Journal of Research in Clinical Medicine

J Res Clin Med, 2024, 12: 9
doi: 10.34172/jrcm.32218
https://jrcm.tbzmed.ac.ir

TUOMS PRESS

Original Article

Evaluation of the causes and diagnosis of acute hepatitis in children admitted to Tabriz Children Hospital

Babak Abdinia[1], Maryam Shoaran[1,2*], Orang Abdollahi[1], Zahra Golchinfar[2]

[1]Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Clinical Research Development Unit of Children Educational and Treatment Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article info

Article History:
Received: March 6, 2022
Accepted: May 27, 2023
ePublished: April 16, 2024

Keywords:
Hepatitis, Diagnosis, Children

Abstract

Introduction: The hepatotropic viruses are the most common causes of hepatitis worldwide; however, other infectious and non-infectious reasons can play a role in disease progress. In this study, we examined the infectious and non-infectious causes, and diagnoses of clinical signs of acute hepatitis in children admitted to Tabriz Children Hospital.

Methods: In this study, the files of the children hospitalized between 2006 and 2016 with acute viral and non-viral clinical signs were extracted in Tabriz Children Hospital and patients' information including age, sex, place of residence, type of disease, and their recovery status were investigated.

Results: Of all patients, 62 were boys (48.4%) and the mean age of the hospitalized children was 6.92 ± 0.46 years. The most common cause was hepatitis A, followed by autoimmune hepatitis. There was no significant relationship between age, gender, and place of residence with diagnosis, but there was a significant relationship between diagnosis and hepatitis type.

Conclusion: The most common type of hepatitis in our study was hepatitis A, and according to its method of transmission, observing health tips is of high significance. Based on the obtained results, autoimmune hepatitis is chronic and requires long-term follow-up.

Introduction

Hepatitis refers to the inflammation of the liver parenchyma and can occur for a variety of reasons, ranging from a temporary asymptomatic viral disease to chronic liver disease, and progressive liver failure.[1,2] Hepatotropic viruses are the most common causes of hepatitis worldwide, nevertheless, other infectious agents, drugs, toxins, and autoimmune and metabolic diseases can also affect a person with this clinical sign. Other viruses causing hepatitis include Epstein-Barr virus (EBV), chickenpox (VZV), herpes virus (HSV), and cytomegalovirus (CMV), that are non-hepatotropic viruses infecting the liver as a part of a systemic infection.[3] The viruses are the causes of five main types of hepatitis A, B, C, D, and E.[4] About 400 million people worldwide are chronic carriers of the hepatitis virus.[5] Getting older increases the emergence of the symptoms. When the symptoms of hepatitis appear, it is usually between 15 days and 6 months after the onset of the disease.[6-8] The early stage of hepatitis is called the acute phase. Symptoms of this phase are similar to the mild flu and include diarrhea, fatigue, anorexia, mild fever, muscle or joint pain, nausea, mild heartburn, vomiting, and weight loss. Symptoms like jaundice, pain in the upper right quadrant of the abdomen, and evidence of hepatic dysfunction may gradually occur. Autoimmune hepatitis is a serious disease that has unpleasant side effects in children if not diagnosed and treated in time. It is estimated that the global prevalence of autoimmune hepatitis is 2 to 17 per 100 000 children.[7-12] The etiology of hepatitis plays a major role in determining the diagnosis and treatment. Most cases of acute viral hepatitis do not require special treatment and only supportive measures suffice. In some cases, antiviral drugs for the treatment of chronic hepatitis B and C are helpful. Specific immunosuppressive therapy is required for autoimmune hepatitis. According to the mentioned problems and scarcity of former comprehensive studies in the region examining the cause and diagnosis of children with hepatitis, this study aimed at evaluating the cause and diagnosis of viral and non-viral hepatitis in Tabriz Children's Hospital. Given the importance of this issue, we tried to determine the common causes and diagnosis of the disease in this age group to pave the way for further studies and general national health policies and, therefore, reduce the complications of hepatitis in children in the future. In any research design and study, a myriad of factors plays a role and makes their results inconsistent with each other, culminating in a call for more studies to

***Corresponding Author:** Maryam Shoaran, Email: maryamshoaran1@gmail.com

arrive at definite solutions.

Methods

In this study, the files of children with acute viral and non-viral hepatitis, who were hospitalized after the approval of the ethics committee and observing the principles of fiduciary and medical ethics in Tabriz Children's Hospital between 2006 and 2016, were extracted and examined. Using the prepared checklist, the file information of these patients, including age, sex, place of residence, type of disease, recovery status or illness, and the fate of the patients were entered into the mentioned form to a traceable extent. If necessary, additional information was collected by telephone and patient calls. The inclusion criteria were children aged 0-15 years with a clinical sign of acute viral and non-viral hepatitis in Children Hospital between 2006 and 2016; and exclusion criteria were the presence of known liver disease, age over 15 years, and incomplete records. Totally, 128 patients were included in the study. The data were analyzed through the SPSS 22. To investigate the correlation between the qualitative variables, the chi-square and Pearson tests were used. For comparing the means of the quantitative variables in the analysis group the P-value variance was employed and a P value of < 0.05 was considered significant. In this study, descriptive statistics, chi-square, Fisher's exact tests, and logistic regression analysis were used to analyze the data.

Results

In this study, 128 patients with inclusion criteria participated, of which 62 were boys (48.4%) and 66 were girls (51.6%). The mean age of hospitalized children was 6.92 ± 0.46 years. The residence of the patients was 56.3% urban and 43.8% rural. Table 1 describes the cause of the disease and the percentage of the patients, according to that the most common cause has been hepatitis A, followed by autoimmune hepatitis. In terms of diagnosis, in subsequent follow-ups, 6.3% of the children died, 68.8% completely recovered, 23.4% had chronic hepatitis, and 1.5% had cirrhosis. In the patients with hepatitis A, the recovery rate was 100% and in patients with autoimmune hepatitis, all cases were chronic and 10% of them developed liver cirrhosis during follow-up. Wilson's disease was diagnosed in 11 patients (8.6%), one of whom underwent liver transplantation. Other patients with Wilson's disease were treated with medication and discharged in good general condition. Of the patients with hepatitis B, one patient recovered, one patient died with fulminant plaque, and the rest were treated and followed up chronically. There were two cases of hepatitis C, both of which became chronic. In cases of hepatitis, the cure rate was 100% and none of the patients died. Due to the inability of the diagnostic methods to classify some patients, a percentage of patients were classified as hepatitis without a cause. In the latter group, the recovery rate was 100% and none of the patients died. In patients with EBV and CMV-induced hepatitis, the recovery rate was 100% and none of the patients died. There was no significant relationship between age, sex, and place of residence with diagnosis ($P = 0.842$, $P = 0.788$, and $P = 0.316$, respectively), while there was a significant relationship between the hepatitis type and good or bad diagnosis ($P = 0.00$)

Table 1. Number of patients by the cause of hepatitis

Type of hepatitis	Frequency	Percent
HAV	44	34.3
Autoimmune	30	23.3
Wilson disease	11	8.6
No cause	11	8.6
HBV	10	7.9
Medicinal	8	6.3
EBV	6	4.7
CMV	6	4.7
HCV	2	1.6
Total	128	100

HAV, hepatitis A virus; HBV, hepatitis B virus; EBV, Epstein-Barr virus; CMV, cytomegalovirus; HCV, hepatitis C virus.

Discussion

In the present study, the most common cause was hepatitis A, with a 100% recovery rate. The type of hepatitis had a statistically significant relationship with patients' diagnoses. In this study, no case of hepatitis E was observed in the hospitalized patients. A previous study at the center reported a 3.6% prevalence of hepatitis E antibodies in outpatients; however, none of the significant clinical cases required hospitalization.[8] Unfortunately, vaccination against the hepatitis A virus (HAV) is not routinely performed in Iran, which could explain the high prevalence of this type of viral hepatitis in children in our hospital. In a study conducted by Babamahmoodi and Haghshenas, 439 patients with viral hepatitis were admitted to Razi Hospital in Ghaemshahr from the beginning of 2003 to the end of 2008, of which 40 patients (9.11%) were infected with hepatitis A. However, in our study, 44 patients (34.4%) were infected with hepatitis A, two patients (1.6%) with hepatitis C, 10 patients (7.9%) with hepatitis B, six patients (4.7%) with hepatitis CMV, and six patients (4.7%) had hepatitis EBV. In the study of this group, six people (7.5%) died due to fulminant hepatitis A, but in our study, despite the maximum prevalence of hepatitis A among the patients, no death was reported. In this study, after hepatitis B and C, hepatitis A had the highest prevalence and hepatitis E was in the next place.[13] On the other hand, in our study, after hepatitis A, autoimmune hepatitis, Wilson's disease, unexplained hepatitis, hepatitis B, and drug-induced hepatitis were the most common diseases observed. Despite the benign course of hepatitis A in our patients, it is necessary to vaccinate the children against this type of hepatitis due to its high prevalence. In a study by Taylor et al, conducted in

the United States, it was reported that there were 29 patients with hepatitis A, 16 of whom recovered, 9 underwent liver transplants, and 4 died, indicating that the diagnosis of hepatitis A was weak and the risk of acute liver failure leading to transplantation or death was high in this study. The results of this study contradict our study, which can be explained by differences in the age group of patients and different clinical manifestations of the disease.[14] In a 2014 study in India, the clinical course of hepatitis A in children was examined. The mean age of the patients was 7.85 and the mortality rate was 1.3% due to hepatic fulminant insufficiency. Most patients recovered completely within two months and prolonged cholestasis was observed in two patients.[15] In our study, 44 cases of hepatitis A were reported, none of which resulted in death or evidence of hepatic impairment as a coagulation disorder. In a 2005 study by Matthew et al., examining the patients admitted to California hospitals for hepatitis A between 1989 and 2000 was conducted, and a death rate of 1.2 per million population was reported. Aging had increased the rate of death and there was a statistically significant relationship between aging and mortality. But in our study, there was no significant relationship between age and diagnosis; it should be noted that our study was generally carried out in the age group of children.[16] In another study conducted in 2006 by Hussain et al, it was found that the pattern of hepatitis A in children was asymptomatic and it was more symptomatic than acute hepatitis in adults.[17] In line with our study, a study by Chadha et al in India revealed that the most common cause of hepatitis was the HAV. However, hepatitis E and hepatitis B were also in the next ranks and hepatitis E virus was reported as the main cause of acute hepatitis and sporadic fulminant.[18] These results were inconsistent with our study, which may require to justify the diagnostic limitations for hepatitis E at our center. The role of the hepatitis C virus (HCV) in the development of acute and fulminant hepatitis was negligible, which was also the case in our study. It should be noted that in our study, due to the lack of hepatitis C cases, judgments about related statistical findings such as diagnosis may not seem accurate. In our study, all patients with CMV recovered. However, in some studies, there have been reports of chronic liver disease and fatal manifestations of CMV infection in the form of hepatitis, carditis, and coagulation disorders.[19] Another study by Kanzler et al, found that 29.1% of the patients with autoimmune hepatitis developed cirrhosis of the liver, and 69.9% developed chronic hepatitis without evidence of cirrhosis. However, in our study, all patients had chronic inflammation and 10% had evidence of liver cirrhosis.[20] In a study by Manolaki et al. in Greece, patients with Wilson disease had a favorable clinical course. In our study, one deceased patient had the Wilson disease.[21] In a study by Aydoğdu et al from Turkey, Wilson's disease accounted for 12.5 percent of the fulminant hepatitis cases, which was close to the percentage reported in our study. However, it should be noted that in this study, patients with good general conditions were not included in the analysis.[22]

Conclusion

According to the findings of our study, it can be concluded that the most common type of hepatitis in our region is hepatitis A, which due to the transmission method of this disease, observing hygienic points, and the inclusion of hepatitis A vaccine in the national vaccination program is recommended. Autoimmune hepatitis and Wilson's disease constitute a significant percentage of patients with clinical hepatitis and the need to pay attention to the diagnostic and therapeutic methods of these two diseases is of high significance. Although hepatitis B and C have a higher prevalence in adults, the age groups of children also need to be taken into account. Further studies are needed to accurately assess the relationship between age, gender, and place of residence with diagnosis in patients with acute hepatitis.

Acknowledgements

We would like to thank the Clinical Research Development Unit of Zahra Mardani Azari Children's Hospital, Tabriz University of Medical Sciences, Tabriz ,Iran for their support.

Authors Contribution

Conceptualization: Babak Abdinia, Maryam Shoaran.
Data curation: Babak Abdinia, Maryam Shoaran, Orang Abdollahi, Zahra Golchinfar.
Formal analysis: Orang Abdollahi, Zahra Golchinfar.
Funding acquisition: Babak Abdinia, Maryam Shoaran.
Investigation: Babak Abdinia, Maryam Shoaran, Orang Abdollahi, Zahra Golchinfar.
Methodology: Babak Abdinia, Maryam Shoaran, Orang Abdollahi, Zahra Golchinfar.
Project administration: Babak Abdinia, Maryam Shoaran, Orang Abdollahi, Zahra Golchinfar.
Resources: Babak Abdinia, Maryam Shoaran, Orang Abdollahi, Zahra Golchinfar.
Software: Orang Abdollahi, Zahra Golchinfar.
Supervision: Babak Abdinia, Maryam Shoaran.
Validation: Babak Abdinia, Maryam Shoaran.
Visualization: Babak Abdinia, Maryam Shoaran.
Writing–original draft: Babak Abdinia, Maryam Shoaran, Orang

Study Highlights

What is current knowledge?

- Hepatotropic viruses are the most common causes of hepatitis worldwide.
- The etiology of hepatitis plays a major role in determining the diagnosis and treatment.

What is new here?

- The most common cause of hepatitis is hepatitis A virus, followed by autoimmune hepatitis.
- There is no significant relationship between age and sex with the diagnosis.
- There is a significant relationship between the cause of hepatitis and patient's outcome.

Abdollahi, Zahra Golchinfar.
Writing–review & editing: Babak Abdinia, Maryam Shoaran, Zahra Golchinfar.

Competing Interests
The authors have no conflicts of interest to declare.

Ethical Approval
The study was approved by the regional ethics committee under the code number of IR.TBZMED.REC.1396.1109.

Funding
None.

References
1. Iorio R, Giannattasio A, Cirillo F, L DA, Vegnente A. Long-term outcome in children with chronic hepatitis B: a 24-year observation period. Clin Infect Dis. 2007;45(8):943-9. doi: 10.1086/521864.
2. Jonas MM, Mizerski J, Badia IB, Areias JA, Schwarz KB, Little NR, et al. Clinical trial of lamivudine in children with chronic hepatitis B. N Engl J Med. 2002;346(22):1706-13. doi: 10.1056/NEJMoa012452.
3. Malik R, Hardikar W. Hepatitis B and C in children. Indian J Pediatr. 2016;83(11):1303-10. doi: 10.1007/s12098-016-2076-4.
4. Mendizabal M, Dip M, Demirdjian E, Lauferman L, Lopez S, Minetto J, et al. Changing etiologies and prognostic factors in pediatric acute liver failure. Liver Transpl. 2020;26(2):268-75. doi: 10.1002/lt.25658.
5. Gregorio GV, Portmann B, Karani J, Harrison P, Donaldson PT, Vergani D, et al. Autoimmune hepatitis/sclerosing cholangitis overlap syndrome in childhood: a 16-year prospective study. Hepatology. 2001;33(3):544-53. doi: 10.1053/jhep.2001.22131.
6. Sokal EM, Kelly DA, Mizerski J, Badia IB, Areias JA, Schwarz KB, et al. Long-term lamivudine therapy for children with HBeAg-positive chronic hepatitis B. Hepatology. 2006;43(2):225-32. doi: 10.1002/hep.21020.
7. Rafeey M. Prevalence and risk factors of hepatitis a in children in Tabriz, Iran. J Res Clin Med. 2014;2(4):183-6.
8. Rafeey M, Sari Sorkhabi R, Ghanbari A, Shoaran M. Evaluation of prevalence and risk factors for hepatitis E in pediatric patients in Tabriz children hospital. Med J Tabriz Univ Med Sci Health Serv. 2016;38(1):32-7.
9. Pathak S, Kamat D. Autoimmune hepatitis in children. Pediatr Ann.2018;47(2):e81-6.doi:10.3928/19382359-20180126-01.
10. Mieli-Vergani G, Vergani D, Baumann U, Czubkowski P, Debray D, Dezsofi A, et al. Diagnosis and management of pediatric autoimmune liver disease: ESPGHAN hepatology committee position statement. J Pediatr Gastroenterol Nutr. 2018;66(2):345-60. doi: 10.1097/mpg.0000000000001801.
11. Hom X, Little NR, Gardner SD, Jonas MM. Predictors of virologic response to lamivudine treatment in children with chronic hepatitis B infection. Pediatr Infect Dis J. 2004;23(5):441-5. doi: 10.1097/01.inf.0000126412.93562.f5.
12. Chu CM, Liaw YF. Chronic hepatitis B virus infection acquired in childhood: special emphasis on prognostic and therapeutic implication of delayed HBeAg seroconversion. J Viral Hepat. 2007;14(3):147-52. doi: 10.1111/j.1365-2893.2006.00810.x.
13. Babamahmoodi F, Haghshenas M. Treatment of chronic hepatitis B virus infection. J Clin Exc. 2013;1(1):2-26. [Persian].
14. Taylor RM, Davern T, Munoz S, Han SH, McGuire B, Larson AM, et al. Fulminant hepatitis A virus infection in the United States: incidence, prognosis, and outcomes. Hepatology. 2006;44(6):1589-97. doi: 10.1002/hep.21439.
15. Kumar KJ, Kumar HC, Manjunath VG, Anitha C, Mamatha S. Hepatitis A in children- clinical course, complications and laboratory profile. Indian J Pediatr. 2014;81(1):15-9. doi: 10.1007/s12098-013-1114-8.
16. Wise ME, Sorvillo F. Hepatitis A--related mortality in California, 1989-2000: analysis of multiple cause-coded death data. Am J Public Health. 2005;95(5):900-5. doi: 10.2105/ajph.2003.035485.
17. Hussain Z, Das BC, Husain SA, Murthy NS, Kar P. Increasing trend of acute hepatitis A in north India: need for identification of high-risk population for vaccination. J Gastroenterol Hepatol. 2006;21(4):689-93. doi: 10.1111/j.1440-1746.2006.04232.x.
18. Chadha MS, Walimbe AM, Chobe LP, Arankalle VA. Comparison of etiology of sporadic acute and fulminant viral hepatitis in hospitalized patients in Pune, India during 1978-81 and 1994-97. Indian J Gastroenterol. 2003;22(1):11-5.
19. Vancíková Z, Kucerová T, Pelikán L, Zikmundová L, Priglová M. Perinatal cytomegalovirus hepatitis: to treat or not to treat with ganciclovir. J Paediatr Child Health. 2004;40(8):444-8. doi: 10.1111/j.1440-1754.2004.00430.x.
20. Kanzler S, Löhr H, Gerken G, Galle PR, Lohse AW. Long-term management and prognosis of autoimmune hepatitis (AIH): a single center experience. Z Gastroenterol. 2001;39(5):339-8. doi: 10.1055/s-2001-13708.
21. Manolaki N, Nikolopoulou G, Daikos GL, Panagiotakaki E, Tzetis M, Roma E, et al. Wilson disease in children: analysis of 57 cases. J Pediatr Gastroenterol Nutr. 2009;48(1):72-7. doi: 10.1097/MPG.0b013e31817d80b8.
22. Aydoğdu S, Ozgenç F, Yurtsever S, Akman SA, Tokat Y, Yağci RV. Our experience with fulminant hepatic failure in Turkish children: etiology and outcome. J Trop Pediatr. 2003;49(6):367-70. doi: 10.1093/tropej/49.6.367.