

Frequency of Cholestasis Among the Patients Suffering from Hepatitis E Virus

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ABSTRACT

Introduction: Acute viral hepatitis (AVH) is a major health concern in developing nations in regard to morbidity and mortality. Cholestasis in the form of bile thrombi in canaliculi is common in acute hepatitis but rare in chronic hepatitis. This study was designed to find the influence of cholestasis among the patients suffering from hepatitis E virus. The aim of this study was to determine the frequency of cholestasis among the patients suffering from viral hepatitis E.

Methods: The design of this study was Descriptive Cross-Sectional Study design, and the duration of this study was from 30 January 2022 to 20 September 2022 at Department of Gastroenterology Sheikh Zayed Hospital Lahore. A total of 189 patients were enrolled were observed to determine the frequency of cholestasis among the patients suffering from viral hepatitis E. Consecutive non-probability sampling technique was used to collect data from the patients. All the collected data were entered and analyzed into SPSS version 24. Data were stratified for age, gender and history of diabetes. Post stratification Chi-square test were applied taking p value of <0.05 as statistically significant.

Results: Age wise distribution among 189 patients were analyzed as n= 15-20 Years 11(5.8%) 21-30 Years 13(6.9%) 31-40 Years 45(23.8%) 41-50 Years 86(45.5%) 51-60 Years 16(8.5%) 61-70 Years 18(9.5%). Mean age was 47.95 years + 14.176 SD. Gender wise distribution among 189 patients were analyzed as n= Male was 110(58.2%) Female was 79(41.8%). Duration of Disease among 189 patients were analyzed as n= Less than 3 months was 103(54.5%) and more than 3 months was 86(45.5%). History of diabetes among 189 patients were analyzed as n= Yes was found 94(49.7%) and No was found 95(50.3%). Distribution of cholestasis among 189 patients were analyzed as n= Yes was found 90 (47.6%) and No was found 99(52.4%).

Conclusion: Based on our findings, the prevalence of cholestasis was 49.7% is in the range of that found in general population. However, this is an evolving area with ongoing research and further assessments in prospective large studies are warranted. It is not possible to differentiate viral hepatitis based on clinical features, biochemical parameters, and severity of illness. Serological markers are essential for correct etiological diagnosis. However, cholestasis is found to be significantly associated with hepatitis-E infection.

Keywords: cholestasis, viral hepatitis E, infection, ELISA

INTRODUCTION

Hepatitis-E infection is a major form of enterically transmitted non-A, non-B Hepatitis. It is the leading cause of acute Hepatitis in the world, with the highest number of cases reported in the developing regions. Data from Pakistan showed that samples obtained from sewerage water in Rawalpindi and Islamabad discovering 40.7% of the sewerage samples to be contaminated with HEV [1,2]. HEV has eight genotypes. Genotypes 1 and 2 only infect humans, are detected mainly in Asia and Mexico, respectively and they spread through fecal-oral route. HEV infection is usually self-limiting and causes acute mild illness. However, HEV infection during pregnancy, especially in the third trimester may lead to acute liver failure. Chronic HEV infection is rare and may develop in immunocompromised patients, such as organ transplant recipients. In addition, HEV has been associated with a range of extrahepatic manifestations, including a spectrum of neurological symptoms and diseases, hematological disorders, renal diseases, acute pancreatitis, myocarditis, arthritis, and autoimmune thyroiditis [3,4,5]. Cholestasis in the form of bile thrombi in canaliculi is common in acute hepatitis but rare in chronic hepatitis, which is diagnostically helpful [5]. It is a result of damage to the bile secretory apparatus of the hepatocytes but may also result from interference with bile flow at the level of the portal tracts [6,7]. Desai et al. In 2020 conducted a study on the frequency of cholestasis among the patients suffering from hepatitis E virus was 14.28% [8,9]. There are no local publish data present on this topic to the best of the candidates knowledge and as the frequency of HEV infection in the Pakistani population is increasing, and the association of HEV with the cholestasis there is a need to conduct this study in local population so that the frequency of this complication among the patients suffering from HEV could be determined which can help us in identifying the burden of this complication in local population and can help us in monitoring the local population suffering from I-HEV keeping in mind this complication frequency in local population so that these patients can be screened and managed properly for this complication which can

help in reducing the morbidity, mortality associated with it and improve the quality of life in the patients suffering from it.

MATERIAL AND METHODS

The design of this study was a Descriptive Cross-Sectional Study design, and the duration of this study were from 30 January 2022 to 20 September 2022 at Department of Gastroenterology Sheikh Zayed Hospital Lahore. A total of 189 patients were enrolled to determine the frequency of cholestasis among the patients suffering from viral hepatitis E. Consecutive non-probability sampling technique was used to collect data from the patients. All the Patients of both gender with ages in the range of 16-70 years suffering from hepatitis E virus as per operative definition and patients who sign written informed consent was taken to include in the study. All the Patients having cirrhotic liver dilated extra and intrahepatic ducts on ultrasound as per ultrasound examination and patients having hepatitis A, B or C on ELISA as per investigations. After approval from ethical review committee of the hospital, 189 patients with HEV who were present in the outpatient department of Gastroenterology Sheikh Zayed Hospital Lahore and who fulfill the above criteria were counseled and explained the details of the study. Written informed consent and detailed history were taken from each patient. The patients presenting with symptoms of hepatitis virus induced jaundice were undergoing screening by ELISA. 5ml of blood were drawn under aseptic measures and were sent to the lab. HEV infection was labelled as per operational definition. These patients were followed till IgM on ELISA is negative in two consecutive tests 24 hours apart and weekly screening was done for cholestasis. The presence of cholestasis was done as per operational definition. All the data were noted and recorded into the attached proforma along with demographic details of the neonates. All the tests were done in the hospital lab to eliminate bias and confounding variables were controlled by exclusion. All the collected data were entered and analyzed into SPSS version 22. Data were stratified for age, gender and history of diabetes. Post stratification Chi-square test were applied taking p value of <0.05 as statistically significant

RESULTS

Age wise distribution among 189 patients were analyzed as n= 15-20 Years 11(5. 8%) 21-30 Years 13(6. 9%) 31-40 Years 45(23. 8%)41-50 Years 86(45. 5%) 51-60 Years16(8. 5%) 61-70 Years18(9. 5%). Mean age was 47. 95 years+ 14. 176 SD (Table No: 1) Gender wise distribution among 189 patients were analyzed as n= Male was110(58. 2%) Female was 79(41. 8%) (Table No: 2)Duration of Disease among 189 patients were analyzed as n= Less than 3 months was 103(54. 5%) and more than 3 months was 86(45. 5%) (Table No: 3)History of diabetes among 189 patients were analyzed as n= Yes was found 94(49. 7%) and No was found 95(50. 3%) (Table No: 4)Distribution of cholestasis among 189 patients were analyzed as n= Yes was found 90 (47. 6%) and No was found 99(52. 4%) (Table No: 5)

Table 1: Age Wise Distribution (n=189)

Age	Frequency	Percent
15-20 Years	11	5. 8
21-30 Years	13	6. 9
31-40 Years	45	23. 8
41-50 Years	86	45. 5
51-60 Years	16	8. 5
61-70 Years	18	9. 5
Total	189	100. 0

Mean age was 47. 95 years+ 14. 176 SD

Table 2: Gender Wise Distribution (n=189)

Gender wise Distribution	Frequency	Percent
Male	110	58. 2
Female	79	41. 8
Total	189	100. 0

Table 3: Duration of Disease Wise Distribution (n=189)

Duration of Disease	Frequency	Percent
Less than 3 months	103	54. 5%
More than 3 months	86	45. 5%
Total	189	100. 0

Table 4: History of Diabetes (n=189)

History of Diabetes	Frequency	Percent
Yes	94	49. 7
No	95	50. 3
Total	189	100. 0

Table 5: Distribution of Cholestasis (n=189)

Cholestasis	Frequency	Percent
Yes	90	47. 6
No	99	52. 4
Total	189	100. 0

Table 6: stratification W. R. T Age of Distribution of Cholestasis (n=189)

Age Wise Distribution	Cholestasis		Total	P. Value
	Present	Absent		
15-20 Years	11(5. 8%)	0(0%)	11(5. 8%)	0. 000
21-30 Years	10(5. 29%)	3(1. 58%)	13(6. 8%)	0. 000
31-40 Years	31(16. 4%)	14(29. 6%)	45(23. 8%)	0. 000
41-50 Years	25(13. 22%)	61(32. 2%)	86(45. 5%)	0. 000
51-60 Years	4(2. 11%)	12(6. 3%)	16(8. 4%)	0. 000
61-70 Years	9(4. 7%)	9(4. 7%)	18(9. 5%)	0. 000
Total	99(52. 3%)	99(52. 3%)	189(100%)	

Table 7: Stratification W. R. T Gender of Distribution of Cholestasis (n=189)

Gender wise distribution	Cholestasis		Total	P. Value
	Present	Absent		
Male	62(32. 8%)	48(25. 4%)	110(58. 2%)	0. 005
Female	28(14. 8%)	51(27. 0%)	79(41. 8%)	0. 005
Total	90(47. 6%)	99(52. 4%)	189(100. 0%)	

DISCUSSION

In current study the Age wise distribution among 189 patients were analyzed as n= 15-20 Years 11(5. 8%) 21-30 Years 13(6. 9%) 31-

40 Years 45(23. 8%)41-50 Years 86(45. 5%) 51-60 Years16(8. 5%) 61-70 Years18(9. 5%). Mean age was 47. 95 years+ 14. 176 SD. Gender wise distribution among 189 patients were analyzed as n= Male was110(58. 2%) Female was 79(41. 8%). Duration of Disease among 189 patients were analyzed as n= Less than 3 months was 103(54. 5%) and more than 3 months was 86(45. 5%). History of diabetes among 189 patients were analyzed as n= Yes was found 94(49. 7%) and No was found 95(50. 3%). Distribution of cholestasis among 189 patients were analyzed as n= Yes was found 90 (47. 6%) and No was found 99(52. 4%). Study done by Nishar Ahmed Shah et al. also found that hepatitis E was most common cause of AVH accounting for 50% of patients in their study group [10]. From this study it can be concluded that HEV is the major etiological agents of AVH in young adults. Important fact noted in the present study was the frequency of HAV among adults. In the present study 12. 8% patients suffering from hepatitis A. Seroprevalence studies reveal that 90–100% of the population acquires anti-HAV antibody and becomes immune by adolescence [11]. A study conducted by Behera MR et al. found that hepatitis A infection is more common among children which accounting for 62. 5% [12]. India is thought to be endemic for HAV and by age of 15 most of the population are observed to be protected against HAV due to subclinical exposure to HAV in childhood [13]. This observation indicates that in India, due to developmental progress, certain population are not exposed to HAV. In childhood and adult population involvement could be due to developmental progress [12,13]. In the present study, AVH was commonly seen in the age group of 21–30 years with a mean age of 27. 25 years among them hepatitis E were majority accounting for 55. 1%. In this study, mean age of presentation was 27. 25±9. 5 years which was slightly lower with other studies Nishar Ahmed et al. 30±12. 4 years and Birajdar SV et al. 36. 2±3. 5 years [7,10] Study done by Varsha Dabadghao et al. and study by Birajdar SV et al. found that maximum number of patients were young adults [14] Male were affected slightly more than female.

A study done by Nishar Ahmed Shah et al. , most common symptoms observed were jaundice (86. 10%) followed by anorexia (76. 50%), dark-colored urine (73%), fever with chills (66. 1%), and abdominal pain in (36. 3%) [15,16]. Another study done by Zhang et al. also observed that the common clinical symptoms were jaundice, fatigue, and anorexia [15]. In the present study, the most common presenting symptoms was yellowish discoloration of urine (84. 2%) followed by yellowish discoloration of sclera (81. 2%). Next common symptoms were anorexia (65. 7%), nausea and vomiting (40%), abdominal pain (38%), and fever (37%). In the present study, anemia was seen in 27 (38. 6%) patients and mean hemoglobin was 10. 99 gm%. TLC was raised in all cases except two (18. 1%) cases of acute hepatitis B. Study done by Ali SJ, et al. also observed increase TLC in HBV patients Mean TLC was 10115. 74 cu/mm. Low platelet count was found in 14 (20%). Study done by Rahman MM et al, low platelet count was observed in 36 cases of HEV patients. 16 Anemia was observed in 24% of patients in Perseghin P et al. is not unusual in AVH [17]. This is attributed to a temporary bone marrow suppression and autoimmune hemolytic anemia, which may accompany viral hepatitis [18,19]. Dilutional anemia is another possible explanation for this observation, as plasma volume is frequently increased in active hepatic disease. Study done by Changgeng Yi Xue Za Zhi Zhi et al. found that leukocytosis and leucopenia in 10. 8% and 7. 4% respectively. This is attributed to a virus interfering with leucopoiesis supports the more frequent finding of leucopenia rather than leukocytosis. In contrast, study done by Ahmad AE et. al found that there were no significant changes in TLC, RBC count, Platelet count in patients with CHB, whereas this study was strictly [20].

CONCLUSION

Based on our findings, the prevalence of cholestasis was 47. 6% is in the range of that found in general population. However, this is an evolving area with ongoing research and further assessments in

prospective large studies are warranted. It is not possible to differentiate viral hepatitis based on clinical features, biochemical parameters, and severity of illness. Serological markers are essential for correct etiological diagnosis. However, cholestasis is found to be significantly associated with hepatitis-E infection.

Recommendation: Our data is consistent with prior studies and substantiates that the frequency of HEV infection in Pakistan is not negligible. It also suggests that the diagnostic investigation for HEV undertaken by the public health system should be extended to encompass all cases of liver disease that are unrelated to the most investigated hepatotropic viruses, considering the possibility of clinical complications associated with this infection

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REFERENCES

- Mast EE, Krawczynski K. Hepatitis E: an overview. *Annu Rev Med.* 2018. 47:257-66.
- Purdy MA, Krawczynski K. Hepatitis E. *Gastroenterol Clin North Am.* 2019 Sep. 23(3):537-46.
- Harrison TJ. Hepatitis E virus -- an update. *Liver.* 2015 Jun. 19(3):171-6.
- Skidmore SJ. Factors in spread of hepatitis E. *Lancet.* 2017 Sep 25. 354(9184):1049-50.
- Kamar N, Bendall R, Legrand-Abravanel F, et al. Hepatitis E. *Lancet.* 2019 Jun 30. 379(9835):2477-88.
- Puoti M, Muioli MC, Travi G, Rossotti R. The burden of liver disease in human immunodeficiency virus-infected patients. *Semin Liver Dis.* 2019 May. 32(2):103-13.
- Dalton HR, Bendall RP, Keane FE, Tedder RS, Ijaz S. Persistent carriage of hepatitis E virus in patients with HIV infection. *N Engl J Med.* 2019 Sep 3. 361(10):1025-7.
- Ollier L, Tieulie N, Sanderson F, et al. Chronic hepatitis after hepatitis E virus infection in a patient with non-Hodgkin lymphoma taking rituximab. *Ann Intern Med.* 2019 Mar 17. 150(6):430-1.
- Kamar N, Selves J, Mansuy JM, et al. Hepatitis E virus and chronic hepatitis in organ-transplant recipients. *N Engl J Med.* 2018 Feb 21. 358(8):811-7.
- Harrison A, Scobie L, Crossan C, et al. Hepatitis E seroprevalence in recipients of renal transplants or haemodialysis in southwest England: a case-control study. *J Med Virol.* 2015 Feb. 85(2):266-71.
- Shrestha MP, Scott RM, Joshi DM, et al. Safety and efficacy of a recombinant hepatitis E vaccine. *N Engl J Med.* 2017 Mar 1. 356(9):895-903.
- Zhu FC, Zhang J, Zhang XF, et al. Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomised, double-blind placebo-controlled, phase 3 trial. *Lancet.* 2018 Sep 11. 376(9744):895-902.
- Hoofnagle JH, Nelson KE, Purcell RH. Hepatitis E. *N Engl J Med.* 2019 Sep 27. 367(13):1237-44.
- Mushahwar IK. Hepatitis E virus: molecular virology, clinical features, diagnosis, transmission, epidemiology, and prevention. *J Med Virol.* 2018 Apr. 80(4):646-58.
- Kuniholm MH, Purcell RH, McQuillan GM, Engle RE, Wasley A, Nelson KE. Epidemiology of hepatitis E virus in the United States: results from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Infect Dis.* 2019 Jul 1. 200(1):48-56.
- Thomas DL, Yarbough PO, Vlahov D, et al. Seroreactivity to hepatitis E virus in areas where the disease is not endemic. *J Clin Microbiol.* 2019 May. 35(5):1244-7.
- Feagins AR, Opriessnig T, Guenette DK, Halbur PG, Meng XJ. Inactivation of infectious hepatitis E virus present in commercial pig livers sold in local grocery stores in the United States. *Int J Food Microbiol.* 2018 Mar 31. 123(1-2):32-7.
- Rein DB, Stevens GA, Theaker J, Wittenborn JS, Wiersma ST. The global burden of hepatitis E virus genotypes 1 and 2 in 2005. *Hepatology.* 2018 Apr. 55(4):988-97.
- Zhuang H, Cao XY, Liu CB, Wang GM. Epidemiology of hepatitis E in China. *Gastroenterol Jpn.* 2020 Jul. 26(Suppl 3):135-8.
- Purcell RH, Emerson SU. Hepatitis E: an emerging awareness of an old disease. *J Hepatol.* 2018 Mar. 48(3):494-503.