Original Research Article

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

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 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}

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 spread by direct contact with the infected person or through consumption of contaminated a food

and water [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 mild 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 that has been 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 a week at a one week interval without any history of pre existing liver disease [38].

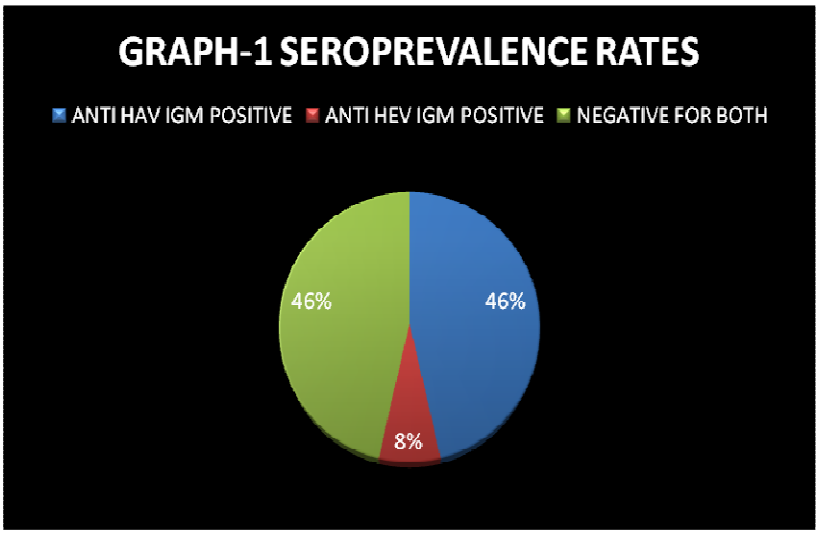
As per the above case definition a total of one hundred and eight subjects with signs and symptoms of acute viral hepatitis referred from paediatric and gastroenterology department during the period from January 2013 to January 2014 were included in the study.

About 5ml blood under aseptic precautions was collected from all the patients in gel tubes from BD vacutainers. 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.

3. RESULTS AND DISCUSSION

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

Majority of the subject's positive for IgM antibodies were males 65.5%. The overall mean age for the Anti HAV IgM positive individuals was 10.84 ± 6.08. For males the mean age observed was 9.60 ±4.68 and females as 12.70 ± 7.48. In case of Anti HEV positive individuals the overall mean age noticed was 26.25 ± 9.40. For males it is 26.57 ±10.11 and females 24.00 ± 0.00 respectively. Therefore it is evident from the above data that hepatitis A infection is more prevalent in young children than in

grownups and adults which is seen with hepatitis E infection with a significant *P value* of less than 0.05. For hepatitis A virus maximum exposures occurred in the age group 6-10 years as 44% followed by 11-15 as 24% and then 0-5 years as 16%. In case of hepatitis E virus infection the age at which maximum exposure occurred is in adolescent and adult hood being 37.5 % for 16-20 years age group followed by 21-25 years and 36-40 years of age group each accounting for 25% as shown in the Table 1.

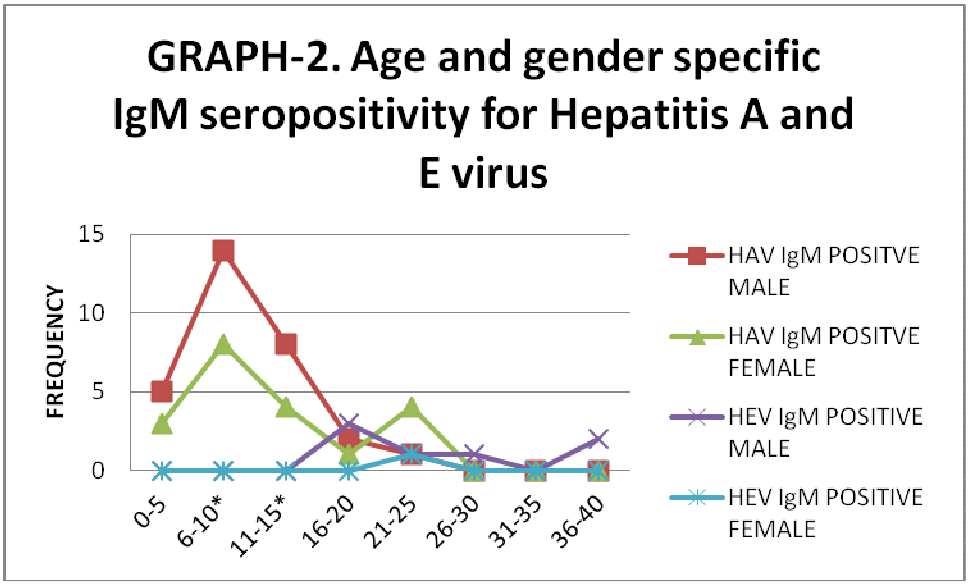
TABLE 1- AGE SPECIFIC DISTRIBUTION OF ANTI -HAV AND ANTI - HEV IgM POSITIVE PATIENTS.

AGEGROUP	TOTAL N=108	HAV IGM POSITVE			HEV IGM POSITIVE		
		MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
0-5	12	5	3	8	0	0	0
6-10*	24	14	8	22	0	0	0
11-15*	15	8	4	12	0	0	0
16-20*	14	2	1	3	3	0	3
21-25*	13	1	4	5	1	1	2
26-30	11	0	0	0	1	0	1
31-35	9	0	0	0	0	0	0
36-40	10	0	0	0	2	0	2
TOTAL	108	30	20	50	7	1	8

{*- indicates majority of the subjects positive for anti IgM antibodies in a particular age group}.

With respect to gender both Hepatitis A and E infection are seen to be common in males accounting for 60% and 87.5% 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 graph -2



INFLUENCE OF ENVIRONMENTAL FACTORS ON DISEASE PREVALENCE - While taking history we have noticed that for Hepatitis A infection 95% of the people belonged to below poverty line and didn't have any access to protected water supply. 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 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. India is the homeland with high endemicity rates for both the infections [39] .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 my many authors [20 30,39,47-49,]

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 together like Deepak et al has shown co infections rates of 7.5%, 8.6% by B Mohan valli and 8.9% by SR et al which is not observed 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 is the early outside association of the male gender which is correlating with the findings of [44 ,52-54].

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 [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. 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 infections 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 vaccination HAV in the national immunization program. And 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].

REFERENCES

1. Hollinger FB, Ticehurst JR. Hepatitis A virus. In: Fields BN, Knipe DM, Howley PM, editors. Fields Virology. 3 rd ed. Philadelphia: Lippincott-Raven; 1996. p. 735-82.

2. Stapleton JT, Lemon SM. Hepatitis A and hepatitis E. In: Hoeprich PD, Jordan MC, Ronald AR, editors. Infectious Diseases. 5 th ed. Philadelphia: Lippincott Co.; 1994. p. 790-7.

3. Lemon SM. Type A viral hepatitis: Epidemiology, diagnosis, and prevention. Clin Chem 1997;43:1494-9.

4. Lemon SM. Hepatitis A virus. In: Webster RG, Granoff A, editors. Encyclopedia of Virology. London: Academic Press Ltd.; 1994. p. 546-54.

5. Gust ID. Epidemiological patterns of hepatitis A in different parts of the world. Vaccine 1992;10 Suppl 1:S56-8.

6. Hadler SC, Webster HM, Erben JJ, Swanson JE, Maynard JE. Hepatitis A in day-care centers. A community-wide assessment. NEngl J Med 1980;302:1222-7.

7. Lednar WM, Lemon SM, Kirkpatrick JW, Redfield RR, Fields ML, Kelley PW. Frequency of illness associated with epidemic hepatitis A virus infection in adults. Am J Epidemiol 1985;122:226-33.
8. Kamar N, Selves J, Mansuy JM, Ouezzani L, Péron JM, Guitard J, Cointault O, Esposito L, Abravanel F, Danjoux M, Hepatitis E virus and chronic hepatitis in organ-transplant recipients *N Engl J Med* 2008 358:811-17.
9. Kunasol P, Cooksley G, Chan VF, Isahak I, John J, Loleka S, et al. Hepatitis A virus declining seroprevalence in children and adolescents in Southeast Asia. Southeast Asian J Trop Med Public Health 1998; 29(2):255-262.
10. Arankalle VA. Hepatitis A vaccine strategies and their relevance in the present scenario. Indian J Med Res 2004; 119 (5): iii-vi

11. Amela C, Pachon I, Bueno R, Miguel de C, Navarro MF. Trends in hepatitis A virus infection with reference to theprocess of urbanization in the greater Madrid area (Spain).*Eur J Epidemiol* 1995; *11* : 569-73.

12. Kremastinou J, Kalapothaki V, Trichopoulos D. The changing epidemiologic pattern of hepatitis A infection in urban Greece. *Am J Epidemiol* 1984; *120* : 703-6.
13. Schwartz Eli, Raveh D. The prevalence of hepatitis A antibodies among Israeli Travelers and the economic feasibility of screening before vaccination. *Int J Epidemiol* 1998; *27* : 118-20.

14. Shaw FE, Halder SC Jr, Maynard JE. Hepatitis A in Mauritius: an apparent transition from endemic to epidemic transmission patterns. *Ann Trop Med Parasitol* 1989; *83* : 179-85.

15. Shapiro CN, Margolis HS. Worldwide epidemiology of hepatitis A virus infection. *J Hepatol* 1993; *18* (Suppl 2): S11-4.

16. Arankalle VA, Tsarev SA, Chadha MS, Alling DW, Emerson SU, Banerjee K, *et al*. Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. J Infect Dis 1995;171:447-50.

17. Mall ML, Rai RR, Philip M, Naik G, Parekh P, Bhawnani SC, *et al*. Seroepidemiology of hepatitis A infection in India: Changing pattern. Indian J Gastroenterol2001;20:132-5.

18. Das K, Jain A, Gupta S, Kapoor S, Gupta RK, Chakravorty A, *et al*. The changing epidemiological pattern of hepatitis A in an urban population of India: Emergence of a trend similar to the European countries. Eur J Epidemiol 2000;16:507-10.

19. Dhawan PS, Shah SS, Alvares JF, Kher A, Shankaran, Kandoth PW, *et al*. Seroprevalence of hepatitis A virus in Mumbai, and immunogenicity and safety of hepatitis A vaccine. Indian J Gastroenterol 1998;17:16-8.

20. Mathur P,Arora NK.Epdidemiological transition of hepatitis A in india:Issues for vaccination in developing countries.Ind.J.Med.Res.128 Dec 2008:699-704.

21. Arankalle VA, Sarada Devi KL, Lole KS, Shenoy KT, Verma V, Haneephabi M. Molecular characterization of hepatitis A virus from a large outbreak from Kerala, India. Indian J Med Res 2006;123:760-9.

22. Chobe LP, Arankalle VA. Investigation of a hepatitis A outbreak from Shimla Himachal Pradesh. Indian J Med Res 2009;130:179-84.

23. Sowmyanarayanan TV, Mukhopadhya A, Gladstone BP, Sarkar R, Kang G. Investigation of a hepatitis A outbreak in children in an urban slum in Vellore, Tamil Nadu, using geographic information systems. Indian J Med Res 2008;128:32-7.

24. Chadha MS, Lole KS, Bora MH, Arankalle VA. Outbreaks of hepatitis A among children in western India. Trans R Soc Trop Med Hyg 2009;103:911-6.

25. Salahuddin M, Bazlul Karim A.S.M. 2Jahangir Alam , Md. 3.Age-specific prevalence of antibodies to Hepatitis A virus among Bangladeshi children .DS (Child) H J 2012; 28 (1) : 31-34
26. Kamath SR, Sathiyasekaran M, Raja TE, Sudha M. Profile of viral hepatitis A in Chennai. *Indian Pediatrics* 2009; **46**: 642-43.
27. Agboatwalla M, Isomura S, Miyake K, Yamashita T, Morishita T, Akram DS. Hepatitis A, B and C seroprevalence in Pakistan. *The Indian Journal ofPediatrics* 1994; **61:** 545-49.
28. WHO. Department of communicable disease surveiliance and response, *Hepatitis A* 2000; 1-39.
29. Saha SK, Setarunnahar S, Shakur S, Hanif M, Habib MA, Dutta SK, et al. Seroprevalence of hepatitis A infection by age group and socioeconomic status of Bangladesh. *13th International Congress on Infectious Diseases Abstracts, Poster Presentations* 2008; **16**(43):101-02.
30. Raharimanga V, Carod JF, Ramarokoto CE, Chertien JB, Rakotomanana F, Talarmin A, et al. Age specific seroprevalence of hepatitis A in Antananarivo (Madagascar). *BMC Infectious Diseases* 2008; **8(78):** 1-6.
31. Sheikh A, Sugitani M, Kinukawa N, Moriyama M, Arakawa Y, Komiyama K, et al. Hepatitis E virus infection in fulmimant hepatitis pattern and an apparently healthy population in Bangladesh. *American Journal of Tropical Medicine and Hygiene* 2002; **66**(6): 721-24.
32. Mohanavalli B, Dhevahi E, Menon T, Malathi S, Thyagarajan SP . Prevalence of antibodies to hepatitis A and hepatitis E virus in urban school children in Chennai. Indian Pediatr 2003; 40 : 328-31.
33. Thapa BR, Singh K, Singh V, Broor S, Singh V, Nain CK. Pattern of hepatitis A and hepatitis B virus markers in cases of acute sporadic hepatitis and in healthy school children from North West India. J Trop Pediatr 1995; 41: 328-329.
34. Aggarwal R, Naik S, Yachha SK, Naik SR. Seroprevalence of antibodies to hepatitis A virus among children in Northern India. Indian Pediatr 1999; 36: 1248-1250

35. Tsarev SA, Emerson SU, Reyes GR, Tsarevq TS, Kapikian AZ, Ticehurst J *et al*. Characterization of a prototype strain of hepatitis E virus. Proc Natl Acad Sci USA, 1992; 89: 559-563.

36. Ahmed M,Munshi SU, Nessa A.High prevalence of hepatitis A virus antibody among Bangladeshi children and young adults warrants pr-immunization screening of antibody in HAV vaccination strategy. IJMM2009; vol27 issue 1

37. Batra Y, Bhatkal B, Ojha B, Kaur K, Saraya A, Panda SK, *et al*. Vaccination against hepatitis A virus may not be required for school children in northern India: results of a seroepidemiological survey. *Bull World Health Organ* 2002; *80* : 728-31.

38. United States Centers for Disease Control and Prevention. 2012 National Notifiable Diseases and Conditions and Current case Definitions. Available from: http://www.cdc.gov/nndss/document/2012_Case%20Definitions.pdf. [Last accessed on 2012 May 16].

39. Tandon BN, Gandhi BM, Joshi YK, Etiological spectrum of viral hepatitis and prevalence of markers of Hepatitis-A and B virus infection in North India *Bull World Health Organ* 1984 62(1):67-73.

40. Dittman S. International congress on viral hepatitis A and B: Experience in education and prevention. Vaccine 2000;18:S1-2.

41. Rakesh p, Sherin D, Sankar Hari. Investigating a community – wide outbreak of hepatitis A in india.Journal of global infectious disease 2014;vol6 issue 2.

42. Arora D,Jindal N, Shukla RK.Water borne hepatitis A and E in malwa region Punjab India .JClinDiag Res.2013;vol7 issue 10-2163-66.

43. Mehta K, Shruti S, Shingala H.Prevalence of Hepatitis A in clinically suspected cases of acute viral hepatitis in jamnagar ,Gujarat ,India.IJSR.2013:Vol2 issue 4 13-14.

44. Syed R et al. Seroepidemiology of hepatitis A virus in Hyderabad, South India. J Med A lli e d S c i 2 0 1 2 ; 2 (2) : 58-61.

45. Verma YS,Rajput SS, Rajput N.Seroprevalence of hepatitis A infection in children .SJAMS.2014;2(3D):1144-47.

46. Chadha MS,Chitabar SD,Arankalle VA.Exposure of indianchildren to hepatitis A virus and vaccination ageIJMed.Res.1999;jan ;109:11-15.

47. Mittal SK, Rastogi A, Kumar N, Talukdar B, Kar P. Seroprevalence of hepatitis A in children - Implications for hepatitis A vaccine. *Trop Gastroenterol* 1998; *19* : 120-1.

48. Joshi N, Nagarjuna KYR, Kumar A. Age related seroprevalence of antibodies to hepatitis A virus in Hyderabad, India. *Trop Gastroenterol* 2000; *21* : 63-5.

49. Kar P. Is there a change in seroepidemiology of hepatitis A infection in India? Indian J Med Res 2006; 123(6):727-729.

50. Singh J, Prakash C, Gupta RS, Bora D, Jain DC, Datta KK. Epidemiology of endemic viral hepatitis in an urban area of India: a retrospective community study in Alwar. *Bull WorldHealth Organ* 1997; *75* : 463-8.

51. Aggarwal R, Krawczynski K, Hepatitis E.An overview and recent advances in clinical and laboratory research *J Gastroenterol Hepatol* 2000 15(1):9-20.

52. Amarapurkar DS, Agar Baijal P, Gupte P, Kamani N, Epidemiology of Hepatitis E Virus Infection in Western India *Journal of Hepatic Monthly Original Article Volume: 8* 2008 8(4):258-62.

53. Aggarwal R, Shahi H, Naik S, Yachha SK, Naik SR, Evidence in favour of high infection rate with hepatitis E virus among young children in India *J Hepatol* 1997 6(6):1425-6.

54. Rao P, Shenoy SM, Baliga S, Joon A, Prevalence of HAV and HEV in the patients presenting with acute viral hepatitis *BMC Infectious Diseases* 2012 12(Suppl 1):1471-2334-12-S1-P30.

55. Dutta AK, Aggarwal A, Kapoor AK, Ray GN, Batra S.Seroepidemiology of hepatitis A in children in Delhi. Indian J Pediatr 2000; 67 : 77-9.

56. Zago MP, Stantolin GC, Perazzio S, Prevalence of antihepatitis A antibodies in children of different socioeconomic conditions in Vila Velha *Rev Soc bras Med trop* 2005 38:285-89.

57. Pereira FE, GonÃ§alves SC, Hepatite A *Rev Soc bras Med trop* 2003 36:387-400.

58. Das K, Kar P, Chakraborty A, Gupta S, Das BC. Is vaccination program against hepatitis A needed in India? *Indian J Gastroenterol* 1998; *17* : 158.

ABBREVIATIONS

HAV – HEPATITIS A VIRUS

HEV – HEPTITIS E VIRUS

WHO – WORLD HEALTH ORGANIZATION

ANTI HAV IGM – HEPATITIS A IGM ANTIBODIES

ANTI HEV – HEPATITIS E IGM ANTIBODIES

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