SEROPREVALENCE OF HEPATITIS A AND E VIRUS INFECTIONS IN PATIENTS WITH ACUTE VIRAL HEPATITIS IN HYDERABAD, INDIA - A ONE YEAR STUDY.

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ABSTRACT

INTRODUCTION: Acute viral hepatitis due to faeco- oral group of hepatitis viruses is endemic in India. Outbreaks of Hepatitis E virus infection are more common than the hepatitis A virus.

AIM: The present study aimed at determining the seroprevalence of IgM antibodies to hepatitis A and E virus in clinically diagnosed acute viral hepatitis cases**.** And to determine its usefulness against the disease prevention.

Study design: A cross sectional study was carried out on symptomatic patients referred from paediatric and gastro enterology department of Princess Esra hospital.

PLACE AND DURATION OF STUDY: Around one hundred and eight subjects were analyzed for anti IgM antibodies to hepatitis A and E virus and liver function test in the department of laboratory medicine for Microbiology and biochemistry at Princess Esra hospital, Deccan College of Medical Sciences between January 2013 and January 2014.

METHODOLOGY: Blood samples were collected under strict aseptic precautions and tested for anti-HAV and Anti-HEV IgM antibodies using capture elisa from diasorin. Biochemical analysis included estimation of serum aminotransferases, alkaline phosphatase and bilirubin levels.

RESULTS: An overall seropositivity of 54% was observed in the present study. More number of the subjects as 46.29% tested positive for anti HAV IgM than for anti HEV IgM as 7.4%. Co-infections were not noticed. Acute viral hepatitis due to hepatitis A virus is more common in children in the age group 6-10 years followed by 11-15 years and lastly 0-5 years indicating the epidemiological shift. Infection with hepatitis E virus was common in adolescent and adults. Males were more susceptible to both the infections than females. Liver function test results correlated well with viral markers indicating damage to the liver parenchyma. The socioeconomic status of the individuals revealed that 95% of the subjects were below poverty line and didn't have access to proper drinking water and sanitary facilities. None were vaccinated against Hepatitis A virus.

Conclusion: The present data suggest that we need to have a dual pronged approach against prevention of acute viral hepatitis caused by A and E virus. Government authorities should prioritize on bringing a uniform improvement in the living standards of the society and make vaccine available to the high risk group at a subsidized rate.

Keywords: [Hepatitis A virus, Hepatitis E virus, Acute viral Hepatitis, Anti HAV IgM, Anti HEV IgM, Serum aminotransferases, Seroprevalence, HAV Vaccine}

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1. INTRODUCTION

Viral hepatitis is an important epidemiological disease caused by any one of the known hepatitis virus and less commonly by some miscellaneous viruses. Among the various hepatitis virus the faecooral group; the Hepatitis A and E virus are highly contagious and spread through consumption of contaminated food and water or by direct contact [1-5]. Moreover it is known to be shed in the faeces of both symptomatic and asymptomatic cases and as well during the convalescence phase. It is able to survive in the environment for months which increases the chances of spread in the community [2, 5]. Hepatitis A virus is known to cause asymptomatic infection in 70% of the children below six years [5,6]. Whereas in grown up children and adults it leads to symptomatic infection [7-9]. On the contrary Hepatitis E virus is known to cause symptomatic infection in adults and fulminant infection in pregnant women especially in the third trimester with high case fatality rate of 20% [10].

The sero epidemiological studies on hepatitis A and E are very limited. Off late several studies have demonstrated a gradual decline in the seroprevalence of the disease from 70% - 45% in highly endemic regions and in intermediate region from 45.34 – 3.01 % [11-12] due to socio economical development or urbanization of the society brought about by increased income levels and improved water and sanitation facilities [13-19]. But the findings are not uniform throughout the country therefore epidemiology of the disease caused by hepatitis A is variable and is influenced by heterogenecity observed in the host susceptibility and environmental factors [20].Therefore from time to time outbreaks keep occurring in the developing countries [21-24] .

The role of vaccine in prevention of diseases is biased or debatable as most of the authors are of the opinion that vaccine is not essential. The present data shows that majority of the children between 5-10 years of age show presence of anti HAV antibodies in the range of 90 - 96.9% respectively. Hence vaccine is not permissible in highly endemic regions [17, 25 – 37].

Aim –To determine the seroprevalence of Hepatitis A and E virus infections in acute viral hepatitis cases attending princess Esra hospital a tertiary care hospital in Hyderabad during a one year period from Jan. 2013- Jan. 2014. To determine the significance of this data in HAV vaccination planning and other protective measures for prevention of HAV infection.

2. MATERIAL AND METHODS

Case definition as per [WHO] WORLD HEALTH ORGANIZATION

An acute viral hepatitis case was defined as a person having an acute illness of < 15 days duration with a discrete onset of any sign or symptom of fever,

headache, malaise, anorexia, nausea , vomiting, diarrhoea and abdominal pain with jaundice or elevated levels of aminotransferases levels > 100 IU/L documented at least twice at a one week interval without any history of pre existing liver disease [38].

EXCLUSION CRITERIA

Patients with symptoms of alcoholic liver disease, Chronic liver disease and those with the history of HAV vaccination were excluded from the study.

A prospective cross sectional study on one hundred and eight patients fulfilling the above case definition criteria of acute viral hepatitis referred from paediatric and gastroenterology department of Princess Esra hospital during the period from January 2013 to January 2014 were included in the study.

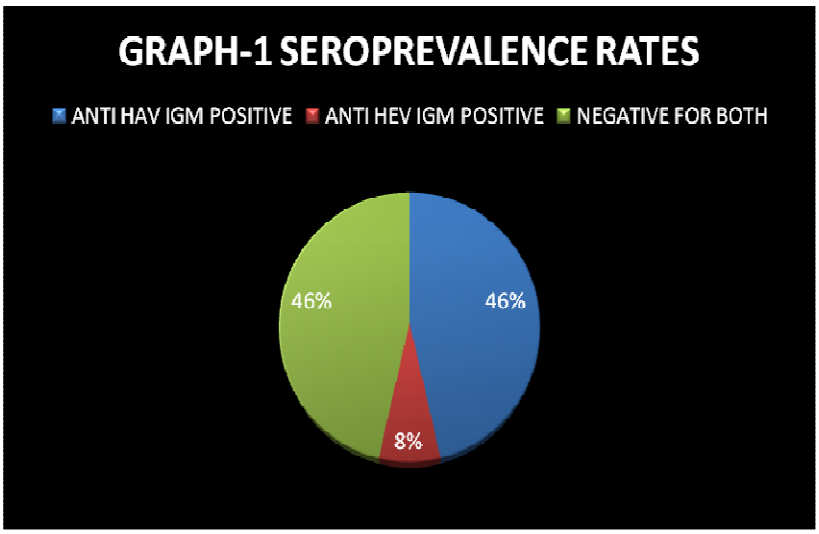
After obtaining an informed oral consent from each patient about 5ml blood was collected in BD vacutianers under aseptic precautions. Blood was allowed to clot and serum used for liver function test and hepatitis markers like Anti HAV IgM and Anti HEV IgM from Diasorin Italy. Assay based on IgM capture ELISA.

Quality control – was achieved by running the internal and external quality control samples during the run and repeating the positive test samples twice.

DATA ANALYSIS – The study data was analyzed using the EPI INFO 7 software from [CDC] Centers for Disease Control and Prevention.

3. RESULTS

Of the one hundred and eight individuals with sign and symptoms of acute viral hepatitis 54% gave a positive serological result for Hepatitis A and E Anti IgM. Hepatitis A alone accounted for 46.29 % and hepatitis E for 7.40% respectively.



THE DEMOGRAPHIC PROFILE

Table 1 shows the demographic data of the subjects in study with specific reference to seropositive individuals. More number of males were symptomatic for the disease than females. The overall mean age for the Anti HAV IgM positive individuals is significantly less when compared to anti HEV IgM positive individuals with a *P* value of 0.001 . Further, it is seen that there is an age specific variation in the exposure rates to hepatitis A and E virus .Hepatitis A infection is more prevalent in young children than in grownups and adults which is common with hepatitis E infection with a significant *P value* of less than 0.05. Majority of the subject's positive for acute viral hepatitis were males 64% than females as 36%.

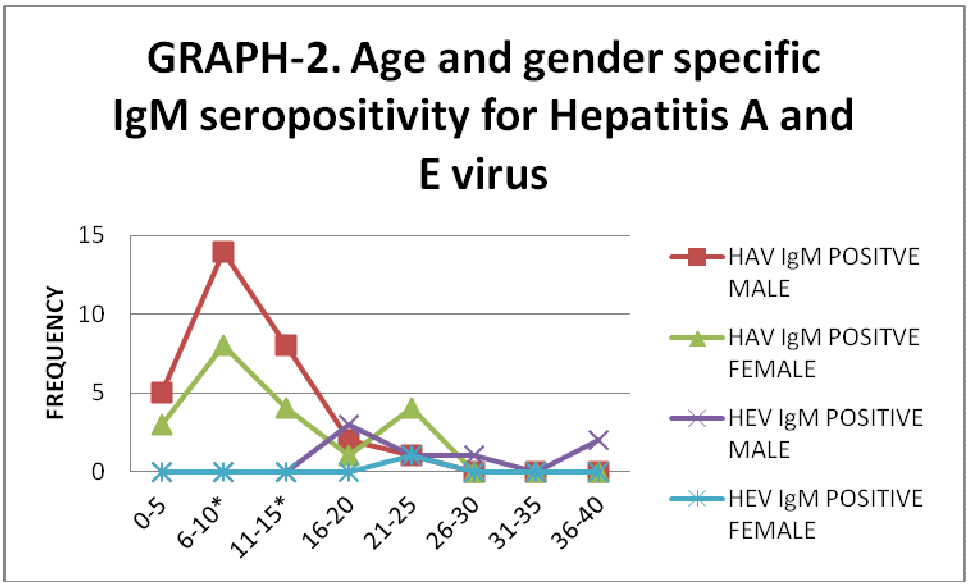
TABLE 1- DEMOGRAPHIC PROFILE OF SUBJECTS IN STUDY.

Factor	Number	Percentage
SEX		
Male	74	68.5
Female	34	31.5
AGE		
Mean age for anti HAV Positive subjects	10.84±6.08	
Males	9.60 ± 4.68	
Females	12. 70 ± 7.489	
Mean age for Anti HEV IgM Positive subjects	26.25 ± 9.40	
Males	26.57 ± 10.11	
Females	24.00 ±0.00	
SEROPOSITIVE SUBJECTS		
Anti HAV IgM Positive	50	46

Males	30	34
Females	20	18.5
Anti HEV IgM Positive	8	7.4
Males	7	6.48
Females	1	0.92
AGE OF MAXIMUM EXPOSURE TO HAV INFECTION		
0-5	8	16
6-10	22	44
11-15	12	24
16-20	3	6
21-25	5	10
AGE OF MAXIMUM EXPOSURE TO HEV INFECTION		
16-20	3	37.5
21-25	2	25
26-30	1	12.5
36-40	2	25
SOCIOECONOMIC STATUS OF ANTI HAV IgM POSITIVE SUBJECTS		
Group	Number	Percentage
Low socioeconomic group	48	95
Lower middle socioeconomic group	2	5
SOCIOECONOMIC STATUS FOR ANTI HEV IgM POSITIVE SUBJECTS		
Lower middle socioeconomic group	6	75
Upper middle socioeconomic group	2	25
Facilities available	Yes %	No %

Access to potable water	5	95
Toilet facility	5	95
Education	4	96
Occupation petty jobs	96	4
Slum dwellers [migrants]	95	5

With respect to gender both Hepatitis A and E infection are seen to be common in males accounting for 60% and 87.5% of the infections respectively. Therefore based on gender and age the above findings show that HAV infection is more common in the age group 6-10years whereas HEV infection is common in the age group 16-20 followed by 21-25 years. Further in the study it is observed that in females aged 21-25 years the prevalence of acute HAV infection is comparatively higher than HEV infection due to reasons unknown. Graph -2



INFLUENCE OF ENVIRONMENTAL FACTORS ON DISEASE PREVALENCE - While taking history from seropositive patients we have noticed that for Hepatitis A infection 95% of the people belonged to below poverty line and didn't have any access to potable water. They were migrants and slum dwellers with no proper sanitation facilities and knowledge about personal hygiene. On the other side hepatitis E infection were seen in low and upper middle socioeconomic group of the society. None were vaccinated against HAV.

The results of liver function test showed a significant correlation with the viral markers for HAV and HEV. Except for two cases of acute viral hepatitis 96% of them had raised aminotranferases, alkaline phosphatase and bilirubin levels in their serum. The mean serum levels for these parameters were as follows for alanine aminotransferase 708.5 ± 650.774 IU/L, for aspartate aminotransferase as 375.5 ± 571.818 IU/L and for alkaline phosphatase as 344.00 ± 149.563IU/L. The mean serum total bilirubin level was about 5.0 ± 3.00. Hence it is evident that all patients were facing severe hepatocellular injury due to viral infection.

DISCUSSION

Hepatitis A and E viral infection are endemic in many developing countries [39]. India is the homeland with high endemicity rates for both the infections [16,37, 40,41]. The seroprevalence rates for hepatitis A IgG antibodies are almost 100% in adult population [27,36,40]. The virus continues to lurk in some pockets of the society due to various environmental and host factors and causes sporadic and epidemics from time to time [41]. There are hardly few studies providing data on acute viral hepatitis caused by hepatitis A and E virus from India [32,42-44]. Most of the studies done so far in India have either determined the serum anti HAV IgG or total antibodies i.e. anti HAV IgM and IgG together which indicate convalescence following infection or immunity against infection due to infection or immunization and are useful in epidemiological studies and developing vaccination strategies [25,32,45-46]. Our study aimed at determining the anti HAV IgM response which signifies acute infection rates in the society after the so called epidemiological shift or transition that has been documented by many authors [20 30, 40, 47-48]

We observed an overall seroprevalence rate of 54% which is less when compared to the one reported as 96.9% by B Mohanvalli et al and 81.88% by Deepak arora et al 2013 from Punjab. Out of this hepatitis A alone accounted for 46.29 % of the cases and E for 7.40 % which is almost reverse of what has been documented by Deepak arora as 13.9% for hepatitis A and 78.78% for hepatitis E and Singh et al as 32.1%, [42, 50] . In some studies very low prevalence rates for hepatitis A has been recorded like the one reported by by Mehta et al 2013 as 19.15% and 6.87% by SR

et al 2012 [43-44] . Further some authors have reported co-infections too in their studies resulting from simultaneous infection by both hepatitis A and E virus like the one by Deepak et al as 7.5%, 8.6% by B Mohan valli and 8.9% by SR et al which is not seen in our case [32,42, 44] . The differences in the seroprevalence rates for the two viruses observed in various geographical region of the same country from North West to south India could be because of the heterogenicity in the host and environmental factors influencing it [51]. In the present study we noticed that disease is more common in males 65.5% which is consistent with the report by SR et al of 67.5% and others [42-44] one of the reasons for this male predominance could be the early outside association of the male gender as mentioned by other authors [44 ,52-54]. Males get exposed to the environment earlier than females in some orthodox societies and cultures.

On the basis of age we noticed that for reasons unknown hepatitis A infection is more common in childhood whereas hepatitis E is more common in adults which corroborates with findings of Aggarwal R et al [51].As per the data on the seropeidemiology of hepatitis A it is known that 96.9 % of the children by the age of 15 years acquire protective antibodies indicating exposure to the virus at an early age of less than 5 years [32].In our study we have seen that maximum exposure to infection occurred in the age group order of 6-10 years followed 11-15 years and then 0-5 years which signifies an epidemiological transition [20, 32 ,55]. On the contrary most of the hepatitis E virus infections occurred in the age group 16-20 years followed by 21-25 and then 36-40 years. Age specific variations in the epidemiology of the two viruses in a same place are not very much explained [16]. Poverty and inadequate personal hygiene are strongly associated with the infection rates [42]. It is said that seroprevalence rates of hepatitis A and E are inversely proportional to the economic status of the individuals, supply of protected water supply and personal and environmental hygiene. There are several reports demonstrating the association between living standards and prevalence of hepatitis A and E. between the high and low income groups and the rural and urban population. It is noticed that 80-90 % of the seropositivity is seen in low socioeconomic and rural

population than in urban and high income group same has been observed in our study too [19,32,40,56,57]. Ninety five percent of the exposed people in case of hepatitis A infection belonged to below poverty line and were migrants from neighboring states or countries with nil personal and environmental hygiene measures [17, 20, 30, 36, 37, 46, 48, 56- 58] But in case of hepatitis E infection positive individuals were from both from low and middle economic class and had access to protected water supply or sanitation.

Therefore the thought to include vaccination against HAV in the universal immunization programme needs to be contemplated before being implemented as lack of appropriate epidemiological data from the various corners of the country and of course the cost of the vaccine are the major obstacles noticed. Disease prevention by provision of protected water supply and improved sanitary conditions still remains a dream in many areas of the Indian subcontinent. Therefore at this stage of economical development it is difficult to comment on inclusion of HAV vaccine in the national immunization program and it is the decision of the policy makers. But of course disease prevention by improving living standards holds relevance.

In acute viral hepatitis the biochemical markers are 96% sensitive for the viral etiology of the disease. Therefore it is always good to monitor the patients along with the viral markers the serum aminotrasferases and bilirubin levels.

4. CONCLUSION

Therefore it appears cognizant to have a target approach with vaccination of the high risk group at a subsidized rate by the ministry of health and family welfare and focus on economical and environmental development which will definitely reduce the seroprevalence of acute viral hepatitis by faeco-oral group of virus as it is quoted that these infections are an index of socio economical status of a country [36].

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COMPETING INTERESTS

None

AUTHORS' CONTRIBUTIONS

'Author Dr. Sarwat Fatima' designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript did review of the literature. 'Author B' managed the biochemical analyses of the study. 'Author C' managed the analyses of viral markers. All authors read and approved the final manuscript."

CONSENT

An informed oral consent was obtained from all the study subjects prior to testing.

ETHICAL APPROVAL

Ethical approval was obtained from institutional ethics committee.

LIMITATIONS

We regret our inability to obtain complete demographic data from all the study subjects which is essential for establishing the role of various environmental factors in disease etiology due to lack of technical support. Any how we tried our level best to get proper information from at least the seropositive group.

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ABBREVIATIONS

HAV – HEPATITIS A VIRUS

HEV – HEPTITIS E VIRUS

WHO – WORLD HEALTH ORGANIZATION

ANTI HAV IGM – HEPATITIS A IGM ANTIBODIES

ANTI HEV IGM – HEPATITIS E IGM ANTIBODIES

CDC – CENTRE FOR DISEASE CONTROL AND PREVENTION

APPENDIX

TITLE

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