CHAPTER – I

INTRODUCTION

1. Study Area

Nepal is a Himalayan country. It is situated in between latitude 26^0 22' N to 30^0 27N and longitude 80^0 4' E to 88^0 12'E and elevation ranges from 90 to 8848 meters. The total area of the country is 1, 47,181 sq. km. The average length is 885 km. east to west and average breadth is 193 km. north to south.

Nepal is landlocked country and situated in between China and India. The northern range is covered with snow over years. The highest peak of the world 'Mount Everest' is situated in it. The middle range is cover with hills, rivers, valleys, lakes. The southern region consists of dense forest, national parks, wild life reserves and conservation area. There are 23.2 million people of 60 casts/ethnic groups accommodated in the country. Geographically, the country is divided into mountain, hill and Terai region. There are 7.3 % population in mountain, 44.3 % in hill and 48.4 % of population in Terai region. The temperature and rainfall differ from place to place.

There are five development regions, 14 zones and 75 districts. Districts are further divided into Village Development Committee (VDC) and Municipality. Currently, there are 3,915 VDCs and 58 municipalities.

Health services in the country are organized into a hierarchy of management, under the Department of Health Service (DHS) of the Ministry of Health (MOH). At the central level, there are 7 divisions, 5 national centers. At the regional level, 5 Regional Health Directorates (RHD) are responsible for public health services.

The private sector provides a significant proportion of health care. In rural areas this is predominantly by traditional healers and in urban areas by pharmacies and doctors and NGOs make contribution to health care services. The Hepatitis-B, other communicable and non-communicable diseases pose significant threat to the population.

1.1 Bir Hospital

Bir Hospital is the oldest medical institution in the country. It was established in 1890 A.D. It is located in the heart of Kathmandu in Mahabaudha. It serves as a primary facility as well as tertiary referral centre. It is the largest hospital in the country. There are 20 departments in general O.P.D. The referral cases from all over the country attend Bir Hospital. About 300 thousands patients visit the Bir Hospital in one year. It is a teaching hospital as well. Now, it is called National Academy of Medical Sciences (NAMS).

2. Background Information of Hepatitis-B

Hepatitis-B was formerly known as serum hepatitis or long incubation hepatitis. There is no clear cut description of hepatitis-B in Ayurveda and other ancient Hindu text but it is mentioned as 'Kamala' in Ayurveda.

Hepatitis-B is endemic throughout the world, especially in tropical and developing countries and also in some regions of Europe. (Zuckerman and Howard, 1990). Viral hepatitis, an infectious disease has been accepted universally as one of the most serious problems in mankind. Its clinical manifestation has been documented from different countries during last three decades.

The term ‘Hepatitis-B’ was first introduced by Mac Callum in 1947. In 1963, Blumberg discovered and termed the protein, in blood from an Australian aborigine as Austria (AU) antigen. By 1968, other investigators, notably Prince and Okochi and Murakami, had established that Au antigen (Now known as Hepatitis-B Surface Antigen or HBsAg) was specially found in the serum of type B hepatitis infected patients and in 1973, Dane found the virus like particles. These particles were considered to be HBV (WHO Report 1973).

Human HBV is a DNA virus, member of the family Hepadna viridae, adopted as a new family in 1984. Efforts to grow this virus have been so far unsuccessful (WHO Report, 1983, No.691).

3. Taxonomy of Hepatitis-B Virus

The HBV, which replicates characteristically by the mechanism of reverse transcription, is classified as a member of Hepadna virus of family Hapadnaviridae. The family Hepadnaviridae possesses enveloped DNA- containing animal viruses that can cause hepatitis in man, animals or birds. The genome of the hepadnavirus virion isolated from the blood of an infected host has a characteristic structure. It consists of a circular (but not covalently closed) partially double-stranded DNA molecule in which one strand [long, L or (-) strand] is of fixed length (3000-3300 nucleotides long) and has a unique 3' and 5' ends and a protein covalently attached to the 5' end. The other strand [short, s or (+) strand] has a fixed 5' end but a variable 3' end, and various in length from 50-100% of that of the L (-) strand (Hollinger, *et al .,1*991).

4. Structure of HBV

Examination by electron microscopy of negatively stained sera containing HBV antigen reveals at least three morphological forms, all of which are

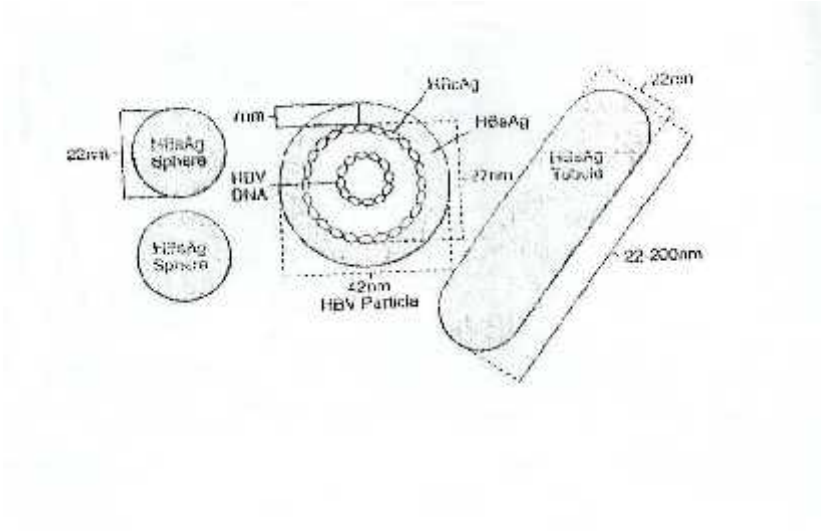


Figure 1: Diagrammatic representation for Hepatitis –B virion and its associated particles

(Source: Koff, 1993)

agglutinated by antibodies directed against the outer surface antigen of the virus particles. These three morphological structures are the hepatitis-B virion itself, and its two forms of surface antigens.

The hepatitis-B virion is a large double shelled spherical particle with a diameter of 42 nm. The structure of virion as a large double shelled particle was described originally by Dane and colleagues in 1970, hence commonly termed Dane antigen (HBeAg.). The HBeAg, which consists of three components, referred as

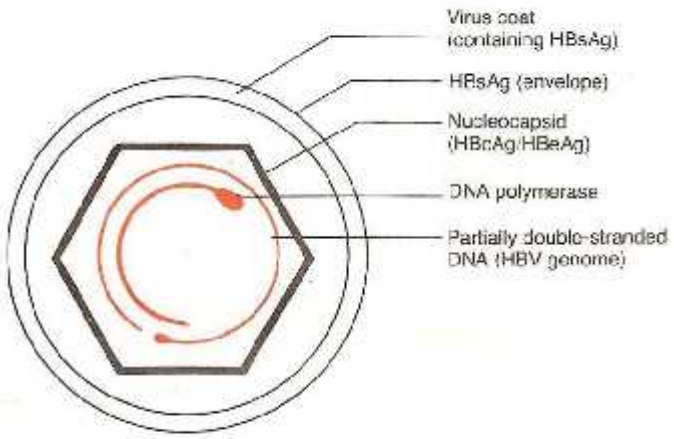


Figure 2: Diagrammatic representation of structure and components of Hepatitis-B

(Source: Gerber et.al.1985)

HBeAg/1, HBeAg/2 and HBeAg/3 (Cheesbrough, 1984), is an integral component of the HBV core particle, presumably resisting in a cryptic form. In the serum, HBeAg remains as a soluble protein with a molecular weight of 15000 D, which results from proteolytic cleavage of the other core protein. The other two morphological forms seen under microscopy include the surface antigens, which are produced in excess by the infected hepatocytes. Out of these two forms, one secreted in the form of 22 nm particles (initially referred to an Australia antigen) and the other in the form of tubular structures of the same diameter with varying length from less than 50 to over 200 nm. Within the infected hepatocytes, filaments are the predominant morphological form, whereas the Dane particles are scantier than the filaments or the abundant smaller spherical particles.

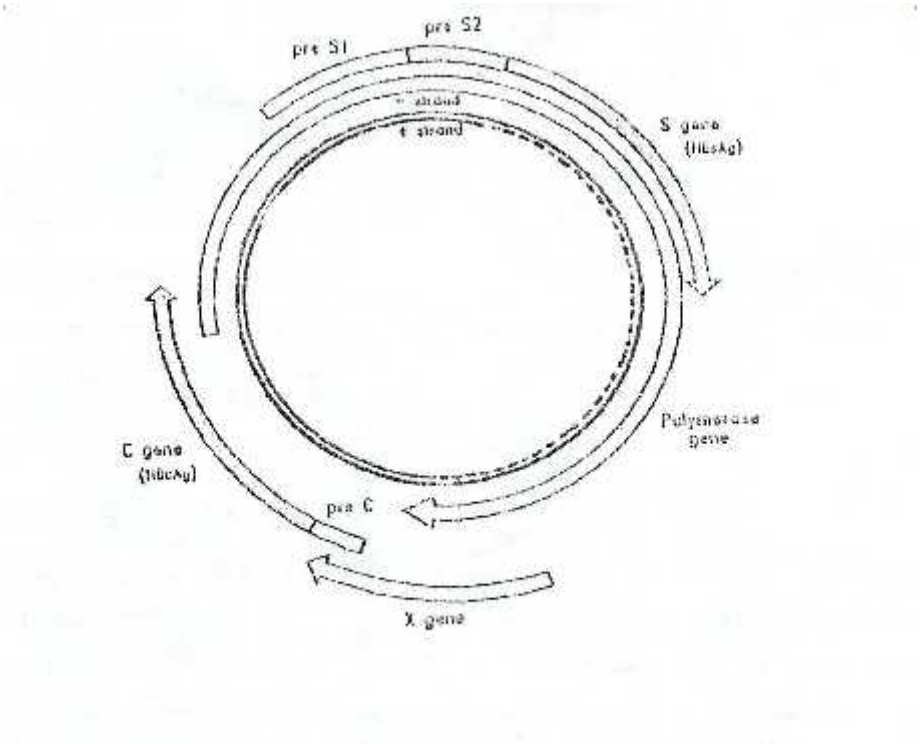


Figure 3: Structure of Hepatitis-B Viral Genome

(Source: Moxon, 1990)

Several studies have shown that, a high proportion of hepatitis-B viral genome is partially double stranded DNA molecule held in a circular particle (Howard et. al, 1990). The virion (Dane particles) comprises an electron-dense nucleocapsid of 27 nm diameter surrounded by another envelop of the surface protein (called Hepatitis-B surface antigen-HBsAg) embedded in the membranous lipid derived from the host cell. The core of nucleocapsid of virion consist the viral genome-HBV DNA, the hepatitis core antigen (HBcAg) and non-structural antigen called the hepatitis-B 'e' antigen (HBeAg).

5. Hepatitis-B Virus Marker

There are various HBV antigens and antibodies. All these antigen and antibody together with the viral DNA polymerase can be detected in the blood at various times after infection and are referred to as "markers",

because their presence or absence in an individual patient mark the course of the disease. It also gives a good idea of the degree of infectivity for others. HBcAg is readily detectable only in the hepatocytes nuclei and not readily detectable in blood and is not used as "marker" (collier and Oxford, 1993).

The Hepatitis-B virus has three distinct antigen a surface antigen, also known as "Australia antigen" (HBsAg), a core antigen (HBcAg), and an "e" antigen (HBeAg). They stimulate the production of corresponding antibodies e.g. surface antibody (anti-HBs), core antibody (anti-HBc) and "e" antibody (anti-HBe). These antibodies and their antigens constitute very useful markers of HBV infection. Patients with HBV infection are expected to have one or more HBV markers.

6. Table: 1 Serological markers of HBV infection

Marker Antigen	**Remarks**	**Present in**
HBsAg	Surface Antigen, not infective	Acute and chronic infection including antigenaemia
HBeAg	Found in core of virion, present in blood indicates infectivity	Acute and chronic Hepatitis
Viral DNA Polymerase	As for HBeAg above	----------

Antibodies	Remarks	Present in
Anti-HBs	Indicates recovery, protect against reinfection	Convalescence
Anti-HBe	Presence indicates little or no infectivity	Convalescence
Anti-HBc	In IgM form indicates recent infection	Convalescence

Note: HBcAg, the core antigen, is not readily detectable in blood and is not used as marker **(Source: Collier, 1993)**

7. Serological and clinical patterns of different markers of hepatitis-B viral infection observed during acute HBV infection.

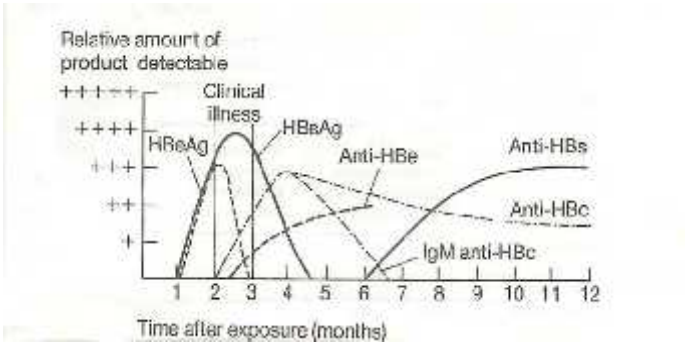


Figure 4: Serological responses to Hepatitis –B Virus infection

(Source: Kumar *et.al.1992)*

8.HBV subtypes:

As well as the main antigen already mentioned, HBcAg, HBeAg, HBsAg, the surface antigen is endowed with serological specificities that enable us to define sub types of the virus. There is a group specific antigenic determinants'd' or 'y'. These in turn may be associated with either of two determinants 'w' or 'r'. Thus, there are four antigenic types of HBsAg- adw, adr, ayw, ayr.

Table:2 Sub types of HBsAg and their determinants

Types	Subtypes	Distribution
Adw	Adw 2	Worldwide
	Adw 4	Worldwide
adr	Adr	Asia(South East)
ayw	ayw 1	Africa, India, Russia
	ayw 2	Africa, India, Russia
	ayw 3	Africa, India, Russia
	ayw 4	Africa, India, Russia
ayr	ayr 1	Africa, India, Russia
Others	Adyw and adywr	-

These sub determinants are of no clinical significance but are useful epidemiologically since there geographical distribution differ. For e.g. Type adw is predominant in Europe and USA, ayw in West Asia, Iran, and Pakistan to India and adr in South Asia. (Collier, 1993).

Additional surface antigens of HBV (q, s, f, t, j, n and g) are described which have not been fully characterized. (Chakravarty, 1995).

9. Stability

It is difficult to assess the stability of HBV due to lack of a suitable laboratory culture system. It was established that heating to 60^0 C for 10 hours in- activates virus by a factor of 100 to 1000 folds. The Chimpanzees inoculation experiment shows that treatment with hypochlorite (10,000 Ppm. available chlorine) and 2% glutaraldehyde for 10 minutes will inactive virus 100,000 fold. Studies based on the survival

of HBsAg shows that this is much more resistant to destruction, (David *et al*, 1992). HBV is readily destroyed by heat sterilization in an autoclave for thirty to sixty minutes (Park and Park, 1997).

10. Hepatitis-B Carriers

There are two types of hepatitis –B carriers based on serological markers.

i. **Super Carrier:** Person with HBeAg in blood is called super carrier. They are highly infectious since only 1 ml. of plasma can transmit the disease. Their blood contains high titre of HBsAg and DNA polymerase. HBV virus may be demonstrable in blood.

ii. **Simple Carrier:** Persons who do not have HBeAg but low titer of HBsAg in blood are called simple carriers. They are most common type of carriers in whom HBV and DNA polymerase are absent. They contain anti-HBc in blood and the infection is transmitted only with large volume of blood. (Chakravatry, 1995).

11. Mode of Transmission

a. Parenteral or percutaneous: Blood, Plasma factors VIII and IX, contaminated needles, dental extraction, operation, tattooing, acupuncture needles, ear piercing, sharing needles and syringes (especially in drug addicts), razors, nail clippers, tooth brushes – all could transmit HBV.

b. Vertical or perinatal spread: Transmission of HBV from mother to infant can occur either from chronic carrier mothers or when the mother suffers from acute viral hepatitis during last trimester of pregnancy.

Infection occurs during birth (ingestion of amniotic fluid or blood) or due to close contact in post natal period. 90% infants, who are infected by their mothers, become chronic carriers probably because their immature immunological system is not able to clear the virus. Risk of transmission to the neonate is about 90% in HBsAg and HBeAg positive mother, about 30% in HBsAg positive, HBeAg and anti- HBe negative mother, and less than 1% in HBsAg positive and anti-HBe positive mothers.

C. Venereal or permucosal spread: Among male homosexuals due to anal intercourse. Bisexual contact also transmits HBV.

D. Oral-oral spread: Since HBsAg has been shown to be present in Saliva, kissing may be a method of transmission. Accidental ingestion of HBsAg positive blood during pipetting can cause HBV hepatitis, as oral ingestion of large viral dose can cause hepatitis (Golwalla, 2000).

Transmission by blood sucking arthropods (e.g. mosquitoes, bed bugs) is suspected but there is no convincing evidence to support suggestion (Park and Park, 1997).

12. Incubation Period

45 to 180 days, lower doses of the virus result often in longer incubation period. The median incubation period is said to be lower than 100 days (Park & Park, 1997).

The incubation period varies inversely with the dose of the virus.

13. Clinical Features:

In case of hepatitis-B, prodromal phase of the infection is often prolonged and more insidious (Howard, *et.al*. 1990). The complications of the infection gradually appear with jaundice and other symptoms like

dark urine, clay colored stool, nausea, malaise, pains in muscles & joints, low grade fever and skin rashes. In some cases, occasionally acute hepatic failure may occur (Singleton and Sainsbury, 1988).

Chronic liver disease may be severe, and may progress to primary liver cancer which in some parts of the world is one of the commonest human cancers, particularly in man (Zuckerman, A.J. 1987, World Health Dec. 1987).

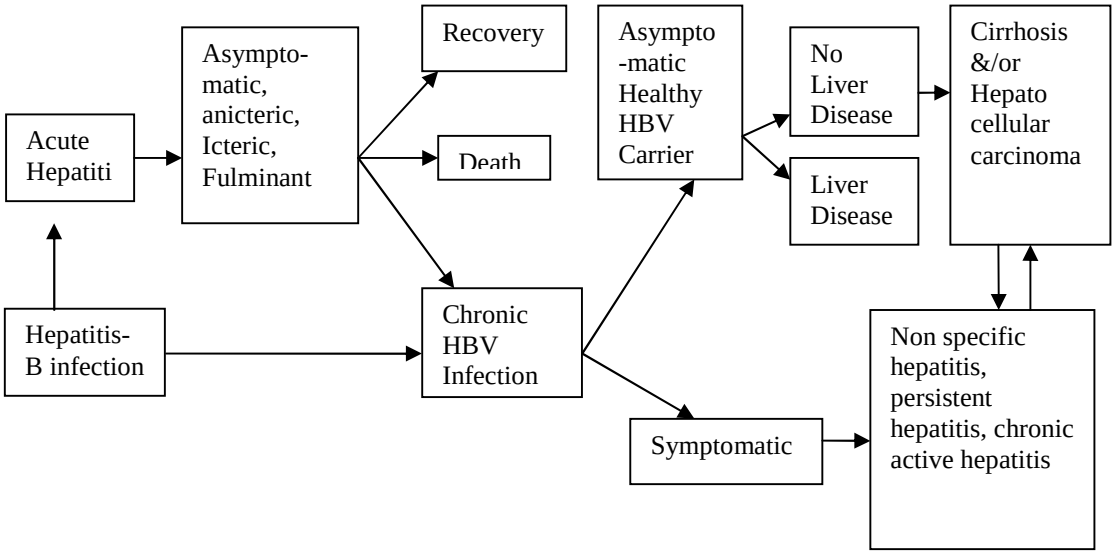
14. High risk groups

This term specifies to people who by reason of their country of birth, way of life or type of work at higher than average risk of acquiring HBV infection.

Table: 3 Groups at higher than average risk of HBV infection:

Category	Risk factor or group
General Community	Sexually promiscuous people, intravenous drug abusers, sexual partner of HBeAg.
Patient	Repeated blood transfusion, long term treatment with blood products e.g. Hemophiliac
Health Care Staff	Work in mental institutions, surgical and dental operation, and some pathological lab work including autopsies, work in STD clinics.

15. Hepatitis-B infection :Range of possible clinical outcome



(Christopher et.al., 1993).

16. Pathology and pathogenesis

In healthy carrier and in chronic hepatitis due to HBV, infected bulky cytoplasm has a ground glass appearance. They are found in clumps and by electron microscopy HBsAg is found to be associated with the endoplasmic reticulum. Naked core particles containing HBcAg are present in cell nuclei.

The morphological lesions in liver produced by all types of hepatitis viruses are similar and consist of pan lobular infiltration with mononuclear cells (mainly lymphocytes), hepatic cell necrosis, hyperplasia of kupffer cells & variable degree of cholesteasis. Parenchymal cell damage consists of hepatic cell degeneration and

necrosis, ballooning of single cells and acidophilic degeneration of hepatocytes as they die.

17. Hepatocellular carcinoma(HCC)

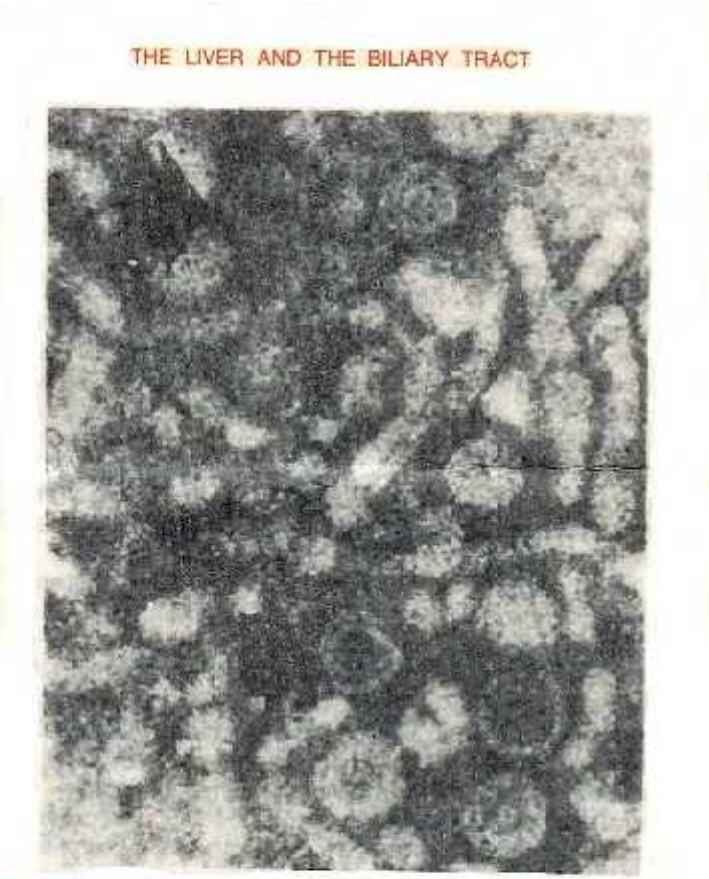


Figure 5 Hepatitis B virus. Electron micrograph (× 220,000) of negatively stained pellet prepared from the serum of a patient with chronic hepatitis. Numerous Dane particles *(arrows)* and 22-nm tubules (consisting of HBsAg) are present. (Courtesy of Dr. Michael Gerber, Professor of Pathology, Tulane University School of Medicine, New Orleans.)

(Source: Kumar *et.al*.1992)

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world, which is found more common in males than females and the incidence of the complication increases with age, reaching a peak in the 30-50 age groups (Howard, *et.al*. 1990).

HCC or primary liver cancer arises as a result of integration of viral genome into the DNA of hepatocytes (liver cells).

In round figures, 80% of patient with acute hepatitis-B recover completely, 15% develop chronic persistent hepatitis (a benign condition) and 5% develop chronic active hepatitis. 5% with chronic active hepatitis, which in about half of them will progress to cirrhosis and in some cases Hepatocellular carcinoma.

18. Interpretation of Results of Serological tests for Hepatitis-B.

Table: 4 Interpretations of Results of Serological Tests for Hepatitis-B

HBsAg	HBeAg	Anti HBc	IgM	IgG	Anti-HBs	Interpretation
+	+	-	-	-	-	Incubation period
+	+	-	+	+	-	Acute hepatitis B or persistent carrier
+	+	-	-	+	-	Persistent carrier state
+	-	+	+/-	+	-	Persistent carrier state
-	-	+	+/-	+	+	Convalescence
-	-	-	-	+	+	Recovery
-	-	-	+	-	-	Infection with HBV without detectable HBsAg
-	-	-	-	+	-	Recovery with loss of detectable anti-HBs
-	-	-	-	-	+	Immunization with infection. Repeated exposure to Ag without infection or recovery from infection from infection with loss of detectable anti-HBc

(Source: Howard and Zuckerman, 1990).

19. Table: 5 Detection of HBs Ag

Generation	Technique	Relative sensitivity	Minimum HBs Ag particle for detection
1st Generation	Agar gel diffusion (AGD)	1 (low)	10^{13}
2nd Generation	CEP/CFT	2-10 (Intermediate)	10^{12}
3rd Generation	RPHA/RIA/ELISA	100-1000 (High)	10^{9}

(Source: Cheesbrough, 1984)

20. Prevention and Control

Hepatitis-B infection though being one of the most infectious and prevalent disease of the world is now preventable with safe and effective vaccines. It is the first vaccine against cancer ever developed (Kane *et. al*. 1993).

However, the vaccine only given prior to infection found effective to prevent disease and the carrier state from developing in almost all individuals.

The vaccines, though become commercially available in 1982, most of the developing countries with high prevalence rate could not afford it. On the other hand, more than 80 countries have already met the call by the Global Advisory Group of the WHO Expanded Programme on immunization (EPI) to introduce the Hepatitis-B vaccine into their national immunization programme by 1997. This programme was run by WHO with the aim of reducing the incidence of new carriers among

children by 80% by 2001, as most HBV infection occurs during childhood (Kane, 1996).

According to the EPI, the first dose of vaccine should be administered to new born with BCG near birth, if possible or with the first dose of DPT, if there is no immunization contact at birth. The second dose should be given with the next dose or DPT and the third dose with the last dose of DPT or at the time of the measles immunization. In case of adult, the vaccine should be given at any age with the interval of 0 – 1 – 6 or 0 – 1 – 2 – 12 months (Kane *et. al*. 1993).

a. Vaccines

Hepatitis-B vaccines are alum adjuvented highly purified preparations of hepatitis-B surface antigen, the glycoprotein that forms the outer coat of the hepatitis B virus. Hepatitis B surface antigen can either be purified from the plasma of HBV carriers (Plasma derived vaccines) or produced in yeast or mammalian cells by recombinant technology (recombinant vaccines). Hepatitis B vaccines are highly immunogenic, even in newborns; and can induce protective anti-hepatitis B surface antibody in 90 to 97 percent of healthy individuals (Kane *et. al*. 1993).

Though having such a high effective sero-conversion rate, there will always be some people who do not respond to the vaccination. The vaccination response is influenced by age, obesity, smoking, immuno competence and gender. Moreover, small percentages of people are genetically or immunologically incapable to response the vaccine (Hallauer, 1996).

Plasma Derived Vaccines

In natural HBV infections, liver cells produce much more HBsAg than is needed to coat viral particles, and the excess HBsAg forms 22 nm spherical and long tubular particles. Plasma derived hepatitis B vaccines are prepared by purifying these particles from the plasma of HBsAg positive donor. These vaccines are inactivated to ensure that no infectious virus or other micro-organisms are present and then alum is added as an adjuvant.

Though the plasma derived vaccine was approved by FAD in 16 Nov, 1981 its use had been limited because of high cost and fear of Acquired immune deficiency syndrome, which could be transmitted through blood products (World News Digest, 1981).

Recombinant Hepatitis B Vaccines

These vaccines are produced by using recombinant DNA technology from HBsAg derived from yeast or mammalian cells in which replicating plasmids containing the viral HBsAg gene are inserted. The HBsAg forms spherical particles similar to the natural 22 nm spherical particle in both chemical composition and immunogenicity.

Other vaccines against hepatitis B which are in progress of clinical trials (Zuckerman and Harrison, 1990) include Hybrid Virus Vaccines, Naval Hepatitis B Vaccines and Chemically synthesized Hepatitis B Vaccines.

b. Immune Globulin

Hepatitis B immune globulin (HBIG) is the antisera containing antibodies to HBV. If the hepatitis B immune globulin is given to

newborns of HBeAg positive mothers in addition to hepatitis B vaccines, the efficacy may be increased to 80 to 90 percent (Zuckerman, 1994; Kane *et. al*. 1993).

21. Treatment

Many antiviral compounds have been proposed for the treatment of hepatitis B infection. Interferon is one such compound, which is still being evaluated for the treatment of chronic hepatitis B in many countries. A number of reports indicate that the administration of an interferon in persistently infected patients has an inhibitory effect on replication of HBV in 40 – 60% of carefully selected patients with chronic active hepatitis B infection. In one another study, out of 169 people treated with interferon, the compound stopped further liver damaged in nearly half of them. Again out of ten subjects one was found entirely cured (World News Digest, 1990).

Similarly, several clinical studies with Ribavirin (Virozole), another well known antiviral chemical, appeared to show encouraging result in acute hepatitis as well as in persistent carriers. Two another synthetic compounds – Suramin (a poly basic anion) and Acycloguanosin (acyclovir) have been shown to exert antiviral activities in experimental hepadnavirus infection. Unfortunately, Suramin has been found to be too toxic (Zuckerman and Harrison, 1990) in clinical trial in patients with chronic hepatitis B.

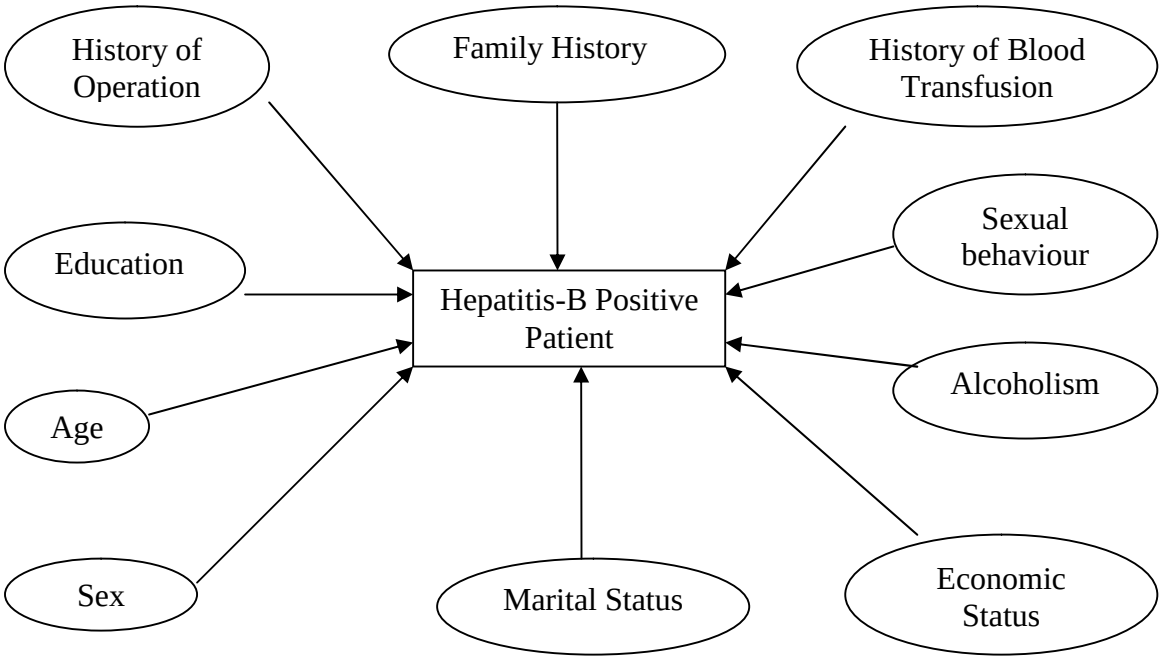
In addition to these antiviral chemicals, herbs of the genus Phyllanthus also believed to possess antiviral properties against HBV (Meixia *et. al.* 1995).

22. Epidemiology

The age at which an individual is infected determines the likelihood of a chronic infection developing. 90% of the adult infected with HBV successfully clear the acute infection and become immune naturally. 9% proceed to chronicity and become chronic carriers. This 9% also forms the human reservoir for the spread of infection in the community. 1% is seen to suffer from fulminant hepatic failure and die early in the acute stage. Fulminant hepatitis refers to a clinical condition with rapid onset and development of acute hepatic failure, with encephalopathy, coma & death in more than 70% cases (Mc Intyre N et.al.).

It is due to an enhanced immune response with more rapid clearing of virus. Where as, 98% of babies born to mothers with chronic HBV infection become infected, and 95% of these will develop a persistent infection (Jawetz *et.al*.)

23.Conceptual Framework



CHAPTER – II

OBJECTIVES OF THE STUDY

General Objective

- To conduct the serological survey on representative samples of clinically suspected patients.

Specific Objective

-To determine the sero-prevalence of Hepatitis-B surface antigen (HBsAg) among blood samples collected from Bir Hospital.

-To find the most susceptible age group and sex group for the infection.

- To recommend the preventive and control measures against Hepatitis-B

Research Questions

- What is the prevalence of Hepatitis-B?
- Which is the most susceptible age group and sex group?
- What are the preventive and control measures of Hepatitis-B?

Study Variables

Dependent variable

- Hepatitis-B

Independent variables

- Age
- Sex
- Socio-economic Status
- Education Status
- Marital Status
- History of Blood donation
- History of Blood Transfusion
- History of Operation
- History of Alcoholism
- Family History of Hepatitis-B
- More Than one Sexual Partner
- IV drug user

CHAPTER – III

LITERATURE REVIEW

Hepatitis-B Research in Global Perspectives

Large volume of literature exists in Hepatitis-B because it is a major public health problem. There is growing concern globally about it. Major research efforts have been directed towards chemotherapy, immunology and vaccines, molecular biology etc. in recent years. Some works regarding prevalence of Hepatitis-B have been mentioned here.

Hollinger *et.al*, (1991) reported that 300 million individuals worldwide are chronically infected with HBV and worldwide one million deaths per year are directly related to HBV infection.

Kane *et.al.,* (1993) published a report on viral hepatitis by viral Hepatitis prevention Board, WHO indicates that, though plasma derived and recombinant vaccines are approved for use in most parts of the world, more than two billion individuals alive today have been infected with HBV at sometime in their lives.

Kane and Mc cloy (1994), reported the situation in many developing countries is too miserable as more than half the population have been infected by the virus.

Hallauer (1996) concluded that the countries with high prevalence rate of HBV infection usually have low economic standard and are unable to afford vaccine for immunization.

de Francisco *et.al*., (1999) – In order to estimate the relative importance of perinatal transmission of HBV in rural Bangladesh a cross

sectional study was carried out. In total 107 (32.4%) positive for HBcAg, 18 (5.4%) for HBsAg. Of infant 1 (0.3%) for HBs Ag. Of the 18 HBsAg positive mothers, 4(22%) were HBe Ag positive.

This survey indicates that HBV is prevalent in rural Bangladesh and that the perinatal transmission mode may be relatively low

Table:6 Prevalence of Hapatitis-B throughout the world

Category	Low	Intermediate	High
Areas	North Europe, Western Europe Central Europe North America, Australia	Eastern Europe, Mediterranean, Former USSR South West Asia, Central America, South America	Parts of China, South East-Asia, tropical Africa
HBsAg Anti-HBsAg Neonatal infection Childhood infection	0.2 – 0.5 % 4 – 6 % Rare Infrequent	1 – 7 % 20 – 55 % Frequent Frequent	8 – 20 % 70 – 95 % Very frequent Very frequent

(Source: Zuckerman & Harrison, 1990)

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Nakai, K. *et.al*, (2001) found on the study population of 403 subjects in Yangon, Myanmar that infection rate of viruses was 8% for HBV.

O' Connel *et.al*, (2000) estimated anti-HBc prevalence in Republic of Ireland is 0.51%.

Oliveira, *et.al*, (1999) found high prevalence of HBV (7.8%) among injecting drug users in Rio de Janeiro, Brazil.

Chunlertrith, *et.al*, (2000), noticed clinico-epidemiology of Hepatitis-B viral infection in North Eastern Thailand that the clinical feature of acute hepatitis was 2.36% and chronic hepatitis was 34.12%. Hepatitis B virus (HBV) infection is a global health problem. Two billion people have been infected worldwide; 360 million suffer from chronic HBV infection; over 520,000 die each year (50,000 from acute hepatitis B and 470,000 from cirrhosis or liver cancer). In Africa and Asian Countries the prevalence of chronic infection is more than 8%, in North Western Europe, North America, and Australia the prevalence of chronic infection is less than 1%. (EASL jury)

Sherlock, S. &Dooley, J. (1997), the carrier rate of HBsAg varies worldwide from 0.1 to 0.2% in Britain, the USA and Scandinavia to more than 3% in Greece and Southern Italy, and even up to 10 to 15% in Africa and the Far East. The rate of exposure to HBV in any community is even higher. Carrier rate of HBsAg is very high in some isolated communities; 45% in Alaskan Eskimos and 85% in Australian Aborigines.

Lee, WM (1977), South East Asia, China and Africa, where the prevalence is high, more than half the population is infected at sometime in their lives and more than 8% are chronic carriers of the virus, the result of either neonatal transmission (vertical) or transmission from one child to another (horizontal).

Tandon, BN et.al. (1996), in 1995, the population of India was reported to be around 900 million. The average estimated carrier rate of HBV in India was 4% with a total pool of approximately 36 million carriers. Among the estimated 350 million HBsAg carriers worldwide, therefore, India alone contributes 9% of global pool.

Litch, JA *et.al*, (1998), the seroprevalence of HBsAg in certain population in India, especially of low socio-economic group, is much higher. Tibetan refuges in northern India were found to have a HBsAg seroprevalence of 21% about five times higher than that of general population.

Live, DB, Wang, HM *et.al*. Reported that the general population of Taiwan has 15-20% carrier rate, which is one of the highest in the world. Approximately, 80 to 90% of the general population was shown to be infected by the age of thirty.

Table:7 Prevalence of HBs Ag in South East Asia

Country	Hepatitis-B Carrier
Bangladesh	9 %
Myanmar	12 %
Nepal	1 %
Maldives	6 %
India	5 %
Thailand	10 %
Bhutan	6 %
Sri Lanka	0.9 %
Indonesia	5 %

Hepatitis-B Research in National Perspectives

Mishra, A.K. (2002), studied on prevalence of HBeAg positive cases among Hepatitis-B virus infected patients. Among 97 patients, 19 patients were found to be positive for HBeAg, indicating that percentage of positivity is 19.6%. The HBsAg and HBeAg were both found to be most prevalent in the age group of 20-29.

Shrestha, S.M. (2000), Showed that prevalence of hepatitis-B in general population is low (HBsAg 1%, anti HBsAg 8%).

Bhatta, *et.al*. (1993), In a study done in Kathmandu Valley, the prevalence of Hepatitis-B among commercial sex workers was found to be 10.9% which is higher in this because the study was done in higher risk groups.

Gyawali, *et.al*. (2002), A study on correlation between hepatitis-B surface antigen and liver function test and the possible factors responsible for hepatitis-B among the patients attending TUTH was conducted in TUTH. Total 78 HBsAg reactive sera and patients along with 54 liver function elevated were studied to explore the facts tracing the possible source of infection hetero-sexual activity was found most common (23%).

Shrestha, SK. (2002), Antibodies to HBV core antigen were found in 21 (14.5%) of 145 HCWs. HBV surface antigens were detected in 2(1.4%) HCWs.

Shrestha, S.M. (1990), In Nepal, HBsAg positive was in 0.9% (1.5% male & 0.5% female). The prevalence of HBsAg is higher in urban than in rural area.

Manandhar, K. & Shrestha, B. (2000), Nepal has been reported to fall in intermediate endemicity (3.97%) and the prevalence was reported

4% in Western Development Region.

Shrestha, S.M. (1987), sero-epidemiological study on Surkhet district of Mid- Western Development Region showed that 6.6% of the healthy population was found carrier of HBsAg.

Shrestha, B. (2003), Of the 177 subjects, 9 was found positive for HBsAg making the prevalence of HBV carriers 5.08% in the target population. The prevalence was greatest 8.69% in active young age group 16-20.

CHAPTER – IV

RESEARCH METHODOLOGY

4.1 Research design:

It is a cross sectional prospective study conducted between 15th July 2002 –15th May 2003.

4.2 Sampling technique:

Purposive Sampling Technique.

4.3 Sample size:

275 patients.

4.4 Study area:

The selected study area is the Bir Hospital, Kathmandu. It is a Central, tertiary level hospital of the country.

4.5 Research population:

Patients of varying ages and different sexes who had attended different OPD of Bir Hospital.

4.6 Collection of Sample:

Samples were collected between 15th July, 2002 – 15th May, 2003. Before filling the questionnaire, each individual was informed about the research procedure and objective of study and taken verbal consent. Then questionnaires were filled.

Blood samples were drawn by lab technicians of Bir Hospital pathology under strict aseptic precaution. The blood samples were serologically investigated by lab technicians of Bir Hospital pathology themselves. The result is based upon the test result given by them.

4.7 Reliability and Validity

- Questionnaire was prepared in simple language.
- Pre-testing of the questionnaire was done.
- Principle investigator was directly involved in the interview and report collection.
- The filled up questionnaire were checked by the investigator after completion of the questionnaire session.

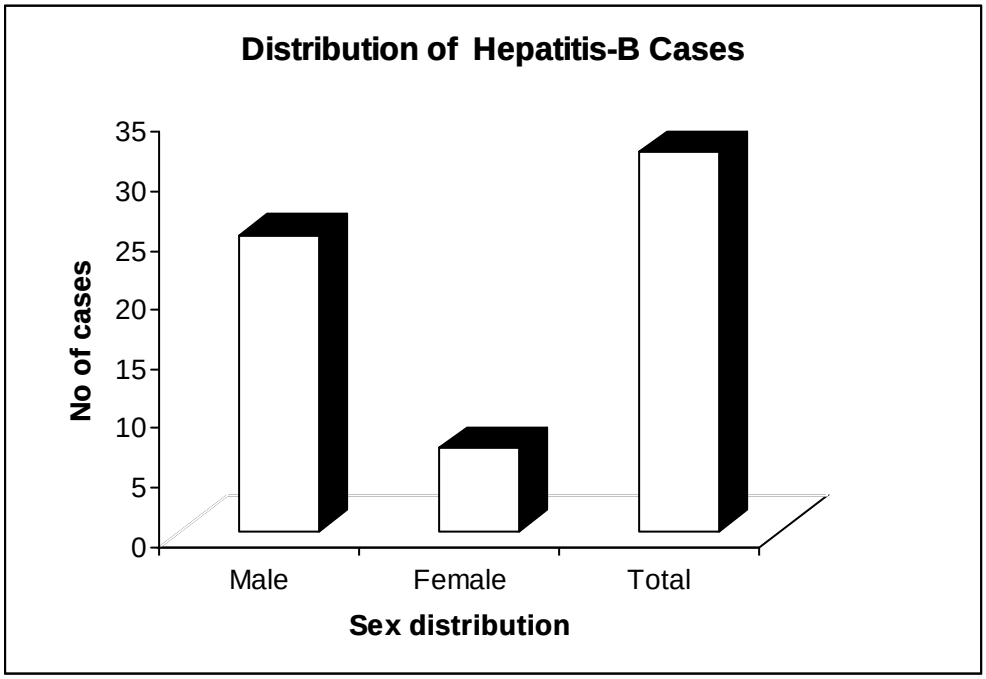
4.8 Limitation of Study:

The study is limited due to time, area, budget and adequate literature.

CHAPTER V

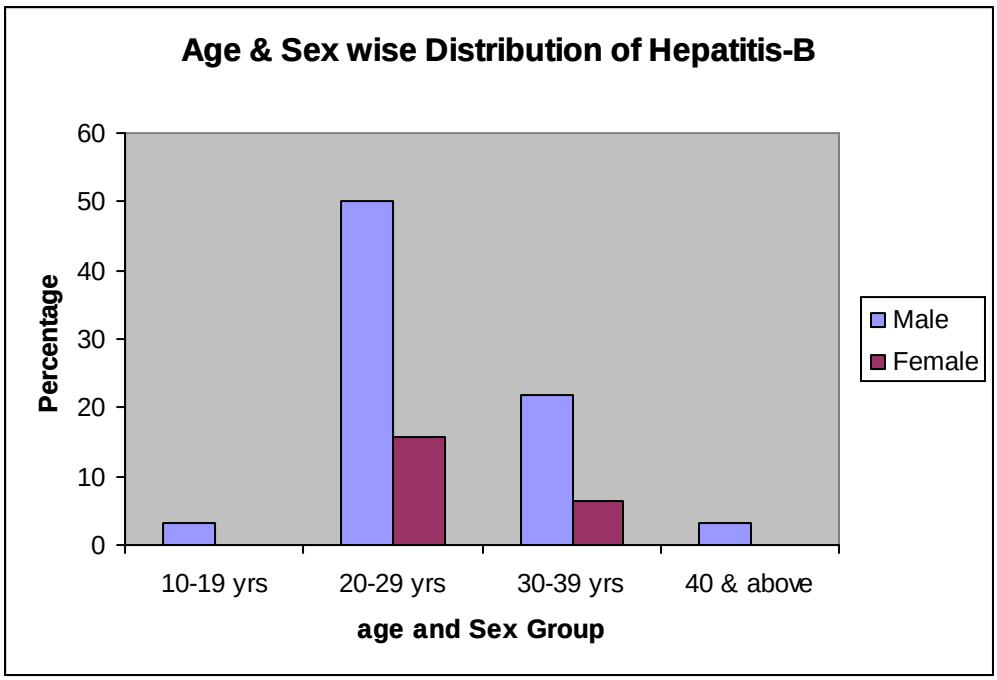
Findings

Total collected samples	-	275
Male samples	-	203
Female samples	-	72



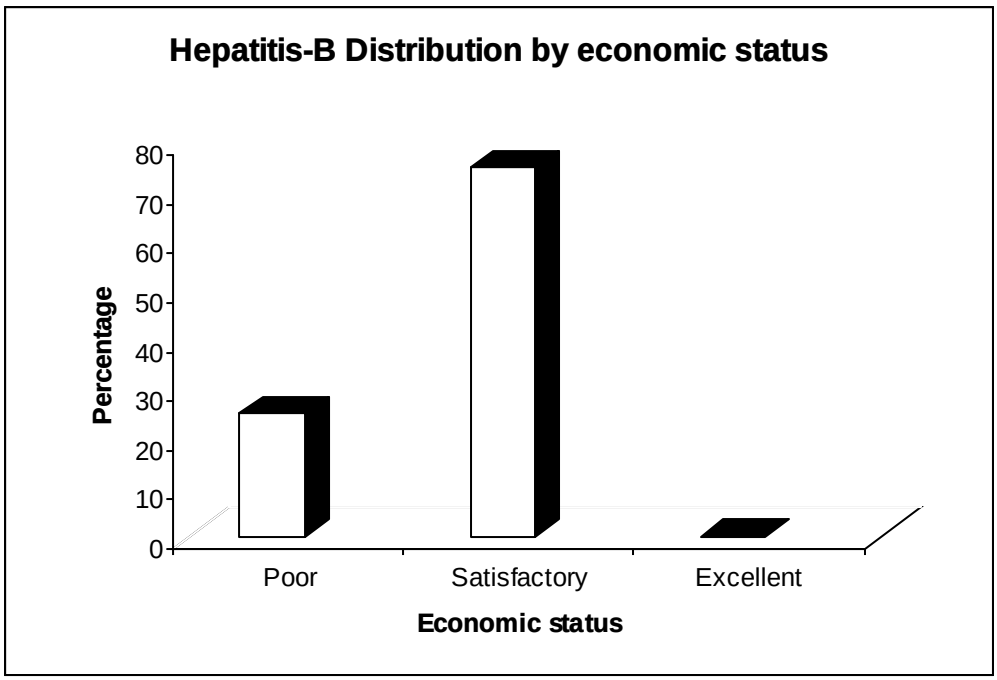
Graph No. 1: Sex-wise distribution of hepatitis-B cases

Total positive cases	-	32
Male positive cases	-	25
Female positive cases	-	7



Graph No. 2: Age and Sex-wise % distribution of hepatitis-B cases

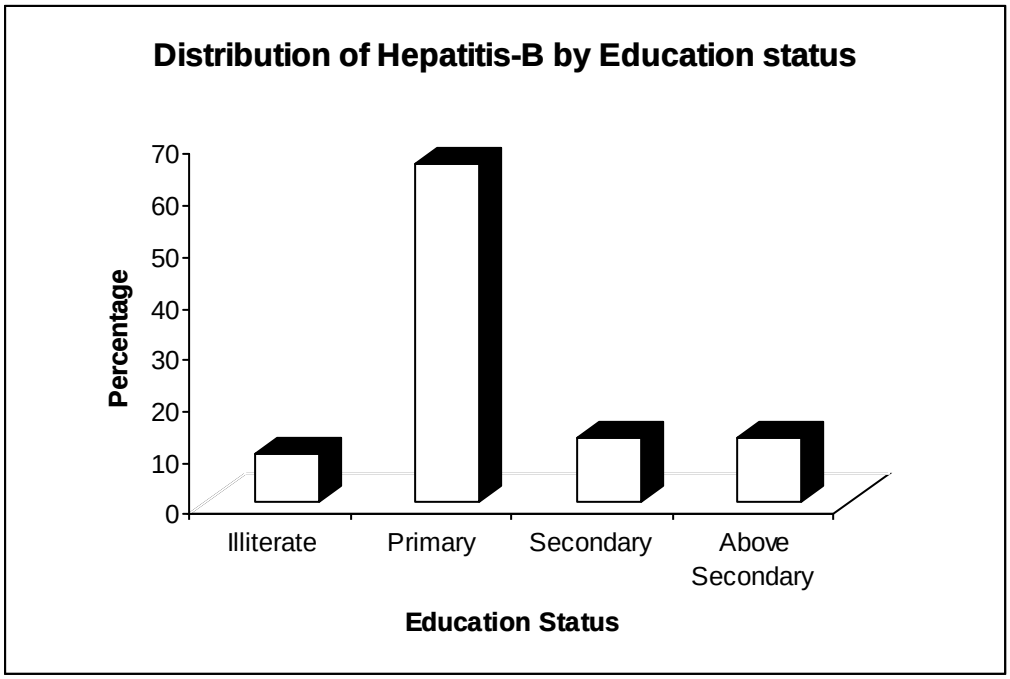
			Total	+ve	%
Marital Status:	Married	=	157	19	59
	Unmarried	=	118	13	41



Graph No. 3: Socio-economic status of hepatitis-B Patients

Socio-economic condition:	Poor	=	54	8	25
	Satisfactory	=	209	24	75
	Excellent	=	12	0	00
History of blood donation:	Yes	=	7	1	3.1
	No	=	268	31	96.9
History of blood transfusion:	Yes	=	3	1	3.1
	No	=	272	32	96.9
History of operation:	Yes	=	9	1	3.1
	No	=	266	31	96.1

More than one	Yes	=	11	4	12.5
Sexual partner	No	=	264	28	87.5
Family History of Hepatitis-B:	Yes	=	00	00	00
	No	=	47	6	18.8
	Don't know	=	228	26	81.2
IV Drug user:	Yes	=	2	1	3.1
	No	=	273	31	96.9
History of Alcoholism:	Non-drinkers	=	67	4	12.5
	Occasional drinker	=	196	26	81.2
	Regular drinker	=	12	2	6.3



Graph No.4: Education status of hepatitis-B Patients

Education:	Illiterate	= 27	3	9.4
	Primary education	= 134	21	65.6
	Secondary ,,	= 66	4	12.5
	Above Secondary,,	= 48	4	12.5

Table:8 Prevalence Of Hepatitis-B

Age group (in years)	Male			Female			Total		
	Total No. of Sample	Positive (HBs Ag)	%	Total No. of Sample	Positive HBs Ag	%	Total No. of Sample	Positive HBs Ag	%
10 – 14	4	0	0	0	0	0	4	0	0
15 – 19	23	1	4.35	6	0	0	29	1	3.45
20 – 24	49	7	14.29	21	2	9.52	70	9	12.86
25 – 29	45	9	20	19	3	15.79	64	12	18.75
30 – 34	33	4	12.12	13	1	7.7	46	5	10.87
35 – 39	23	3	13.04	11	1	9.09	34	4	11.76
40 – 44	15	1	6.67	2	0	0	17	1	5.88
Above 45	11	0	0	0	0	0	11	0	0
Total	203	25	12.32	72	7	9.72	275	32	11.63

CHAPTER – VI

DISCUSSION

Hepatitis-B is a disease of clinical importance. It is a kind of DNA virus, member of family Hapadnaviridae (WHO report, 1983).

It has three morphological forms. They are Dane particle, sphere and tubules. Of the three, only Dane particle is considered as infectious. (Chakravarty, 1995).

There exist various HBV antigens. They are HBsAg, HBcAg and HBeAg. (Howard & Allison, 1995).

Clinical picture of viral hepatitis are almost indistinguishable. Although, occasionally, jaundice may be the first symptom of acute hepatitis in most cases, there is prodromal period of non-specific symptoms prior to jaundice, which is clinically difficult to distinguish (Sherlock, 1980).

Present study is based on the cases suspected by physicians of different departments of Bir Hospital during their treatment period. During the study period, 275 blood samples were collected. Among total Hepatitis-B cases, 12.32% and 9.72% were found among male and female respectively.

Hepatitis-B is highly infectious disease. At present, it is a global health problem. Hollinger, *et.al.* (1991) reported that 300 million individuals worldwide are chronically infected with HBV and worldwide one million deaths per year are directly related to HBV infection.

Age groups of the studied human population were categorized into the difference of 5 years up to 45 and above. Among total blood samples, 203 were from male and 72 were from female. The study showed that

male and female of age group 25-29 were found to be highest prevalence rate i.e. male 20% and female 15.8%

Thus, the result clearly indicates that both male and female of age group 25-29 were very susceptible to hepatitis-B infection.

Mishra, A.K. (2002) showed that HBsAg and HBeAg were both found to be most prevalent in the age group of 20-29. The present study also showed that the HBsAg most prevalent in age group 25-29. Hence, it is consistent with the previous report.

No cases of Hepatitis-B were reported from 10-14 and above 45 years of male as well as below 20 years and above 35 years of female. The least prevalence rate was reported from age group 15-19 in male as well as 30-34 in female.

Shrestha S.M. (1990) reported that in Nepal, HBsAg positive was in 0.9% (1.5% male and 0.5% female). The prevalence of HBsAg is higher in urban than in rural area.

But present study shows that HBsAg positive is 11.63% (Male 12.32% and female 9.72%). It is higher result because the study was done in clinically suspected cases (High risk group).

The educated and uneducated both are suffering from Hepatitis-B. There is no significant reduction in the HBsAg prevalence in educated person. Hence, the school education is not effective in Nepal.

This study shows that people from poor or satisfactory economic status are more susceptible for the hepatitis-B. It may be due to insufficient sample collected from the people of excellent economic status.