Chapter 1- Introduction

Liver is the second largest organ in human body and is affected by several different infections. These include hepatotropic viral infections, bacterial infectionsand protozoal infections, each having their own specific clinical features that require targeted therapies.

Among these, Hepatitis is a very common medical condition of the liver where the disease causes inflammation and swelling that potentially leads to permanent damage in the liver tissues.Globally it has become a major public health concern since the morbidity and mortality rate of the disease is increasing andis becoming more visible as the second major killer infectious disease after tuberculosis. Millions of people are getting infected annually with some leading to hepatocellular carcinoma (HCC). In fact, liver cirrhosis and fatalities have been reported among significant proportion of patients. (WHO, 2012)

Hepatitis, in general, is a non-specific prodromalillness with no symptoms in some people, whereas yellow discoloration of the skin and whites of the eyes (jaundice), poor appetite, vomiting, tiredness, abdominal pain, nausea, arthralgia, myalgia, diarrhea, dark urine and pale stool may develop with preceding jaundice. Moreover, if the infection is acute then it resolves within six months, and last longer if the condition is chronic. There are many different causes and factors that include chemical toxins, infectious organisms,autoimmune diseases, drugs, and alcohol causing hepatitis(Cook, 1998)(Malaguarnera, et al., 2012)

There are five known hepatitis viruses among which three cause persistent infection and chronic hepatitis: Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Hepatitis D virus (HDV). (Lau & Wright TL, 1993) while the other two cause acute self-limited disease:Hepatitis A and Hepatitis E (Hoofnagle & Di Bisceglie, 1997). Recent findings propose that an additional form of viral hepatitis is present, to which two freshly discovered human viruses; the Hepatitis G virus (HGV) and the Hepatitis GB virus C (HGBV-C)have been related. HGV and HGBV-C are probably the same virus and their role in causing acute and chronic hepatitis is yet to be studied. (Muerhoff , et al., 1995)

The different viruses differ in their mode of transmission, populations for affecting andfinally results in different health outcomes.Hepatitis A and E viral

infections are food and water borne and can result in acute outbreaks within communities where unsafe water supply and poor sanitation is practiced. Hepatitis B and C are blood-borne infections, with transmissions occurring through unsafe use of needles and not so hygiene medical procedures. Hepatitis D is also transmitted through contact with infected blood; however, it occurs only in people who are infected with hepatitis B virus. (WHO, 2016)

Worldwide incidence of viral hepatitis is enormous and has taken a heavy toll on lives, communities, and health systems with 1.3 million people dying from viral hepatitis-related cirrhosis and liver cancer in 2015. Among these deaths, approximately 47% are due to hepatitis B virus, 48% to hepatitis C virus and the rest are attributed to hepatitis A and hepatitis E viruses. (WHO, 2016) The World Health Organization (WHO) estimated that 1 in 3 people in the world have been infected by either HBV or HCV,(Hajarizadeh, et al., 2013) About 2.3 billion people of the world are infected with one or more of the hepatitis viruses among whichapproximately 240 million people have chronic hepatitis B virus infection and 130–150 million have chronic hepatitis C virus infection. In East Asia and sub-Saharan Africa 5–10% of the adult population are estimated to have chronic HBV infection (CDC, 2020).Without an expanded and accelerated response, the number of people living with hepatitis B virus are assumedincrease in number in thenext 40–50 years, with a cumulative 20 million deaths occurring between 2015 and 2030. The number of people living with hepatitis C virus is increasing, despite the existence of an effective cure. (WHO, 2016)

Bangladesh, a South Asian country, surrounded by India on its 3 sides and the Bay of Bengal on the fourth side also shares a small land boundary with Myanmar. Viral hepatitis is a major burden to the health care system as well as to the economy of Bangladesh. Despite being a member of the developing world, Bangladesh have significant poverty and poor hygienic conditions which offer a favorable condition for nurturing Hepatitis B, C, and E.Hepatitis E virus is the leading cause of acute hepatitis in this country, however with improvement of economic status and sanitation practices, this appears to be on the decline. Hepatitis B virus remains the leading cause in all forms of chronic liver diseases in the country.(Mahtab, 2016)About 8 million people in Bangladesh were infected with chronic hepatitis B virus (HBV) and chronic hepatitis C virus HCV. (Shelton, 2014)(Mahtab, et al., 2008). Also, there are

frequent outbreak of viral acute hepatitis that are caused by hepatitis A virus (HAV) and hepatitis E virus (HEV).

Prevention and control strategies must be ensured to reduce the number of viral hepatitis such as raising awareness through public education, vaccination, blood transfusion safety strategies, food hygiene, safe water early diagnosis and effective medical support are being implemented to reduce the number of infections.

Table 1. Main Hepatitis viruses

	HAV	HBV	HCV	HDV	HEV
Acute Hepatitis	Case fatality increases with age	Case fatality increases with age	Uncommon	Superinfecton HBV may lead to fulminant disease	Higher case fatality in pregnant women
Chronic Infection	No	5% of adults and 90% of chldren	55-85%	Complicates chronic hepatitis B	Very rara
Hepatocellular Carcinoma	No	Yes	Yes	Yes	No
Route of transmssion	person-person, food borne, waterborne	Perinatal, bloodborne, sexual	perinatal, bloodborne, sexual	bloodborne	waterborne, foodborne
Vaccination	Yes	Yes	No	HBV vaccine	No
Treatment optons	None	Available	Available	Modified treatment of HBV	None

source: WHO, Introduction to hepatitis. Pg 13

1.1 Rationale

Hepatitis is one of the most complicated diseases which has affected approximately more than 2 billion people in the world (Jefferies, et al.,2018). The infection rate and death ratio are rising worldwide including Bangladesh. Being a global burden hepatitis requires substantial and additional resources to minimize the number of infection and death rate. Studies are conducted nationwide to identify the exact prevalence of Hepatitis; however, no such studies were found specific to the district of Chattogram. Hence this study was under taken to observe the current situation of hepatitis in this district.

1.2 Objectives

General

- To find the prevalence of hepatitis in Chattogram district.

Specific

- Evaluation of seasonal variation in the prevalence of different types of viral hepatitis.
- Comparing the prevalence of different viral hepatitis among gender
- Examining the trends of Viral hepatitis prevalence or severity over time
- Identify the risk factors of different viral Hepatitis

Chapter 2- Literature Review

Over the past three decades public health activities to control viral hepatitis have progressively increased. There are five viruses that are responsible for most cases of viral hepatitis, an inflammation of the liver where the virus uses the liver as the primary site for replication. These are the hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV) belonging to different virus families, having unique morphology, genomic organization and replication strategy. All these viruses can cause acute hepatitis. However, only HBV, HCV and HDV cause chronic hepatitis frequently, leading to progressive scarring of the liver (cirrhosis) followed by primary cancer of the liver (hepatocellular carcinoma). Among these 96% of the mortality was due to HBV and HCV which are therefore the major focus for research. Nearly 20% of all hepatitis cases show no markers, though there are specific serological tests available for some of the viruses.

In May 2016, the World Health Assembly recognized the Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021. The GHSS called for the abolition of viral hepatitis as a public health threat by 2030, aiming to reducing new infections by 90% and the mortality rate by 65%. New strategic processes are being applied to reduce the number of new infections and saving lives between 2015 and 2030. (WHO, 2017)

2.1.1 Hepatitis A

The hepatitis A virus belong to the picornavirus group of enteroviruses. HAV is highly infectious and is the major cause of acute viral hepatitis that spreads through fecal oral route. It was first identified by an American virologist, Stephen Mark Fein stone during World War II (1973). (Chakravarti & Bharara, 2019) In developing countries like Africa, Asia and parts of South America, transmission rates are high, and most infections occur in early childhood due to poor sanitation, overcrowding and living conditions. The cases in these regions arise from traveling to endemic areas, spreading from person-to-person or from contaminated food. (Anastee & Jones, 2017) In occasional outbreaks water and shellfish have been the vehicle for transmission.

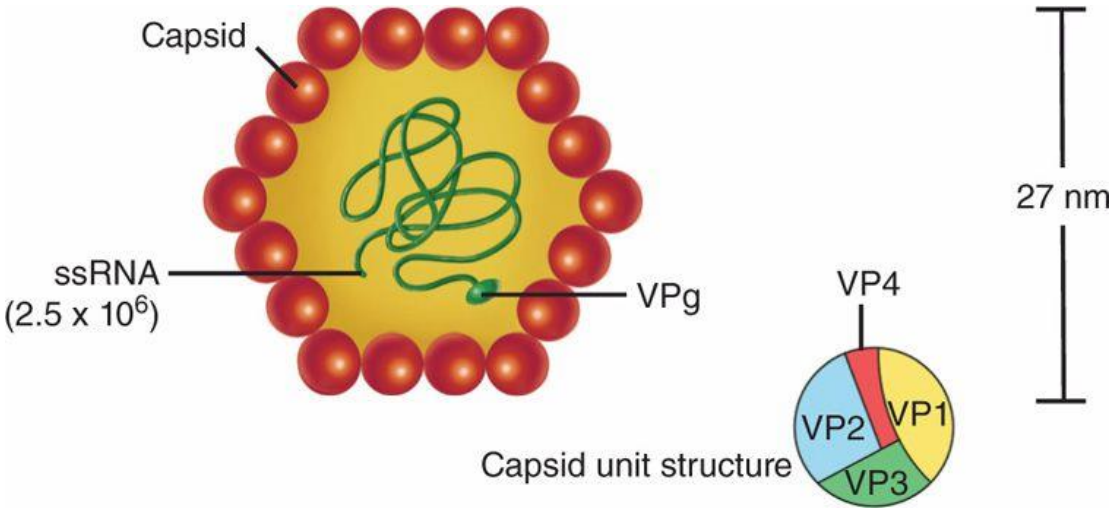

Fig. 1Structure of Hepatitis A virus

Source:Dr. J. H. Hoofnagle and of Abbot Laboratories, Diagnostic Division, North Chicago, Illinois.

The number of global hepatitis A cases was >1.4 million with 27,731 deaths in 2010.(Havelaar AH, et al., 2015)Owing to development in the socioeconomic sector and public health improvement, incidence of HAV infection has been decreasing globally. However, infection of older aged people are increasing leading to more severe clinical manifestations and greater disease burden. (Murphy, et al., 2016)There is no specific treatment for acute hepatitis A except for supportive care and liver transplantation in the rare cases with liver failure. (Burroughs & Westaby, 2005) According to World Health Organization (WHO) estimates, there were 126 million cases of acute hepatitis A in 2005. (WHO, 2012)

Several outbreaks have been reported throughout the world over the last 10 years. The table belowshows the different out breaks that have taken place in the past years.

Table2. Outbreaks of Hepatitis A around the world from 2009-2018

S. No.	Year	Geographical Location	No. of documented cases	Route of transmission	Source of infection
1.	2009	Autralia	Not specified	Feco-oral	Semi-dried tomatoes
2.	2010	London	5	Feco-oral	-
3	2011	Korea	16	Feco-oral	-
2.	2013	India (Lucknow)	267	Feco-oral	-
3.	2014	India (Mylapore village)	45	Feco-oral	Contaminated water
4.	2015	Taiwan	Not specified	Sexual	MSM
5.	2016	USA (9 states)	134	Feco-oral	Strawberries
6.	2016	USA (Hawaii)	292	Feco-oral	Scallops
7.	2016	Europe	Not specified	Sexual	MSM
8.	2016	India (Kerala)	223	Feco-oral	Food from newly opened hotel
9.	2017	USA (California)	694	?Feco-oral	Illicit drug users/homeless
10.	2018	Europe	163	? Feco-oral	Travel

Source: (Chakravarti & Bharara, 2019)

Globally, with the improvement of hygienic conditions and childhood vaccination, the morbidity of HAV infection has been substantially reduced in both developed and developing countries. But if the virus is introduced in a region, either by contaminated food or by person-to-person contact, outbreaks with an extensive spread of HAV may be triggered, and the morbidity and mortality that are associated with these outbreaks within in low endemiccountries can become severe.This phenomenon was demonstrated recently in the United States where >15,000 HAV infection cases have been reported since 2016, with increased rates of hospitalization (1073 cases, 71%) and deaths (41 cases, 3%) than usual. (Foster, et al., 2018)

The first hepatitis A vaccine that was commercially produced, was launched in 1992. (Van Herck & Van Damme, 2005) Both inactivated (HepA-I) and live attenuated vaccines (HepA-L) against hepatitis A are currently available where the immune protection postvaccination can persist for at least 20 years. (Zhang, 2020) The live attenuated vaccines are mostly used in china whereas most other countries use inactivated vaccines. (Van Damme & Van Herck, 2005)

The virus is relatively stable at low pH levels, moderate temperatures, and detergents. But can be inactivated by high temperature that requires heating foods (>85°C) for 1 min or disinfecting surfaces with a 1:100 dilution of sodium hypochlorite (household bleach) for 1 min. (Nainan, et al., 2006) Foodborne HAV outbreaks are often caused by contaminated frozen or dried food that is not heated well before consumption. (Petrignani, et al., 2010)(Gallot, et al., 2011)

2.1.2Clinical Features

The clinical course of acute hepatitis is divided in to several phases.

Phase 1: Incubation period is the time between exposure to the virus and the onset of symptoms. This phase ranges from 15 to 50 days (approximately 28 days) and the patient remains asymptomatic despite active viral replication and excretion in feces. The transmission of the virus is very significant during this phase owing to the high viral load that is excreted.

Phase 2: Prodrome stage, characterized by the onset of nonspecific symptoms, ranges from several days to more than a week prior to the onset of jaundice. The clinical course of HAV is indistinguishable from other types of acute viral hepatitis. There is a sudden onset of fever, malaise, nausea, anorexia, abdominal discomfort.

Phase 3: Icteric phase begins with the appearance of dark urine due to bilirubinuria, pale stools and yellowing of the skin and mucous membranes. This begins within 10 days of the initial symptoms in majority of the cases; however, anicteric hepatitis can also occur.

Infected individuals excrete the virus in large amount in feaces for about 2-3 weeks before the onset of symptoms and then for further 2 weeks or so. Clinical illness usually does not last longer than 2 months, although 10%-15% of people have prolonged or relapsing signs and symptoms for up to 6 months. Virus may be excreted during a relapse. The symptomatic illness from HAV is directly related to age. HAV infection is common among children i.e., 70% of children younger than <6 years of age are often asymptomatic, and so 30% adults will have serological evidence of past infection. older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients. In developed countries, HAV transmission during childhood is less frequent. The estimated case fatality ratio varies with age

from 0.1% among children < 15 years of age, to 0.3% among persons 15–39 years of age, to 2.1% among adults aged ≥ 40 years of age.

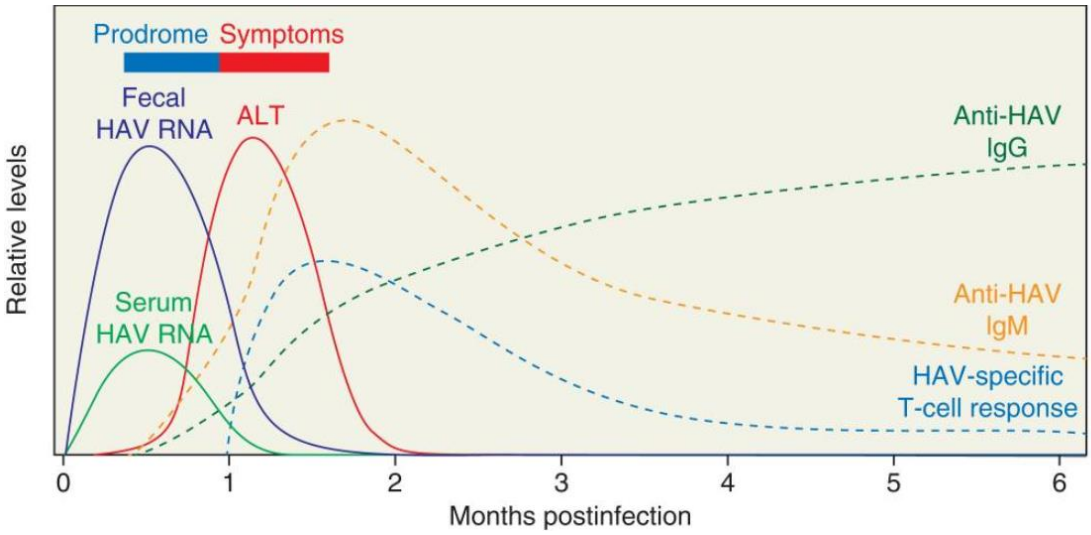

Figure 2. A typical course of hepatitis A

2.1.3Laboratory Diagnosis

Based on clinical or epidemiological features HAV cannot be distinguished from other types of viral hepatitis. Serological test is required to confirm the presence of HAV. Virtually all patients with acute hepatitis A have detectable IgM anti-HAV determined by enzyme immunoassay. Confirmation of acute HAV can be made during the acute or early convalescent by the presence of IgM anti-HAV in serum. Usually this is detectable within 5–10 days before the onset of symptoms and can persist for up to 6 months. IgG anti-HAV appears in the convalescent phase and remains forever. The antibody test for HAV measures both IgG anti-HAV and IgM anti-HAV. Persons who are total anti-HAV positive and IgM anti-HAV negative have serologic markers indicating immunity consistent with either past infection or vaccination.

2.1.4Prevention of HAV

Hepatitis A is a vaccine-preventable disease. HAV can be prevented by:

- Adequate sanitation and housing facilities, as well as personal hygiene.
- Pre- and post-exposure passive prophylaxis with immune globulin (IG).
- Pre- or post-exposure active immunization with an HAV vaccine.

2.2 Hepatitis B

2.2.1 Transmission of HBV

There are three main modes of transmission for Hepatitis B virus: through blood and its products, via sexual intercourse and perinatally from mother to child. Only very small amount of blood is necessary to cause transmission and this was observed by transmission via needle- stick injuries. Thus, it is prevalent in drug addicts who share needles during intravenous drug use. HBV in serum and vaginal fluids suggest that transmission can occur through sexual intercourse. Again, transmission from mother to child during normal delivery is another route, possibly owing to the exposure of the child to its mother's vaginal fluid during delivery. Transplacental transmission is rare and no evidence was found indicating spread through breast feeding.

Since HBV is an enveloped virus, it is sensitive to the outside environment and hence require intimate contact to be transmitted.

2.2.2 Epidemiology

Although found worldwide, this virus is particularly prevalent in Asia. This leads to an increased incidence of hepatocellular carcinoma in many Asian countries. Immunization against HBV has significantly reduced incidences of hepatoma in children and hence is considered as the first vaccine to prevent human cancer.

2.2.3 Clinical course and pathogenesis of Hepatitis B Virus

After a virus enters the blood, it infects the hepatocytes displaying the viral antigens on the cell surface. Cytotoxic T cells induce an immune attack against the viral antigens on infected hepatocytes and this results in a cell mediated immune injury. Some of the early symptoms as well as some of the complications of chronic hepatitis are caused by these antigen-antibody complexes. Due to a less competent immune system, infected newborns are at higher risk of becoming chronic carriers than infected adults. A chronic carrier is some one who has HBsAg persisting in their blood for at least six months. HBV DNA exists as an episome in the nucleus of continuously infected cells with a small number of copies being integrated into the cell cytoplasm. Depending on the adequacy of the cytotoxic T cell response, a person may become clear of an HBV infection are be a chronic carrier.

Chronic carriers can sometimes make the e antigen and therefore have high probability of making infectious virions and transmitting the disease. The e antigen indicates transmissibility since it is encoded by the same gene that encodes the core antigen suggesting HBV DNA genome is present in the host. Some carriers do not produce e antigens and hence are less likely to transmit the disease.

Many infections of HBV are asymptomatic and are only detected by the presence of antibody to HBsAg. The incubation period for hepatitis B is 10- 12 weeks. Clinical symptoms are similar to that of hepatitis A, but tends to be more severe and dangerous.

2.2.4 Laboratory Diagnosis of HBV

Early Hepatitis B virus infection can be diagnosed by testing for HBsAg and the IgM antibodies to the core antigen. HBsAg appears during incubation period and is detectable in most patients during acute phase. In convalescence phase, it is undetectable in most patients. prolonged presence (> 6 months) indicates carrier state. HBsAb is not detectable during these early stages since they are binding to the viruses and trying to control the disease. There is a window phase during which neither Hepatitis B surface antigen nor antibody is detected. At this time, HBcAb is present and can be used to make the diagnosis. This IgM form of HBcAb is present during acute infection and disappears approximately 6 months later. Testing for HBcAg is not readily available. HBeAg can be seen during the incubation, prodromal and early acute disease. It is also found in certain chronic carriers.

Detection of viral DNA within the serum shows that infectious virions are present. Reduction of this viral load in chronic hepatitis B patients are used as an indicator for success of drug therapy.

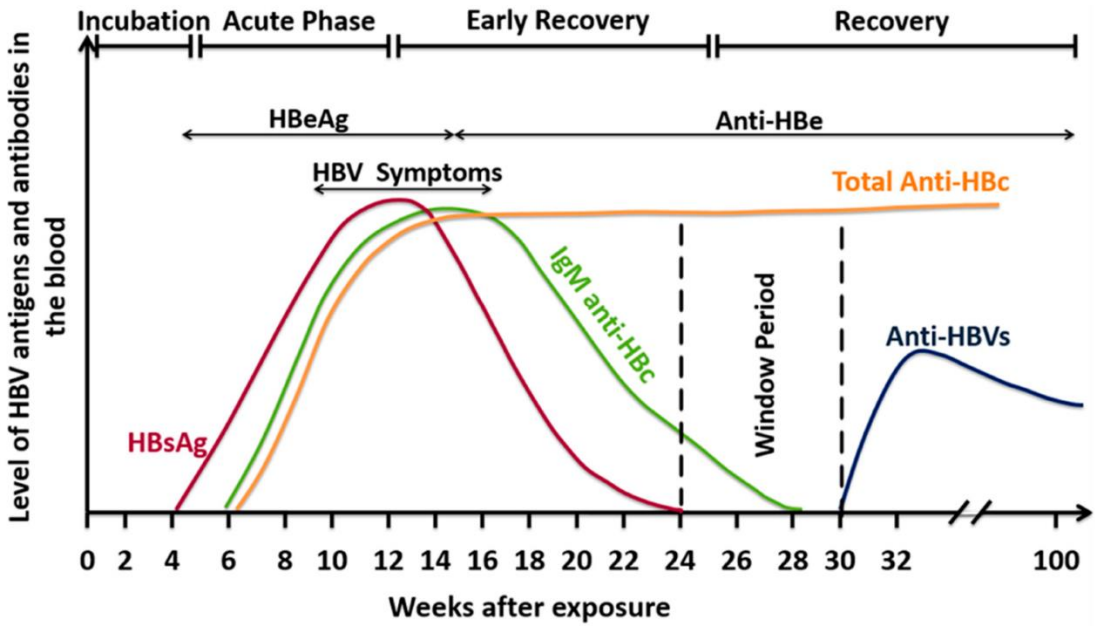

Figure3- Serologic findings in patient with acute Hepatitis B

2.2.5 Prevention of HBV

Prevention can be done by the use of vaccines or hepatitis B immunoglobulin (HBIG). The vaccine contains HBsAg produced in yeast using recombinant DNA technology. It is highly effective in preventing infection and is indicated in people at high risk of infection (e.g., healthcare workers, sex workers, drug users, transfusion recipients, etc.) Many countries have this vaccination in their immunization schedule for children.

In order to provide immediate passive immunization against HBV infection HBIG is used. This immunoglobulin contains a high titer of HBsAb and is provided to individuals following exposure to HBsAg positive blood. In newborns to mothers with HBsAg positive blood, both vaccine and HBIG should be given for passive-active immunization.

2.3 Hepatitis C

2.3.1 Transmission of HCV

HCV is mainly transmitted by blood and humans are the reservoirs. Common modes of transmission are injection drug users, vertical transmission from mother to child during birth, needle stick injuries and sexual intercourse (not so common). Transmission through blood has greatly reduced since any donated blood with HCV antibodies are discarded. Like HBV, there is no evidence of transplacental

transmission or transmission via breast feeding. Since many infections are asymptomatic, high risk groups should be screened for HCV antibodies in their blood. Although some flaviviruses are inset borne, no evidence of transmission by insects has been found for HCV.

2.3.2 Pathogenesis and clinical features

HCV primarily infects hepatocytes; however, cell death is induced by cytotoxic T cells that cause an immune attack. Even though HCV strongly predisposes to hepatocellular carcinoma, no evidence of an oncogene in the viral genome nor insertion of viral genome in to DNA of cancer cells has been found. Although antibodies against HCV are made, about 75% of HCV infected individuals end up as chronic carriers. Chronic carrier rate is much higher for HCV than for HBV. It is yet uncertain if patients previously infected by HCV and healed has developed life long immunity or can be reinfected.

Granted acute infection is often asymptomatic, mild symptoms such as malaise, nausea and pain in right upper quadrant can occur. Other symptoms are fever, anorexia, nausea & vomiting, jaundice, dark urine, clay stools and elevated levels of transaminases are observed. As far as chronic liver disease, cirrhosis and hepatocellular carcinoma, hepatitis C infection is similar to that of HBV infection. Mean incubation period is about eight weeks and HCV infections can lead to many autoimmune conditions such as purpura, membranoproliferative glomerulonephritis, arthralgia, vasculitis, etc.

2.3.3 Laboratory diagnosis

Diagnosis is made by detecting antibodies to HCV using enzyme linked immunosorbent assay (ELISA). In the assay, the antigen is a recombinant protein formed from three HCV proteins that are immunologically stable, excluding the highly variable envelope proteins. The test is unable to distinguish between IgM and IgG or between acute, chronic or resolved infection. If ELISA test is positive PCR-based test that detects the presence of viral RNA in serum needs to be done. Success of treatment is monitored by observing reduction in viral load in the patient. A chronic infection is determined by positive ELISA test, elevated levels of transaminase and detection of viral RNA for six months or more.

2.3.4 Treatment

Treatment using peginterferon alfa have displayed significant reduction of chronic carriers for HCV infection. Hence, acute hepatitis C is treated with this. For chronic hepatitis C combination of drugs from three classes are used. These are NS5A inhibitors, protease inhibitors and RNA polymerase inhibitors.

2.3.5 Prevention

No vaccination or hyperimmune globulins are available for the prevention of HCV

2.4 Hepatitis D

Hepatitis delta virus (HDV) is one of the smallest virus infecting humans which consist of a defective RNA that can infect only individuals who have hepatitis B surface antigen (HBsAg); worldwide more than 15 million people are co-infected. Globally, HBV infection is a major cause of liver-related morbidity and mortality and is widely distributed worldwide. There is a risk of liver cirrhosis and hepatocellular carcinoma in people chronically infected with HBV. (WHO, 2017) Hepatitis D Virus (HDV) is an RNA virus that depends on HBV for propagation. (Hughes, et al., 2011) As is uses the HBsAg as a viral envelope and shares the same hepatocyte receptor of HBV for viral entry. (Botelho-Souza, et al., 2017) Even after being the smallest virus, yet co-infection with HBV is the most severe viral hepatitis.

The HDV is composed of a coat of HBV envelope proteins surrounding the nucleocapsid, which consists of a single-stranded, circular RNA genome complexed with delta antigen, the viral protein. (Hughes, et al., 2011)

2.4.1Epidemiology of HDV

Globally Hepatitis D virus (HDV) affects nearly 5% of people who have a chronic infection with hepatitis B virus (HBV) and 1 in 5 cases of liver disease and liver cancer are due to co-infection of HDV and HBV. A study has identified several geographical hotspots where there is high prevalence of HDV infection which includes Mongolia, the Republic of Moldova, and countries in Western and Middle Africa. In North America, injectable drug users are at the highest risk of contracting HDV. In Bangladesh, information about prevalence of HBV infection is scarce, and there is no available data has been found on HDV infection. HDV infection is common in people who are exposed to blood products or needles previously infected

or contaminated with HBV. Globally around 18 million people are infected with HDV. HDV infection is declining worldwide due to successful HBV immunization, and improvement in socioeconomic status but currently no such data were found to prove this claim. (Jefferies, et al., 2018) New areas of high HDV prevalence have emerged in Albania, , northern India areas of China and Japan. Despite such high rates of hepatitis B in these Asian nations, the incidence of hepatitis D is comparatively lower.

2.4.2Transmission of HDV

HDV transmission routes are similar to HBV: percutaneous or sexually through contact with infected blood, body fluids or blood products. The virus follows two patterns for infection i.e. by coinfection with HBV or superinfection after HBV infection. In-case of coinfection the patient shows two transaminases peaks, the first apparently due to hepatitis B and the second, which occurs weeks later, due to hepatitis D infection. The acute infection is biphasic. In most cases coinfection resolve but in 2.4-4.7% cases the patient become chronic carriers. In around 50-70% cases, superinfectionsgrow in to a severe form of acute hepatitis and 90% of them become chronic carriers. This could be due to the fact that the D virus infects hepatocytes which are heavily colonized by B viruses that give HDV and excellent environment for replication. With both infections, incidence of fulminant hepatitis is more common and the mortality rate is 5% as compared to 1% with hepatitis B alone. It is to be noted that Delta hepatitis is considered to be one of the most severe viral hepatitis. In acute forms it produces more fatalities but in chronic forms it produces more cirrhosis, even in children.

2.4.3Clinical Feature of HDV

The onset of the disease is usually abrupt, with signs and symptoms resembling those of HBV infection. The average incubation period for: HDV Co-infection is 90 days (range 45-160 days) and Superinfection is approximately 2-8 weeks. Acute HDV co-infection is usually self-limiting, whereas superinfection often progresses to chronic hepatitis. Fulminant cases are observed more in superinfections rather than in co-infections. Children can endure a severe clinical course, that often progresses to severe chronic hepatitis. Certain signs of HDV include:

- Yellow skin and eyes (jaundice)
- Stomach upset

- Pain in your belly
- Throwing up
- Fatigue
- Not feeling hungry
- Joint pain
- Dark urine
- Light-colored stool.

2.4.4Laboratory Diagnosis of HDV

Diagnosis of HDV is made by observing high levels of Immunoglobulin G (IgG) and Immunoglobulin M (IgM) by enzyme-linked immunosorbent assay (ELISA), finding of anti-HDV in serum, and established by detection of HDV RNA using RNA polymerase chain reaction (PCR) testing in serum. However, HDV diagnostics are not widely available and so it is difficult to monitor antiviral therapy. HBsAg is useful key to monitor treatment response if quantitative HDV RNA is not available. Decreasing HBsAg levels often indicates surface antigen loss and HDV clearance, although this very rare.

2.4.5Prevention of HDV

Since HDV infection occurance depend on HBV infection it is important to minimize the transmission of HBV. This could be done as follows:

- Vaccination for Hepatitis B
- Latex condoms recommended for people having sex with more than one partner.
- HBV test should be done in pregnant women so that infants born to HBV-infected mothers gets HBIG (hepatitis B immune globulin) and vaccine within 12 hours after birth.
- Patients who had been infected with HBV should not donate blood, organs, or tissue.
- Health care workers should get vaccinated against HBV and always follow routine barrier precautions, and safely handle needles and other sharps objects.
- Contaminated items with blood should not be shared between individuals.
- Injectable drug users should avoid or discontinue the use of such drugs.

- Properly screen and test blood product before use.

2.5 Hepatitis E

Hepatitis E is probably the most common cause of acute viral hepatitis in the developing countries especially in Bangladesh, India, Pakistan and Nepal. It causes infection in both human and animals around the world. In 1983, Mikhail Balayan a Russian virologist visualized the virus through electron microscopy when he examined his own feces self-administration of contaminated material.(Purcell & Emerson, 2008) The hepatitis E virus (HEV) consist of a positive stranded RNA that exists in both enveloped and non-enveloped forms and belong to the viral member Hepeviridae.

Based on the difference in HEV genotype the epidemiology and clinical presentation of HEV infection vary greatly by geographic location. (Teshale & Hu, 2011) Fecal contamination of drinking water is a major route of contamination so the overall burden of the disease is highest in parts of the world where clean drinking water is scarce. (Rein, et al., 2012) Most HEV infections show no symptoms and can lead to the spontaneous clearance of the virus.

HEV infection is a serious public health concern especially in developing countries, where large outbreaks have been reported due to poor sanitation and lack of sewage infrastructures. There is also a growing evidence for the claims that seroprevalence of HEV infection in industrialized countries is increasing day by day. Patients that have chronic liver disease, travelers to endemic areas, people working with animals and pregnant women 3rd trimester living in endemic areas are at high risk of getting infected with HEV.

The incubation period for HEV ranges from 3 weeks to 9 weeks and has a high mortality rate in pregnant women. It has symptoms like Hepatitis A but is comparatively much severe.It occurs mostly in people ageing from 15-40 years.

2.5.1Epidemiology of Hepatitis E

Every year approximately 20 million people around the world are infected with hepatitis E leading to an estimated 3.3 million symptomatic cases. In 2015 approximately 44000 people died due to HEV infection. Waterborne outbreaks (which can be large, often involving hundreds to thousands of people) have occurred

in South and Central Asia, tropical East Asia, Africa, and Central America. In recent years, many large international outbreaks have occurred among refugees and displaced people living in camps. In outbreak-prone areas, interepidemic disease is sporadically encountered. Sporadic disease are also seen in other regions that are not prone to outbreaks, such as the Middle East, temperate East Asia (including China), North and South America, and Europe. People of United States are at highest risk of HEV infection when they travel to epidemics areas, mainly because of drinking contaminated water. When traveling in Japan and Europe, eating raw or inadequately cooked food are also major concern for HEV infection.

In Bangladesh HEV infections occur throughout the year, and is a major (34%) cause of acute jaundice in tertiary hospitals in Bangladesh. Some seasonal outbreak has been recorded in few studies that have confirmed the HEV infection in Bangladesh. In spite of having seasonal outbreak in Bangladesh, the region is imagined as endemic for HEV with the range of sero-prevalence 27% to 60%. A study was conducted in 2008 by International Centre for Diarrhoeal Disease Research, Bangladesh (icddrb) reported jaundice outbreak in a large population having more than 4000 cases in an urban community where it reported high risk of HEV in low income and densely populated areas where mostly men who are working outside and poses risk of illness. High fatality rate was observed in pregnant women with their neonates. Some Bangladeshi travelers were diagnosed with HEV infections followed by an outbreak of hepatitis E virus in Bangladeshi UN peacekeepers in 1990. Between 2003 and 2005, another study provided the baseline of sero-prevalence of hepatitis E virus in rural areas of Bangladesh where found 22.5% positive and result was similar to other south Asian countries

2.5.2Transmission of Hepatitis E

The main route for HEV transmission is by fecal-oral rout which accounts for a very large proportion of clinical cases. Having poor sanitation allows virus excreted in faeces of infected people to reach water supplies as a result contaminating drinking water. There are other routs for transmission but have been smaller number of clinical cases. These routes of transmission include:

- ingestion of undercooked meat or meat products derived from infected animals (e.g. pork liver);

- transfusion of infected blood products; and
- vertical transmission from a pregnant woman to her baby.

2.5.3Clinical Features of Hepatitis E

Following exposure to HEV the incubation period ranges from 2- 10 weeks, with an average of 5-6 weeks. 3-4 weeks after the onset of the disease the person starts to excrete the virus. Symptomatic infection is most common in people aged from 15-40 years. Children are often asymptomatic or possess mild illness without jaundice which goes undiagnosed.

Typical signs and symptoms of hepatitis include:

- an initial phase of mild fever, reduced appetite (anorexia), nausea and vomiting, lasting for a few days; some persons may also have abdominal pain, itching (without skin lesions), skin rash, or joint pain.
- jaundice (yellow colour of the skin and whiteness of the eyes), with dark urine and pale stools; and
- a slightly enlarged, tender liver (hepatomegaly).

These symptoms are often indistinguishable from those experienced during other liver illnesses and typically last 1–6 weeks.

2.5.4Prevention of Hepatitis E

The most effective approach against the disease is prevention. In case of highly populated and dense area transmission of HEV can be prevented by maintaining quality standards for public water supplies and establishing proper disposal systems for human faeces. In case of individual level infection can be avoided by maintaining regular hygienic practices and avoiding consumption of impure water and ice. If possible, to get vaccinated in countries where vaccination is avail

Chapter 3- Materials and Methods

3.1 Description of the study area

Located in the southeastern coast of Bangladesh, Chattogram is a large port city and is considered as the commercial capital of Bangladesh. It has an area of 5,283 km^2 with a metropolitan area of 2,510 km^2. The city boasts a population of more than 8.4 million according to 2016 statistics. It is located between the Chittagong Hill Tracts and the Bay of Bengal and at the banks of the Kornophuli River (BBS, 2016).

Figure 4: Map of the study site

The district of Chattogram is further subdivided into 18 upazillas and the Chattogram Metropolitan Area. The average temperature varies from 13º to 32ºC with a humidity of 70 to 85%. The average rainfall fluctuates from 5.6 mm to 727.0 mm. Due to over-crowding anda very dense population; the district faces many public health challenges including food and water borne diseases. To meet the increasing demands of water

supply, Chattogram Water Supply and Sewerage Authority (CWASA) has taken up the responsibility for supplying water through its distribution network following treatment of water from the Halda River and ground water sources (Zuthi, et al., 2009)

3.2 Study Design

The study conducted was a retrospective onewhere data was collected from a laboratory receiving samples from various patientsreferred by physicians across Chattogram district. All suspected cases who had done a test for viral hepatitis were included in this study. Since patient confidentiality had to be maintained, only gender of the patient could be included in the study. Season was based on the date the sample was collected.

3.3 Case definition

'An acute illness typically including acute jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper quadrant tenderness. Biological signs include increased urine urobilonogen and >2.5 times the upper limit of serum alanine aminotransferase'(WHO, 2000)

If a case was suspected to have hepatitis based on the case definition; he/she was referred to the laboratory for 'confirmatory serological testing'.

3.4 Study period

The study was conducted over a period of 6 months. Three years data (January 2018 to December 2020) was collected for this study.

3.5 Sample collection procedure

Samples were collected from patients that were referred to theQrex Diagnostic & Consultation Centre (Pvt.) Ltd and Prescription Center diagnostic for serological test of viral hepatitis and who voluntarily approached the center. ELISA test was conducted for all these patients in the following way.

Equipments used

- A microwell plate
- A multipette

- Washing device
- Microplate washer

Reagents used

- Coating Buffer-
- A diluting or washing buffer
- Blocking buffer- Bovine serum Albumin
- Enzyme – Horse radish peroxidase
- Chromogenic substrate- Trimethyl Benzidine
- Stop solution

Step 1- The sample was added to plate

Step 2- Blocking buffer was added to block remaining protein binding sites

Step 3- Then a suitable primary antibody was added

Step 4- This was followed by the addition of a suitable secondary antibody (HRPO conjugate) that binds to the primary antibody.

Step 5- TMB substrate was added next and this was converted in to a detectable form by HRPO.

The results were read by measuring the absorbance at 450nm with the help of ELISA reader. These results were then stored in the laboratory database.Wantai Anti HAV IgM Elisa kit ,Bioelisa HBsAg 3, Anti HCV Elisa V 4.0, WANTAI HEV-IgG ELISA were used for detecting IgM against HAV, the HB surface antigen, Ant-HCV and IgG & IgM against HEV respectively. Results that came back positive for Hepatitis B were retested for anti-HDV antibodies using Wantai HDV-IgG ELISA test kit.

After obtaining permission from appropriate authorities, the results were later collected from the laboratory data base, where the lab made sure that the patient's identity was kept confidential.

3.6Data collection

Data from Qrex Diagnostic & Consultation Centre (Pvt.) Ltd and Prescription Center diagnosticwere collected for a total of 3514 patients from Chattogram district who approached physicians with symptoms from January 2018 to December 2020 and

were tested for viral hepatitis. The variables obtained were season, gender, and year of diagnosis. Season was further divided into three types (Summer, Rainy and Winter). Summer months were between March to June, rainy moths between July to October and winter months were November to February.Date of sample collection and gender of patients were recorded from the lab data records.

3.7 Statistical analysis

Data that was collected were compiled on to a Microsoft excel spreadsheet. The data was then analyzed using STATA/IC 13 (StataCorp 4905, Lakeway Drive, College Station, Texas 77845, USA)

Sl No	INVOICE_ID	GENDER	INVOICE_DATE	ITEM_NO	ITEM_NAME	RESULT
142	QR1805000154	Male	19-May-18	100137	Anti-HEV IgM	4.000
143	QR1805000154	Male	19-May-18	100648	HBs Ag (SCREENING)	Positive
146	QR1805000155	Female	19-May-18	100137	Anti-HEV IgM	4.000
147	QR1805000155	Female	19-May-18	100648	HBs Ag (SCREENING)	Negative
153	QR1805000159	Male	19-May-18	100648	HBs Ag (SCREENING)	Negative
154	QR1805000159	Male	19-May-18	100137	Anti-HEV IgM	4.000
155	QR1805000161	Male	19-May-18	100648	HBs Ag (SCREENING)	Negative

Figure 5. Sample of data record

3.8 Descriptive analysis

Prevalence of each type of hepatitis was calculated using positive samples divided by the total number of samples tested expressing the results as a percentage with 95% confidence interval (CI). To observe the existence of any outbreak, prevalence was calculated month wise. Gender, season and yearly variations were observed using tables and charts.

Chapter 4- Results

The study was conducted in the Chattogram district, where data was collected from ten different hospitals over a three-year study period. A total of 3514 patients whose serum samples tested positive for any form of viral hepatitis were included as study subjects. For each type of hepatitis, variation across gender, season and timeline were evaluated. The overall prevalence of Hepatitis A was 1.2% (n=42) with 95% CI: (0.9-1.6), Hepatitis B was 86.06% (n=3,024) with 95% CI: (84.9-87.2), Hepatitis C was 2.93% (n=103) with 95% CI: (2.4-3.5) and Hepatitis E alone was 9.82% (n= 345) with 95% CI: (8.9-10.5).

4.1 Prevalence of Hepatitis A

4.1.1 Univariate association between Hepatitis A and selected variables

The percentage of Hepatitis A was found significantly higher in male patient (2.1%; 95% CI: 1.4-3.1) than that of female patient (0.7%; 95% CI: 0.4-1.2) (p=0.001). Other two variables, season and year didn't show any significant difference in case of Hepatitis A (Table 1).χ^2test was used to find the significant value.

Table 3: Frequency distribution of Hepatitis A

Variables	Categories	N	n (%)	95% CI	P value
Gender	Male	1202	25 (2.1)	1.4-3.1	0.001
	Female	2312	17 (0.7)	0.4-1.2	
Season	Rainy	1874	22 (1.2)	0.7-1.8	0.946
	Summer	683	9 (1.3)	0.6-2.5	
	Winter	956	11 (1.2)	0.6-2.0	
Year	2018	1454	23 (1.6)	1.0-2.4	0.105
	2019	1448	16 (1.1)	0.6-1.8	
	2020	612	3 (0.5)	0.1-1.4	

4.1.2 Gender wise percentage of Hepatitis A:

Hepatitis A was found higher in Male patients than that of female patients throughout the year. Higher positive percentage identified in male in August (4.21%) followed by November (4.05%) and February (3.61%). There was no positive in male in the month of January, March and December. In case of Female, highest percentage of Hepatitis A observed in May (2.81%). All female patient was negative in January, March, September and October. (Figure 1)

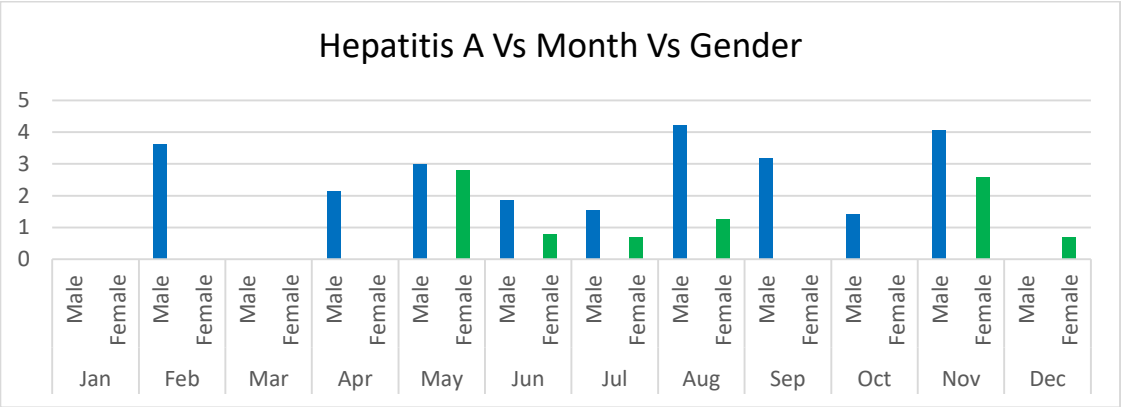

Figure 6: Percentage of Hepatitis A by gender

4.1.3 Yearly variation of incidences of Hepatitis A

Hepatitis A was found higher in the year of 2018 (1.58%) and lowest percentage was in 2020 (0.49%) (Figure 2).

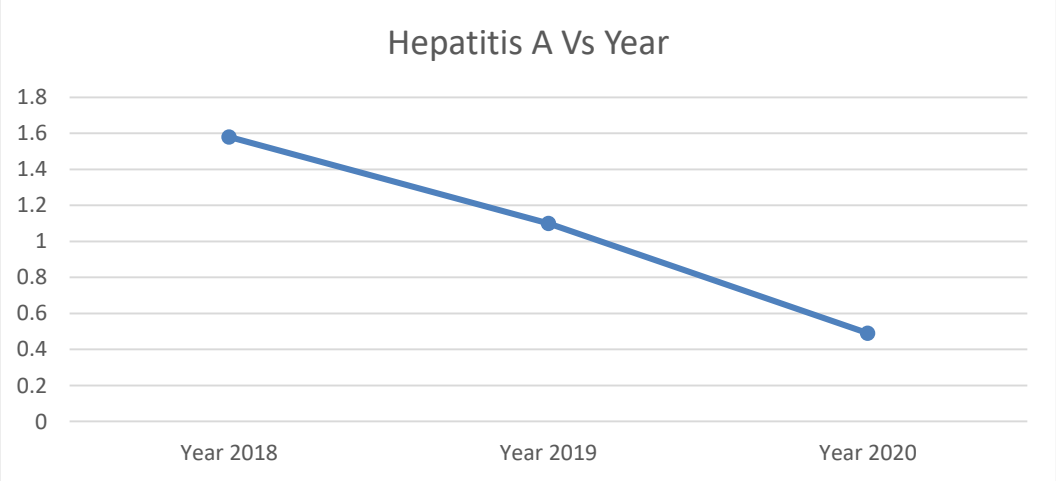

Figure 7: Percentage of Hepatitis A by year

4.2 Prevalence of Hepatitis B

4.2.1 Univariate association between Hepatitis B and selected variables

Hepatitis B was most prevalent in female patient (91.3%; 95% CI: 90.0-92.4) than that of male patient (76%; 95%CI: 73.5-78.4) (p <0.001). The Hepatitis B percentage was higher in winter season (93.1%; 95% CI: 91.3-94.6), whereas the significantly the lowest percentage found in the rainy season (81.1%) (p<0.001). In case of three-years, hepatitis B was mostly prevalent in 2020 (94.1%; 95% Ci: 91.9-95.8) than other two years (p<0.001).

Table 4: Frequency distribution of hepatitis B

Variables	Categories	N	n (%)	95% CI	P value
Gender	Male	1202	914 (76.0)	73.5-78.4	<0.001
	Female	2312	2110 (91.3)	90.0-92.4	
Season	Rainy	1874	1520 (81.1)	79.3-82.9	<0.001
	Summer	683	613 (89.8)	87.2-91.9	
	Winter	956	890 (93.1)	91.3-94.6	
Year	2018	1454	1100 (75.7)	73.3-77.8	<0.001
	2019	1448	1348 (93.1)	91.7-94.3	
	2020	612	576 (94.1)	91.9-95.8	

4.2.2 Gender wise percentage of Hepatitis B:

Hepatitis B was frequently found in higher percentage in all months in female patients than the male patients. The month April showed the highest (99.09%) positive female patients. on the other hand, the month January showed the lowest (79.58%) in hepatitis B of female patients. In case of male patients, highest positive percentage was observed in January (92.65%) and lowest positive was in June (63.84%) (Figure 3).

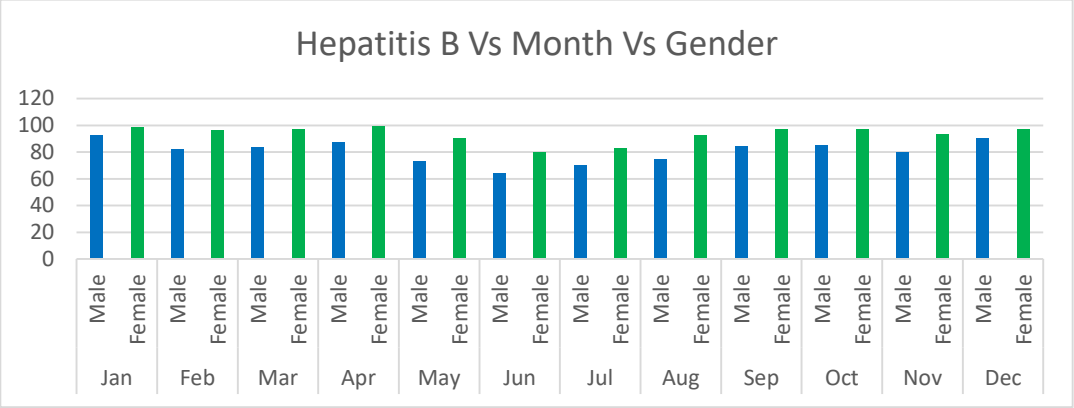

Figure 8: Percentage of Hepatitis B by gender

4.2.3 Yearly variation in detection of Hepatitis B

The line graph showed the higher amount of positive Hepatitis B patients were in the year 2020 (94.12%) and lower were in 2018 (75.65%) (Figure 4).

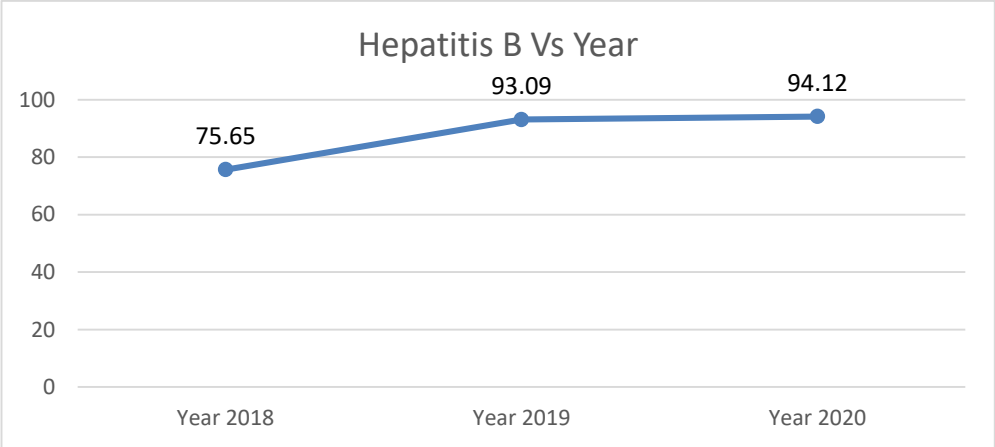

Figure 9: Percentage of Hepatitis B by year

4.3 Prevalence of Hepatitis C

4.3.1 Univariate association between Hepatitis C and selected variables

There is a significant difference in the presence of hepatitis C in the gender variable where, male patients were higher (5.6%; 95% CI: 4.3-7.0) and female patients were lower (1.6%; 95% CI: 1.1-2.1) ($p<0.001$). There was no significant difference in season and year variables.

Table 5: Frequency distribution of Hepatitis C

Variables	Categories	N	n (%)	95% CI	P value
Gender	Male	1202	67 (5.6)	4.3-7.0	<0.001
	Female	2312	36 (1.6)	1.1-2.1	
Season	Rainy	1874	52 (2.8)	2.1-3.6	0.672
	Summer	683	19 (2.8)	1.7-4.3	
	Winter	956	32 (3.4)	2.3-4.7	
Year	2018	1454	34 (2.3)	1.6-3.2	0.063
	2019	1448	43 (2.9)	2.1-3.9	
	2020	612	26 (4.3)	2.8-6.1	

4.3.2 Gender wise percentage of Hepatitis C

Hepatitis C was observed higher in male patients in every month. 11.11% male patients were infected with hepatitis C in march which is the highest and 1.54% in July which is the lowest. In case of female, highest 3.14% was infected with hepatitis C in June and lowest 0.56% was infected in May.

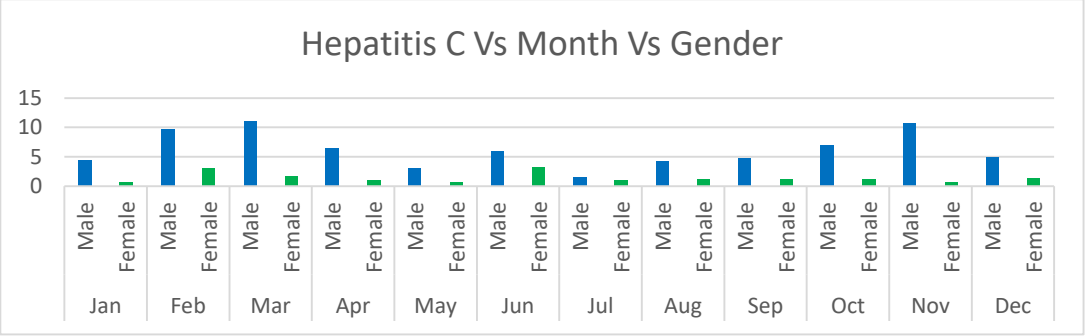

Figure 10: Percentage of Hepatitis C by gender.

4.3.3 Yearly variation in detection of Hepatitis C

In the year of 2020, hepatitis C infection was highest (4.25%) among those three year. Lowest infection was observed in 2018 (2.34%) (Figure 6).

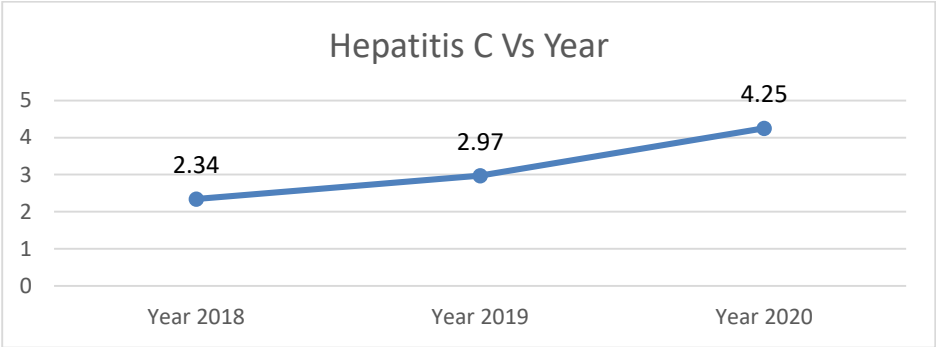

Figure 11: Percentage of Hepatitis C by year

4.4 Prevalence of Hepatitis E

4.4.1 Univariate association between Hepatitis E and selected variables

A total of 374 patients were found with Hepatitis E. Among them 345 patients had Hepatitis E alone, while the remaining 29 had co-infection with at least one other type of viral hepatitis. There was significant variation detected in all three variables in case of hepatitis E. Male patients were identified with higher infection (19.4%; 95% CI: 17.2-21.7) with hepatitis E than that of female patients (p<0.001). Moreover, rainy season showed significantly higher infection with hepatitis E (12.3%; 95% CI: 10.8-13.8) than the other two seasons summer and winter (p=0.001). In case of year, significantly higher amount of hepatitis E found in 2018 (16.4%; 95% CI: 14.5-18.4) than the other two year.

Table 6: Frequency distribution of Hepatitis E

Variables	Categories	N	n (%)	95% CI	P value
Gender	Male	1202	233 (19.4)	17.2-21.7	<0.001
	Female	2312	141 (6.1)	5.2-7.2	
Season	Rainy	1874	230 (12.3)	10.8-13.8	0.001
	Summer	683	71 (10.4)	8.2-12.9	
	Winter	956	73 (7.6)	6.0-9.5	
Year	2018	1454	238 (16.4)	14.5-18.4	<0.001
	2019	1448	111 (7.7)	6.3-9.2	
	2020	612	25 (4.1)	2.7-5.9	

4.4.2 Gender wise percentage of Hepatitis E

Hepatitis E was witnessed significantly higher in male patients. Highest amount 28.71% of hepatitis E was identified in male patients in May and lowest 12.16% identified in November. In case of female, highest 11.52% detected in June and lowest 1.19% detected in January.

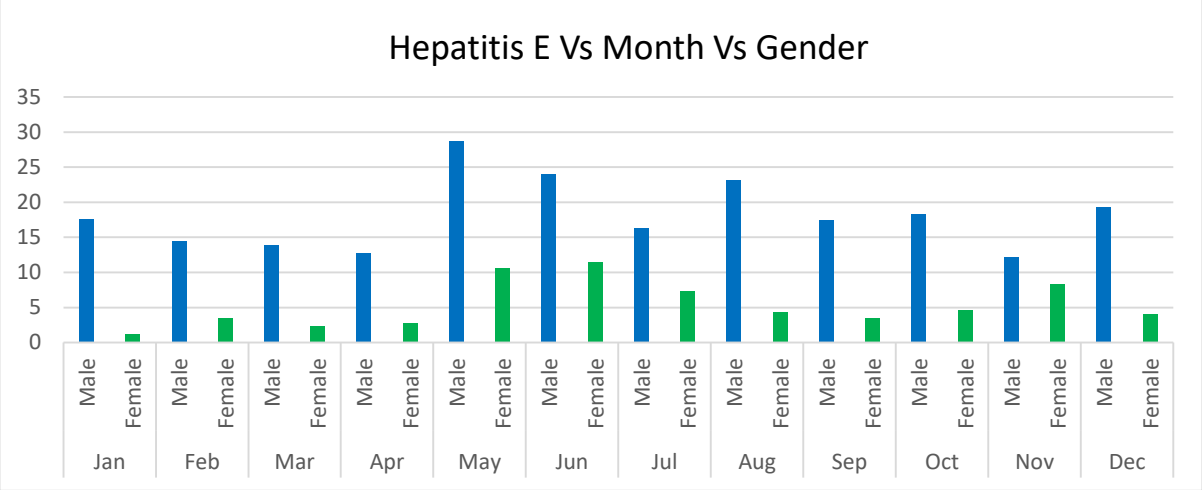

Figure 12: Percentage of Hepatitis E by gender

4.4.3 Yearly variation in detection of Hepatitis E

Hepatitis E was detected highest in 2018 (16.37%) and lowest in 2020 (4.08%).

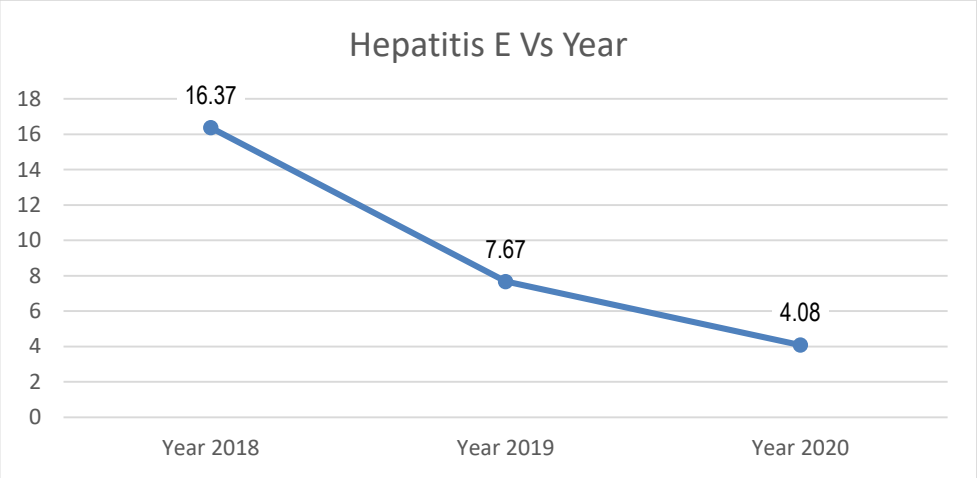

Figure 13: Percentage of Hepatitis E by year

Chapter 5- Discussion

Infections from acute viral hepatitis are seen sporadically throughout the year in Bangladesh. Hepatitis A, B, C, D and E are of greatest concern since they have the potential for outbreaks and epidemic spread leading to severe illness and death. (Mahtab, et al., 2009). Hepatitis B and C in particular can lead to chronic liver diseases and is the most common cause of liver cirrhosis, cancer and hepatitis related deaths when combined together (WHO, 2021). However, while all five viruses cause liver diseases, they vary in their mode of transmission, severity of illness, geographic distribution as well as methods of prevention.

The current study provides an insight to the seroprevalence of different types of Hepatitis among the residents of Chattogram. This includes variation across gender, seasons and timeline. Although there are multiple causes of Hepatitis in Bangladesh, this study has focused on Viral hepatitis in particular since most cases of hepatitis in Bangladesh are attributable to viral causes. (Parvin, et al., 2011).

From the study, it was revealed that the most common type of viral hepatitis found in the residents of Chattogram was Hepatitis B, where 86.06% of the respondents were infected by this. One explanation for this could be that infections with Hepatitis B virus could become chronic and hence lead to an increased prevalence of the disease as compared to Hepatitis A and E where the viruses do not last for a long period of time within the host; or Hepatitis C, for which there are treatments available unlike Hepatitis B.

The second most common viral hepatitis found among respondents was infection with Hepatitis E (9.82%). In contrast, another study on the seroprevalence of different viral hepatitis that was conducted in rural area of Bangladesh, about 22.5% were found to have had previous infection with HEV, while the most common seroprevalence was that for HAV infection (93.5%) (Labrique, et al., 2009). Both of these are waterborne diseases and hence unhygienic practices and lack of proper knowledge of water purification and maintaining sanitation could have led to this finding. In the same study, 35.2% and 1.5% tested positive for HBcAg and Anti- HCV respectively. This suggests although hepatitis B is not the most frequent viral hepatitis in the location, it still made up a substantial percentage of the study population. Another study that was published much earlier (Khan, et al., 2000) showed seroprevalence of HEV to be the most common (53%), followed by HAV (39%), HBV (19%) and HCV (13%). In this

study 100% of children six years of age or below were affected by HAV. From the above-mentioned studies and our recent results, it can be agreed upon that prevalence of acute viral hepatitis (Hepatitis A and E) are gradually decreasing, while the prevalence of choric viral Hepatitis (Hepatitis B and C) is gradually increasing.

On observing the prevalence of HAV infection, a significant number of males were affected as compared to the females ($p= 0.001$). The male: female ratio was 1.47:1. A similar result was observed in a serological study of HAV among medical students in Delhi. (Jindal, et al., 2002) For seasonal variation, although not significant, the disease was more prevalent in rainy season and the number of cases decreased gradually with each passing year. In contrast to a study by Villar et al (Villar, et al., 2002), incidences were highest in spring and summer. However, the study also agreed that a seasonal variation was observed with more cases emerging the rainy season.

Incase of HBV, significant variation was observed in both gender ($p<0.001$), season ($p<0.001$) as well as cases per year ($p<0.001$). The number of females affected were significantly higher and the cases were more frequent in winter season. The prevalence of hepatitis B increased significantly according to the timeline with most cases being seen in the year 2020. While multiple studies were published on the prevalence of HBV among different study populations (Chen, et al., 2007), (Kumar, et al., 2015), no study was found that mentioned the impact of weather conditions on the prevalence of Hepatitis B. One study was found that discussed the seasonal variations across the clinical course of chronic hepatitis B patients. (Zhang, et al., 2006). in this study, disease flareups and remissions were observed in summer and spring seasons, a finding contrary to our study. As mentioned before, with time trend, a rise in cases of HBV was seen. This was not observed in the study by Chen (Chen, et al., 2007) probably due to nationwide vaccination programs against HBV infections.

The gender variable showed significant difference in case of HCV infection, where male patients had a higher incidence than female patients ($p<0.001$). In an African study, on prevalence of hepatitis c infections, isolated infections with HCV were relatively more common in females than in males, while co-infections were more frequent in males than in females. (Pennap, et al., 2010). In almost every month of the year, a higher number of male patients were affected than female ones. Though not significant, incidences of HCV infections are gradually rising over the years in

Bangladesh. In contrast, incidences have been on the decline in Egypt (Kandeel, et al., 2017)

Significant variation was observed in the variables gender, season and year in case of HEV infection. Male patients were more susceptible to HEV infection than female ones and a significantly higher number of cases were observed in the rainy season. When looking at the timeline, a decline in number of cases over the years have been observed, with highest number of cases in 2018.

Looking at the results in its entirety, females were more affected than males and incidences were higher in rainy season. When segregated into types of viral hepatitis, prevalence was higher in males for all types of viral hepatitis except for hepatitis B where prevalence in females was unusually high. The case of female predominance in cases of Hepatitis B is still unknown since most studies show a higher prevalence in the male population. The overall number of viral hepatitis cases detected fell drastically from 1454 cases detected in 2018 to only 612 cases in 2020, probably due to the introduction of yet another infectious disease COVID-19.

Chapter 6- Conclusion

From this study, we can come to this conclusion that cases of viral hepatitis are frequently detected in the district of Chattogram.Hepatitis B was the most common type of viral hepatitis detected making up a major portion of all cases detected. Although reduction in food and water borne viral hepatitis (HAV & HEV) was observed in the most recent years, the rise in prevalence of Hepatitis B and C are a concerning issue. Except for hepatitis B, all cases of viral hepatitis had a male predominance.

Chapter 7 - Recommendation

Incidences of viral hepatitis are on the rise and adequate measures need to be taken in order to control them. Further emphasis should be placed on vaccination and constant check should be done on blood and blood products that help in the spread of chronic hepatitis. Additionally, health education on practicing good hygiene as well as safe sex, provisions of safe water and taking precautions when travelling to endemic areas can help prevent the spread of this disease.

Chapter 8–Limitations

Since this study collected data from a laboratory for analysis, quite a few limitations were present.

- No data on patient demographics other than gender could be obtained due to confidentiality issues.
- Risk factors could not be evaluated due to lack of contact with patients.
- Data collection was limited to just two laboratories. Using more laboratories could increase the number of cases detected and a comparison could have been made between different regions of the district based on the location of these labs.

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