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A clinico – epidemiological profile of acute viral hepatitis in Northern India

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Abstract
A study to examine the clinic – epidemiological profile of acute viral hepatitis was carried in the region. It was found that in a total of 90 serologically positive acute viral hepatitis patients, Hepatitis E was most frequently found and with most fatalities among pregnant women. Overall, hepatitis B had the most fulminant course followed by hepatitis E. The disease was statistically insignificantly distributed age, sex and rural/urbanwise. The individual courses of the different types of acute viral hepatitis were thereby studied and discussed.

Keywords: Acute viral hepatitis, Hepatitis B, Hepatitis E

1. Introduction
In a country like India, acute viral hepatitis (AVH) is one of the frequently encountered conditions in medicine OPD due to existence of unsanitary conditions. Despite it being a major health problem, not many studies in India have explored the prevalence, etiology or clinic-epidemiological profile of the cases at length besides few conducted in New Delhi and Chandigarh [1, 2]. The limiting factor remains the high cost of these diagnostic kits, but serological studies are essential from epidemiological and prognostic point of view. Therefore, this study was undertaken to determine the prevalence, etiology and epidemiological profile of AVH in Northern India so that appropriate management and preventive strategies for this part of the country could be planned.

2. Method and Materials
This study was undertaken on suspected cases of acute viral hepatitis (AVH). This was a hospital based, prospective, observational, non-interventional and comparative study and conducted at J N Medical College, AMU, and ALIGARH.
An AVH case was defined as a person having an acute illness of <15 days duration with a discrete onset of any sign/symptom (e.g. Fever,, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain) and either a) jaundice or b) elevated serum alanine transferase (ALT) > 100IU/L documented atleast twice at a 1 week interval without any history of pre-existing liver disease [3].

2.1 Methods
Serum samples were collected from all the affected and persons of AVH from the outdoor and indoor services of the dept. of medicine, JN Med college and hospital, AMU, Aligarh during the study period and subjected to routine investigations and serological detection of IgM HAV, HBsAg, Anti HCV antibodies and IgM HEV. A detailed history of each patient was recorded, including travel history, blood transfusion and food intake and water from outside sources. Those with alcoholic, autoimmune, hemolytic, malarial, drug induced hepatitis or cholestatic jaundice were excluded from the study.

2.2 Sample size
90 Consecutive cases of acute viral hepatitis were enrolled. Eligible subjects (15years and above) were chosen for the study.

2.3 Controls
Healthy blood donors with no clinical evidence of present or past involvement of liver disease.

2.4 Study Design
This was a hospital based, Prospective, Observational, non-interventional and comparative study.
An informed consent was obtained from each patient prior to entering into the study. A detailed history and physical examination was carried out and samples were collected for every subject who entered
The study was approved by the institutional ethical committee.

2.5 Collection and Transport of Samples
A sample of 7-10 ml of blood was collected aseptically from all the patients. Serum was separated by centrifugation, aliquoted & stored at -20 degree till further tests were performed.

2.6 Investigations
Hemoglobin (Hb), TLC, DLC, ESR, PT/INR, RFT, LFT, anti-HAV IgM ELISA, IgM HBsAg ELISA, anti- HCV IgM ELISA, anti HEV IgM ELISA assay.

2.7 Statistical analysis
Analysis was performed using SPSS Statistical package for windows (SPSS, 15.0, Chicago, IL). Continuous variables were expressed as mean ±standard deviation (Gaussian distribution) or range and qualitative data was expressed as percentage. Unpaired t test for independent samples was used in comparing continuous data between two groups. Linear relationship between variables was analysed using Pearson's correlation coefficient. All p values were two tailed and values of <0.05 were considered to indicate statistical significance. All confidence intervals were calculated at 95% level.

3. Results

In this study, out of a total of 90 AVH subjects enrolled 47(52.22%) were female and 43(47.78 %) males [Table 1]. The mean age of study was 37.4±15.9 years with maximum no. of patients (52.22%) in the age group 15-35 years. 43(47.77%) patients out of total 90 cases belonged to rural area against 47(52.23%) from urban [Table 2].

Maximum seropositive were due to hepatitis E (38.9%), followed by hepatitis B (12.2%), hepatitis C (5.6%) and hepatitis A (3.3%) [Fig 1]

2 cases were co –infected with both hepatitis B and C.

Total seropositive cases were 54 out of total 90 study cases. 17 (31.48%) of them developed a fulminant course. This was maximum in hepatitis B cases (36.36%) followed by hepatitis E (31.48%) [Table 6]. Fulminant course in pregnant females with HEV was 50% [Table 4 and 5].

The outcome of the seropositive cases was analyzed too. 31 (57.40%) cases improved, 8 (14.81%) absconded/LAMA and 15 (27.77%) expired. The mortality rate was highest among the HBV cases (36.36%) followed by HEV (28.57%) [Table 7].

Table 1: Age and sex distribution of study cases.

Age group(years)	Sex		
	Males (%)	Females (%)	Total
15-35	20(42.6)	27(57.4)	47(100)
36-55	16(59.3)	11 (40.7)	27(100)
>55	7(43.8)	9(56.3)	16(100)
Total	43(47.8)	47(52.2)	90(100)

Chi square = 2.1, df = 2, $p > 0.05$; not significant

Table 2: Age distribution of study cases with respect to locality of residence

Age group	rural	urban
15-35	18	27
36-55	15	12
>55	10	8
total	43(47.77%)	47(52.23%)

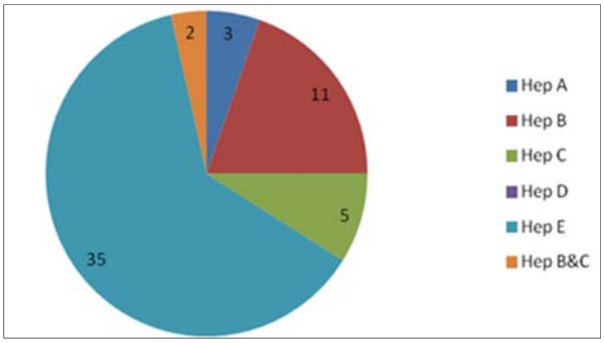

Fig 1: Pie chart showing distribution of serologically positive cases

Table 3: Distribution of IgM HEV among pregnant and non-pregnant females.

Pregnancy	HEV IgM	
	Positive	Negative
Yes	10	10
No	6	21
Total	16	31

Chi square = 3.948, df = 1, $p < 0.05$, significant

Table 5: Frequency of clinical features and signs in individual subtypes of Hepatitis.

Variable	Frequency			
	Hepatitis A(n=3)	Hepatitis B(n=11)	Hepatitis C(n=5)	Hepatitis E(n=35)
Pallor	1	1	1	10
Icterus	2	9	4	35
Pruritis	0	1	0	3
Hepatomegaly	1	3	2	11
Splenomegaly	0	1	1	1
Fever	1	2	1	12
Nausea	2	7	3	22
Vomiting	2	7	2	18
Pedal edema	0	1	0	11
Ascites	0	2	3	3
Anorexia	3	10	4	26
Encephalopathy	0	3	1	5
S.Bil.>5mg%	0	7	4	27
High SGOT(>40IU/l)	2	9	5	31
High SGPT(>40IU/l)	2	10	3	31
ARF	0	1	0	4

Table 6: Distribution of fulminant hepatitis cases in the various subtypes.

Fulminant hepatitis	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E	Total
Yes	0 (0%)	4(36.36%)	1(20%)	12(34.28%)	17(31.48%)
No	3	7	4	23	37
Total	3	11	5	35	54

Chi square = 5.1, df = 3, $p > 0.05$; not significant

Table 7: Clinical outcome in different subtypes of Acute Viral Hepatitis

Clinical outcome	Hepatitis subtype				
	Hepatitis A (n=3)	Hepatitis B (n=11)	Hepatitis C (n=5)	Hepatitis E (n=35)	Total (54)
Improved	2	6	4	19	31 (57.40%)
Expired	0	4	1	10	15 (27.77%)
LAMA / Absconded	1	1	0	6	8 (14.81%)

Chi square = 3.6, df = 6, $p > 0.05$; not significant

4. Discussion

The present hospital based study dealt with the magnitude and risk factors associated with acute viral hepatitis in incumbent outdoor and indoor patients. In all, 90 subjects were enrolled for the study; of which 43 (47.8%) were males and 47 (52.2%) were females. The mean age of the study cases was 37.4+_15.9 years. Our findings of a male preponderance among cases was consistent with those of Ahmed *et al.*, [4] who observed a male prevalence of 62.5% among 5193 cases in a large retrospective study in Pakistan.

The rural vs urban distribution of cases was 47.77% and 52.235 respectively so not much purposive. Studies from abroad (Baaten *et al.*,) have however shown a higher prevalence of acute viral hepatitis in urban population. The difference can be attributed to difference in methodologies, a small sample size in our study and also the fact that the Western countries are

already low endemic areas for Viral Hepatitis and thus can show higher endemicity in urban regions, indicating the need for differentiated regional studies and prevention strategies.

The overall distribution of serologically positive cases in the present study was as follows in decreasing order of magnitude: Hepatitis E (n=35), Hepatitis B (11), Hepatitis C (5) and Hepatitis A (3). There was a remarkably high magnitude of cases positive for IgM antibodies for Hepatitis E virus in our study. This observation was similar to several other region specific studies like those of Arankalle *et al.,* [5] Amrapurkar D *et al.,* [6] from India and from Bangladesh (Alain B *et al.,*) [7] and Pakistan (Altaf B *et al.,*) [8]. The World Health Organization (WHO) in its reports has also noted a very high prevalence of Hepatitis E sero -positivity from other international communities as well [9]. A majority of our cases belonged to lower socio economic groups and had poor sanitation practices. Diseases that spread from feco oral route thus occur at higher rates in such populations. Hepatitis E also has a feco oral transmission, and this could be the reason for a high prevalence among the studied cases. A confounding factor in this context is that Hepatitis A (which also has a faeco-oral transmission) was not observed that frequently (3 cases) vs those of Hepatitis E (35 cases). This is in contrast to the observation made in few other studies (Aland *et al.,* 2000; Bartoloni *et al.,* 1999) wherein the authors have reported a relatively higher population specific prevalence of Hepatitis A than Hepatitis E. It is suggested that the low prevalence of anti-HEV IgG in the study population (9%), particularly when compared with anti-HAV IgG (97%), represents a more sporadic than epidemic type occurrence. The difference can be explained by the fact that these have been community studies with large sample sizes recruited in a more representative manner than ours, which involved a smaller sample with consecutive hospital patients. However, a high area specific prevalence of HEV observed in the aforementioned studies reflects a 'local and focal' nature of the disease and a tendency of epidemic spread.

In our study, only two cases of co-infection of HBV and HCV was detected. Dual infection has been reported in as high as 12% cases of chronic liver disease and 11.7% cases of hepatocellular carcinoma from India (Thyagarajan SP *et al.,* [10]; Arora DR *et al.,* [11]). These findings are in contrast to our study probably because these studies comprised of proven cases of chronic liver disease and hepatocellular carcinoma whereas the cases in our study were included on the criterion of raised liver function enzymes and exclusion of other causes of hepatitis such as alcoholism and drug toxicity.

The outcome of Hepatitis E was particularly woeful in pregnancy in terms of higher rates of abortions, fulminant hepatitis and mortality. The association of pregnancy and the incidence of Hepatitis E infection and also mortality due to Hepatitis E in pregnancy were both statistically significant($p<0.05$). This finding is supported from that of a vast body of research conducted in India and abroad (Dahiya M *et al.,* [12]; Beniwal M *et al.,* [13]; Hussaini SH *et al.,* [14]). Investigators are exploring a possible role of cytokines like IL-6, TGF-beta, IFN-g and TNF-α in the pathogenesis of fulminant hepatitis and consequent high mortality among pregnant women (Navaneethan U *et al.,* [15]).

The rates of fulminant hepatitis in both Hepatitis B and C were fairly high in our study (36.36% and 20% respectively); and also the mortality due to these infections. This was probably because the sickest of the patients had a higher chance of being admitted to the hospital and more probability of dying due to complications of the illness.

5. Conclusion

The study has a few inherent shortcomings as well. It was conducted among subjects recruited from the hospital and not from the community. The sample size was relatively small due to logistic constraints. The methodology included consecutive patients who fulfilled the inclusion criteria and there was no specific sampling frame for the same in order to ensure better representativeness. Only selected hepatotropic viruses were studied. Follow up was not done to check for chronicity. Variables like pregnancy outcome in Hepatitis other than Hepatitis E and sero-prevalence in family members could not be studied. Despite the fallacies, the study however lays ground for planning and conducting more analytical studies like case control and prospective studies in this context, so that more information can be generated regarding trends over time, risk factors and natural history of disease.

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