http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i9.98

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Clinico-Epidemiological Study and Laboratory Profile of Viral Hepatitis- A in Children

Authors
Sudipta Dhak[1], Shibasish Banerjee[2*]
[1]Medical Officer (Specialist), Department of Paediatrics, Jhargram District & Super-speciality Hospital, Jhargram, West Bengal, India
[2]Demonstrator, Department of Community Medicine, Medical College, Kolkata, West Bengal, India
*Corresponding Author
Shibasish Banerjee
Demonstrator, Department of Community Medicine, Medical College, Kolkata, West Bengal, India

Abstract
Purpose: *Acute viral hepatitis A is a widespread, usually self-limited disease in children. This study was conducted to see any change in the pattern of clinico-epidemiological and laboratory profile of this disease and to find out hepatic and extra-hepatic complication in children.*
Methodology: *43 children diagnosed as acute viral hepatitis A by HAV IgM serology (ELISA) were included in this Hospital based cohort study.*
Results: *Mean age was 6.65 ± 2.46 y (48.8% male, 51.2% female).29 children were from lower socio-economic status. Anicteric hepatitis was found in 6.98%. Fever, dark colored urine and hepatomegaly were present in all. Other signs and symptoms were icterus (93.02%), nausea (83.72%), vomiting (76.74%), pain abdomen, abdominal distention, clay colored stool, pruritus and splenomegaly (16.28%). Most common complication was prolonged (> 12 weeks) cholestasis (16.3%) followed by ascites (6.99%), bleeding manifestations (4.65%), fulminant hepatic failure (4.65%). By comparative study, in children with prolonged cholestasis and/or palpable left lobe of liver(20.9%) with the rest of the study populations: it showed that the serum bilirubin (mean14.48 mg/dl), AST(p 0.001)and ALP(p 0.008) value were much higher with statistically significant hypoalbuminemia (p 0.042), edema (p 0.011), splenomegaly (p 0.008), altered hepatic echotexture (p 0.010),GB wall thickening (p 0.003) and altered ALT : AST ratio(p 0.005) at initial presentation.*
Conclusion: *This study showed that there is a changing trend in terms of increased frequency of prolonged cholestasis and left lobe hepatomegaly with significant changes of some relevant laboratory parameters.*
Keywords: *Hepatitis A, Cholestasis , Palpable left lobe of liver, Hypoalbuminemia, Cohort study.*

Introduction

Hepatitis A virus (HAV) infection is a widespread disease, accounting for 1.4 million cases annually worldwide[1]. In high endemic areas the reported incidence of HAV is 150 per 100,000 per year[1]. Hepatitis means inflammation of the hepatocytes and can be caused by a variety of different viruses such as hepatitis A, B, C, D and E. Since the development of jaundice is a characteristic feature of liver disease, a correct diagnosis can only be made by testing patients' sera for the presence of specific anti-viral antibodies[2,3]. Hepatitis A, a non enveloped, positive stranded RNA virus of the

picornavirus family, is a significant cause of morbidity and socio-economic losses worldwide [3,4,5].

Hepatitis A is an enteric infection spread by contaminated excreta[5,6]. The course of disease is extremely variable and divided into four clinical phases: incubation period, pre-icteric, icteric, convalescent period[3,4]. Recent studies shows a shift in epidemiology of HAV infection over the past decade[7,8] with increased frequency in the paediatric age group 12, tend to present with non-specific gastrointestinal symptoms and jaundice with prolonged cholestasis (jaundice persists beyond 12 weeks)[9]. Children from low socioeconomic classes (SECs) have a high prevalence of anti-HAV antibodies[10].

Since the first officially reported epidemic of viral hepatitis in 1955 at Delhi[11], many outbreaks of hepatitis have occurred in different parts of the country[11-13]. In India, hepatitis A virus (HAV) is still a major cause of sporadic acute hepatitis[14,15] in children. In the year 2000 study showed that nearly 90% of adolescents, adults, and most children acquired immunity to HAV infection in their preschool years[7].

The mortality rate is low (0.2% of icteric cases). Occasionally, extensive necrosis of the liver occurs during the first 6 -8 weeks of illness. Marked abdominal pain, vomiting, jaundice and the development of hepatic encephalopathy associated with coma and seizures, are the signs of fulminant hepatitis, leading to death in 70-90% of the patients. HAV is the main etiological agent of Fulmimant Hepatic Failure (FHF)in children[16]. Among patients with chronic hepatitis B or C or underlying liver disease, who are super-infected with HAV, the mortality rate increases considerably. There are limited data regarding present scenario of clinic-epidemiological course of hepatitis-A in West Bengal.Therefore this study has been undertaken to see any changing pattern of clinico-epidemiological and biochemical profile & clinical course including complications of viral hepatitis-A in children .

Materials and Methods

Hospital based prospective cohort study was conducted at In-patients and Out-patients department of Pediatric Medicine, IPGME&R/ SSKM Hospital, Kolkata-700020, a tertiary center in West Bengal. Duration of the study was 1½ year (February 2015 – July 2016). 43 children including both male & female diagnosed as acute viral hepatitis- A by HAV IgM (ELISA) serology were included in this study as non-randomized allocation. All children attended the study place in presence of the investigator satisfied the inclusion criteria and not had any of exclusion criteria were included in the study during the first fifteen months of the study period.

Inclusion criteria were- 1.Age – 1-12 y, 2.IgM Anti-HAV – Reactive,3. Duration of jaundice <3months, 4. Icteric & anicteric hepatitis. Exclusion criteria were- Jaundice persist >3 months duration, Haemolytic jaundice, IgM HAV – Non reactive , Chronic liver disease, Age <1y / >12y,Parents not giving consent.

Data were collected by oral questionnaire method regarding relevant history from parents or patient's family members, analyzing previous medical records, using bedside clinical instruments and sending required investigations to the Institutional laboratories and recording the reports in the pre-structured case study proforma. The study protocol was reviewed and approved by the Institutional Ethics Committee of IPGME & R, Kolkata. Study was conducted after taking written informed consent from the guardian/parents.

During the first 15 months of the study period all children (1-12 y) presented with features of acute hepatitis was enrolled but those satisfied the inclusion/exclusion criteria were included for the study. All study populations were clinically examined thoroughly and laboratory investigations were done from different laboratories of this institution as per the study proforma. All children were monitored for complications during hospital stay. They were discharged when clinically stable and afebrile for >24 hrs with modest increase in appetite & general well-being. Follow-up was done

at 2 weeks & 4 weeks of discharge. Detailed history, clinical examination, LFT were done in all children. All complications during this follow-up were recorded.

Clinical history such as fever, pain abdomen, nausea, vomiting, hepatomegaly, splenomegaly, any bleeding manifestation, dark urine, abdominal distension, mental status, any features of hepatic & extrahepatic complications were studied. Socio-economic history such as per capita income, education of parents & patient, source of drinking water , mode of excreta disposal were recorded. Diagnosis was confirmed by specific Viral serology [IgM anti HAV positive, Method- Enzyme Linked Immunosorbent Assay (ELISA)]. Liver function test (LFT), prothrombin time(PT), activated partial thromboplastin time (aPTT), blood sugar ,blood urea, serum creatinine ,other viral hepatitis markers (HBsAg, Anti-HCV, Anti-HEV) were used. Routine test such as Complete blood count including Hb%, total WBC count (TC), differential count (DC), platelet count were done. Ultrasonography (USG) of abdomen was advised with special emphasis to hepatobiliary system.

Data were collected, recorded & compiled on Microsoft Excel data sheet. Statistical methods (mean, standard deviation) were used to analyse the data. Data were analysed by the software Statistical version 6 [Tulsa, Oklahoma: StatSoft Inc., 2001]. Frequencies of various signs were expressed as percentage of total cases. Study of significance were analysed by Chi square test for qualitative data and Student unpaired t-test and Mann-Whitney U test for quantitative data. P value <0.05 is considered significant. Numerical variables are normally distributed by Kolmogorov-Smirnoff goodness-of-fit test other than HAV IgM, PT, APTT, INR.

Results

In this study a total 43 children were included. The mean age of children was 6.65 ± 2.46 y, 46.5% were belonging from socio-economic class IV as per modified Kuppuswamy's Socio-Economic Status Scale, 16.3% used to purify water at home either by boiling, using filter. Among them 21 (48.8 %) were male & 22 (51.2 %) were female .In this cohort study children under study divided into two groups ,in Group 1 – children had no features of prolong cholestasis at follow up &/ had palpable left lobe of liver (which is usually a sign of chronic liver disease) and in Group 2 - children had features of prolong cholestasis at follow up &/ had palpable left lobe of liver. 11 children (25.6%) out of 43 children were belonging from Group -2.Among Group 2, 5 children (45.5%) had both prolong cholestasis & palpable left lobe of liver , 2 children (18.2%) had prolong cholestasis. Only and 4 children (36.3%) had palpable left lobe of liver only and all children were HAV IgM positive with mean titre of 3.08 ± 1.54.

Most common symptoms were fever & dark colored urine (100%). Tender hepatomegaly was present in all cases(100%), Splenomegaly was present in 7 cases (16.28%) , bleeding manifestations in 2 cases (4.65%) , edema in 5 cases (11.63%) , ascites in 3 cases (6.99%), altered sensorium in 2 cases (4.65%). Majority of children had serum bilirubin in range 2-10 mg/dl (33 cases, 76.74%) and only 2 had above 20 mg/dl . More than 2000 U/L of ALT and AST were seen in 3 cases (6.97%) and 4 cases (9.3%) respectively. ALP was elevated in 11 cases (25.58%), hypoproteinemia in 5 cases (11.63%), hypoalbuminemia in 14 cases (32.56%), INR >1.5 in 5 cases (11.63%) , abnormal aPTT (>1.5 times of control) in 3 cases (6.98%). INR was highest 7.1, PT 88 sec, aPTT 96 sec in a child with FHF. FHF seen in only 2 cases (4.65%).16 cases (37.21%) had altered hepatic echotexture, 23 cases (53.49%) had contracted Gall Bladder (GB) and 4 cases (9.3%) had GB wall thickening [Table 1].

Follow up was done after 2 weeks and 4 weeks of discharge. For statistical analysis t-test was used. In children with prolonged cholestasis and/or palpable left lobe of liver (group 2) AST value was much higher (p 0.001) with significant hypoalbuminemia (p 0.042).At onset of disease total bilirubin level was much higher (mean – 14.48 mg/dl). ALP value was significantly higher during follow up (mean 274.4, p 0.008). Statistically significant findings were noted in children with prolonged cholestasis

and/or palpable left lobe of liver with following variables: Clay colored stool (p 0.045), edema (0.011), abdominal distention (p 0.011), splenomegaly (p 0.008), altered echotexture of liver (p 0.010), contacted Gall Bladder (p 0.005) and GB wall thickening (p 0.003) [Table 2].

Table 1: Frequency Distribution of various parameters (signs, symptoms, bio-chemical & USG findings)

Parameters	Cases (n = 43)	Percent (%)
Icterus	40	93.02
Nausea	36	83.72
Vomiting	33	76.74
Dark Urine	43	100
Pruritus	6	13.95
Clay colored stool	17	39.5
Pain abdomen	31	72.09
Abdominal Distention	23	53.49
Bleeding manifestation	2	4.65
Edema	5	11.63
Ascites	3	6.99
Altered Sensorium	2	4.65
Hepatomegaly	43	100
Left lobe of liver Palpable	9	20.93
Splenomegaly	7	16.28
Sanitation	37	86.05
Water purification at home	7	16.28
ALT (>40 U / L)	43	100
AST (>40 U / L)	43	100
Elevated ALP	11	25.58
Serum Protein (<6gm/dl)	5	11.63
Serum Albumin (<3.5gm/dl)	14	32.56
Serum Globulin(<2.5gm/dl)	2	4.65
INR (>1.5)	5	11.63
Abnormal aPTT	3	6.98
Altered liver echotexture	16	37.21
Contracted GB	23	53.49
GB Wall thickening	4	9.30
FHF	2	4.65

Normal levels of ALP : 1 – 9 y :145 - 420 ; 10 – 11 y : 130 – 550;12 – 13 y: Male : 200 – 495; Female : 105 – 420. Abnormal aPTT - > 1.5 times the control

Table 2: Comparison of numerical variables between Groups 1 and 2 – Student's unpaired t test

	Mean std dev.	Mean std dev.	t-value	p-value	Valid N	Valid N	Std dev.	Std dev.
Group	**1**	**2**			**1**	**2**	**1**	**2**
***Bil_B**	**6.86**	**14.48**	**-4.055**	**0.000**	32	11	2.84	9.66
***AST_B**	463.19	1400.64	-3.756	**0.001**	32	11	380.81	1280.97
*Protein_B	7.18	6.55	2.562	**0.014**	32	11	0.73	0.56
***Alb_B**	3.68	3.31	2.100	**0.042**	32	11	0.45	0.64
***Bil_2W**	3.66	11.93	-3.907	**0.000**	32	11	4.56	9.26
***AST_2W**	116.50	769.27	-4.131	**0.000**	32	11	76.87	905.33
***ALP_2W**	214.59	330.18	-2.484	**0.017**	32	11	121.29	164.53
***Protein_2W**	7.23	6.29	3.849	**0.000**	32	11	0.47	0.74
***Alb_2W**	3.73	3.31	2.691	**0.010**	32	11	0.37	0.62
***ALP_4W**	155.13	274.40	-3.041	**0.008**	8	10	31.71	106.64
***Alb_4W**	3.98	3.45	2.655	**0.017**	8	10	0.47	0.4

*statistically significant

B: baseline , 2W : follow up after 2weeks, 4W: follow up after 4 weeks

Discussion

Arankalle V, Mitra M, Bhave S, Ghosh A, Balasubramanian S, Chatterjee S et al conducted study in 928 children an reported a higher seroprevalence among older children (9–10 years 60.9%), most of belonging from lower socio-economic class - 46.5% from class IV & 27.9% from class V, only in 16.3% parents used to purify water at home, only 33.1%were belonging from a household with a private toilet .Most common symptoms were fever & dark colored urine (100%), others - icterus (93.02%), nausea (83.72%), vomiting (76.74%), pruritus (13.95%), clay colored stool (39.5%) , pain abdomen (73.09%), abdominal distention (53.49 %). Tender hepatomegaly (100%), Splenomegaly (16.28%), bleeding manifestations (4.65%), edema (11.63%), ascites (6.99%), altered sensorium in (4.65%) were also seen[17].

K. Jagadish Kumar, H. C. Krishna Kumar, V. G. Manjunath, C. Anitha, S. Mamatha in their study in 117 children with Hepatitis-A showed that most common symptoms fever (82.1).Other symptoms were nausea / vomiting (67.9%), dark urine (51.3%), pain abdomen (48.7%), anorexia (39.7%0, bleeding (3.8%). Hepatomegaly (98.7%), Splenomegaly (39.2%) of children. Anicteric hepatitis was found in 3 cases (6.98%). Serum bilirubin was in range 2-10 mg/dl (33 cases , 76.74%) and in 2 cases had above 20 mg/dl .More than 2000 U/L of ALT and AST were seen in 6.97% and 9.3%of cases respectively. ALP was elevated in 25.58%, hypoproteinemia (11.63%), hypoalbuminemia (32.56%), INR >1.5 (11.63%), abnormal aPTT (6.98%). INR was highest 7.1, aPTT 96 sec in a child with FHF. FHF seen in only 2 cases (4.65%).No mortality occurred during this study.K. Jagadish Kumar, H. C. Krishna Kumar, V. G. Manjunath, C. Anitha, S. Mamatha 16 showed >5 folds rise in AST & ALT in 79.5% and 70.5% cases respectively, hypoproteinemia in 10.3% , INR >1.5 in 15.4% and abnormal aPTT in 12.8% of cases[12].

According to WHO Life threatening complication of hepatitis-A is fulminant hepatic failure (FHF), which occurs in less than 1% of cases & mortality rate is 0.2%[1].

Though palpable left lobe of liver usually seen in chronic liver disease but in this study 5 children(11.6%) had both prolonged cholestasis & palpable left lobe of liver, 2 children (4.6%) had prolonged cholestasis only and 4 children (9.3%) had palpable left lobe of liver only. In children with prolonged cholestasis and/or palpable left lobe of liver AST value was much higher (p 0.001) with significant hypoalbuminemia (p 0.042), total bilirubin level was much higher (mean – 14.48 mg/dl) at onset , ALP value was significantly higher during follow up (mean 274.4 , p 0.008), 27.28% had pruritus , clay colored stool (p value 0.045), edema (p value 0.011), abdominal distention (p 0.011), splenomegaly (p 0.008), 72.72% had altered echotexture of liver (p 0.010), 90.91% had contacted Gall Bladder (p 0.005) and 36.36% had GB wall thickening (p 0.003)[18].

As per Jeong SH, Lee HS. Signs and symptoms of prolonged cholestasis are pruritic skin, fatigue, loose stool and weight loss[19]. K. Jagadish Kumar, H. C. Krishna Kumar, V. G. Manjunath, C. Anitha, S. Mamatha showed in their study that 6.4% had altered hepatic echo-texture and 41 % had GB wall thickening[12].In viral hepatitis the AST: ALT ratio is usually less than one[20]. Statistically significant altered ALT: AST ratio i.e. AST>ALT seen in children with prolonged cholestasis and/or palpable left lobe of liver (p value 0.005).

Limitation of this study were small sample size (n=43), short duration of follow-up , tertiary care based study ,all children belonged to same ethnicity, so conclusion may not be true universally.

Conclusion

This study showed that there is a changing trend in terms of increased frequency of prolonged cholestasis and signs of chronicity like enlargement of left lobe of liver with significant changes of some relevant laboratory parameters.

Acknowledgement

The authors would like to thank the children for participation in the study

Contributions

Sudipta Dhak: Planned the study and enrolled the children, Collected and analyzed the data;

Shibasish Banerjee: drafted and revised the manuscripts. All authors approved the final manuscripts. Sudipta Dhak will act as guarantor for the paper.

Compliance with Ethical Standards

Conflicts of Interest: None

Source of Funding: None

References

1. WHO/CDS/CSR/EDC/2000.7. Hepatitis A. World Health Organization. Department of communicable disease surveillance and response: available at: http://www.who.int/cs/disease/hepatitis/Hep

atitisA_whocdsredc2000_7.pdf .Accessed 1st December 2014.

2. Lemon SM. Hepatitis A virus. In: Webster RG and Granoff A, eds. Encyclopedia of Virology, London, Academic Press Ltd, 1994:546-554.
3. Stapleton JT and Lemon SM. Hepatitis A and hepatitis E. In:Hoeprich PD, Jordan MC, and Ronald AR, eds. Infectious Diseases, 5th ed. Philadelphia, Lippincott Co, 1994:790-797.
4. Hollinger FB and Ticehurst JR. Hepatitis A virus. In: Fields BN, Knipe DM, and Howley PM, eds. Fields Virology, 3rd ed. Philadelphia, Lippincott -Raven, 1996:735-782.
5. Lemon SM. Type A viral hepatitis: epidemiology, diagnosis, and prevention. Clinical Chemistry,1997, 43(8(B)):1494-1499.
6. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices. Morbidity and Mortality Weekly Report, 1996, 45(RR15):1 -30.
7. Jacobsen K. The Global Prevalence of Hepatitis a Virus Infection and Susceptibility: A Systematic Review. Immunization, Vaccines and Biologicals. Geneva:WorldHealthOrganization;2009.Available from:http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.01_eng.pdf. Accessed December 26, 2012.
8. Kar P. Is there a change in seroepidemiology of hepatitis A infection in India? Indian J Med Res. 2006;123:727–729.
9. Acharya SK, Batra Y, Bhatkal B, Ojha B, Kaur K, Hazari S, et al. Seroepidemiology of hepatitis A virus infection among school children in Delhi and north Indian patients with chronic liver disease: Implications for HAV vaccination. J Gastroenterol Hepatol 2003; 18: 822-7.
10. Dhawan PS, Shah SS, Alvares JF, et al. Seroprevalence of hepatitis A virus in Mumbai, and immunogenicity and safety of hepatitis A vaccine. Indian J Gastroenterol. 1998;17:16–18.
11. Dhamdhere MR, Nadkarni MG. Infectious hepatitis at Aurangabad. Report of an outbreak. *Indian J Med Sci* 1962;*16* : 1006-15.
12. K. Jagadish Kumar, H. C. Krishna Kumar, V. G. Manjunath, C. Anitha, S. Mamatha,: Hepatitis A in Children- Clinical Course, Complications and Laboratory Profile; The Indian Journal of Pediatrics ,January 2014, Volume 81, Issue 1, pp 15-19 Date: 01 Aug 2013 .
13. Naik SR, Aggarwal R, Salunke PN, Mehrotra NN. A large waterborne viral hepatitis E epidemic in Kanpur. India. *Bull World Health Organ* 1992; *70* : 597-604.
14. 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 fromnorth west India. *J Trop Pediatr*1995; *41* : 328-9.
15. Malathi S, Mohanavalli B, Menon T, Srilatha P, Sankaranarayanan VS, Reju B, *et al*. Clinical and viral markers pattern of acute sporadic hepatitis in children at Madras, South India. *J Trop Pediatr*1998; *44* : 275-8.
16. Samanta T, Ganguly S. Aetiology, clinical profile and prognostic indicators for children with acute liver failure admitted in a teaching hospital in Kolkata. Trop. Gastroenterol.2007 Jul-Sep;28(3):135-9
17. Arankalle V, Mitra M ,Bhave S, Ghosh A , Balasubramanian S , Chatterjee S et al: changing epidemiology of hepatitis a virus in indian children ; Dovepress journal : Vaccine: Development and Therapy;18th January Volume 2014:4, p 7-13. https://doi.org/10.2147/VDT.S53324

18. Kliegman R M., Stanton B F. , St. Geme J.W., Schor N. F. , Behrman R. E.: Nelson Textbook of Pediatrics; 19th Edition, an imprint of Elsevier Inc.,p1374.
19. Jeong SH, Lee HS. Hepatitis A: Clinical manifestations and management. Intervirol 2010;53:15-19. https://doi.org/10.1159/000252779 [last accessed on 8th June,2019]
20. Park GJH, Lin BPC, Ngu MC et al. Aspartate aminotransferases: alanine aminotransferases ratio in chronic hepatitis C infection : is it a predictor of cirrhosis? 2000; 15 : 386-389.