A research paper submitted to the Department of Pharmacy, East West University in conformity with the requirements for the degree of Bachelor of Pharmacy

Submitted by

Monjurul Islam

ID: 2013-1-70-016

Department of Pharmacy

East West University



Dedicated to my parents, my sister, my respected teachers and my friends, for their love and support...

# **Declaration by the Research Candidate**

I, Monjurul Islam, hereby declare that the dissertation entitled "A Study on Knowledge and Awareness about Hepatitis B among the School and College going students of Dhaka City" submitted by me to the Department of Pharmacy, East West University, in the partial fulfilment of the requirement for the award of the degree Bachelor of Pharmacy is a complete record of original research work carried out by me during 2017, under the supervision and guidance of Nishat Nasrin, Assistant Professor, Department of Pharmacy, East West University. The formed the basis for the thesis has not award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

Monjurul Islam ID: 2013-1-70-016 Department of Pharmacy East West University, Dhaka.

# **Certificate by the Supervisor**

This is to certify that the thesis entitled "A Survey on Knowledge and Awareness about Hepatitis B among the School and College going students of Dhaka City" submitted to the Department of Pharmacy, East West University, in the partial fulfilment of the requirement for the degree of Bachelor of pharmacy was carried out by Monjurul Islam, ID: 2013-1-70-016 in 2017, under the supervision and guidance of me. The thesis has not formed the basis for the award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

Nishat Nasrin

**Assistant Professor & Supervisor** 

**Department of Pharmacy,** 

East West University, Dhaka

# **Endorsement by the Chairperson**

This is to certify that the thesis submitted to the Department of Pharmacy, East West University, Dhaka-1212, in partial fulfilment of the requirement for the Degree of Bachelor in Pharmacy, was carried out by **Monjurul Islam, ID: 2013-1-70-016**.

Dr. Chowdhury Faiz Hossain Professor & Chairperson Department of Pharmacy East West University, Dhaka

# Acknowledgement

Firstly, all admires to **Almighty Allah** who has given me patience and capability as a gift to complete this project. I would like to give thanks to my family for their moral and financial support and for their unconditional inspiration.

I am very much willing to express my sincere indebtedness to my honorable supervisor, **Nishat Nasrin**, Assistant Professor, Department of Pharmacy, East West University for her expert supervision, constructive criticism, valuable advice, optimistic counseling, constant support & continuous backup and encouragement throughout every phase of the project as well as to prepare this dissertation.

I would also like to put forward my most sincere regards and profound gratitude to **Dr. Chowdhury Faiz Hossain,** Professor and Chairperson, Department of Pharmacy, East West University, for giving me the opportunity to conduct such an interesting project and for facilitating a smooth conduction of my study.

I would like to acknowledge that this dissertation has only been possible through the remarkable support of my friends **Sayyed Md. Jubair & Nusrat Yasmin** who helped me instantaneously when I needed the most while working on this research paper.

And at the end, I would like to thank my family for their endless inspiration, support and care during my research work.

# **Table of Contents**

Serial No.	Name of the content	Page No.
	List of Figures	Ι
	List of Abbreviations	II
	Abstract	III
	Chapter One: Introduction	1-22
1.1	Overview	1
1.2	Types of Infection	1
1.2.1	Acute Infection	1-2
1.2.2	Chronic Hepatitis B	2-3
1.2.3	Latent Hepatitis B	3-4
1.3	Extr5ahepatic Manifestation of Hepatitis B	4-5
1.4	Virology	6-8
1.5	Etiology	8-9
1.6	Transmission	10
1.6.1	Perinatal Transmission	10
1.6.2	Sexual Transmission	10-11
1.6.3	Parenteral Transmission	11

1.6.4	Mother to Child Transmission	11
1.6.4.1	Pre-embryonic and Assisted Reproductive Therapy	12
1.6.4.2	Prenatal	12
1.6.4.3	Intrapartum	12
1.6.4.4	Breastfeeding	13
1.6.5	Healthcare Associated	13
1.6.6	Sporadic Cases	13
1.7	Sign and Symptoms	13
1.7.1	Symptoms of Acute Hepatitis B	13-14
1.7.2	Symptoms of Chronic Hepatitis B	14
1.7.3	Cirrhosis of The Liver due to Hepatitis B	14-15
1.8	Prevention and Treatment	15
1.8.1	Treatment	15
1.8.1.1	Available Treatments	16
1.8.1.2	Interferon Therapy	16
1.8.1.3	Treatment in Children	17
1.8.1.4	Pregnancy	17
1.8.1.5	Treatment of Acute HBV	17
1.8.2	Prevention	17
1.8.2.1	Vaccination	17-18
1.8.2.2	HBV Vaccination Programme	18-19

1.8.2.3	Occupational HBV Vaccination	19
1.8.2.4	Post-exposure prophylaxis	19
1.8.2.5	Prevention of Mother to child Transmission	20
1.8.2.6	Other Prevention Measures	20
1.9	Epidemiology	20
1.9.1	High-Prevalence Populations	20-21
1.9.2	Intermediate-Prevalence Populations	21
1.9.3	Low-Prevalence Populations	22

# **Chapter 2: Literature Review**

Serial No.	Name of Content	Page No.
2.1	Hepatitis B Knowledge Among Iranian Adolescents: A National Survey	23
2.2	A survey of knowledge about Hepatitis B among new military recruits in China	23
2.3	Hepatitis B Awareness Among Medical Students and Their vaccination Status at Syrian Private University	24
2.4	Hepatitis B Awareness and knowledge in Asian Communities in British Columbia	24-25
2.5	Awareness and Opinions about Hepatitis B among Secondary School Teachers in Irepodun Local Government Area of Kwara State, Nigeria	25
2.6	Hepatitis B Virus Infections Among Children and Adolescents	25-26

	in Germany: Migration Background as a Risk Factor in a Low Seroprevalence Population	
2.7	Hepatitis B Awareness, Testing, and knowledge among Vietnamese American men and women	26-27
	Significance of Study	28-29
	Aims and Objective of study	30

# **Chapter 3: Methodology**

Serial No.	Name of Contents	Page No.
3.1	Type of the Study	31
3.2	Study Area	31
3.3	Study Population	31
3.4	Study Period	31
3.5	Questionnaire Development	31-32
3.6	Sampling Technique	32
3.7	Data Analysis	32

# Chapter 4: Results

Serial No.	Name of Contents	Page No.
4.1	Gender Distribution of Students	33
4.2	Age Distribution of Students	33
4.3	Class Distribution of Students	34
4.4	Group distribution of the student	34
4.5	Knowledge about Hepatitis B	35
4.6	Source of Information	35
4.7.1	Knowledge about the body part affected by the Hepatitis B	35
4.7.2	Knowledge about the body part affected by the Hepatitis B	36
4.8	Knowledge About the virus of Hepatitis B	36
4.9	Knowledge about Treatment of Hepatitis B	37
4.10	Knowledge about Vaccine Availability	37
4.11	Knowledge About vaccine	38
4.12	Knowledge about the family member or friends have Hepatitis B	38
4.13	Knowledge about Mode of	39
	Transmission	
4.14	Misconception about Mode of Transmission of Hepatitis B	40
4.15	Knowledge of Control and Prevention of Hepatitis B	41

# **Chapter 5: Discussion & Conclusion**

Serial No.	Name of contents	Page No.
5.1	Discussion	43-44
5.2	Conclusion	45

Chapter 6: References46-48

# List of Figures

Serial No.	Name of Figures	Page No.
4.1	Gender Distribution of Students	33
4.2	Age Distribution of Students	33
4.3	Class Distribution of Students	34
4.4	Group distribution of the student	34
4.6	Source of Information	35
4.7.1	Knowledge about the body part affected by the Hepatitis B	35
4.7.2	Knowledge about the body part affected by the Hepatitis B	36
4.8	Knowledge About the virus of Hepatitis B	36
4.9	Knowledge about Treatment of Hepatitis B	37
4.10	Knowledge about Vaccine Availability	37
4.11	Knowledge About vaccine	38
4.12	Knowledge about the family member or friends have	38
	Hepatitis B	
4.13	Knowledge about Mode of Transmission	39
4.14	Misconception about Mode of Transmission of Hepatitis B	40
4.15	Knowledge of Control and Prevention of Hepatitis B	41
4.16	Attitude towards Hepatitis B Infected Person	42

# List of Abbreviations

HBV	Hepatitis B Virus
FHF	Fulminant Hepatic Failure
ALT	Alanine Aminotransferase
ORF	Open Reading Frames
DR	Direct Repeat
GRE	Glucocorticoid-responsive Element
STD	Sexually Transmitted Disease
MTCT	Mother to Child Transmission
PEP	Post-exposure Prophylaxis
HLA	Human Leukocyte Antigen

#### Abstract

Hepatitis B is a potentially life-threatening liver infection caused by the Hepatitis B virus (HBV). It is a major global health problem. It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer. In Bangladesh Hepatitis B is one of the biggest threat due to lack of knowledge and awareness about it. The aim of the study was to assess the knowledge and awareness about Hepatitis B among the school and college going students in Bangladesh. A total of 203 subjects aged between 13 to 19 years' age, who were students of different schools and colleges participated in the study representing the adolescent of the nation. They responded to a structured questionnaire where all the respondents have heard about Hepatitis B. According to 51.23% of the respondents, Hepatitis B can be transmitted through blood transfusion. About 41.87% informed that Hepatitis B can be transmitted by breast feeding. Majority of them have little knowledge or misconception about the mode of transmission like eating and drinking from same plates or glasses of patient (21.67%) and kissing or talking (19.70%). From this study we found 72.90% respondents thought that proper knowledge and education is the most effective way to control and prevent Hepatitis B. About 59.11% respondents thought another most effect way to prevent Hepatitis B is blood test before marriage. From this study we found that 67% students would behave positively to the Hepatitis B patient if he/she will be one the student or teacher of their educational institute. Another 66.50% respondents said they will continue their relationship with Hepatitis B infected person. Since this study was conducted in only 9 schools and colleges in the Dhaka city, that cannot reflect the overall view of the whole country, further research work should be carried out with more number of schools and colleges across the country. It is also important to increase the level of knowledge and awareness about Hepatitis B; so that misconceptions don't arise among the school and college going students.

**Key Words:** Hepatitis B, School & College, Student, Knowledge, Awareness, Mode of Transmission, Prevention, Attitude, Dhaka.

# Chapter 1 Introduction

# **1.1 Overview**

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem. It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer.

A vaccine against hepatitis B has been available since 1982. The vaccine is 95% effective in preventing infection and the development of chronic disease and liver cancer due to hepatitis B. Hepatitis B is a viral infection of the liver. Along with other hepatitis types (such as hepatitis C and hepatitis E), hepatitis B is caused by transmission (spread) of the virus through blood and body fluids. Some persons infected with hepatitis B develop a chronic infection, become carriers, and are then able to pass on the infection to others. All individuals with hepatitis B are at higher risk of developing liver cancer and cirrhosis of the liver. Hepatitis B affects more than 300 million individuals worldwide and is a serious health problem in many industrialized nations and developing countries. Most people who have chronic hepatitis B were infected at birth or in early childhood.

Hepatitis B virus may be directly cytopathic to hepatocytes. However, immune system mediated cytotoxicity plays a predominant role in causing liver damage. The immune assault is driven by human leukocyte antigen (HLA) class I–restricted CD8 cytotoxic T lymphocytes that recognize hepatitis B core antigen (HBcAg) and hepatitis B e antigen (HBeAg) on the cell membranes of infected hepatocytes (Torpy, Burke and Golub, 2011).

# **1.2 Types of Infection**

# **1.2.1 Acute infection**

The incubation period of HBV infection is 40-150 days (average, approximately 12 weeks). As with acute HAV infection, the clinical illness associated with acute HBV infection may range from mild disease to a disease as severe as FHF (<1% of patients). After acute hepatitis resolves, 95% of adult patients and 5-10% of infected infants ultimately develop antibodies against hepatitis B surface antigen (HBsAg) that is, anti-HBs clear HBsAg (and HBV virions), and fully recover. About 5% of adult patients, 90% of infected infants, and 30-50% of children infected at age 1-5 years develop chronic infection.

Some patients, particularly individuals who are infected as neonates or as young children, have elevated serum levels of HBV DNA and a positive blood test for the presence of HBeAg but have normal alanine aminotransferase (ALT) levels and show minimal histologic evidence of liver damage. These individuals are in the so-called "immune-tolerant phase" of disease. Years later, some but not all of these individuals may enter the "immune-active phase" of disease, in which the HBV DNA may remain elevated as the liver experiences active inflammation and fibrosis. An elevated ALT level is also noted during this period. Typically, the immune-active phase ends with the loss of HBeAg and the development of antibodies to HBeAg (anti-HBe).

Individuals who seroconvert from an HBeAg-positive state to an HBeAg-negative state may enter the "inactive carrier state" (previously known as the "healthy carrier state"). Such individuals are asymptomatic, have normal liver chemistry test results, and have normal or minimally abnormal liver biopsy results. Blood test evidence of HBV replication should be nonexistent or minimal, with a serum HBV DNA level in the range of 0 to 2000 IU/mL.

Inactive carriers remain infectious to others through parenteral or sexual transmission. Inactive carriers may ultimately develop anti-HBs and clear the virus. However, some inactive carriers develop chronic hepatitis, as determined by liver chemistry results, liver biopsy findings, and HBV DNA levels. Inactive carriers remain at risk for hepatocellular carcinoma (HCC), although the risk is low. At this point, no effective antiviral therapies are available for patients in an inactive carrier state.

Other patients who seroconvert may enter the "reactivation phase" of disease. These individuals remain HBeAg-negative but have serum HBV DNA levels higher than 2000 IU/mL and show evidence of active liver inflammation. These patients are said to have HBeAg-negative chronic hepatitis (Samji, 2017).

# **1.2.2 Chronic Hepatitis B**

Chronic hepatitis B is usually diagnosed as a result of a workup for abnormal liver function tests or as a result of screening patients at risk for HBV infection. Many patients with chronic hepatitis B have no symptoms or have nonspecific symptoms such as fatigue or right upper quadrant discomfort.

Acute exacerbations due to HBV e-antigen seroreversion (ie, in which e antigen reappears) occasionally occur in patients with chronic hepatitis B. Most of these exacerbations are asymptomatic, but occasionally an acute hepatitis-like clinical picture with detectable IgMantibody against the core antigen occurs, leading to misdiagnosis of acute HBV infection in patients not previously known to have chronic HBV infection.

In late cases, signs of cirrhosis such as jaundice, ascites, splenomegaly, pedal edema, encephalopathy, or variceal bleeding can be present.

Hepatocellular carcinoma should be suspected in cirrhotic patients with new-onset right upper quadrant pain, rapidly developing ascites, a palpable liver mass, or hepatic encephalopathy. Other nonspecific features of hepatocellular carcinoma include watery diarrhea, hypoglycemia, and certain cutaneous manifestations such as acanthosisnigricans and the Leser-Trelat sign (multiple pruritic seborrheickeratoses of sudden onset).

In chronic hepatitis B, liver enzyme levels can be normal, even in patients with well compensated cirrhosis. ALT levels may range from normal to five times higher than normal. Thrombocytopenia, hypoalbuminemia, direct hyperbilirubinemia, and prolonged prothrombin time suggest cirrhosis.

Findings of chronic hepatitis B on liver biopsy range from minimal inflammation to cirrhosis. The most characteristic histologic feature of chronic HBV infection is the "ground-glass hepatocyte," which is due to intracellular accumulation of HBV surface antigen (Elgouhari, Abu-Rajab Tamimi and Carey, 2008).

# 1.2.3 Latent Hepatitis B

Other atypical HBV infections include seronegative occult or latent HBV infections. This heterogeneous group consists of patients who are HBsAg-negative who are either seronegative for all HBV markers or positive for anti-HBc and/or anti-HBs. Many of these patients are positive for HBV DNA by polymerase chain reaction either in the liver or serum or both. Some of these patients have underlying liver disease, suggestive of ongoing hepatocellular injury from persistent HBV infection. Studies in animal models have demonstrated long-term persistence of viral genomes in the serum and/or liver of animals that have biochemical and serologic evidence of viral clearance

and recovery from infection. The important question is whether this observation represents ongoing viral replication and therefore clinically significant infection in terms of liver disease and transmission. Existing evidence supports the notion that it indeed indicates low-level viral replication, capable of transmission. Studies in liver transplantation revealed transmission of HBV

infection to recipients if the donors carried the anti-HBcmarker. In addition, reactivation of HBV infection in patients with serologic evidence of recovery undergoing immunosuppression or

Chemotherapy has been reported. These observations, together with the immunologic studies described above, provide compelling evidence that one may not be able to completely eliminate HBV infection. Patients with serologic evidence of recovery probably have low-level viral replication that is effectively controlled by an active immune response. The possibility that these occult infections are caused by HBV mutants has been proposed. Although mutations have been reported in various regions of the viral genome, definitive evidence in support of a pathogenic role of these mutants is lacking. Furthermore, whether liver disease can indeed result from these occult HBV infections is controversial. At present, there are no convincing studies in support of a causal relationship. Therefore, these occult HBV infections, other than the special situations described above, may not be clinically important (Liang, 2009).

# **1.3 Extrahepatic Manifestation of Hepatitis B**

Extrahepatic manifestations of hepatitis B are present in 1–10% of HBV-infected patients and include serum-sickness–like syndrome, acute necrotizing vasculitis (polyarteritisnodosa), membranous glomerulonephritis, and popular acrodermatitis of childhood (Gianotti-Crosti syndrome). Although the pathogenesis of these disorders is unclear, immune complex–mediated injury related to high level of HBV antigenemia is thought to be the cause.

The serum-sickness like syndrome occurs in the setting of acute hepatitis B, often preceding the onset of jaundice. The clinical features are fever, skin rash, and poly-arteritis. The symptoms often subside shortly after the onset of jaundice, but can persist throughout the duration of acute hepatitis B. The course of this syndrome often parallels the duration and level of HBV viremia: rapid clearance of the virus leads to rapid resolution of the illness. This disorder resembles experimental

serum sickness, in which immune complexes activate the complement pathways leading to complement-mediated injury. Patients with this syndrome have low complement levels and high-level circulating immune complexes containing HBV antigens and complement components.

About 30%–50% of patients with acute necrotizing vacuities (polyarteritisnodosa) are HBV carriers. This entity is more commonly seen in patients with recent exposure to HBV. Immunemediated vascular injury can involve large, medium, and small vessels. Early clinical features are marked constitutional symptoms, high fever, anemia, and leukocytosis.

Multisystem involvement is common, including arthritis, renal disease (proteinuria and hematuria), heart disease (pericarditis and congestive heart failure), hypertension, gastrointestinal disease (acute abdominal pain and bleeding), skin involvement (vasculitis lesions), and neurological disorders (mono-neuritis multiplex and central nervous system abnormalities). The disease is highly variable and has a mortality rate of 30% within 5 years if not treated.

HBV-associated nephropathy has been described in adults but is more common in children. Membranous glomerulonephritis is the most common form. Liver disease may be mild or absent in many of these patients. This disorder is frequently observed in countries with high prevalence of HBV infection. About 30%–60% of children with this disorder experience spontaneous remission, especially with HBeAg seroconversion. However, about 30% of adults with this condition can progress to renal failure with as many as 10% requiring dialysis or renal transplant.

Popular acrodermatitis (Gianotti-Crosti syndrome) is a distinct skin manifestation of acute HBV infection in childhood. Skin lesions are maculopapular, erythematous, and non-pruritic, and involve the face and extremities. The syndrome lasts about 15–20 days and can either precede or follow the onset of jaundice in acute hepatitis B. Generalized lymphadenopathy and hepatomegaly have been described.

Other immune-mediated hematological disorders, such as essential mixed cryoglobulinemia and aplastic anemia have been described as part of the extrahepatic manifestations of HBV infection, but their association is not as well-defined; therefore, they probably should not be considered etiologically linked to HBV (Han, 2004)

# **1.4 Virology**

The hepatitis B virus (HBV) is a small DNA virus with unusual features similar to retroviruses. It is a prototype virus of the *Hepadnaviridae* family. Related viruses are found in woodchucks, ground squirrels, tree squirrels, Peking ducks, and herons. Based on sequence comparison, HBV is classified into eight genotypes, A to H. Each genotype has a distinct geographic distribution. Three types of viral particles are visualized in infectious serum by electron microscopy. Two of the viral particles are smaller spherical structures with a diameter of 20 nm and filaments of variable lengths with a width of 22 nm.

The spheres and filaments are composed of hepatitis B surface antigen (HBsAg) and host-derived lipids without viral nucleic acids and are therefore noninfectious. The infectious HBV virion (Dane particle) has a spherical, double-shelled structure 42 nm in diameter, consisting of a lipid envelope containing HBsAg that surrounds an inner nucleocapsid composed of hepatitis B core antigen (HBcAg) complexed with virally encoded polymerase and the viral DNA genome. The genome of HBV is a partially double-stranded circular DNA of about 3.2 kilobase (kb) pairs. The viral polymerase is covalently attached to the 5' end of the minus strand. The viral genome encodes four overlapping open reading frames (ORFs: S, C, P, and X). The S ORF encodes the viral surface envelope proteins, the HBsAg, and can be structurally and functionally divided into the pre-S1, pre-S2, and S regions. The core or C gene has the precore and core regions. Multiple in-frame translation initiation codons are a feature of the S and C genes, which give rise to related but functionally distinct proteins. The CORF encodes either the viral neucleocapsidHBcAg or hepatitis B e antigen (HBeAg) depending on whether translation is initiated from the core or precore regions, respectively. The core protein has the intrinsic property to self-assemble into a capsid-like structure and contains a highly basic cluster of amino acids at its C-terminus with RNAbinding activity. Therefore, ORF codes for a signal peptide that directs the translation product to the endoplasmic reticulum, where the protein is further processed to form the secreted HBeAg. The function of HBeAg remains largely undefined, although it has been implicated as an immune tolerogen, whose function is to promote persistent infection. The polymerase (pol) is a large protein (about 800 amino acids) encoded by the PORF and is functionally divided into three domains: the terminal protein domain, which is involved in encapsidation and initiation of minusstrand synthesis; the reverse transcriptase (RT) domain, which catalyzes genome synthesis; and

the ribonuclease H domain, which degrades pre-genomic RNA and facilitates replication. The HBV *X* ORF encodes a 16.5-kd protein (HBxAg) with multiple functions, including signal transduction, transcriptional activation, DNA repair, and inhibition of protein degradation. The mechanism of this activity and the biologic function of HBxAg in the viral life-cycle remain largely unknown. However, it is well established that HBxAg is necessary for productive HBV infection in vivo and may contribute to the oncogenic potential of HBV. Other functionally important elements within the HBV genome include two direct repeats (DR1 and DR2) in the 5' ends of the plus strand, which are required for strand-specific DNA synthesis during replication. Two enhancer elements, designated as En1 and En2, confer liver-specific expression of viral gene products. A glucocorticoid-responsive element (GRE) sequence within the S domain, apolyadenylation signal within the core gene, and a posttranscriptional regulatory element overlapping En1 and part of HBxAg ORF have also been described.

The HBV replication pathway has been studied in great detail and is summarized in. The initial phase of HBV infection involves the attachment of mature virions to host cell membranes, likely involving the pre-S domain of the surface protein. Various cellular factors have been proposed to be the viral receptors, but only carboxypeptidase D has been shown to play an essential role in viral entry for the duck HBV. Mechanisms of viral disassembly and intracellular transport of the viral genome into the nucleus are not well understood and probably involve modification of the nucleocapsid core protein. After entry of the viral genome into the nucleus, the single-stranded gap region in the viral genome is repaired by the viral pol protein, and the viral DNA is circularized to the covalently closed circular (cccDNA) form. This form of HBV DNA serves as the template for transcription of several species of genomic and sub-genomic RNAs and is the stable component of the replication cycle that is relatively resistant to antiviral action and immune clearance. The transcripts from the cccDNA are unspliced, polyadenylated, and possess a 5' cap structure. The 3.5-kb genomic transcripts consist of two species with different 5' ends: the pre-genomic and the pre-core RNAs. The pre-genomic RNA (pgRNA) serves as the template for reverse transcription and the messenger RNA for core and polymerase; the pre-core RNA directs the translation of the pre-core gene product. The polymerase translation is initiated at the pol start codon of the pgRNA, probably as a result of a ribosomal scanning mechanism. The large HBsAg (L-HBsAg) protein is translated from the 2.4-kb sub-genomic RNA, the middle (M-HBsAg) and small HBsAg (S-

HBsAg) proteins from the various forms of 2.1-kb RNAs, and the HBxAg protein from the 0.7-kb RNA.

The S-HBsAg is the major *S* gene product and the L and M proteins are the minor species. Each surface protein has a glycosylation site in the S domain. Additional modifications of the L and M proteins occur at the pre-S2 domain with an N-linked oligosaccharide and a myristic acid at the amino-terminal glycine residue of the pre-S1 domain. The distribution of the three envelope glycoproteins varies among the types of viral particles, with little or no L and M protein in the 20-nm particles but relatively more L protein in the Dane particles.

Replication of HBV begins with encapsidation of the genome. The packaging signal is a *cis*-acting element referred to as epsilon, which contains a stem-loop structure. The terminal protein of the pol interacts with the epsilon and in concert with the core protein forms the nucleocapsid. After encapsidation, the pol mediates the reverse transcription of the pgRNA to minus-strand DNA and subsequent positive-strand synthesis. The circular form of the DNA is completed through several complicated steps of strand transfer. The nucleocapsid then interacts with the envelope proteins in the endoplasmic reticulum to assemble into mature virions, which are then secreted into the extracellular milieu (Liang, 2009).

# **1.5 Etiology**

HBV, a member of the Hepadnaviridae family, is a 3.2-kb partially doubled-stranded DNA virus. The positive strand is incomplete. The complete negative strand has four overlapping genes, as follows:

- Gene S codes for hepatitis B surface antigen (HBsAg), a viral surface polypeptide
- Gene *C* codes for hepatitis B core antigen (HBcAg), the nucleocapsid protein; it also codes for hepatitis B e antigen (HBeAg), whose function is unknown
- Gene *P* codes for a DNA polymerase that has reverse transcriptase activity
- Gene *X* codes for the X protein that has transcription-regulating activity

The viral core particle consists of a nucleocapsid, HBcAg, which surrounds HBV DNA, and DNA polymerase. The nucleocapsid is coated with HBsAg. The intact HBV virion is known as the Dane particle. Dane particles and spheres and tubules containing only HBsAg are found in the blood of

infected patients. In contrast, HBcAg is not detected in the circulation. It can be identified by immune histochemical staining of infected liver tissue.

HBV is known to have eight genotypic variants (genotypes A-H). Although preliminary studies suggest that particular HBV genotypes may predict the virus's response to therapy or may be associated with more aggressive disease, it would be premature to incorporate HBV genotype testing into clinical practice on a routine basis.

HBV is readily detected in serum, and it is seen at very low levels in semen, vaginal mucus, saliva, and tears. The virus is not detected in urine, stool, or sweat.

HBV can survive storage at  $-20^{\circ}$ C and heating at  $60^{\circ}$ C for 4 hours. It is inactivated by heating at  $100^{\circ}$ C for 10 minutes or by washing with sodium hypochlorite (bleach).

The major reservoir of HBV in the United States consists of the 850,000 to 2.2 million people with chronic HBV infection. In this group, those with HBeAg in their serum tend to have higher viral titers and thus greater infectivity.

HBV is transmitted both parenterally and sexually, most often by mucous membrane exposure or percutaneous exposure to infectious body fluids. Saliva, serum, and semen all have been determined to be infectious. Percutaneous exposures leading to the transmission of HBV include transfusion of blood or blood products, injection drug use with shared needles, hemodialysis, and needlesticks (or other wounds caused by sharp implements) in healthcare workers.

Globally and in the United States, perinatal transmission is one of the major modes of HBV transmission. The greatest risk of perinatal transmission occurs in infants of HBeAg-positive women. By age 6 months, these children have a 70-90% risk of infection, and of those who become infected, about 90% will go on to develop chronic infection with HBV.

For infants born to HBeAg-negative women, the risk of infection is approximately 10-40%, with a chronic infection rate of 40-70%. Even if transmission does not occur in the perinatal period, these children are still at significant risk for the development of infection during early childhood. Groups at high risk for HBV infection include intravenous (IV) drug users, persons born in endemic areas, and men who have sex with men. Others at risk include healthcare workers exposed to infected blood or bodily fluids, recipients of multiple blood transfusions, patients undergoing hemodialysis, heterosexual persons with multiple partners or a history of sexually transmitted disease, institutionalized persons (e.g., prisoners), and household contacts or sexual partners of HBV carriers (Samji, 2017).

# **1.6 Transmission**

The hepatitis B virus can survive outside the body for at least 7 days. During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. The incubation period of the hepatitis B virus is 75 days on average, but can vary from 30 to 180 days. The virus may be detected within 30 to 60 days after infection and can persist and develop into chronic hepatitis B.

In highly endemic areas, hepatitis B is most commonly spread from mother to child at birth (perinatal transmission), or through horizontal transmission (exposure to infected blood), especially from an infected child to an uninfected child during the first 5 years of life. The development of chronic infection is very common in infants infected from their mothers or before the age of 5 years.

Hepatitis B is also spread by percutaneous or mucosal exposure to infected blood and various body fluids, as well as through saliva, menstrual, vaginal, and seminal fluids. Sexual transmission of hepatitis B may occur, particularly in unvaccinated men who have sex with men and heterosexual persons with multiple sex partners or contact with sex workers. Infection in adulthood leads to chronic hepatitis in less than 5% of cases. Transmission of the virus may also occur through the reuse of needles and syringes either in health-care settings or among persons who inject drugs. In addition, infection can occur during medical, surgical and dental procedures, through tattooing, or through the use of razors and similar objects that are contaminated with infected blood (Samji, 2017).

# **1.6.1 Perinatal transmission**

The vast majority of HBV cases around the world result from perinatal transmission. Infection appears to occur during the intrapartum period or, rarely, in utero. Neonates infected via perinatal infection are usually asymptomatic. Although breast milk can contain HBV virions, the role of breastfeeding in transmission is unclear (Samji, 2017).

## **1.6.2 Sexual Transmission**

Sexual transmission of hepatitis B is a major source of infection in all areas of the world, especially in the low endemic areas, such as North America. Hepatitis B is considered to be a sexually

transmitted disease (STD). For a long time, homosexual men have been considered to be at the highest risk of infection due to sexual contact (70% of homosexual men were infected after 5 years of sexual activity). However, heterosexual transmission accounts for an increasing proportion of HBV infections. In heterosexuals, factors associated with increased risk of HBV infection include duration of sexual activity, number of sexual partners, history of sexual transmitted disease, and positive serology for syphilis. Sexual partners of injection drug users, prostitutes, and clients of prostitutes are at particularly high risk for infection (Hou, Liu and Gu, 2005).

# **1.6.3 Parenteral transmission**

HBV was once a common cause of post transfusion hepatitis. Screening of US blood donors for anti-HBc, beginning in the early 1970s, dramatically reduced the rate of HBV infection associated with blood transfusion. According to the National Heart, Lung and Blood Institute, the risk that a blood donation is infected with hepatitis B is 1 in 205,000.

Patients with hemophilia, those on renal dialysis, and those who have undergone organ transplantation remain at increased risk of HBV infection. IDU accounts for 20% of US cases of HBV. A history of HBV exposure is identified in approximately 50% of IDUs. The risk of acquiring HBV after a needle stick from an infected patient is estimated to be as high as 5% (Samji, 2017).

# **1.6.4 Mother to child transmission**

Approximately 90% of infants of HBsAg-positive, HBeAg-positive women and 5%–20% of infants of HBsAg-positive, HBeAg-negative women become infected without intervention. The most important risk factor for MTCT is the maternal HBV DNA level. Most MTCT infant PEP failures occur at thresholds of maternal HBV DNA levels of  $\geq 10^6$  to  $\geq 10^8$  copies/mL. When HBV is acquired during pregnancy, third-trimester infections carry the highest risk for MTCT. MTCT can occur during pregnancy or intrapartum (Nelson, Jamieson and Murphy, 2014).

# **1.6.4.1 Pre-embryonic and Assisted Reproductive Therapy**

HBV has been detected in sperm, oocytes, and embryos. Limited data suggest HBV transmission can occur in germ line cells. The risk of HBV transmission from persons with chronic HBV during assisted reproductive therapy is unknown, but transmission is theoretically possible. Storage of cryopreserved sperm and embryos in the nitrogen vapor state, sperm washing, and double-sealing cryocontainers are suggested methods for reducing the possible risk of transmission (Nelson, Jamieson and Murphy, 2014).

## 1.6.4.2 Prenatal

The rate of intrauterine transmission is unknown but considered to be low. The presence of maternal HBeAg is associated with higher HBV DNA levels, and HBeAg is the only structural HBV protein that can pass through the placenta. Some authors speculate HBeAg might establish chronic HBV infection through induction of T-cell tolerance to HBV in utero. A case-control study found significantly greater MTCT following amniocentesis (3 of 6) compared with controls (3 of 67) only when maternal HBV DNA levels were  $\geq 10^7$  copies/mL (Nelson, Jamieson and Murphy, 2014).

# 1.6.4.3 Intrapartum

MTCT during delivery is most common. Exposure occurs through micro-transfusion or hematologic leaks of mother's blood to the fetus during contractions, or through inoculation of mucosal membranes or breaks in the skin (eg, scalp electrodes). Detection of HBV DNA in cord blood might indicate MTCT, but HBV DNA detection could represent maternal-fetal transfusion during labor and delivery or contamination of cord blood samples.

Most studies find no difference in MTCT among babies delivered by operative/spontaneous vaginal delivery or caesarean section when the infants receive PEP. One study found elective caesarian section reduced MTCT rates in HBeAg-positive mothers with predelivery levels of HBV DNA  $\geq 10^{6}$  copies/mL. Caesarian section is not recommended for reducing MTCT in the US (Nelson, Jamieson and Murphy, 2014).

# **1.6.4.4 Breastfeeding**

Markers of HBV are detectable in breast milk and colostrum from HBsAg-positive women. Reported rates of HBV-infection among breastfed and non-breastfed infants are similar, although some studies did not account for maternal HBV DNA levels. A meta-analysis of studies in which the mothers did not have cracked or bleeding nipples did not identify an increase in MTCT when breastfed infants received PEP (Nelson, Jamieson and Murphy, 2014).

# **1.6.5 Healthcare associated**

Hepatitis B outbreaks have been associated with healthcare settings. Between 2008 and 2015, there were 23 outbreaks and 175 outbreak-associated cases of hepatitis B associated with healthcare settings reported in the United States. Outbreaks were reported in long-term care facilities and outpatient clinic settings. The CDC noted that these numbers likely underestimate the true incidence of healthcare-associated outbreaks because of the asymptomatic course of hepatitis B infection as well as the long incubation period. Additionally, there is no requirement to report these cases to the CDC if they have been investigated by state and local health authorities (Samji, 2017).

# **1.6.6 Sporadic cases**

In approximately 27% of cases, the cause of HBV infection is unknown. Some of these cases, in fact, may be due to sexual transmission or contact with blood (Samji, 2017).

# 1.7 Sign and symptoms

# **1.7.1 Symptoms of Acute Hepatitis B**

Acute hepatitis B is the period of illness that occurs during the first one to four months after acquiring the virus. Only 30% to 50% of adults develop significant symptoms during acute infection. Early symptoms may be non-specific, including fever, a flu-like illness, and joint pains. Symptoms of acute hepatitis may include:

- fatigue,
- loss of apatite
- nausea,
- jaundice (yellowing of the skin and eyes), and
- pain in the upper right abdomen (due to the inflamed liver).

Acute hepatitis damages the liver so badly it can no longer function. This life-threatening condition is called "fulminant hepatitis." Patients with fulminant hepatitis are at risk of developing bleeding problems and coma resulting from the failure of the liver. Patients with fulminant hepatitis should be evaluated for liver transplantation (Nettleman and El Mortada, 2017).

# 1.7.2 Symptoms of chronic Hepatitis B

The liver is a vital organ that has many functions. These include a role in the immune system, production of clotting factors, producing bile for **digestion**; storing nutrients including sugars, fats and minerals for use by the body later; processing medications; and breaking down toxic substances. Patients with chronic hepatitis B develop symptoms in proportion to the degree of abnormalities in these functions. The signs and symptoms of chronic hepatitis B vary widely depending on the severity of the liver damage. They range from few and relatively mild signs and symptoms to signs and symptoms of severe liver **disease** (cirrhosis or liver failure).

Most individuals with chronic hepatitis B remain symptom free for many years or decades. During this time, the patient's liver function blood tests usually are normal or only mildly abnormal. Some patients may deteriorate and develop inflammation or symptoms, putting them at risk for developing cirrhosis (Aspinall et al., 2011).

## 1.7.3 Cirrhosis of the liver due to hepatitis B

Inflammation from chronic hepatitis B can progress to cirrhosis (severe scarring) of the liver. Significant amounts of scarring and cirrhosis lead to liver dysfunction.

Symptoms may include:

- weakness,
- fatigue,
- loss of appetite,
- weightloss,
- breast enlargement in men,
- a rash on the palms,
- difficulty with blood clotting, and
- spider-like blood vessels on the skin.

Decreased absorption of vitamins A and D can cause impaired vision at night and thinning of bones (osteoporosis). Patients with liver cirrhosis also are at risk of infections because the liver plays an important role in the immune system (Aspinall et al., 2011).

# **1.8 Prevention and Treatment**

## **1.8.1 Treatment**

The goal of treatment is clearance of HBV DNA (and, if possible, clearance of HBeAg and HBsAg) to prevent the development of cirrhosis, liver failure and HCC [23]. Long-term treatment is often required, although some individuals maintain a low or undetectable HBV DNA level >6 months after stopping treatment, which is classed as a 'sustained virological response' (SVR). Complete eradication of HBV infection does not occur, due to the persistence of HBV DNA within the nuclei of host hepatocytes.

Treatment should be considered for patients in either the HBeAg-positive CHB or the HBeAgnegative CHB phases and those with cirrhosis, irrespective of eAg status. Treatment is not indicated for individuals in the immune tolerant phase, where liver damage has not yet occurred. The phase of infection or extent of liver damage may be difficult to assess, in which case a liver biopsy can be helpful. Patients and clinicians are often keen to avoid liver biopsy, and new noninvasive tests, including serum markers and transient elastography (fibroscanning), may avoid the need for biopsy in the future (Aspinall et al., 2011).

# **1.8.1.1** Available treatments

There are currently seven drugs available for the treatment of CHB:

- Five nucleostide analogues (NUCs) (lamivudine, adefovir, entecavir, tenofovir and telbivudine)
- Two interferon-based therapies (conventional interferon and pegylated interferon alpha)

NUCs suppress viral replication by inhibiting HBV viral polymerase, whereas interferon therapy works by enhancing the host immune response. The two main treatment strategies are finite therapy with interferon or NUC therapy (for those who maintain an SVR off treatment), or long-term therapy with one or more NUCs, for those with cirrhosis or who do not maintain an SVR.

Treatment native patients. However, some experts recommend the use of *de novo* combination therapy in those with a high risk of viral resistance, or in patients with cirrhosis, for whom the development of resistance may have life-threatening consequences (Aspinall et al., 2011).

# **1.8.1.2 Interferon therapy**

The advantages of interferon therapy are the absence of viral resistance, the finite course of treatment (normally 48 weeks) and an increased chance of SVR and HBeAg and HBsAg clearance compared with those taking NUC therapy. Long-term studies have demonstrated that interferon treatment is associated with a significant reduction in the risk of cirrhosis and HCC, even in those who fail to clear HBeAg. However, interferon has a poor side-effect profile (including persistent flu-like symptoms and psychiatric complications) compared with NUC therapy, requires subcutaneous injection and is not recommended for patients with decompensated cirrhosis. The use of interferon is therefore restricted to patients who are most likely to benefit; in particular, younger patients who have more potential years in which to develop complications from their CHB and thus have more to gain from achieving an SVR (Aspinall et al., 2011).

# **1.8.1.3 Treatment in children**

Treatment should be considered as soon as there is evidence of the immune reactive phase, regardless of the patient's age. Interferon therapy, lamivudine and adefovir are approved for use in children, but the newer antivirals (tenofovir and entecavir) have not yet been fully evaluated in younger children and are only recommended for individuals >15 years of age (Aspinall et al., 2011).

# 1.8.1.4 Pregnancy

Treatment in women of childbearing age should take into account the likelihood of spontaneous reversion, the anticipated duration of treatment and the immediacy of pregnancy plans. Treatment of pregnant women with antivirals is sometimes considered, but interferon therapy is contraindicated in pregnancy. The most recent EASL guidelines suggest testing the viral load in eAg-positive mothers and considering the use of antivirals in the mother in the third trimester to reduce the viral load and vertical transmission. HBV infected women should be monitored closely after delivery as exacerbations of CHB may occur (Aspinall et al., 2011).

# 1.8.1.5 Treatment of acute HBV

Most cases of acute HBV can be managed with supportive treatment, although there is some evidence that NUC therapy can improve prognosis in patients with severe or fulminant infection (Aspinall et al., 2011).

# **1.8.2 Prevention**

# **1.8.2.1 Vaccination**

Safe and effective hepatitis B vaccines containing inactivated HBsAg have been available since the early 1980s. The first vaccines were plasma derived; however, these have been replaced over

the years by vaccines manufactured in yeast or mammalian cells using recombinant DNA technology. In general, the vaccine is administered using a three-dose schedule. Vaccine efficacy (defined as anti-HBs concentration of  $\geq 10$  mIU/ml) is greatest in infants, children and young adults with protective antibody levels achieved in ~95% of those vaccinated. After the age of 40 years, the proportion of persons who have a protective antibody response following vaccination declines to <90% and to ~75% in those vaccinated over the age of 60 years. Other factors associated with a reduced response to vaccination include immunosuppression, liver disease, renal failure, smoking and obesity. Protection conferred by hepatitis B vaccination has been shown to be long lasting, with the risk of HBV infection significantly reduced even when anti-HBs concentrations decline to  $\leq 10$  mIU/ml over time (Aspinall et al., 2011).

## **1.8.2.2 HBV Vaccination programme**

In 1992, the WHO recommended that all countries should introduce universal HBV vaccination into their routine immunization programmes. The impact of universal infant HBV vaccination has been reported in a variety of countries and settings. In general, studies in high endemicity areas have shown a decline in the prevalence of CHB infections in children to <2%, and a reduction in the incidence of HCC in children and young adults has also been reported in some South East Asian countries where universal infant vaccination programmes have been in operation for up to 20 years. In the USA, the number of newly acquired HBV infections has declined substantially since the introduction of a national immunization strategy which includes the universal vaccination of infants beginning at birth and the identification and vaccination of adults at increased risk of infection. Between 1990 and 2007, the annual incidence of HBV infection in the USA declined by >80% overall, and by 98% in children <15 years old. In Europe, studies in Italy and Bulgaria have demonstrated a dramatic decline in the incidence of acute HBV infections and the prevalence of CHB following the introduction of universal HBV vaccination programmes.

As of 2008, 177 of 193 WHO member states (92%) had integrated HBV vaccination into their national infant vaccination schedules. In Europe, 22 of 29 EU/EEA countries have implemented a universal infant or adolescent HBV vaccination programmes. The remaining seven countries,

including the UK, have adopted a selective vaccination programme targeting at-risk groups based on the local epidemiology of HBV infection (Aspinall et al., 2011).

# **1.8.2.3 Occupational HBV vaccination**

Vaccination and post-vaccination testing of response is recommended for individuals at occupational risk of exposure to HBV. In the UK, vaccination is recommended for the following occupational groups.

- Health care workers (HCWs)
- Laboratory workers
- Staff of residential and other accommodation for those with learning difficulties.
- Other occupational groups at increased risk, e.g. morticians, embalmers and prison service staff.

Similar recommendations for occupational HBV vaccination have been made elsewhere (Aspinall et al., 2011).

# **1.8.2.4 Post-exposure prophylaxis**

Post-exposure prophylaxis (PEP) with HBV vaccination alone or a combination of HBV vaccination and passive immunisation with HBV immunoglobulin (HBIG) has been shown to be highly effective in preventing HBV transmission following exposure to infected blood or body fluids, e.g. via contaminated sharps injury, sexual contact or perinatal exposure. In order to maximize efficacy, PEP should be initiated as soon as possible following exposure. The choice of PEP and dose regimen will depend on the timing and nature of the exposure, the vaccination status of the exposed person and the HBsAg status of the source (Aspinall et al., 2011).

# 1.8.2.5 Prevention of mother to child transmission

PEP, initiated at birth, is recommended for all infants of HBV infected mothers. PEP using a combination of HBIG and an accelerated course of HBV vaccine has been shown to be effective in preventing perinatal HBV transmission in ~90% of cases. Many countries, including the USA and the UK, have introduced routine antenatal screening of all pregnant women to identify HBsAgpositive mothers and maximize opportunities to prevent mother to child transmission of HBV infection (Aspinall et al., 2011).

#### **1.8.2.6 Other prevention measures**

In addition to vaccination, the risk of HBV transmission can be reduced through other prevention measures including: routine testing of blood, organ and tissue donors, screening of blood and blood products, harm reduction advice and provision of needle exchange programmes for injecting drug users and condom use to reduce the risk of sexual transmission (Aspinall et al., 2011).

# 1.9 Epidemiology

The epidemiology of hepatitis B can be described in terms of the prevalence of hepatitis B surface antigen (HBsAg) in a population, broadly classified into high- (>8% HBsAg prevalence), intermediate- (2%–7%) and low-prevalence (<2%) areas. These broad categories are useful for understanding the predominant patterns of transmission and outcomes for infection, as well as the relative population burden of the consequences of chronic hepatitis B, including liver cancer (MacLachlan and Benjamin C., 2017).

# **1.9.1 High-Prevalence Populations**

In countries where chronic HBV infection affects more than 8% of the population, the majority of these individuals were infected at birth or in early childhood, when the risk of progression to chronicity is high. High-HBV prevalence is common in much of the Asia Pacific and sub-Saharan African regions of the world. Globally, it has been estimated that 45% of the world's population

Page | 20

lives in an area of high prevalence. There is evidence to suggest that vertical transmission is more common in Asia than in Africa, where a greater proportion of women are highly infectious at childbearing age, relating in part to predominant HBV genotypes that influence the likelihood of HBeAg positivity and high levels of HBV DNA during peak childbearing ages.

The potential impact of infant vaccination against HBV is obviously greatest in high-prevalence populations. In such populations where universal infant vaccination was implemented early, not only has HBsAg dropped profoundly, but there is some evidence for significant reductions in liver cancer incidence among age cohorts eligible for free vaccine. In China, the prevalence of HBsAg fell from 9.7% to 1.0% in children aged less than 5 years, preventing an estimated 16 to 20 million cases of chronic hepatitis B. In other settings, such as the Gambia Hepatitis Intervention Study, the protective efficacy of infant vaccination in preventing chronic HBV infection was reported as  $\sim$ 95% (MacLachlan and Benjamin C., 2017).

#### **1.9.2 Intermediate-Prevalence Populations**

Regions of the world in which HBV prevalence is classified as intermediate (2%–7%) include North Africa and the Middle East, parts of Eastern and Southern Europe, parts of Latin America, and South Asia. These represent a similar proportion of the global population to high-prevalence areas (slightly more than 40%). In these regions, transmission occurs either perinatally or horizontally. Although the predominant mode of transmission varies according to country, perinatal acquisition is thought to be less common in intermediate compared with high-prevalence countries, owing to a lower prevalence of high infectivity among women of childbearing age.

As discussed above, the categorization of prevalence is subject to change with the impact of immunization and other prevention programs, and a number of countries previously categorized as high prevalence are now estimated to have a population seroprevalence below 8%. This decrease in prevalence through the impact of vaccination has also been shown in intermediate-prevalence countries in Europe (MacLachlan and Benjamin C., 2017).

#### **1.9.3 Low-Prevalence Populations**

People living in low-HBV-prevalence countries make up the minority of the global population ( $\sim$ 12%), and include Australia, Asia, Northern and Western Europe, Japan, North America, and some countries in South America.

In low-prevalence areas, the incidence of vertical and horizontal transmission in childhood is low, with most incident infections occurring in adolescence and adulthood through sexual contact, injecting drug use, and other blood-related exposures, including historically in healthcare settings.

A recent systematic review suggested that worldwide, 1.2 million people who inject drugs (PWID) are living with chronic hepatitis B (range 0.3–2.7 million), and 6.4 million have previously been exposed. Regions with a low overall prevalence of chronic hepatitis B (CHB) but a relatively high burden of PWID living with CHB include Eastern Europe (280,000; 22.8% of the global total), and North America (272,500; 22.2% of the global total). Other people at increased risk of acquiring HBV in adulthood include those who are or who have been incarcerated, men who have sex with men, sex workers, and homeless people.

Global migration from higher prevalence to lower-prevalence countries is also an important determinant of the burden of chronic hepatitis B in many countries, where the prevalence in migrants generally reflects that of their country of origin. In many otherwise low-prevalence countries, the majority of people living with chronic HBV were born overseas in endemic areas (MacLachlan and Benjamin C., 2017).

# Chapter 2 Literature Review

#### 2.1 Hepatitis B Knowledge Among Iranian Adolescents: A National Survey

Roushan et al (2013) conducted a national survey to assess Iranian adolescents' knowledge about hepatitis B (HBV) and associated factors. They conducted a questionnaire-based national survey of 18-year-old adolescents according to stratified cluster random sampling in Iran during 2007. The Response rate was 87%. Most adolescents (60%) knew that HBV infects the liver. Percentage of adolescents who gave correct answers to major routes of HBV transmission were as follows: spouse of an infected person 59%, multi-partners 66%, intravenous drug use 73%, body piercing 55% and personal belongings 55%. Higher levels of education, living in rural areas, marriage and (except for body piercing) female gender were associated with better knowledge. The knowledge of HBV infected individuals about major routes of HBV transmission was low (P < 0.001). There are important deficits in adolescents' knowledge about HBV that requires attention of health educators to tailor educational programs for specific groups.

#### 2.2 A survey of knowledge about hepatitis B among new military recruits in China

Li et al (2017) conducted a survey to assess knowledge about Hepatitis B among new military recruits in China. They conducted a questionnaire-based cross-sectional study among 800 new military recruits in China during 2017. A self-administered, structured questionnaire was used to collect information, and 727 questionnaires were returned completed. Analysis was performed using SPSS 18.0, and P < 0.05 was considered statistically significant. Results: Of the respondents, 665 (91.5%) were male and 62 (8.5%) were female. The mean age was  $18.9 \pm 1.7$  years. A total of 608 respondents (83.6%) demonstrated poor knowledge and 119 (16.4%) adequate knowledge about HBV. Older age, female and higher education level were statistically associated with a higher mean knowledge score. Multivariate logistic regression showed that age (OR = 3.040, 95%CI 1.724–5.359, P < 0.001) and gender (OR = 1.791, 95%CI 1.325–2.421, P < 0.001) were significantly associated with appropriate behavioral practices towards prevention of HBV. Against a backdrop of high HBV prevalence in China, new military recruits had poor knowledge of HBV. New recruits need better education about HBV to assist in reducing and preventing HBV infection.

#### **2.3 Hepatitis B Awareness among Medical Students and Their Vaccination Status at Syrian Private University**

Ibrahim and Idris (2014) conducted a survey to assess medical students about their awareness and vaccination status of Hepatitis B. They conducted a questionnaire-based study at Syrian Private University (SPU), Faculty of Medicine, in 2014 to assess the knowledge and awareness about hepatitis B, the status of hepatitis B vaccination, and the reasons for not getting vaccinated among the first- and the fifth-year medical students. The study demonstrated surprising results and raises issues about the high number of medical students who are not vaccinated or not sure about their vaccination status, which puts them at a higher risk of being infected in the future. Another important issue is the medical students' overall knowledge about this life-threating infection. The students have not been totally educated about the gravity of the situation which requires the need of further HBV education. It is highly recommended that SPU provides the HBV vaccine to all non-vaccinated students attending the faculty of medicine at no cost to encourage them to take the HBV vaccine and to reform some of its educational curriculum to effectively limit the hazardous effects of this disease and elaborate on the serious health consequences of HBV.

#### 2.4 Hepatitis B Awareness and Knowledge in Asian Communities in British Columbia

Yau et al (2016) conducted a survey to assess Asian Communities in British Columbia regarding awareness and knowledge about Hepatitis B. They conducted a telephone based survey of Chinese, Korean, Filipino, South Asian, and Southeast Asian populations in 2016. Multiple logistic regression analysis was performed to identify predictors of HBV knowledge. General awareness of HBV was reported in 78.8% (798/1013). HBV awareness was the highest in Chinese (89%) and Filipino (88%) populations and the lowest in the South Asian (56%) population. "Reasonable" knowledge of HBV was elicited in 76.8% (778/1013). Higher HBV knowledge was associated with younger age (p = 0.014), higher education (p < 0.0001), Chinese ethnicity (p < 0.0001), and use of media (p = 0.014) and Internet (p = 0.024) for health information. Compared to the Chinese (OR = 1.0) population, "reasonable" knowledge of HBV was lower in Korean (OR = 0.3, 95% CI: 0.1–0.5), Filipino (OR = 0.3, 95% CI: 0.2–0.6), South Asian (OR = 0.3, 95% CI: 0.2–0.4), and Southeast Asian (OR = 0.3, 95% CI: 0.1–0.6) populations. 54.8% (555/1013) felt that HBV

education was inadequate and 80.1% (811/1013) preferred HBV education in their native languages. Compared to the Chinese population, other Asian communities in BC have lower HBV awareness and knowledge. Public education should target older and less educated and Korean, Filipino, South Asian, and Southeast Asian populations in their native languages via media and Internet.

#### 2.5Awareness and Opinions about Hepatitis B among Secondary School Teachers in Irepodun Local Government Area of Kwara State, Nigeria

Eredoro, (2017) conducted a survey to assess the knowledge and opinions of secondary school teachers in Irepodun Local Government Area of Kwara State, Nigeria about Hepatitis B Virus Infection. He conducted a questionnaire-based survey on 150 teachers in Nigeria during 2017. Data on the knowledge score on facts, mode of transmission, and prevention of HBV infection for all the respondents were 4.6 out of 8, 8.7 out of 17 and 4.7 out of 8 respectively. Television (54%), radio (44%), newspaper (42%) and friends (39%) was the main sources of information on HBV infection, while least utilized source of information was internet (23%), church/ mosque (21%), tertiary institution (21%) and library/ librarian (18%). The factors militating against the teaching of Hepatitis B to students as identified were teacher's inadequate knowledge, lack of formal training, lack of teaching aids, teacher's poor motivation and HBV infection not being part of school subject's curriculum. Recommendation that hepatitis B as well as other trending health issue should be introduced into teacher educational programs and those teachers themselves should take advantage of the vast collection of information available in the interest to improve their knowledge on HBV infection and general health was given.

#### 2.6 Hepatitis B Virus Infections Among Children and Adolescents in Germany: Migration Background as a Risk Factor in a Low Seroprevalence Population

Cai et al (2011) conducted a survey to assess German children and adolescent's Status of Hepatitis B virus infection and Migration Background as a Risk Factor in a Low Seroprevalence Population. They conducted a questionnaire-based survey on Children and Adolescents in Germany during

2003 to 2006. Data on age, gender, migration background, and socioeconomic status were collected through questionnaires. A child was defined as having a 2-sided migration background if both parents, or the child and 1 parent, immigrated, and a 1-sided migration background if only 1 parent immigrated. Among children with migration background, a first-generation migrant was defined as born outside Germany; a second-generation migrant was born in Germany. Information on HB vaccination status was obtained from vaccination cards. Serologic samples from participants were tested for anti-hepatitis B core antigen (anti-HBc) and hepatitis B surface antigen. We performed weighted univariable and multivariable logistic regression analyses to assess determinants for HB infection. Of 13,065 participants (3-17 years), 0.5% (95% confidence interval [CI], 0.4–0.7) were anti-HBc positive, among whom 38.7% (95% CI, 20.0–57.5) were hepatitis B surface antigen positive. Two-sided migration background and being a first- or secondgeneration migrant were significantly associated with anti-HBc positivity (odds ratio [OR]: 8.3, 95% CI: 4.0–17.4; OR: 11.0, 95% CI: 3.5–35.0; OR: 3.0, 95% CI: 1.2–7.3). No further determinants were found. HB infection is rare among children and adolescents in Germany. Firstand second-generation migrant children can be considered to be at risk for HB infection, 2-sided migration background or being a first-generation migrant carried the greatest risk. Targeted testing for HB infection and early HB vaccination should be provided to immigrants' children.

### 2.7 Hepatitis B Awareness, Testing, and knowledge among Vietnamese American men and women

Taylor et al (2005) conducted a survey to assess Vietnamese American's awareness, testing and knowledge about Hepatitis B. They conducted a community-based, in-person survey of Vietnamese men and women was conducted in Seattle during 2002. Seven hundred and fifteen individuals (345 men and 370 women) completed the questionnaire. Eighty-one percent of the respondents had heard of hepatitis B (76% of men, 86% of women) and 67% reported HBV testing (66% of men, 68% of women). A majority of the participants knew that HBV can be transmitted during sexual intercourse (71% of men, 68% of women), by sharing toothbrushes (67% of men, 77% of women), and by sharing razors (59% of men, 67% of women). Less than one-half knew that hepatitis B is not spread by eating food prepared by an infected person (46% of men, 27% of

women), nor by coughing (39% of men, 25% of women). One-third of our respondents did not recall being tested for HBV. Important knowledge deficits about routes of hepatitis B transmission were identified. Continued efforts should be made to develop and implement hepatitis B educational campaigns for Vietnamese immigrant communities. These efforts might be tailored to male and female audiences.

#### Significance of Study

Hepatitis B is a potentially life-threatening liver infection caused by the Hepatitis B virus (HBV). It is a major global health problem. It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer. A vaccine against Hepatitis B has been available since 1982. The vaccine is 95% effective in preventing infection and the development of chronic disease and liver cancer due to hepatitis B (WHO, 2017).

According to WHO 6.2% of adult people are infected in Hepatitis B in Western Pacific Region. In Africa 6.1% adult people are infected in Hepatitis B. In the Eastern Mediterranean Region, the South-East Asia Region and the European Region, an estimated 3.3%, 2.0% and 1.6%% of the general population is infected, respectively. 0.7% of the population of the America is infected in Hepatitis B. An estimated 257 million people are living with hepatitis B virus infection in The World and In 2015, hepatitis B resulted in 887 000 deaths, mostly from complications (including cirrhosis and hepatocellular carcinoma) (WHO, 2017).

In Bangladesh, about 4-7% of the population is HBV infected, and 3.5% of pregnant women have the virus. These virus-infected persons are the potential source of infection to their neonates, members of the family and other individuals. According to the National Liver Foundation, about 60-70% of the infected individuals are not aware about the existence of HBV in their body (Chaity, 2017).

In order to prevent Hepatitis B knowledge and awareness about Hepatitis B is very important. The World Health Organization (WHO) believes that globally, this lack of awareness and poor access to diagnostic tests means 95% of the 400 million people who live with Hepatitis may not know they are infected. Along with vaccination program, Government should run awareness campaign across the country to aware people about Hepatitis B (Chaity, 2017).

To our knowledge, very few research works have been carried out to assess the level of knowledge regarding Hepatitis B among the school and college going children of our country.

Therefore, the present study was designed having the aim of assessing the level of knowledge and attitude about the disease among the adolescents.

#### Aims and Objective of the Study

The aims and objectives of this study were to:

- To assess the awareness and knowledge levels about Hepatitis B among the students of Schools and Colleges.
- To assess the attitudes of the students of School and colleges toward the Hepatitis B patients.

# Chapter 3 Methodology

#### 3.1 Type of the Study

It was a survey based study.

#### 3.2 Study Area

The survey was conducted in 9 Schools & Colleges in different areas inside Dhaka City. The Schools & Colleges were:

- 1. Shohid Buddhijibi School & College
- 2. Mirpur Bangla High School & College
- 3. Mirpur Govt. High School
- 4. Monipur High School & college
- 5. BCIC College Mirpur
- 6. Mirpur University College
- 7. Ideal School & College
- 8. Dhaka Imperial College
- 9. FM International School & College

#### **3.3 Study Population**

In this study, a total number of 203 students of different groups were surveyed with a questionnaire in order to assess the awareness and knowledge about Hepatitis B. Informed consent was obtained from the eligible participants before interviewed and participants who agreed to join the study provided the required information for the studies.

#### **3.4 Study Period**

This study was started from January 2017. During this period, we analyzed the literature and within July to October 2017 we collected data.

#### **3.5 Questionnaire Development**

The questionnaire was specially designed to collect the simple background data and the needed information. The questionnaire was written in simple English and also translated in Bengali in order to ensure it was understandable by the participants. Extra space was however, allowed after

some questions for the participants' comments; and in most cases, these were used as qualifying remarks which aided considerably in giving answers to questions and in providing additional information which assisted the interviewers in drawing up conclusions.

#### 3.6 Sampling Technique

In this study convenience sampling technique was followed.

#### **3.7 Data Analysis**

After collecting, the data were checked and analyzed with the help of Microsoft Excel 2010. The result was shown in bar, pie and column chart and calculated the percentage of the knowledge and awareness about Hepatitis B among the students.

## Chapter 4

## **Results**

#### **4.1 Gender Distribution of Students**

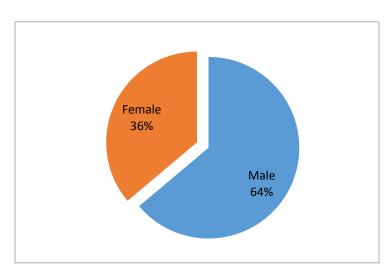
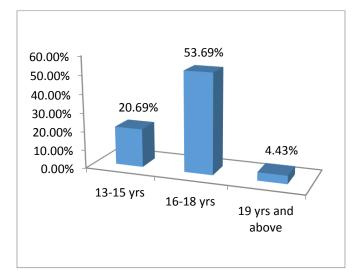


Figure 4.1: Gender Distribution of Students

In our study we found about 64% students were male and 36% were female students.



#### 4.2 Age Distribution of Students

#### Figure 4.2: Age distribution

In this survey about 53.69% students were in the age range between 16-18 years, 20.69% were in age range between 13-15 years, and 4.43% were in age range 19 years and above.

#### 4.3 Class Distribution of Students

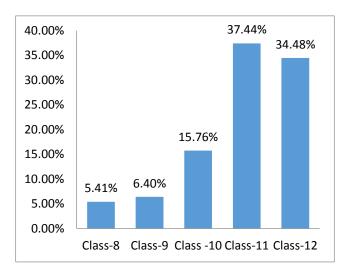
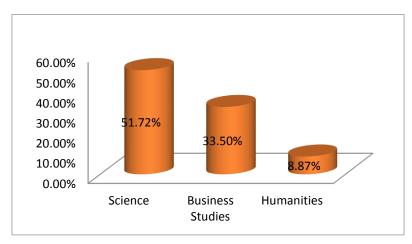


Figure 4.3: Class distribution of student

Majority of the students who studied in class-11 (37.44%) and class-12 (34.48%). Also, there were 5.41% of the students who studied in class-8, 6.40% of the students who studied in class-9 and 15.76% students who studied in class-10.



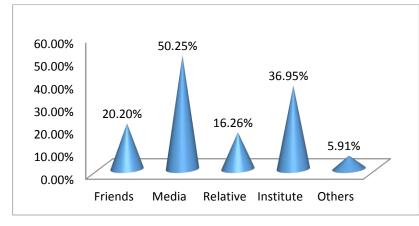
#### 4.4 Group distribution of the student

Figure 4.4: Group distribution of students

In this study, majority of the students studied in Science Group (51.72%). Also, there were 33.50% students were studied in Business Studies and 8.87% students were studied in Humanities.

#### 4.5 Knowledge about Hepatitis B

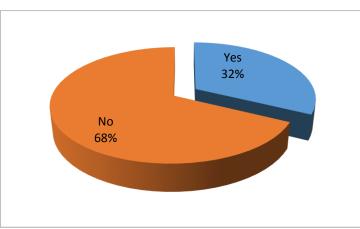
In this study all responders confirmed that they heard about Hepatitis B.



#### **4.6 Source of Information**

Figure 4.6: Source of Information

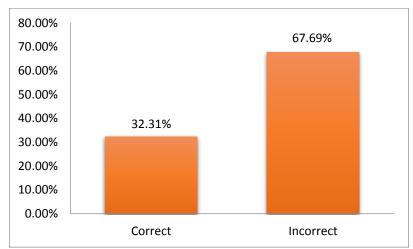
Among the study population,50.25% told that they were informed about Hepatitis B through media (TV, Radio, Newspaper), 36.95% from Educational institutes and 20.20%, 16.26% and 5.91%, students were informed from Friends, and other sources respectively.



#### 4.7.1 Knowledge about the body part affected by the Hepatitis B

Figure 4.7.1: Knowledge about the body part Affected by the disease

Majority of the students did not know which body part was affected by Hepatitis B. Only 32% students confirmed that they knew which body part was affected by Hepatitis B.



#### 4.7.2 Knowledge about the body part affected by the Hepatitis B

Figure 4.7.2: Knowledge about the body part Affected by the disease

Among the student who confirmed they knew about the body part affected by the disease, only 32.31% were correct and 67.69 % were incorrect.

#### 4.8 Knowledge About the virus of Hepatitis B

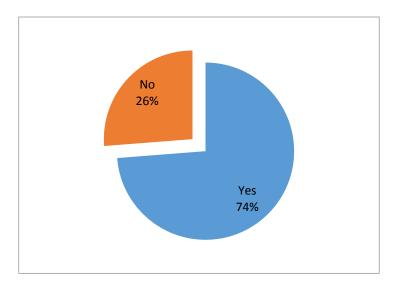
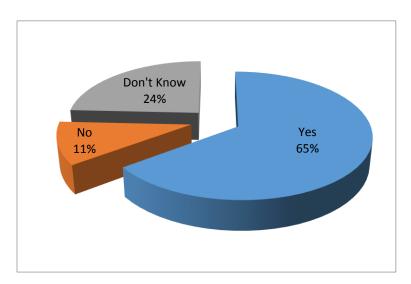
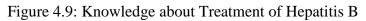


Figure 4.8: Knowledge about the Virus of Hepatitis B

Majority of the study populations confirmed that Hepatitis B is caused by the virus. Only 26% students did not know about this.



#### 4.9 Knowledge about Treatment of Hepatitis B



In this study 65% students informed Hepatitis B can be treatable 11% students confirmed it is not treatable, 24%% had no idea about this.

#### 4.10 Knowledge about Vaccine Availability

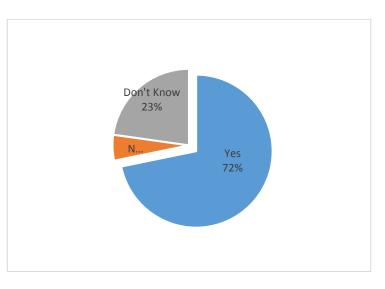


Figure 4.10: Knowledge about Vaccine Availability

72% students informed that vaccine is available for Hepatitis B. Only 5% students confirmed that there is no vaccine available for Hepatitis B and 23% students did not know about the vaccine.

#### 4.11 Knowledge About vaccine

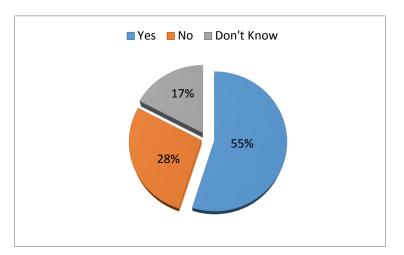
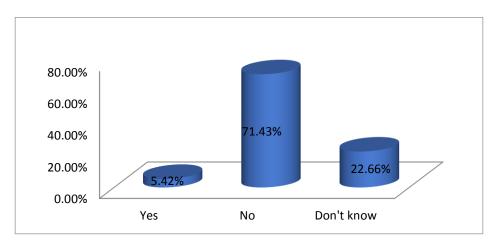


Figure 4.11: Knowledge about vaccine

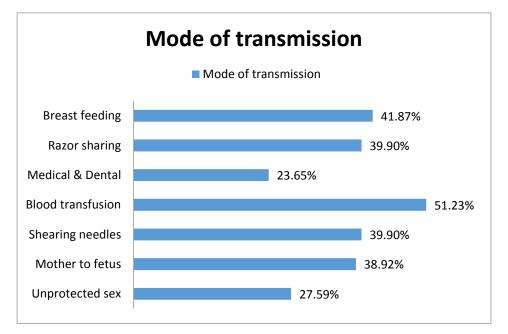
In this study 55% students confirmed that they took vaccine. 28% students informed that they did not take vaccine and 15% students did not know whether they took vaccine or not.



#### 4.12 Knowledge about the family member or friend have Hepatitis B

Figure 4.12: Knowledge about the family member or friend have Hepatitis B

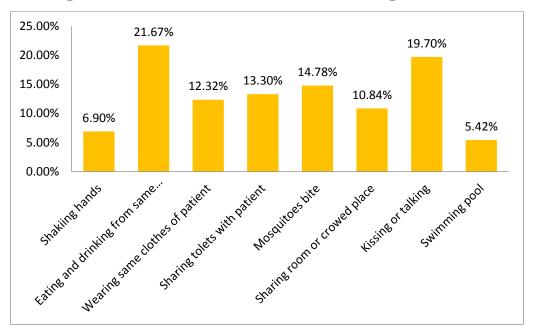
In this study majority of the students informed that no family member or friend had Hepatitis B. Only 5.42% students confirmed about their family member or friend had Hepatitis B. Among them few students specified their relationship with the affected people. 22.66% did not know about this.



#### 4.13 Knowledge about Mode of Transmission

Figure 4.13: Knowledge about Mode of Transmission

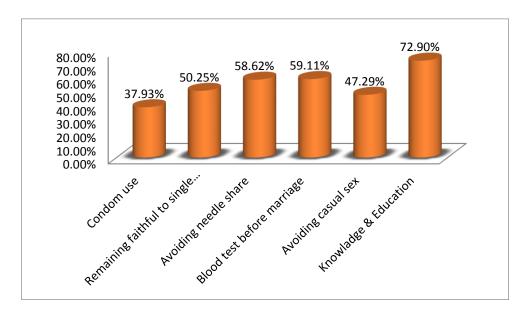
Most of the respondents (51.23%) supported that Hepatitis B can be transmitted by blood transfusion. About 41.87% students said Hepatitis B can be transmitted by breast feeding. On the other hand, 39.90% Students said Hepatitis B can be transmitted by sharing infected needles or syringe and by razor sharing. Whereas 27.59%, 38.92% and 23.65% population informed Hepatitis B can be transmitted by unprotected sex, mother to fetus and medical & dental respectively.



#### 4.14 Misconception about Mode of Transmission of Hepatitis B



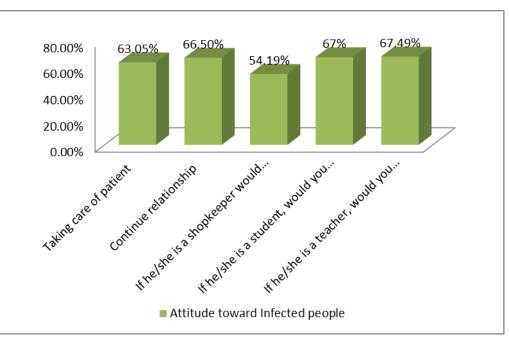
Among the students some don't have clear concept regarding this topic. Some of them (6.90%0) confirmed that by shaking hand Hepatitis B can be transmitted and 21.67% said by drinking and eating on same glass or plate HVB can be transmitted. About 12.32% respondents said by wearing same cloth it can also be transmitted. About 13.30% said by sharing toilet with infected person Hepatitis B can be transmitted whereas 14.78%, 10.84%, 19.70% and 5.42% of the respondents marked mosquito bites, sharing room or crowded places, kissing or talking and swimming in the same pool as a mode of transmission respectively.



#### 4.15 Knowledge of Control and Prevention of Hepatitis B

Figure 4.15: Knowledge of Control and Prevention of Hepatitis B

During this study we found, most of the students (72.90%) thought knowledge & education can prevent and control this disease. Whereas 37.93%, 50.25%, 58.62%, 59.11% and 47.29% of them marked condom use, remaining faithful to single partner, avoiding needle share, blood test before marriage and avoiding casual sex respectively as the control and prevention method.



#### **4.16** Attitude towards Hepatitis B Infected Person

#### Figure 4.16: Attitude towards Hepatitis B Infected Person

From the study, 63.05% of the respondent wanted to take care of the infected person and 66.50% %) of respondents wanted to continue relationship with infected person. About 54.19% of the respondents said that they won't mind buying food from the infected shopkeeper and will be positive towards the infected person. Approximately 67% students said that they would be positive about Hepatitis B infected student in the school and 67.49% student said that if Hepatitis B infected person is their teacher they won't mind his/her presence in the school and they will be positive towards him/her.

# Chapter 5 Discussion & Conclusion

#### **5.1 Discussion**

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem. It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer (WHO, 2017).

This study was conducted over 203 School and College going students in Dhaka city and among the students most of them were male (64%) and 34% students were female but Roushan et al (2013) found 42.5% male and 57.5% female in their study, where percentage of female respondent was high.

In our study, all the respondents confirmed that they heard about Hepatitis B. On the other hand, Ibrahim and Idris (2014) found that 8% Medical students of Syrian Private University never heard about Hepatitis B. It indicates that the Bangladeshi school and college students have higher knowledge about Hepatitis B than the Syrian medical students.

In our study, we found majority of the students (68%) did not know which body part was affected in Hepatitis B. Roushan et al (2013) found in their study 60.3% Iranian adolescents had known which body part was affected in Hepatitis B which was quite opposite to our result.

During this study, majority of the respondents (74%) confirmed that Hepatitis B is caused by virus. Ibrahim and Idris (2014) also found similar kind of result where 83.6% respondent confirm that virus is the causative agent of Hepatitis B.

From the study we found 72% students knew about the availibity of vaccine and 55% students confirmed that they took vaccine, 28% students did not take vaccine and 15% students did not know whether they took vaccine or not. Ibrahim and Idris(2014) also found 43.65% Syrian medical students took vaccine, 29.69% did not take vaccine and 26.56% did not know they took vaccine or not. It shows us a similar kind of vaccination status among the Bangladeshi school & college going students and the Syrian medical students of Syrian private University.

We have noticed that most of the respondents (51.23%) believed that Hepatitis B is transmitted by blood transfusion. About 41.87% students said that Hepatitis B can be transmitted by breast feeding. Also 39.90%, 27.59%, 38.92% and 23.65% students confirmed that Hepatitis B can be transmitted by sharing needles, unprotected sex, mother to fetus and medical & dental respectively.

A study conducted by Roushan et al (2013) on Iranian adolescents found 70% respondents supported that Hepatitis B can be transmitted by blood transfusion. They also found 66 % and 55% respondents thought that Hepatitis B can also be transmitted by unprotected sex and razor sharing. Ibrahim and Idris (2014) showed that 70%, 53% and 53% medical students of Syrian Private University informed that Hepatitis B can be transmitted by blood transfusion, unprotected sex and mother to fetus respectively.

We also found some misconception about the mode of transmission about Hepatitis B. Some of the respondent thought that Hepatitis B can be transmitted by Shaking hands (6.90%), eating and drinking from same plates or glasses of patient (21.67%), wearing same clothes of the patient (12.32%), sharing toilet (13.30%), mosquito bites (14.78%), sharing room (10.84%), kissing or talking (19.70%) and swimming pool (5.42%). Li et al (2017) found in their study that 12% new military recruits in china thought that Hepatitis B can be transmitted by hand shaking.

During this study we also found that majority of the respondents informed that a good level of knowledge and awareness is required for the control and prevention of Hepatitis B. We also found that the majority of the respondents showed positive attitude towards Hepatitis B infected people.

#### **5.2 Conclusion**

Based on all the facts, it can be concluded that knowledge and awareness about Hepatitis B among the school and college going students are not satisfactory. They have lack of knowledge about Hepatitis B and it's mode of transmission, which leads to a high risk of Hepatitis B. However, to overcome this situation and to increase the knowledge and awareness about Hepatitis B along with The Government, some private and health care organization need to be come forward and organized programs such as vaccination programs in the school across the country and awareness campaign to increase awareness and knowledge about Hepatitis B among the adolescents in Bangladesh. However, a very few research work have been done in this field, so there is a large scope for research in this field. It is however need to mention that this research was conducted on randomly chosen school s and colleges in Dhaka city in a very small scale, so it does not reflect the whole idea. Therefore, it is suggested that if a conclusive result about the knowledge and awareness is desired, further large scale researches should be conducted.

## Chapter 6

## References

#### **6** References

Aspinall, E., Hawkins, G., Fraser, A., Hutchinson, S. and Goldberg, D. (2011). Hepatitis B prevention, diagnosis, treatment and care: a review. Occupational Medicine, [online] 61(8), pp.531-540. Available at: https://academic.oup.com/occmed/article/61/8/531/1541366/Hepatitis-B-prevention- [Accessed 8 Oct. 2017].

Cai, W., Poethko-Müller, C., Hamouda, O. and Radun, D. (2011). Hepatitis B Virus Infections Among Children and Adolescents in Germany. The Pediatric Infectious Disease Journal, [online] 30(1), pp.19-24. Available at:

http://journals.lww.com/pidj/Abstract/2011/01000/Hepatitis\_B\_Virus\_Infections\_Among\_Childr en\_and.7.aspx [Accessed 1 Oct. 2017].

Chaity, A. (2017). Why 10 million Bangladeshis have Hepatitis B. [online] Dhaka Tribune. Available at: http://www.dhakatribune.com/health/2017/07/28/10-million-bangladeshishepatitis-b/ [Accessed 5 Nov. 2017].

Elgouhari, H., Abu-Rajab Tamimi, T. and Carey, W. (2008). Hepatitis B virus infection: Understanding its epidemiology, course, and diagnosis. Cleveland Clinic Journal of Medicine, [online] 75(12), pp.881-889. Available at:

http://www.mdedge.com/ccjm/article/94870/gastroenterology/hepatitis-b-virus-infectionunderstanding-its-epidemiology [Accessed 5 Oct. 2017].

Eredoro, C. (2017). Awareness and Opinions about Hepatitis B among Secondary School Teachers in Irepodun Local Government Area of Kwara State, Nigeria. Health Science Journal, [online] 11 No.5:530(1791-809X). Available at: http://www.hsj.gr/medicine/awareness-and-opinions-about-hepatitis-b-among-secondary-school-teachers-in-irepodun-local-government-area-of-kwara-state-nigeria.php?aid=20918 [Accessed 27 Nov. 2017].

Han, S. (2004). Extrahepatic manifestations of chronic hepatitis B. Clinics in Liver Disease, [online] 8(2), pp.403-418. Available at: http://www.hepatitisbannual.org/article.asp?issn=0972-9747;year=2006;volume=3;issue=1;spage=128;epage=154;aulast=Shim [Accessed 6 Oct. 2017].

Hou, J., Liu, Z. and Gu, F. (2005). Epidemiology and Prevention of Hepatitis B Virus Infection. International Journal of Medical Sciences, [online] pp.50-57. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nlm.gov/pmc/articles/PMC114225/lttps://www.ncbi.nlm.nlm.gov/pmc/

Ibrahim, N. and Idris, A. (2014). Hepatitis B Awareness among Medical Students and Their Vaccination Status at Syrian Private University. Hepatitis Research and Treatment, [online] 2014, pp.1-7. Available at: https://www.hindawi.com/journals/heprt/2014/131920/ [Accessed 1 Oct. 2017].

Li, Y., Chen, W., Wei, L., Xie, Y., Wang, L., Fu, J. and Wang, F. (2017). A survey of knowledge about hepatitis B among new military recruits in China. Military Medical Research, [online] 4(1), pp.1-6. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5241974/ [Accessed 1 Oct. 2017].

Liang, T. (2009). Hepatitis B: The virus and disease. Hepatology, [online] 49(S5), pp.S13-S21. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2809016/ [Accessed 6 Oct. 2017].

MacLachlan, J. and Benjamin C., B. (2017). Hepatitis B Virus Epidemiology. Cold Spring Harbor Perspectives in Medicine, [online] 7(10).

Available at: http://perspectivesinmedicine.cshlp.org/content/5/5/a021410.full [Accessed 8 Oct. 2017].

Nelson, N., Jamieson, D. and Murphy, T. (2014). Prevention of Perinatal Hepatitis B Virus Transmission. Journal of the Pediatric Infectious Diseases Society, [online] 3(suppl 1), pp.S7-S12. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164184/ [Accessed 7 Oct. 2017].

Nettleman, M. and El Mortada, M. (2017). Hepatitis B Symptoms, Vaccine, Treament& Prevention. [online] MedicineNet.

Available at: https://www.medicinenet.com/hepatitis\_b/article.htm [Accessed 7 Oct. 2017].

Roushan, N., NasiriToosi, M., Meysamie, A., Esteghamati, A. and Hajrassuliha, H. (2013). Hepatitis B Knowledge Among Iranian Adolescents: A National Survey. Iranian Red Crescent Medical Journal, [online] 15(12), pp.1-7.

Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3955498/ [Accessed 1 Oct. 2017].

Samji, N. (2017). Viral Hepatitis: Background, Pathophysiology, Etiology. [online] Emedicine.medscape.com. Available at: http://emedicine.medscape.com/article/775507-overview#a2 [Accessed 8 Oct. 2017].

Taylor, V., Choe, J., Yasui, Y., Li, L., Burke, N. and Jackson, J. (2005). Hepatitis B Awareness, Testing, and Knowledge among Vietnamese American Men and Women. Journal of Community Health, [online] 30(6), pp.477-490.

Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1810895/ [Accessed 1 Oct. 2017].

Torpy, J., Burke, A. and Golub, R. (2011). Hepatitis B. JAMA, [online] 305(14), p.1500. Available at: https://jamanetwork.com/journals/jama/fullarticle/896712 [Accessed 7 Oct. 2017].

World Health Organization. (2017). Hepatitis B. [online] Available at: http://www.who.int/mediacentre/factsheets/fs204/en/ [Accessed 4 Nov. 2017].

Yau, A., Ford, J., Kwan, P., Chan, J., Choo, Q., Lee, T., Kwong, W., Huang, A. and Yoshida, E. (2016). Hepatitis B Awareness and Knowledge in Asian Communities in British Columbia. Canadian Journal of Gastroenterology and Hepatology, [online] 2016, pp.1-8. Available at: https://www.hindawi.com/journals/cjgh/2016/4278724/ [Accessed 1 Oct. 2017].