype 2 and 3 in Asia are more common. HCV is sensitive and destroyed by stomach acid (Achord et al., 2002) and is sensitive to Ether.(Brooks et al., 2013)

### 4.2.1 Transmission:

HCV in transmitted through: (Slonczewski et al., 2009; Levinson, 2012; WHO 2019; Brooks et al., 2013)

- Blood transfusion primarily
- Can be through needle stick injury
- Parenteral from mother to child
- Sexual transmission, but last two methods are less frequently.
- Tattooing is associated to infection with HCV.

### 4.2.2 Pathogenesis:

HCV through blood enter liver, infect hepatocytes, replicate inside but does not destroy or kill them, there is no effect or evidence to cytopathic effect to liver cells. Cytotoxic T cell immunity attack hepatocyte and cause death of them, so; none types of hepatitis viruses are cytopathogenic specifically or typically, while cellular damage appeared in hepatitis disease, but it caused by immune response. (Levinson, 2012; Brooks et al., 2013)
HCV can cause both acute and chronic infection, approximately 80% of infected persons do not exhibit symptoms. (Slonczewski et al., 2009/WHO 2019) HCV infection from mild disease going during few weeks to serious hepatocellular carcinoma, lifelong disease.

### 4.2.3 Symptoms:

Infection period for HCV ranges from 15 to 160 days (Brooks et al., 2013) or 2 weeks to 6 months. (WHO 2019) Those who have symptoms may have:

- Decreased appetite
- Fever
- Nausea
- Anorexia
- Vomiting
- Dark urine
- Pale faeces
- Jaundice (yellowish discoloration of skin, whites of eyes)
- Increasing alanine aminotransferase (ALT) Level

### 4.2.4 Diagnosis:

Diagnosing of HCV done by testing and detecting of anti-HCV antibodies serologically, if the test was positive then ELISA need to confirm by HCV RNA testing, that is confirming chronic infection of HCV (Levinson, 2012; Achord et al., 2002; WHO 2019) after confirming HCV chronic infection, liver biopsy used to determine degree of liver damage (cirrhosis).(Slonczewski et al., 2009/WHO 2019) Chronic infection detection depends on the HCV RNA detection for at least 6 months. Approximately 90% of HCV patients are anti-HCV positive within five months. (Brooks et al., 2013)

### 4.2.5 Treatment:

According to genotypes of HCV virus there is some drug treatments which they effect on viral replication or viral elimination in chronic infected patients. IFN-α is a recombinant drug which is cytokine released by host cells, then used to inhibit HCV replication.( Brooks et al., 2013; Levinson, 2012; World Health Organization, 2016)
Ribavirin is inhibitor of nucleoside for HCV but a therapy can have more effect and cure on most patients with HCV infection with utilizing for most genotypes HCV is pan-genotypic direct acting antivirals (DAAs) that usually uses for 12 to 24 weeks depending on presence or absence of cirrhosis, DAAs directly inhibit HCV replication cycle.( World Health Organization, 2016; WHO 2019)

### 4.2.6 Prevention:

There is no available vaccine against HCV, (Slonczewski et al., 2009; Brooks et al., 2013; Levinson, 2012; Achord et al., 2002; World Health Organization, 2016) but reducing risks to virus exposure can be prevented, Such as:

- Hand hygiene
- Prevention from blood exposure
- Testing for donated blood.

### 4.2.7 Prevalence:

HCV is the prevalent blood-borne pathogen,( Levinson, 2012; WHO 2019) according data in 2015 by World Health Organization estimated globally around world there were (1.75) million new HCV infections which equal to (23.7) per (100,000) persons, and (71) million persons were living with HCV chronically while (843000) patients recovered or cured and approximately in 2016 about (399000) patients died by HCV, while Hepatitis C Virus caused cirrhosis in most of them.(WHO 2019) Depending on regions of WHO which was divided world upon them, in both data (new infections and chronic infections) highest region is Eastern Mediterranean region that are (409000) new infections with (15) million chronic infections.(WHO 2019) While north of Cyprus is a part of that region, studies show during 5 years from 2010 to 2014 there were (31) HCV infections in there from (25442) persons.(Güler et al., 2018; Güler, 2016)

### 4.2.8 Co-infection:

There is co-infection between HCV and HBV,(World Health Organization, 2017) co-infection between HCV and HIV,( Brooks et al., 2013; Levinson, 2012) co-infection between HCV and Tuberculosis. In that situation, viruses in patients caused more sever liver disease and higher incidence of liver cirrhosis, hepatocellular carcinoma and mortality, So it needs more to treatment, firstly dominant virus will be identified and require treatment it will do to the virus then treatment for the following other virus.

**4.2.9 Specific groups with high risks;** (Brooks et al., 2013; World Health Organization, 2016; WHO 2019)

1- People Who Inject Drugs (PWIDs)
2- Persons with co-infection HCV and other virus or disease like (HBV, HIV and TB).
3- Children born from positive HCV antigen mother.
4- Infected sexual partners.
5- Tattooing persons.

## 4.3. Hepatitis D virus:

HDV is another type in hepatitis viruses which cause hepatitis D disease or hepatitis delta.(Levinson, 2012)
HDV from the nucleus of hepatocytes of patients who had HBsAg positively chronic liver disease by Marcus Rizzetto in 1977 was discovered, (Giersch, 2015; Wedemeyer et al., 2010; Rizzetto et al., 1977; Slonczewski et al., 2009) HDV is a single-stranded, circular, negative sense RNA, enveloped, very small genome which encodes only one internal core protein known as Delta antigen (HD-Ag), HDV has no polymerase virion, therefore; for replication replicates by RNA polymerase of host cells.(Brooks et al., 2013; Levinson, 2012) RNA size of HDV is 1.7 kb. and its particle size is 35-37 nm,(Brooks et al., 2013) and till now 8 genotypes reported to HDV.(Deny, 2006; Giersch, 2015; Wedemeyer et al., 2010)

HDV is a defective virus which is needs a helper virus to replication, HDV uses surface antigen of HBV to itself as HDV envelope protein. HDV due to one serotype of HBsAg as its envelope, it has only one serotype. For infection HDV needs HBV, so HDV infects only those persons who already had infected with HBV regardless to new or chronic HBV infection.(Levinson, 2012; Achord et al., 2002; World Health Organization, 2017; Wedemeyer et al., 2010)

### 4.3.1 Transmission:

Transmission route of HDV is believed similar and same as Hepatitis B Virus (HBV) in (Brooks et al., 2013; Levinson, 2012; Wedemeyer et al., 2010)

- Parenteral
- Through blood exposure (Giersch, 2015)
- Sexually via contact with infected blood person and its products. (WHO 2019)

### 4.3.2 Pathogenesis:

Pathogenesis of HDV in not known completely, through blood HDV entire liver, then infects hepatocytes, after infection immunity response such cytotoxic $CD4^+$ T cells (Wedemeyer et al., 2010) will cause damage of hepatocytes which infected with the virus. (Levinson, 2012)

### 4.3.3 Symptoms:

There is two major types of infection by HDV (acute co-infection and super infection).
In acute, the HDV infection usually recovered completely. Also can develop from mild to severe chronic delta hepatitis rarely. Non-specific symptoms like:

- Nausea
- Fatigue
- Anorexia (Giersch, 2015)

HDV super infection with HBV chronically infected is more severe than HBV itself infection alone in all ages, in 70-90% persons, it cause cirrhosis faster and earlier than HBV infection alone, also leading liver failure significantly in higher. (Levinson, 2012; World Health Organization, 2015; WHO 2019)

### 4.3.4 Diagnosis:

HDV diagnosis and determining in laboratory is made in first step by detecting (IgG) antibody against HDV antigen and (IgM) antibody in serum of patients and confirming by RNA of HDV detection in serum. HDV Antibodies within months to years can disappear.(Giersch, 2015; Wedemeyer et al., 2010; WHO 2019; Brooks et al., 2013; Levinson, 2012)

### 4.3.5 Treatment:

There is no special therapy to HDV but can be used PEGylated interferon alpha for at least 48 weeks, PEG-IFN-α leads about 25% of patients to clearance from HDV, while in end stage of liver disease may be liver transplantation considered. (Levinson, 2012; Giersch, 2015; Wedemeyer et al., 2010; WHO 2019)

### 4.3.6 Prevention:

There is no specific vaccine to HDV but can be prevent by preventing HBV transmission, especially for those who are not infected by HBV through Hepatitis B vaccination. (Brooks et al., 2013; Levinson, 2012; WHO 2019)

### 4.3.7 Prevalence:

HDV infection is coinfection with HBV infection. At least 5% of chronic HBV infected patients are have HDV that is estimated (15-20) million persons have or infected with HDV. (World Health Organization, 2017; Mhalla et al., 2016; Giersch, 2015; Wedemeyer et al., 2010; WHO 2019)

### 4.3.8 Co-Infection:

HDV is a virus to replication and infection needs Hepatitis B Virus (HBV). So in itself is defective virus.

### 4.3.9 Specific groups with high risk:

1- Chronic cirrhosis of Hepatitis B Virus.
2- People Who Inject Drugs (PWIDs)
3- Sexual activity workers (WHO 2019)

## 4.4. Hepatitis E virus:

Hepatitis E virus is a fifth type of hepatitis viruses which causes hepatitis disease.
In 1983 by using Immune Electron Microscope (IEM) Hepatitis E Virus was discovered in stool samples by Dr. Mikhail S. Balayan in Russia.(Lapa et al., 2015; Balayan et al., 1983) HEV is a member of the hepeviridae family, its genome is cloned and is non enveloped, positive-sense, single-strand RNA (Levinson, 2012) with size of 7.2 kb. (Brooks et al., 2013), HEV in size is small 27-34 nm (World Health Organization, 2014) or 30-32 nm, icosahedral symmetry (Brooks et al., 2013), susceptible to heat (60 ̊c for few minutes) inactivates HEV particles (World Health Organization, 2014), mostly causes to acute hepatitis.(World Health Organization, 2017 ) HEV in fulminant hepatitis disease has high mortality of 20% rate in pregnant women.(Brooks et al., 2013; Levinson, 2012; World Health Organization, 2017) The HEV has four distinct genotypes at least 1-4, only 1 and 2 are responsible for human disease.(World Health Organization, 2014)

### 4.4.1 Transmission:

HEV is transmitted through fecal-oral route, especially through contaminated water.(Brooks et al., 2013; World Health Organization, 2017; WHO 2019) HEV is water borne epidemic disease in Asia, Africa, India and Mexico. (Levinson, 2012; World Health Organization, 2014) Also there are some other routes for transmission, such as: (Lapa et al., 2015; WHO 2019)

- Eating or consumption of raw or uncooked meat of pig
- Transfusion from infected blood.
- Vertical transmission from a pregnant to her baby.
- Ingestion of undercooked meat from infected animal.
- Closely pig contact

### 4.4.2 Pathogenesis:

From stool of infected persons HEV is shed, then it contaminates water, after drinking or eating contaminated water or food, the virus enters body through intestine then to liver, HEV infects liver and resolving during (2-6) weeks. HEV can make a progress to acute liver failure meant Fulminant Hepatitis.

### 4.4.3 Symptoms:

Incubation period for HEV varies from 2-10 weeks. Symptoms include:

- Headache
- Mild fever
- Chills
- Fatigue
- Nausea
- Vomiting
- Dark urine and
- Jaundice (yellowing of skin and whitish eyes).(Wedemeyer et al., 2010)

### 4.4.4 Diagnosis:

Laboratory diagnosis useful for detecting HEV in a patient, they are including testing for

- Blood, serologically for Antibodies against HEV (IgM anti-HEV, IgG anti-HEV).
- Genome of the virus (HEV nucleic acid). (Wedemeyer et al., 2010)

### 4.4.5 Treatment:

There is no specific antiviral treatment for HEV, but for symptomatic acute Hepatitis E, it can be treat symptoms, in purpose of that Ribavirin or PEGylated interferon can be use and combination both of them for furthermore effect in co-infection with HIV.( Lapa et al., 2015)

### 4.4.6 Prevention:

- A vaccine against HEV developed but not available in most countries without China. (World Health Organization, 2017 /WHO 2019)
- Using quality standards for water supplies.
- Hygienic practices.

### 4.4.7 Prevalence:

According WHO reports, globally every year 20 million HEV infections are estimated, from those infections 3.3 million are symptomatic acute Hepatitis E. In 2015, there were 44000 deaths caused by Hepatitis E Virus around world.

### 4.4.8 Coinfection:

There is no coinfection between Hepatitis E Virus and other types of Hepatitis viruses. Commonly Hepatitis E Virus does not cause chronic infection. HEV co-infection with HIV has been observed, recently. (Lapa et al., 2015)

### 4.4.9 Special groups with high risk:

- Pregnant women.
- Those persons who often cannot get pure, chlorine and safe water such as refugees and migrants, persons from mobile and cross-border populations. (World Health Organization, 2014)
- Farmer, Butcher and Veterinarians of pigs.
- Persons consume pork commonly. (Lapa et al., 2015)

## 4.5. Hepatitis B virus

### 4.5.1 Discovery stages of Hepatitis B Virus:

Hepatitis B virus HBV is causing potentially life threatening liver disease in human called hepatitis B.(Achord et al., 2002)
It had known hepatitis B as oldest virus which found in human body, discovered from 0.2 to 7 thousand years ago in human skeletons from Asia and Europe.(Sabri, 2018) Despite this hepatitis B virus didn't clinically discover until Second World War (WWII). Due to dying of soldiers by Yellow Fever disease, Dr. F.O. MacCallum British physician produced Yellow Fever Vaccine from soldier's serum and he injected them with the vaccine, he noticed developing Hepatitis disease in most of them, after some researching, he noticed the hepatitis disease may cause by unknown virus from infected serum that used to injection of soldiers. Then the doctor used the hepatitis B term for hepatitis infection from contaminated blood and serum in 1947 (Patlak et al., 2000), hepatitis A term for those hepatitis infections caused by non-sterilized needle during vaccine injection and water contaminated in there. (Sabri, 2018)

In 1965 researcher doctor Baruch Samuel Blumberg and biochemist Harvey Alter after discovered (Aa),(Blumberg et al., 1965) the Australian antigen in blood of Australia aborigines then later named hepatitis B surface antigen HBsAg, in 1970 by D. S. Dane and K.E. Anderson who they discovered whole hepatitis B particles in Aa positive serum. Later Dane particle name used for those particles (Sabri, 2018; Schumann, 2014) which referred to Scientist D. S. Dane while he published for first time electron micrographs of the virion. Figure (4.5.2 A)

### 4.5.2 HBV structure:

Hepatitis B virus is a member hepadnaviridae family, small, enveloped, partially one molecule of double-stranded circular DNA genome, negative sense, icosahedral nucleocapsid core, with having DNA-dependent DNA polymerase, the virus circulate in serum with size of 42 nm, genome size is 3.2 kb. (Brooks et al., 2013; Levinson, 2012; Güler, 2016; World Health Organization, 2015; Sabri, 2018; Schumann, 2014; Cardell, 2009), figure (4.5.2 A), There is a micrograph of the Hepatitis B Virus structure through Transmission Electron Microscopy (TEM) in figure of (4.5.2 B).
HBV has at least eight (8) genotypes from A to H (Schumann, 2014; Cardell, 2009) or nine (9) genotypes from A to I,(World Health Organization, 2015) basis on more than 8% difference in HBV genome.

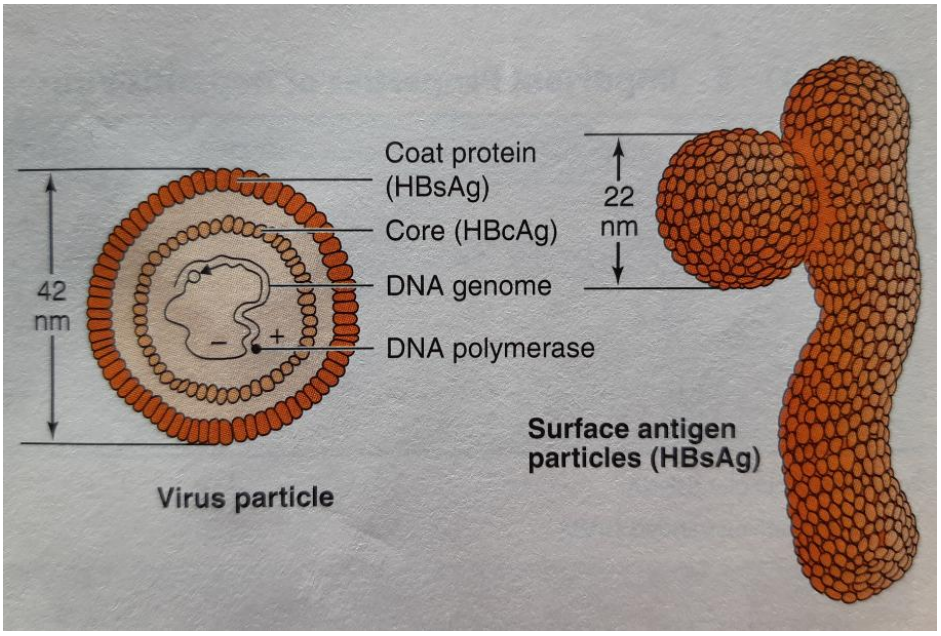


**Figure (4.5.2 A):** Left, Structure of Hepatitis B Virus, which includes DNA genome, Core protein and Coat protein (Surface protein) with 42 nm in size. Right, Coat protein or Surface protein particle (HBsAg) while in wide size of spherical particle of the surface protein is 22 nm. , figure belonged (Levinson, 2012).

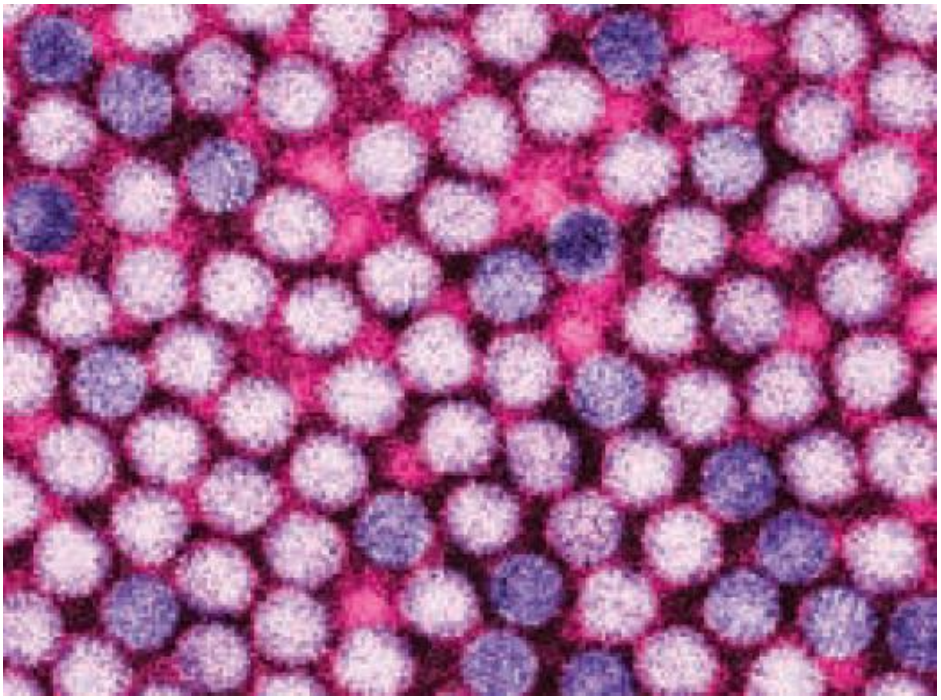

**Figure (4.5.2 B):** Transmission Electron Microscope (TEM) Micrograph of the Hepatitis B Virus structure, they appear in 40 nm. Figure belonged (Slonczewski, et. al., 2009)

### 4.5.3 HBV morphology:

Through Electron Microscopy, Hepatitis B Virion morphologically appears in two types of particles:

1- The infectious Dane particles
2- The smaller non-infectious particles

#### 4.5.3.1 The infectious Dane Particle

Dane Particle is 42 nm, consists of (envelope) and (core) or outer lipid envelope component of surface antigen, contains or includes (HBsAg). And 27 nm inner ico sahedral nucleocapsid core, contains hepatitis B core antigen (HBcAg). Dane Particle is double-layered.

In the core contains DNA genome which DNA polymerase covalently attached with 5' end of the minus long strand of DNA and has activity of reverse transcriptase. Surface proteins which are rooted in outer envelope, they take their rolling in binding and entering target cell during infection period.
Both core protein and surface protein are antigenic molecular, they are recognizing and detecting by both T cells and B cells in immune system during immunity process in human body against them. Left of the Figure (4.5.3.1)

#### 4.5.3.2 The smaller non-infectious particles

They are empty tubular or filamentous and spherical particles, spherical particles are 22 nm, while long filamentous in wide are 22 nm too, but maybe they long more than 200 nm. right of figure (4.5.3.1). This particles are more than from virion in blood of the patients, their ratio to virion is 1000:1. They are non-infectious.
In an electron micrograph of hepatitis B virus reveals/appears all the three particles: HBV virion, spherical and filamentous particles with high number of their particles among some HBV virion which numbers of the virion is too less than non-infectious particles (both empty filamentous and spherical particles). Figure (4.5.3.2)

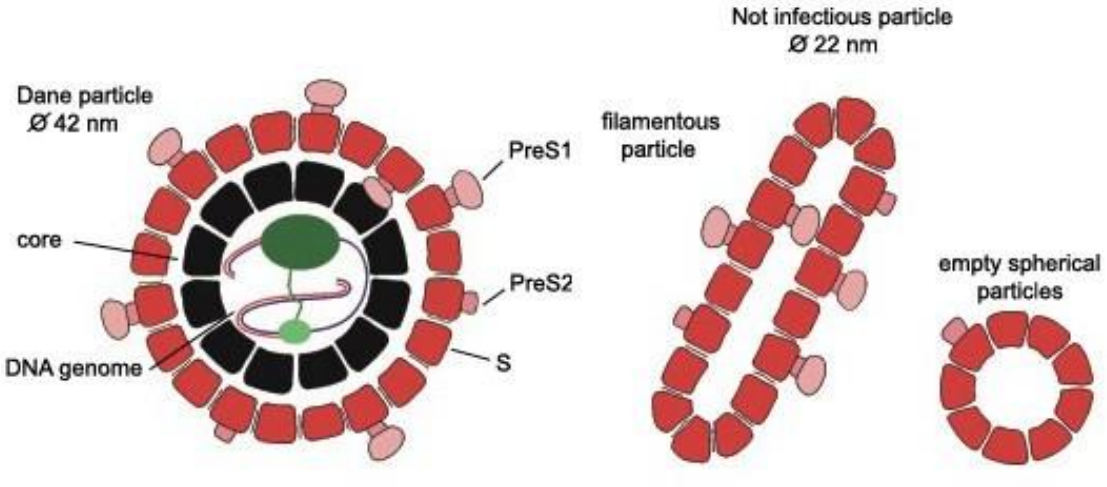


**Figure (4.5.3.1):** Left part, infectious Dane Particle HBsAg Large (PreS1 + PreS2 + s), Medium (PreS2 + s), Small (s) proteins with its core and genome**,** right part, smaller non-infectious particles of Hepatitis B Virus (HBV) empty filamentous and spherical shape. Figure is belonging to Gerlich (Gerlich et al., 2009)

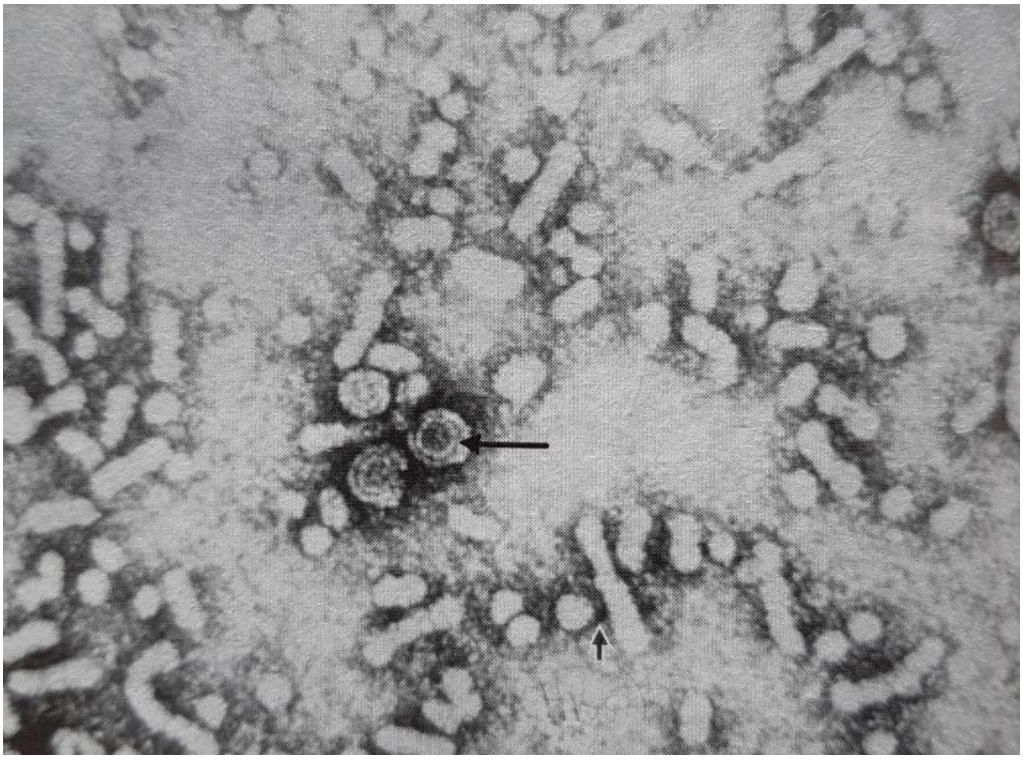

**Figure (4.5.3.2):** An electron micrograph reveal all the three particles of Hepatitis B Virus: HBV virion, spherical and filamentous particles, long arrow focused on HBV virion and short arrow focused on empty filamentous and spherical particles, long right site is empty filamentous and small circle left site of the arrow is empty spherical particle, with high number of their particles among some numbers of the virion. Figure belonged (Warren Levinson, 2012)

### 4.5.4 HBV genome:

Genome of the Hepatitis B Virus is approximately 3200 bp. , it has (9) genotypes (A-I). There are four overlapping Open Reading Frames (ORF) on the HBV genome for encoding and transcription of Surface, Core, (X) proteins and Polymerase (P) protein while (P) protein includes DNA polymerase, RNase H activities and reverse transcriptase.
The S gene has three codons and encodes HBsAg Large (PreS1 + PreS2 + s), Medium (PreS2 + s), Small (s gene) proteins means (L, S, M) protein. The C gene has two codons and encodes HBcAg and HBe proteins. (Cardell, 2009) (Figure 4.5.4 shows all 4 Open Reading Frames (ORF))

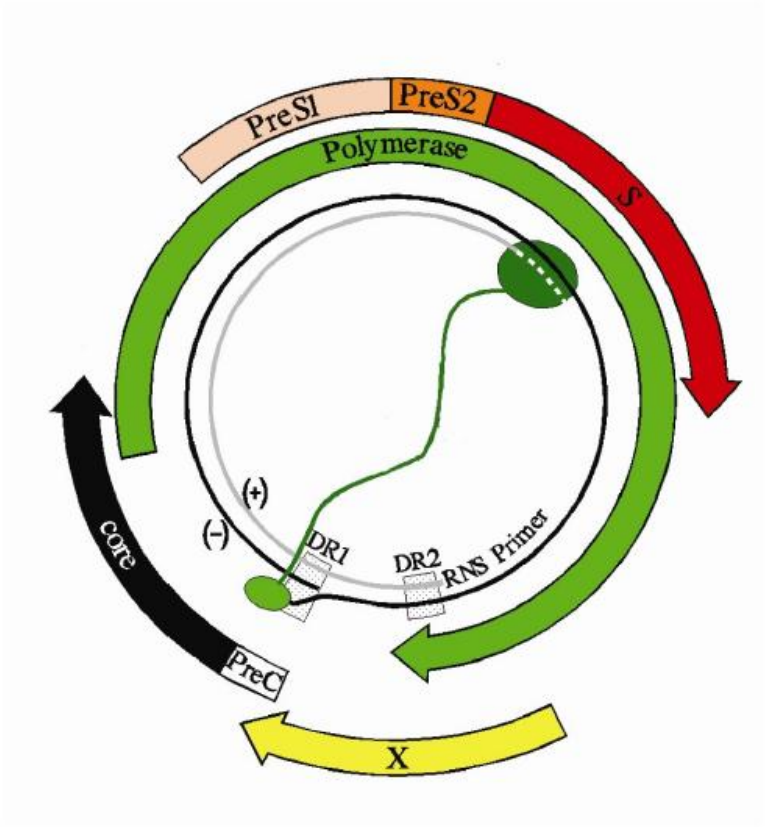


**Figure 4.5.4:** Hepatitis B Virus Genome, includes four open reading frames, they are encoding for transcription of Polymerase, core and surface protein. Polymerase protein is covalently attached to the minus strand of the virus. Figure belonged (Gerlich et al., 2009)

### 4.5.5 Pathogenesis:

After HBV enters the blood, the virus through blood circulation gets liver and infects hepatocytes, due to infection HBV antigens are displayed on the surface of hepatocytes, immune cells such as cytotoxic T cells attack on infected cells then inflammation appeared.
Antigen-Antibody complexes cause some symptoms, such as (icterus, enlarged liver and arthritis). Viral clearance and disease pathogenesis mediate by adaptive immune response. (Brooks et al., 2013; Levinson, 2012; Schumann, 2014)
HBV cause acute infection and chronic infection. Chronic infection develops from acute infection, in hepatitis B when immune response failed in/to control the virus, (Achord et al., 2002) chronic infection mean infecting with HBsAg or persisting HBsAg and the virus at least 6 months in blood, risk of HBV chronic infection development is highest in children,(World Health Organization, 2017) close to 5% patients of HBV become chronic carriers.(Levinson, 2012; Achord et al., 2002; World Health Organization, 2017; World Health Organization, 2015) In chronic infection symptoms more sever and the disease from cirrhosis can develop into hepatocellular carcinoma (HCC) if not treated,(World Health Organization, 2015) maybe HBV is a human tumor virus.(Levinson, 2012)
Incubation period of HBV is 10-12 week or 60 to 90 days. (Brooks et al., 2013) Destroy of infected hepatocytes with HBV caused by immunity response, cytotoxic T cells kill the virus and infected cells with the virus (liver cells). (Achord et al., 2002; Brooks et al., 2013) In acute infection severity depends on host immune response and number of infected cells (Achord et al., 2002). High level of HBV DNA leads to develop cirrhosis of liver and hepatocellular carcinoma (HCC) in chronic infected patients (Schumann, 2014)

### 4.5.6 Transmission:

HBV can transmit through these routes:

- Expose to contaminated or infected blood or any other infected body Fluids (saliva, seminal Fluids...)
- Sexual contact
- Intravenous drug abuse
- Tattooing
- Perinatal transmission from mother to new born (Levinson, 2012; World Health Organization, 2015; Cardell, 2009; WHO 2019) during birth.
- Haemodialysis patients and staff. (Brooks et al., 2013)

### 4.5.7 Symptoms:

Most people with new/acute infection of HBV are asymptomatic (Brooks et al., 2013; Levinson, 2012; Achord et al., 2002; World Health Organization, 2017/World Health Organization, 2015 ) while some people have some symptoms, such as:

- Icteric (yellowing both skin and eyes)
- Fatigue
- Nausea
- Vomiting
- Dark urine.

In some patients the infection can develop to chronic liver infection that can develop to cirrhosis then to hepatocellular carcinoma (HCC). (Brooks et al., 2013; Levinson, 2012/ Schumann, 2014)

### 4.5.8 Diagnosis:

Through serological or biochemical or histological also clinical tests we can assess of HBsAg positive persons. (Schumann, 2014) In early incubation period HBsAg, DNA polymerase activity, HBV DNA and HBeAg exist in blood, HBsAg during 2-6 weeks is detectable and remains until six (6) months after exposure. (Brooks et al., 2013; Levinson, 2012)

There is a gap period for disappearing HBsAg and detecting HBs antibody (HBsAb) that includes several weeks, that time called (window phase). In window phase anti-HBc is positive, so, HBcAb in both acute and chronic infection is present and in recovered persons from acute infection, also.

The figure (4.5.8.A) describes those situations (Brooks et al., 2013; Levinson, 2012). And figure (4.5.8.B) part A and part B shows both acute infection (A) and (B) chronic infection with serological and clinical course profiles of HBV infection (Schumann, 2014; Liang, 2009).

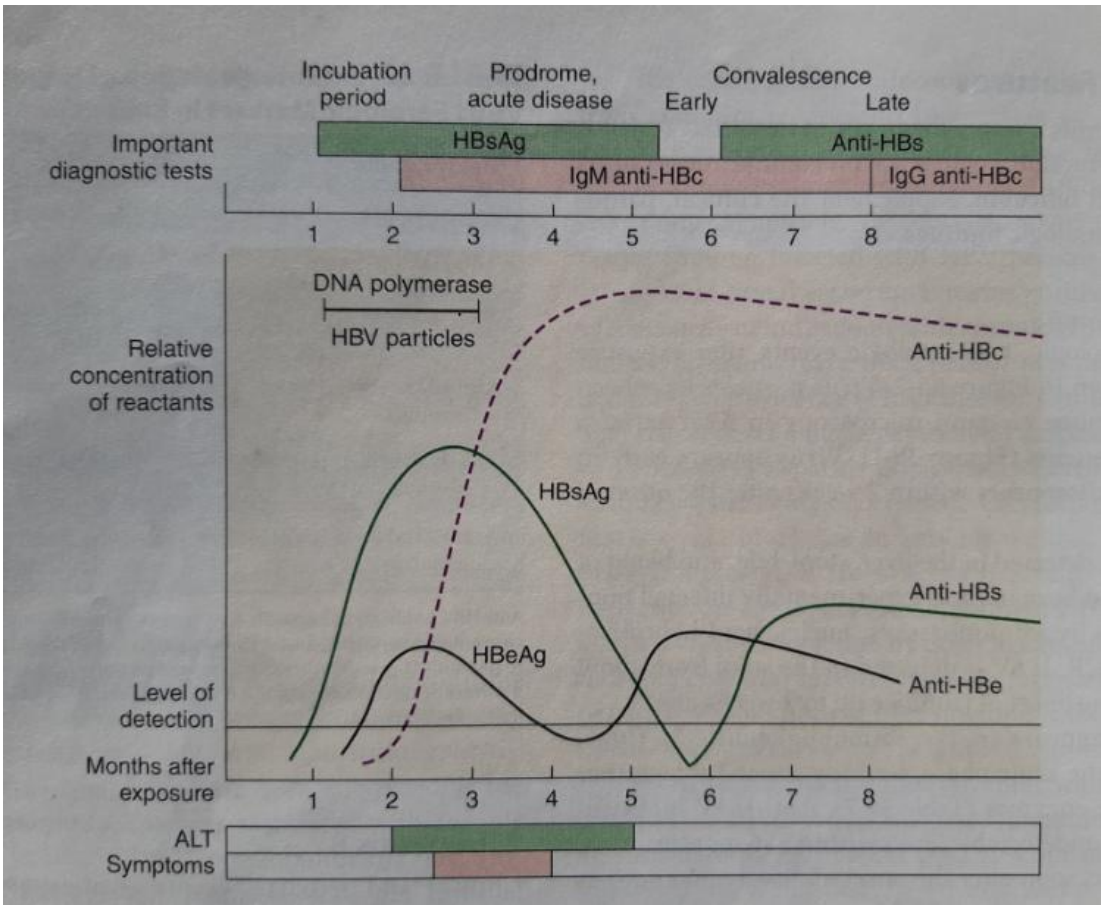


**Figure (4.5.8.A):** shows situations of infected person with Hepatitis B Virus after exposure with the virus by months, from early infection to developing of the disease. Showing existing Particles of the virus in blood at first three months of infection then immunity response against them. Window phase is that gap between HBsAg and Anti-HBs antibody before sixth month after exposure. Figure belonged (Geo. F. Brooks et al., 2013)

### 4.5.8.1 There are some tests for diagnosing, assessment and monitoring of HBV:

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- HBV DNA
- Alfa fetoprotein (AFP) for hepatocellular carcinoma (HCC).

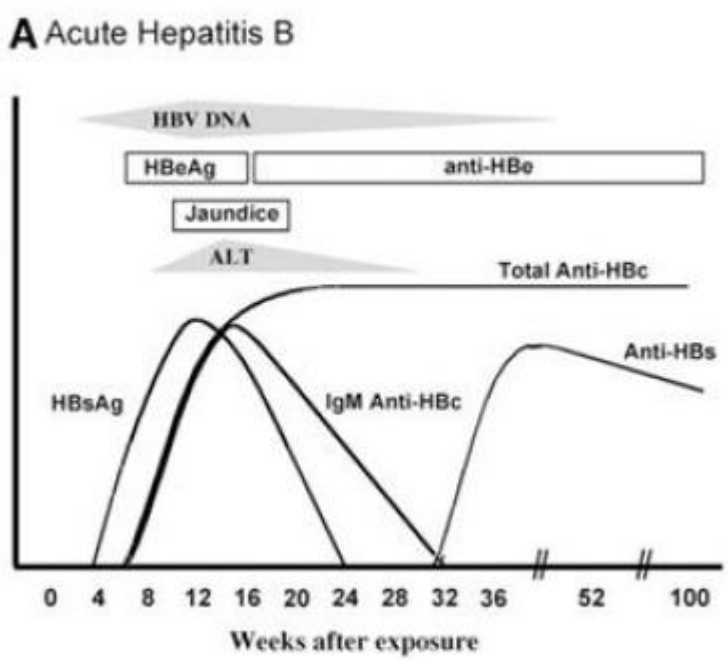


**Figure 4.5.8.B:** Part A- Acute Hepatitis B infection, serological and clinical changes by weeks after exposure of HBV, approximately DNA of the virus can be find during acute Hepatitis B infection period then decreased by immune response. Belong (T. Jake liang 2009)

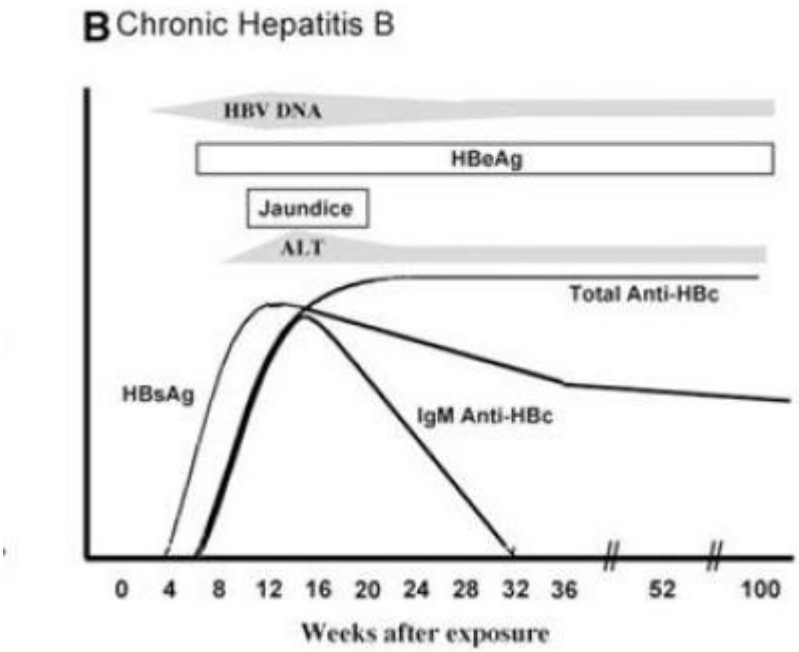


**Figure 4.5.8.B:** Part B- Chronic Hepatitis B infection, serological and clinical changes by weeks after exposure of HBV. HBV DNA and HBeAg remain in blood after six month of infection. Antibody not produced against HBsAg in Chronic phase. Figure Belong (T. Jake liang 2009)

There is some serological markers for HBV in hepatitis patients, they have helping us in interpreting HBV's clinical and serological events, they are (Brooks et al., 2013; Levinson, 2012; Achord et al., 2002; Güler, 2016; Kurugöl et al., 2009; World Health Organization, 2015; Schumann, 2014) HBsAg, HBcAg, HBeAg, anti-HBs, anti-HBc (IgM), anti-HBc (IgG), anti-HBc, anti-HBe and HBV DNA. Table (4.5.8) interprets serological markers of HBV.

| Marker | HBV marker for: |
|---|---|
| HBsAg | HBV infection<br>(acute and chronic) |
| HBeAg | High level HBV replication and infectivity<br>(also marker for treatment response) |
| HBV DNA | Level of HBV replication<br>(also primary marker for treatment response) |
| Anti-HBc (IgM) | Acute HBV infection<br>(sometimes also in flare of chronic infection) |
| Anti-HBc (IgG) | Recovered or chronic HBV infection |
| Anti-HBs | Recovered HBV infection and<br>marker of HBV vaccination<br>(Titer level reflects vaccine efficacy) |
| Anti-HBe | Low-level HBV replication and infectivity<br>(also marker for treatment response) |
| Anti-HBc IgG and (and no)<br>anti-HBs and HBsAg neg | Recovered HBV infection |
| Anti-HBc (IgG) and HBsAg<br>(> 6 Months) | Chronic HBV infection |
| Anti-HBc (IgG) and/or<br>anti-HBs and HBV-DNA | Latent or occult HBV infection |

**Table (4.5.8):** Interpreting Serological and Virological markers, each of them reveals special step/phase of Hepatitis B Infection. HBsAg: hepatitis B surface antigen, HBcAg: hepatitis B core antigen, HBeAg: hepatitis B e antigen, anti-HBs: antibody against hepatitis B surface antigen, anti-HBc (IgM): antibody against hepatitis B core Immunoglobulin M, anti-HBc (IgG): antibody against hepatitis B core Immunoglobulin G, anti-HBc: antibody against hepatitis B core, anti-HBe: antibody against hepatitis B e antigen and HBV DNA: Hepatitis B Virus Deoxyribo Nucleic Acid. Table Belong to (T. Jake Liang 2009)

**4.5.8.2 For diagnosing Hepatitis B Virus, by using these below routes, HBsAg can be detect from patients:**

A- (RDTs) Rapid Diagnostic Tests by lateral flow.

B- Immunoassays Techniques.
- (RIA) Radioimmuno assay
- (CLMIA) Chemiluminescent micro particle Immunoassays
- (ECLIA) Electro Chemiluminescence immunoassays
- (EIA) Enzymeimmunoassays
- (MEIA) Micro particle Enzyme Immunoassays (Amini et al., 2017)

**4.5.9 Treatment:**

Using therapy and treatment for Hepatitis B, supportive and allowing in recovering and repairing damaged hepatocellular. (Brooks et al., 2013) There are seven antivirals therapies against HBV now, they proved to treatment chronic Hepatitis B infections, most of them their targets are nucleoside or nucleotide of HBV.
They are useful for

- Delay progression of Liver cirrhosis.
- Reduce Hepatocellular carcinoma. (Levinson, 2012; Güler, 2016; World Health Organization, 2015; Schumann, 2014)
- Improving survive for long time. (Brooks et al., 2013)

**4.5.9.1 Therapies include:**

- Recombinant interferon alpha (INF-α) or PEGylated IFN-α
- Lamivudine (3TC)
- Telbivudine (TBV)
- Entecavir (ETV)
- Adefovir (ADV)
- Tenofovir (TDF)
- Emtricitabine (FTC)

Activity those antiviral therapies to HBV are displayed in Table (4.5.9.1) also resistances against them. All of them without first (IFN- α) their targets are nucleotide or nucleoside analogue (NAs) from Hepatitis B Virus. HBV has resistance for all of them except Interferons, especially high resistance for Tenofovir (TDF), Entecavir (ETV) and Telbivudine (TBV).

| Antiviral agent | Potency against HBV | Resistance barrier |
|---|---|---|
| **Interferons** | Moderate | Not applicable |
| **Tenofovir** | High | High |
| **Entecavir** | High | High |
| **Emtricitabine** | Moderate | Low |
| **Telbivudine** | High | Low |
| **Lamivudine** | Moderate - high | Low |
| **Adefovir** | Low | Moderate |

**Table (4.5.9.1):** Those antiviral which used against Hepatitis B Virus in disease of Hepatitis B. Tenofovir, Entecavir and Telbivudine have high effect on the virus, but the virus hasn't resistance against Interferons, also Interferons have Moderate effect on the virus. Table belonged (WHO 2015)

Typically in acute infection of HBV does not use antivirals. (Levinson, 2012; Cardell, 2009)

**4.5.9.2 Mechanism action of antivirals:** (Brooks et al., 2013; World Health Organization, 2015; Cardell, 2009)

- Inhibition HBV replication by Entecavir (ETV).
- Inhibition priming of reverse transcription by Adefovir (ADV).
- Inhibition of synthesis of negative strand of HBV DNA by (3TC, FTC and TDF).
- Level reduction of DNA of the HBV by Lamivudine (3TC).
- Enhancement ability of immune system against HBV by Interferon.

### 4.5.10 Prevention:

While hepatitis B distributed throughout the world and it caused a common disease in all countries that it was a public health problem, it is need to prevent its transmission and not allowing to more distribution and infecting anymore human.
Today, there is an effective way to preventing against hepatitis B disease which is vaccine as vaccination against hepatitis B virus ,the vaccine of hepatitis B is the main way to prevention from HBV. (Brooks et al., 2013; WHO 2019)

#### 4.5.10.1 Vaccination as prevention way:

World health organization (WHO) recommends hepatitis B vaccination as main part in childhood vaccination programs throughout world. Current days there is third generation of vaccine against hepatitis B virus, first of them could be purify non-infectious particles of HBsAg from plasma in 1980, second generation was recombinant vaccine small surface protein of HBsAg derived from yeast in 1989, in third generation vaccine middle and large surface protein for the vaccine developed from mammalian Chinese Hamster Ovary cells (CHO), third generation is more effective and stronger than previous vaccine generations.( Brooks et al., 2013; Levinson, 2012; Achord et al., 2002; Güler, 2016; Kurugöl et al., 2009; World Health Organization, 2015; Schumann, 2014; Cardell, 2009)

The vaccination schedule (standard recommendation regime) is: (3) three doses through intramuscular injection at 0, 1 and 6 months.
After completing those doses, should be test for HBsAg antibody (anti-HBs) level in body, 10 mIU/ml or greater than, is protective. (Güler, 2016; World Health Organization, 2015; Cardell, 2009; WHO 2019) Response for the HB vaccine in children better than adults. (Cardell, 2009) Also vaccine reduced hepatoma in them. (Levinson, 2012)

### 4.5.11 Special groups with high risk: (World Health Organization, 2015; WHO 2019; Brooks et al., 2013; World Health Organization, 2017)

In terms of prevalence, special groups differ from others, they are with high risk to infection, and they are these groups below.

- Health care workers (HCWs)
- Prisoners
- Blood donor

• Persons who inject drugs (PWID)
• Indigent people
• Migrant persons
• Homosexual men
• New born infants from infected mother.
• Co-infected persons (HBV/HIV, HBV/HCV and HBV/HDV). (World Health Organization, 2017)

### 4.5.12 Epidemiology:

Prevalence defined by the rate of occurrence of new infection in a population in a period of time, HBV infection had spread worldwide, deaths caused by HBV infection is in high rate with globally deaths caused by tuberculosis, AIDS and malaria. According to published reports of World Health Organization (WHO) in 2015 and 2017, globally (2) billion people have HBV infection, past and present infection (World Health Organization, 2015), from this amount infection (257) million of them are living with chronic hepatitis B that equal to %3.5 of the human population, then (240) million infected person are chronic carries for hepatitis B surface antigen (HBsAg) while about (2.7) million from (36.7) million of infected people with HIV are infected as co-infection with HBV. May (65) million women can potentially during childbearing age period transmit their HBV to their babies.

Annually is estimated (650 000) die from complication of chronic HBV that accounted for %45 of Hepatocellular carcinoma (HCC) and %30 for cirrhosis.

Also, HBV infection causes an economic burden for general and individuals infected, it accounted for %5-10 of liver transplants.(World Health Organization, 2017/World Health Organization, 2015) most of the burden HBV infection comes from those infections that acquired before (5) years old which most of them are chronic (CHB) and asymptomatic, figure (4.5.12.A) shows that burden.

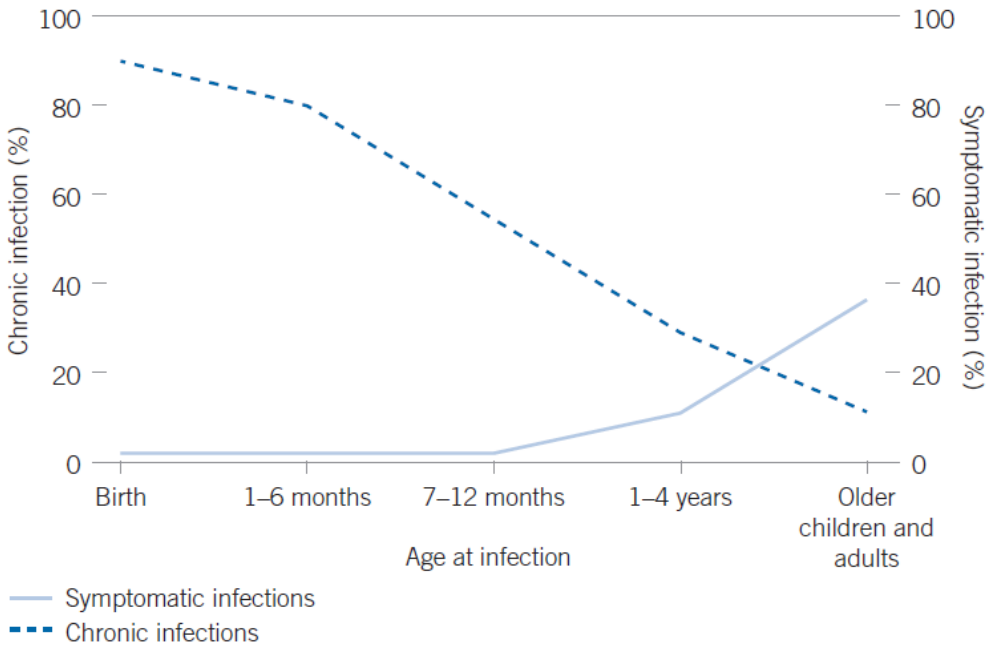


**Figure (4.5.12.A):** Most of Hepatitis B Infections before five years old are chronic Hepatitis B (CHB) with asymptomatic while with infection with the virus in older age is reverse. Figure belonged (WHO 2015)

Prevalence of HBsAg showed in Table (4.5.12), (257) million people in the world which equals %3.5 of human population are living with the HBV, while Western Pacific region (region of WHO) has the highest prevalence in the world that it has (115) million HBV infection, European region has (15) million HBV infection and Eastern Mediterranean region includes 21 million infection.

| | Estimates of the prevalence of HBV infection (%) | | | Estimated number of persons living with HBV (millions) | | |
|---|---|---|---|---|---|---|
| | | Uncertainty interval (95%) | | | Uncertainty interval (95%) | |
| WHO region | Best | Lower | Higher | Best | Lower | Higher |
| African Region | 6.1 | 4.6 | 8.5 | 60 | 45 | 84 |
| Region of the Americas | 0.7 | 0.4 | 1.6 | 7[a] | 4 | 16 |
| Eastern Mediterranean Region | 3.3 | 2.6 | 4.3 | 21 | 17 | 28 |
| European Region | 1.6 | 1.2 | 2.6 | 15 | 11 | 23 |
| South-East Asia Region | 2.0 | 1.5 | 4.0 | 39 | 29 | 77 |
| Western Pacific Region | 6.2 | 5.1 | 7.6 | 115 | 93 | 140 |
| Total | 3.5 | 2.7 | 5.0 | 257 | 199 | 368 |

*Source:* WHO, work conducted by the London School of Hygiene & Tropical Medicine (LSHTM). *See* Annex 2.

**Table (4.5.12):** Prevalence of 3.5% persons from general population who living with Hepatitis B (HBsAg), there is highest prevalence rate in Western Pacific Region then in African Region (according WHO regions), 115 million, and 60 million, respectively. Table belongs (WHO 2015)

There is three rates for estimating endemicity of the HBsAg prevalence around world, they are low, intermediate and high in general population, seroprevalence of (<2%) referred to low endemicity seroprevalence of Hepatitis B Virus, range from (2-7%) referred to intermediate incidence of the HBV, while (2-4%) refer to low intermediate and (5-7%) is high intermediate, also; (≥8%) referred to high endemicity seroprevalence of the virus.

Ages specific prevalence of HBsAg varies in world, figure (4.5.12.B) shows age specific prevalence for children from 5 to 9 years old, depending on geographical countries, there is the highest prevalence in sub-Saharan Africa in children and less than %2 is seen in central Latin America.

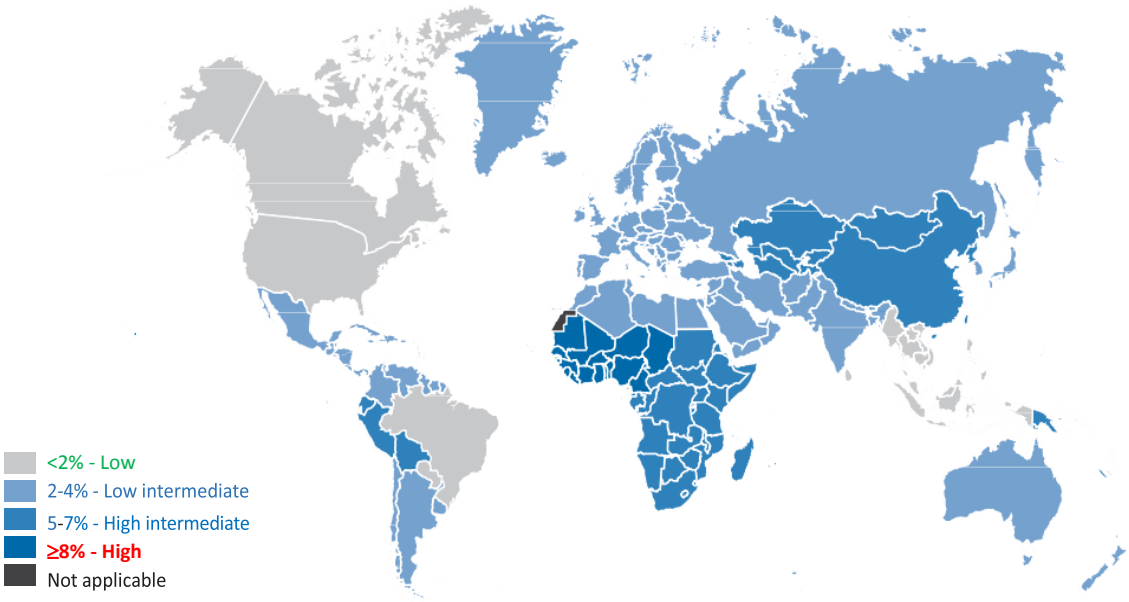


**Figure (4.5.12.B):** Prevalence of HBsAg in world for children from 5 to 9 years old. There is high prevalence of the virus in west of Africa and East of Asia, while in Canada and America is in low endemicity, low-intermediate is appear in Middle-East. Figure belonged (WHO 2015)

Prevalence of HBsAg in world for adults is differ from children, figure (4.5.12.C) in Canada, North America, Central Latin America, Western Europe, Hepatitis B Disease is in low endemicity, they have less than 2% from general population. There is low-intermediate (2-4%) endemicity prevalence of the virus in Russia, Middle-East countries, north of Africa and Australia. Highest prevalence of Hepatitis B Virus (≥8%) occurs in Western Africa countries.

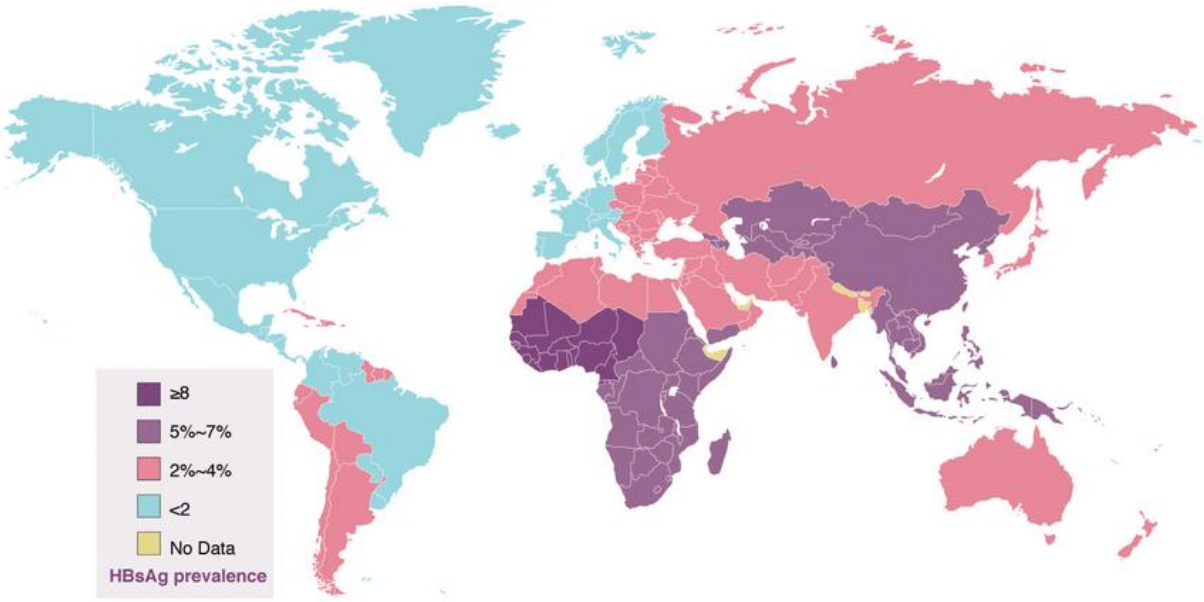


**Figure (4.5.12.C):** Prevalence of HBsAg in world for adults is differ from children. Middle East countries are in low endemicity of Hepatitis B Virus incidence. The figure belonged (Centers for Diseases Control and Prevention, CDC 2010)

Genotypes of Hepatitis B Virus randomly diffused throughout our planet, prevalence of HBV around the world according its (8) genotypes presented in figure (4.5.12.D), dominant genotype of HBV in Europe is type (D) ,also studies showed in Northern Cyprus dominant genotype is (D) (Arıkan et al., 2016; SUMER et al., 2019), while in Asia genotype B and C are dominant.

Eight Genotypes of Hepatitis B Virus dominantly distributed around world like as these:

HBV Genotypes A with D are dominant in Europe, Africa with India,
HBV Genotypes B with C are dominantly appeared in Asia
HBV Genotype E in West Africa
HBV Genotype F dominantly appeared South and Central of United Stated of America
HBV Genotype G is appeared in Germany with France and of United Stated of America
HBV genotype of H is dominant in Central America

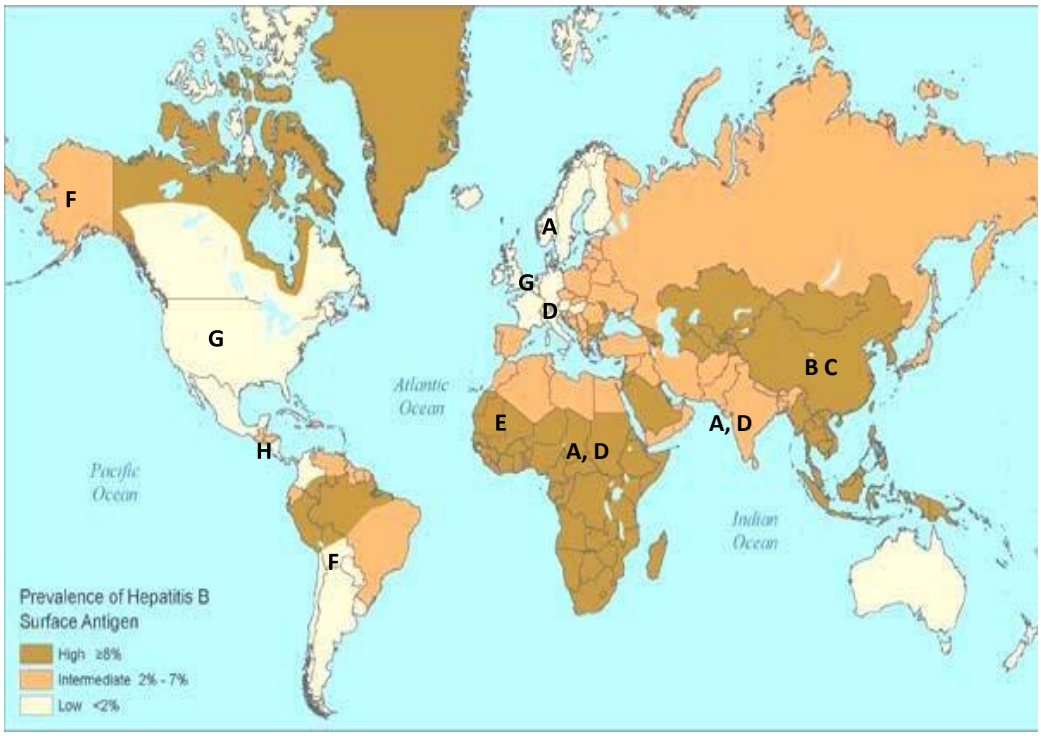


**Figure (4.5.12.D):** prevalence of HBV around the world according eight genotypes of the virus. Dominant genotype in north of Cyprus is genotype D. The figure belongs (Centers for Diseases Control and Prevention, CDC, 2009)

# 5. Material and methods

## 5.1. Population:

This present study was conducted in Near East University Hospital (NEUH) in Lefkosa /Nicosia capital city of Turkish Republic Northern Cyprus (TRNC). Samples was collected from all patients who came to the Hospital in purpose to test, screen and monitoring themselves. Subjects were Civilian Cypriots, Turkish people who live in the Cyprus Island, Blood donors, military persons (Soldiers), Travelers or Tourists, Foreign people who came for work or education purpose in the island. Sampling period was two years from January of 2017 until December of 2018.
Tests done for all of subjects from Medical Microbiology Laboratory in Near East University Hospital (NEUH) during couple of years 2017-2018. All subjects collected from record unit system of NEUH with their age, sex, information.

## 5.2. Serological tests:

All serum samples were tested for marker HBV surface antigen (HBsAg) by using Chemiluminescence immunoassays (CEIA) (Architect i1000 SR, Abbott, USA) according to the manufacture, the cut off test values were accepted (Sample/Cut Off) 1≤ as positive**.**

## 5.3. Statically analysis:

Analyzing data was performed by using software program of Statistical Package for the Social Science (SPSS), version of 18.0 (SPSS Inc., Chicago, IL, USA).

# 6. Results

In this recent study, totally, overall (23,977) persons regardless with their different situation were rolled in this research. In Microbiology Laboratory of NEUH were tested for Hepatitis B surface Antigen (HBsAg) for those all (23,977) persons. HBsAg sero tests had positive result for (314) patients/persons from all, also, negative result for (23,663) patients/persons from all, (1.3%) positive and (98.7%) negative. Table (6.1) describes those results.

| Test Results | Frequency | Percent |
|---|---|---|
| Negative | 23663 | 98.7 |
| Positive | 314 | 1.3 |
| Total | 23977 | 100.0 |

**Table (6.1):** Contains (314) positive results and (23663) negative results from (23,977) subjects, which positive results were 1.3% and negative results were 98.7%.

In terms of Gender, (15,341) of subjects were male (64.0%) and (8636) of subjects were female, it means (36.0%) all of them. Table (6.2) shows Gender groups with their results. In our result for our study, there was not relationship between gender and prevalence of HBsAg result statically, also P value was (P: 0.485).

| | Male | Female | Total |
|---|---|---|---|
| Count | 15341 | 8636 | 23977 |
| Expected Count | 15341.0 | 8636.0 | 23977.0 |
| % within Test Result | 64.0% | 36.0% | 100.0% |
| % within Gender | 100.0% | 100.0% | 100.0% |

**Table (6.2):** Results of the males and females in our study, 64.0% of them were male that equaled (15341), 36.0% of them were female that equaled (8636), statically there was no significant association between our results with gender of subjects.

In terms of Age, ages of persons who rolled in our research starts from less than one year old (from 0 ) to (99) years old, while the mean age was 31.34 and standard deviation was 15.631. Table (6.3)
Most of persons were young in (19 - 40) years old, they were (17,289) persons 72.1%, then adult (41 - 65) ages which they were (3,680) persons 15.3% all of them, and ages from (0 - 18) years old, they were (1,636) which included 6.8% of our research. Table (6.4)

| | All Subjects | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 23977 | 0 | 99 | 31.34 | 15.631 |
| Valid No. | 23977 | | | | |

**Table (6.3):** General age table, age of persons who rolled in our research includes minimum age less than one year to maximum age (99) years old, with mean age of 31,34 ±15,631.

| | 0-18 | 19-40 | 41-65 | >65 | Total |
|---|---|---|---|---|---|
| Frequency | 1,636 | 17,289 | 3,680 | 1,372 | 23,977 |
| Percent % | 6.8 | 72.1 | 15.3 | 5.7 | 100.0 |

**Table (6.4):** General age groups table, highest number of our subjects were included young, which they were 72.1% from all of them, then adults which included 15.3% and children from less than one year to 18 years old, which equaled to 6.8 of all of them.

From (23663) negative results, minimum value was (0.00) and maximum value was (0.99), while mean value was (0.39 ± 0.14). For positive results from (314) results minimum value started from (1.01) until maximum value (6659.38) while mean value was (2165.13 ± 1753.67). Table 6.5.

| | All Subjects | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Negative Value | 23663 | 0.00 | 0.99 | 0.39 | 0.14 |
| Positive Value | 314 | 1.01 | 6659.38 | 2165.13 | 1753.67 |

**Table (6.5):** Minimum and Maximum Value table, for negative results minimum and maximum values were (0.00 – 0. 99) and for positive results minimum and maximum values were (1.01 – 6659.38) in the research.

Samples derived from different departments of the Hospital (NEUH Departments), from 22 departments had been tested for Hepatitis B Virus (HBsAg) in NEUH Microbiology Laboratory, Table (6.6). Highest number of testing had done to Infection Department which included (13751) tests that equaled 57.3% in percentage and (2451) tests to Blood Bank by 10.2% then Gynecology (1795) tests that was 7.5% in percentage. Table (6.6) contains all departments and their HBsAg tests which done to them.

In our research from (23977) samples, we had (314) HBsAg seropositive results, from that number (195) of them were male that equals 1.2% from all males and (119) of them were female that included 1.3% from all females. Table (6.7) displays positive genders with their numbers.
Usually as other studies which done worldwide, in our study, females had lower number of infection with Hepatitis B Virus comparing with males, too,(Ott et al., 2012) they were (37.9%) seropositive HBsAg rate while males were (62.1%) seropositive of HBsAg.

| NEUH Departments | Frequency | Percent |
|---|---|---|
| Blood bank | 2451 | 10.2 |
| Brain surgeon | 193 | 0.8 |
| Cardiology | 1639 | 6.8 |
| Check-up | 1229 | 5.1 |
| Chest Diseases and Allergy | 44 | 0.2 |
| Child Health and Diseases | 21 | 0.1 |
| Dermatology | 93 | 0.4 |
| Dialysis | 97 | 0.4 |
| Emergency | 94 | 0.4 |
| ENT | 403 | 1.7 |
| Eye diseases | 28 | 0.1 |
| Gastroenterology | 42 | 0.2 |
| General Surgery | 406 | 1.7 |
| Gynecology | 1795 | 7.5 |
| Infection | 13751 | 57.3 |
| Internal medicine | 456 | 1.9 |
| Laboratory | 276 | 1.2 |
| Neurology | 17 | 0.1 |
| Oncology | 19 | 0.1 |
| Orthopedics and Traumatology | 412 | 1.7 |
| Plastic surgery | 215 | 0.9 |
| Urology | 299 | 1.2 |
| Total | 23980 | 100.0 |

**Table (6.6):** 22 departments had been tested for Hepatitis B Virus (HBsAg) in NEUH Microbiology Laboratory, highest number of testing had done to Infection Department which included (13751) test and (2451) test to Blood Bank then Gynecology (1795) test.

| Gender | Frequency | Percent |
|---|---|---|
| Male | 195 | 1.2 |
| Female | 119 | 1.3 |
| Total | 314 | |

**Table (6.7):** Positive males and females in results of our research, (195) of them were males who infected with Hepatitis B Virus and (119) of them were females who infected with Hepatitis B Virus.

In relation to ages, our (314) HBsAg seropositive persons were with various ages from (0) minimum age to maximum age that was (94) years old. Mean age for our positive subjects was 34.92 ±16.592 (0-94). Table (6.8) contains age statistics. For positive results, most of persons were young in (19 - 40) years old, they were (207) persons, then adult (41 - 65) ages which they were (75) persons and older persons which their ages more than 65 years old, they were (17) which included in our research. Table (6.9) clears that.
In our result for our study, there was relationship between age and prevalence of Hepatitis B surface Ag result statically, also P value was (P: 0.000).

| | All Subjects | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 314 | 0 | 94 | 34.92 | 16.592 |
| Valid No. | 314 | | | | |

**Table (6.8):** Positive age table, age of infected persons with Hepatitis B Virus in our research includes minimum age less than one year to maximum age (94) years old, with mean age of 34.92 ±16.592.

| | 0 -18 | 19 - 40 | 41- 65 | > 65 | Total |
|---|---|---|---|---|---|
| Frequency | 15 | 207 | 75 | 17 | 314 |
| Percent for age groups | 0.91 | 1.19 | 2.03 | 1.23 | |

**Table (6.9):** Positive age groups table, highest number of our subjects were included young, which they were 207 persons, then adults which included 75 persons and older persons from more than 65 years old, which equaled to 17 persons. In our positive result, there was relationship between age and prevalence of Hepatitis B surface Ag result statically, P value was (P: 0.000).

Departments of NEUH based on HBsAg seropositive results were Infection Department was first department in highest number for HBsAg test positivity that was (168), 53.50% positive result then Internal Medicine Department (27) samples 8.60% and then Cardiology department (26) tests were positive 8.28%. Among (23) departments in the hospital only (18) of them included positive results for HBsAg. Table (6.10) contains all 18 departments and their frequency for positive results from 314 positive results in this research.

| NEUH Departments | Frequency | Percent for positive results |
|---|---|---|
| Blood Bank | 11 | 3.5 |
| Brain Surgeon | 5 | 1.59 |
| Cardiology | 26 | 8.2 |
| Check-up | 16 | 5.0 |
| Chest Diseases and Allergy | 1 | 0.3 |
| Child Health and Diseases | 2 | 0.6 |
| Emergency | 3 | 0.9 |
| ENT | 3 | 0.9 |
| Gastroenterology | 7 | 2.22 |
| General Surgery | 5 | 1.59 |
| Gynecology | 19 | 6.05 |
| Infection | 168 | 53.50 |
| Internal Medicine | 27 | 8.60 |
| Laboratory | 11 | 3.50 |
| Neurology | 1 | 0.3 |
| Orthopedics and Traumatology | 2 | 0.6 |
| Plastic Surgery | 3 | 0.9 |
| Urology | 4 | 1.27 |
| Total | 314 | 100.0 |

**Table (6.10):** NEUH Departments based on HBsAg seropositive results were (18) departments, first department in highest number for HBsAg test positivity that had (168) positive result was Infection Department, 53.50% of positive results then Internal Medicine Department (27) positive result after both Cardiology department (26) tests were positive result from 314 positive results in this study.

# 7. Discussion

Causing high morbidity and mortality by Hepatitis B Virus (HBV) around whole countries in World and had been a serious Public Health Problem (Dahab et al., 2019) also Economic Problem, prevalence and distribution of Hepatitis B surface Antigen (HBsAg) is a ring that calls for challenging against it and stopping the virus. Annually HBsAg threats from more than (650000) persons to die who chronically infected with the virus. (World Health Organization, 2015)

Hepatitis B Virus low endemicity less than (2%) is seen in countries and regions of Canada, North America, Central Latin America, Western Europe and North Europe countries.

Russia, Eastern Europe countries, Middle-east region, North of Africa, Australia, Argentina and New Zealand are in low-intermediate (2-4%) endemicity prevalence of the virus.

(5-7%) high intermediate prevalence of HBV is seen in East Asia, Sub Saharan Africa and China.

Highest prevalence of Hepatitis B Virus (≥8%) occurs in Western Africa countries.

While North Cyprus geographical located in Middle-East region, surrounded by low endemicity or low-intermediate endemicity countries for seroprevalence of HBsAg such as in Turkey in 2005 one research done for (506) persons that (269) 51.4% of them were male and (237) that equals to 43.2% of them were female, out of them, there was (201) HBsAg positive. Rate of the prevalence was 7.0%. (Mehmet et al., 2005) But in 2007 tested for (39,002) persons with mean age 34 (20-60) which males were (22401) 58% and females were 42% (16,601), in that research incidence of (HBV) decreased for (2.55%) (Dilek et al., 2007) while with more researches decreasing rates more than more appeared, in a study which done during (6) years for (80,454) persons with 41 (18-64) mean age at 2013, that 73,133 (90%) of them were male and 7321 of them (9.1%) were female. Only (1054) were positive that revealed prevalence rate in Turkey is in low endemicity. (Uzun et al., 2013)

In Greece studies show prevalence of HBsAg is in low-intermediate endemicity that is 2.1% in 1997-1998 in general population and 3.0% at 2013 in People Who Inject Drugs (PWIDs).(Hahné et al., 2013; Falla et al., 2018)

In Syria, there is no recent study but in a review at 2016, shows prevalence rate in Syria is in low endemicity that it is 1.1%. (Bashour et al., 2016) Also in same year a study done for syrian refugees in Kurdistan Region camps, border of Syria for (880) syrian refugees with mean age of (24), 34 person of them were HBsAg positive and the rate was 3.8%, it means low-intermediate endemicity of HBsAg. (Hussein et al., 2016)

In Lebanon in three studies which done at 2016 and 2018 revealed HBsAg prevalence is in low endemicity (2016\1.6%, 2016\1.74%, 2018\1.2%). (Rached et al., 2016; Rached et al., 2016; Abou Rached et al., 2019) In Palestine studies show prevalence of HBsAg is in low-intermediate endemicity (3.8%) (Al Zabadi et al., 2015), in Israel is same like in Palestine (3.5%).(Loebstein et al., 2008) In Egypt studies tell us HBsAg incidence is in low endemicity (2011\1.4%, 2013\1.6%, 2017\1.4%). (Wasfi et al., 201; Mortada et al., 2013; Ismail et al., 2017)

In Iran there is (1,347) million person in general population that is (1.79%) which is low endemicity in 2017. (Hajarizadeh et al., 2017) From Iraq, researches revealed in 2018 incidence of HBsAg in Kurdistan Region was in low endemicity rate that was (1.14%) (Hussein, 2018) while in South of Iraq was in low intermediate endemicity, in (69915) persons in a study, seropositive rate was 2.3% at 2016, (Al-Rubaye et al., 2016) this rate decreased from previous studies which showed 6.2% HBV seropositivity during 2007 and 2008.(Ali, 2009)

In Saudi Arabia, seroprevalence is 1.6%, studies show Saudi Arabia is in low endemicity. (Abdullah, 2018) Libya is in low intermediate endemicity of Hepatitis B Virus when tested for (65,761) Libyan people, the prevalence rate was 2.2% in 2013 and 2018. (Ismail et al., 2018; Elzouki et al., 2013)

In our research, out of (23,977) samples we had/got (314) seropositive HBsAg in North of Cyprus, which this result equal to (1.3%) of HBsAg seroprevalence in Northern Cyprus during couple of years (2017 - 2018).
This result shows, globally HBsAg in North of Cyprus is in low endemicity which less than 2%. Also, prevalence of the HBsAg in North of Cyprus is less than countries that surrounded it geographically.

## 7.1. Comparing our result with previous results in Northern Cyprus:

In 2006, in a research, tested for (17,545) persons for prevalence of Hepatitis B Virus among them in Northern Cyprus which the study included (13,546) males and (3999) females with 34.5 ± 10.3 mean age. The result for HBsAg rate was 2.46% HBsAg positive. (Altindis et al., 2006)

In 2009, in a research, for (585) blood samples from Turkish population who they are living in Northern Cyprus tested, for determining HBsAg prevalence among/in them. Males in the study included (275) and (310) females. The result for HBsAg prevalence was 0.85%. (Kurugöl et al., 2009)

In 2012, in another research that done for (1500) blood donors in NEUH for evaluation HBsAg in Northern Cyprus, (1296) of subjects were males and (204) of them were females with mean age was 28 years. The result for HBsAg prevalence was 0.6%. (Süer et al., 2012)

In 2014, in a research tested for seropositivity of HBsAg within (16372) persons, the result for prevalence of HBsAg was 1.4%. (233) persons were HBsAg positive from (16372) samples. (Güler et al., 2014) in NEUH, North Cyprus.

In 2015, in another research, tested for (13892) serum for HBV molecular epidemiology and distribution of HBsAg dominant genome in North Cyprus, in NEUH, North Cyprus. The result for HBsAg positivity was 1.1%. (Arıkan et al., 2016)

In 2017, in another research that done for prevalence of HBsAg in North of Cyprus, tested for (25442) persons in NEUH, North of Cyprus, (17529) of them were male and (7913) of them were female, with mean age 34.32 ± 14.24. The rate result for HBsAg was 1.35% seropositive. (Güler et al., 2018)

In 2019, in a research, tested for (140) patients for HBsAg seroprevalence evaluating in hemodialysis patients of NEUH in Northern Cyprus, (85) of them were male and (55) of them were female. The result for HBsAg prevalence was 0.7%. (Güvenir et al., 2019)

Now, in recent research after working on (23977) samples from NEUH, Northern Cyprus, we found (314) HBsAg positive out of total samples that equals to 1.3%. Appending on this rate that we got it in our research comparing with previous researches during previous years, this result shows us/tell us that prevalence of Hepatitis B Virus in Northern Cyprus during couple of years decreased from 2.46% in 2006 to 1.3% at now, fortunately.

## 8. Conclusion

In our research we are thinking low endemicity of Hepatitis B Virus (HBsAg) in Turkish Republic Northern Cyprus (TRNC) may because of:

- There is high rate and widespread Hepatitis B Vaccination Programs in the Island.

- Knowledge, aware and conscious of Cyprus community to monitoring, screening, vaccination and controlling the HBV in their life.

- Performing all series/doses of Hepatitis B Vaccine for children by parents for their child.

As in result we got, persons 19 years old to 40 years old were highest age group in our research who they were HBsAg positive then adults and then older persons (more than 65 years old) means children were lowest group of population in Cyprus to seropositive of HBsAg. This is due to implementation of Hepatitis B Vaccine by Government to all newborn and child in Northern Cyprus.
Public Hepatitis B Vaccination Programs in north of Cyprus is implementing by government since 1995, before that time, individually could be inject the vaccine in the island, because of this high HBsAg infection appear in adults.

# 9. Recommendations

Through this research, we are recommending for:

- Increasing testing, monitoring and screening for Hepatitis B disease, in purpose of early diagnosing the virus in body and early controlling the disease if noticed.
- Enhancement of Hepatitis B Vaccination for all persons who living in Cyprus, Cypriots and Foreign nationals people.
- Increasing education knowledge about the virus, the disease, routes of transmission and infecting human.

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## 11. Curriculum vitae


# Wrya Raouf Mahmud

Nicosia .TRNC Turkish Republic of Northern Cyprus
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Email: wria.236666@gmail.com Postal Code: 1010


### Education Information

- B.Sc. at Medical Microbiology (2011-2015)

Medical Microbiology Dep. Faculty of Science and Health. School of Health. Koya University – Koya city/ Erbil/ Kurdistan Region - F.R. IRAQ

- Seventh ranks from the department.
- Knowledge in the following fields (Medical Bacteriology, Medical Parasitology, Medical Virology, Microbial Physiology, Hematology, Biochemistry, Immunology, Microbial Pathogenicity and Antimicrobial agents, Pharmaceutical, Genetics, Molecular Biology, Biostatistics, Bioinformatics, Vaccination and Epidemiology).
- Graduation project about (ISOLATION OF ANTIBIOTIC PRODUCING STREPTOMYCES FROM DECAYED PLANT MATERIALS).

### Personal Quality & Skills

- Flexible in hard working, multi-culture and conditions.
- Relocation in any city.
- Communication with the team workers.
- Self –motivated & Self-reliant.
- Ability of managing.

### Work Experience

- **Assistant Lecturer**

-In Sulaimani Polytechnic University – Sulaimaniyah\Iraq at Technical College of health\ Medical Laboratory Department (MLD) 1/2017 – 9/2018.

- **Lecturer**

-Halabja Technical Institute - Halabja\ Iraq at Medical Laboratory Technique (MLT) Department **2015-2016**.

- **Assistant Microbiologist**

-Evening Laboratory (Meer Laboratory) 9/2016 – 10/2018, Sulaimaniyah\Iraq.
-Evening Consultant of Hiwa Oncology and Hematology Hospital in 2016, Sulaimaniyah\Iraq.

- **Volunteer in Health sector**

-Hiwa Oncology and Hematology Hospital at 2015-2016, Sulaimaniyah\Iraq.

- **Assistant Laboratory**

-SHAHID Dr. Xalid Hospital in Koya/Erbil - Iraq 2013-2015.
-Sulaimani Teaching Surgical Hospital at 2014, Sulaimaniyah\Iraq

- **Casher**

-In a Market for (2) years in Sulaimaniyah city 2012-2013.

## Computer skill

- Microsoft office (word, excel and power point).
- Internet

## Extra Quality

- Attendance in the third International Conference in IHMSC-SPU (International Health and Medical Sciences Conference - Sulaimani Polytechnic University) on July 2019 in Sulaimaniyah\Iraq.
- Conference Paper in the Second International Conference in IHMSC-SPU (International Health and Medical Sciences Conference - Sulaimani Polytechnic University) on July 2018 in Sulaimaniyah\Iraq.
- Participating in the first International Conference in IHMSC-SPU (International Health and Medical Sciences Conference - Sulaimani Polytechnic University) on August 2017 in Sulaimaniyah\Iraq.
- Attendance in the third International Conference in ICNSB (International Conference of Natural Sciences on Biotechnology - Charmo University) on May 2018 in Sulaimaniyah\Iraq.
- Certificate in English Language course (Elementary) during March-May 2018 in Sulaimaniyah by UPP Org.
- Certificate in COMIX on April 2018 in Sulaimaniyah by UPP Org.
- Certificate in Personal Strategic Planning by IAPTLD (International Academy of Personal Training and Leadership Development) in Erbil - Iraq at April of 2013.

## Languages

- Conversational English language.
- Conversational Arabic.
- Beginner at Turkish.
- Kurdish (native language).

## Hobbies & Interests

- Learning, research on Science, writing, traveling …etc.

## Thesis Plagiarism Report:

prevelance of hepatitis B surface antigen in northern cyprus years 2017-2018

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