REVIEW OF LITERATURE
Review of literature

Although hepatitis was known very early as an infectious disease (Zukermann 1979), the observations leading to our current knowledge of hepatitis began with studies of hepatitis outbreaks during the first world war and the demonstration later by transmission studies with bacteria free filtrates that the disease was caused by a virus. Human volunteer studies distinguished between faeco-oral transmitted, short incubation, epidemic (but also sporadic) hepatitis (hepatitis A) and parenterally transmitted long incubation hepatitis (hepatitis B) and indicated existence of further forms of hepatitis nonA, nonB. The search commencing with hepatitis B in 1963 leading to hepatitis E in 1990 terminated to the present day characterization of the six hepatotropic agents (A,B,C,D,E,G) (Shleizeinger).

All forms of viral hepatitis have a basic pathology. The essential lesion is an acute inflammation of the entire liver. Hepatic cell necrosis is associated with leucocytic and histiocytic reaction and infiltration. (Dible et al 1943).

All of them start with a prodromal period of mild fever, headache, flu like illness or no symptoms at all followed by darkening of urine/ lighting of faeces. Then jaundice develops along with
transient itching. Liver is specially affected and is palpable with a smooth/ tender edge in 70%. After an icteric period of 1-4 weeks the child gradually recovers. Hepatitis A,E and G are such type of self limiting illnesses. On the other hand hepatitis B and C are prone to chronicity.

Tandon et al (1984) studied etiological spectrum of viral hepatitis and the prevalence of serological markers of hepatitis A and B virus infection in healthy persons in North India. Hepatitis A virus was found to be the most common cause of acute hepatitis in children (67%). It was a less frequent cause of this disease in adults (14%). Exposure to HAV occurs in early etiological and by the age of 10 years 90% of healthy persons have serological evidence of hepatitis A virus infection.

Worldwide, there are more than 350 million carriers of HBV, 60 million of whom will die from liver cancer and 45 million from cirrhosis (Shleizeinger). The world wide prevalence of HBV infection is falling (Alberti et al).

It is estimated that there are 300 million carriers of HCV, about 2.5 million in Europe. In USA, it is conservatively estimated that approximately 170 000 cases of acute hepatitis C occur per year. Of
these, between 70 and 80% will maintain infection and develop chronic hepatitis (Alter et al).

Hepatitis E occurs in all epidemic, sporadic, endemic in India. The largest epidemic in India was reported in 1955-56 in New Delhi. Subsequent outbreaks of epidemic and sporadic hepatitis E were documented in North India (Tandon et al, 1982) and in Kashmir, India (Khuroo et al, 1983). Similar outbreaks have been reported in other regions of South East Asia. A high mortality rate (18-20%) has been incurred in pregnant women.

On studying the age related distribution of children with acute viral hepatitis (with complications). We found that various pediatricians.


Malathi et al (1998) also subdivided 127 children with acute viral hepatitis into two years slabs (0-2, 2-4 and so on upto 12 years) they observed maximum incidence 43% of HAV between 2-4 years, 4-
6 years. Majority of Non A and Non B (they didn’t test for HEV and HCV) were between 2-4 years.

Khuroo et al (1983) observed that HAV cases were maximum below 10 years of age.

Thapa et al (1995) subdivided their 324 children of acute viral hepatitis into three broad groups (0-5, 6-10 and 11-15 years) they found HAV in 50% of cases that were below 5 years followed by 36% in between 6-10 years.

In less than 10% patient extra hepatic immune complex mediated manifestations may be present like polyarthritis, (which is typically symmetric involves chiefly the distal joints e.g. proximal interphalangeal joints and subsides with development of jaundice), hematuria and proteinuria reflecting glomerular involvement (Lister-Melman et al 1989), angioedema, urticaria, maculopular rash, polymyalgia rheumatica, neuropathies, myocarditis etc. (Bacon et al, 1975, Tabor 1987, Ussell et al 1984).

Stewart et al (1978), Lemon (1985) reported increased incidence of diarrhoea and vomiting in children with HAV. In a study on 415 patients with hepatitis A, Gust and Feinstone (1988), observed anorexia in 90% cases, Nausea in 87% cases, vomiting in 71% cases, abdominal discomfort in 65% cases, dark coloured urine in 94% cases and fever in 75% cases.

On examination of a case of acute viral hepatitis with or without complication lymphadenopathy, oedema, ascites, spleenomegaly are found with varying incidence. Spleenomegaly is found in 15% cases of acute viral hepatitis (Shleizeinger).

Fulminant hepatitis is marked by clinical features of hepatic synthetic function with associated bleeding diathesis and coma.

The myriad complications of acute viral hepatitis include bleeding manifestation presenting in the form of hematemesis / hemorrhagic RTA, malena, ascites, chronic hepatitis, fulminant hepatic failure, spontaneous bacterial perintonitis, hepatic encephalopathy and lastly acute renal shut down. While community studies of acute viral hepatitis have reported lower incidence of these complications on account of a high proportion/ chunk of self limited/ mild cases the studies on hospitalize children documented higher incidence.
Likewise amongst the community studies Malathi et al (1998), in their study on 127 children with acute viral hepatitis observed HE in 10.2% of cases with HAV, 17.6% cases with HBV and in 33.35 cases with combined A and B hepatitis.

Khuroo et al (1983), in their study on 293 cases with acute viral hepatitis observed that the incidence of HE in Non A and Non B hepatitis group (12.3%) was higher than that in hepatitis B group (4.2%) and hepatitis A group (6.8%).

Tandon et al (1985), and Kar et al (1994) in their study observed hepatic encephalopathy in maximum cases (55%) with Non A and Non B hepatitis.

Coming to studies on those children who were admitted on account of the complications of acute viral hepatitis. Poddar et al (2002) in their 172 children of acute viral hepatitis found ascites in (30%), encephalopathy in 32.6%. 16% children with ascites had spontaneous bacterial peritonitis.

Poddar et al (2000) again studied fulminant hepatic failure in 67% children they found ascites in 34% out of which 26% had spontaneous bacterial peritonitis.
Poddar et al (2000) and again Poddar et al (2002) in both their studies on acute viral hepatitis and fulminant hepatic failure respectively found that mortality was higher in those with spontaneous bacterial peritonitis occurrence.

**BIOCHEMICAL PARAMETERS**

Khuroo et al (1983), studied serum bilirubin levels in 293 children with AVH, the observed mean serum bilirubin levels by them were 2.1±2.1 mg% in HAV, 5.1±4.3 mg% in HBV and 4.8±4.5 mg% in NonA NonB hepatitis respectively. They found high levels of bilirubin in children infected with HBV, as compared to other viral markers.

Khuroo et al, observed that serum bilirubin levels in case of hepatitis A(2.1±2.1 mg%) were significantly less when compared to HBV and Non A and Non B hepatitis (p value <0.05).

Mathiesen et al (1979) in their study on 115 patients in Copenhagen, also observed that the patients with type A hepatitis had a significantly lower levels of maximum bilirubin than those with type B (p value <0.05).

Malathi et al (1998), studied serum bilirubin levels in 127 children with AVH, the observed mean serum bilirubin levels by them were 3.4±2.6 mg% in HAV, 5.8±2.2 mg% in HBV, 9.1±1.4 mg% in A
and B co-infection, and 5.8±2.5mg% in Non A NonB hepatitis. No statistical significant inference was drawn by them.

**SGPT**

Mathiesen et al (1979), in their study on 115 patients found no statistical difference in maximum ALT levels of A,B and Non B hepatitis.

Mean ALT levels observed by Malathi et al (1998) were 227.1±261.4 IU/ml in HAV, 360.8±341.8IU/ml in HBV, 741.3±248.6 IU/ml in A+B co-infection and 407.3±318.7IU/ml in Non A NonB hepatitis. No statistical inference was drawn by them. Higher levels of ALT were observed in children with type B hepatitis alone or in combination with hepatitis A. by Mathiesen et al (1979 and Malathi et al (1998).

**Prothrombin time** It reflects the synthetic function of the liver and being protein with short half-life as compared to albumin. It is a good indicator of liver injury in acute viral hepatitis.

Fulminant hepatitis is marked by clinical features of hepatic synthetic function with associated bleeding e\diathesis and coma and PT is elevated.

Poddar et al (2000) graded PT as the marker of disease activity and the best indicator of prognosis in acute viral hepatitis with
complications. Fulminant hepatic failure was associated with decreased SGPT and increased prothrombin time (Poddar et al 2002).

In their study in hospitalized children with fulminant hepatic failure they found that PT was elevated significantly in those children who died than those who recovered.

**Serological tests** :-: For the purpose of diagnosis of these viruses serological tests have been the main stay to this day on account of being able to confirm/document even asymptomatic cases.

In an attempt to overcome the limited sensitivity of IEM assay have been developed for the detection of specific viral antigens and HAV-RNA. A number of workers (Hollinger et al 1975, Purcell et al 1976) developed sensitive immuno assay, radioimmuno assays (RIA) or ELISA for detection of HAAq in fecal samples.

HAV/HEV is best diagnosed by IgM antibody (detected by ELISA) presence that appears within1-2 weeks and persists for 3-4 m ELISA has the highest sensitivity (99.9%) and specificity (99.9%).

Jansen et al (1985) detected HAV-RNA in fecal samples from patients with hepatitis A by molecular hybridization. This technique has been found to be more sensitive than ELISA or RIA for detection of HAAq.

HBV has three kinds of antigens HbsAg, HbcAg and HbeAg, HbeAg denotes infectivity of the infected person while HbcAg doesn't appear in blood and remain in the liver. HbsAg is the first serological marker to appear in the serum after 1-2 weeks and disappears in 1-2 m following onset of jaundice. Anti HbcAg IgM is a marker of acute infection apart from HbsAg and comes after 1-2 weeks of HbsAg appearance.

Australian antigen of HbsAg could be detected inpatients with acute and chronic disease by simple assay procedures such as agar gel diffusion (AGD) or counterimmunoelectrophoresis (Gerety et al, 1978).

In 1972, a modified radioimmunoassay (RIA) called “Sandwich” RIA was developed by Overby et al, to detect HbsAg. This diagnostic test has a sensitivity 10000 times that of AGD and can detect less than 0.5ng HbsAg per ml of serum. Sandwich assays have remained the methodologies of choice for detecting HbsAg because of their long history of high sensitivity and specificity. Recent modified IEA have
employed microplaricles (MEIAs) and computerized instrumentation to produce very rapid and completely automatic MIAS for HbsAg (Decker 1991, Eble et al 1991).

Sero logical tests for HCV detect antibodies to viral antigens. The first generation ELISA test used recombinant antigen c100. Subsequent tests have used HCV recombinant and synthetic peptides and these have proved more sensitive and specific. The third generation ELISA includes antigens from the putative core, NS3, NS4 and NS5 regions of the virus (Courouce et al, 1994). These have a sensitivity and specificity of 99%.

The original anti c100 appeared only 4-6 months and even up to 1 year after the infection, whereas the antibody to c33 appears early at 11 weeks and always within 20 weeks of the onset. False positives still occurs and the mean period between infection and detection of antibody is 12 weeks (Busch et al, 1994). ELISA blood donor screening is virtually 100% effective in preventing transmission of HCV to recipients (Van der Poel et al, 1994).