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Acute Viral Hepatitis in Zahedan: A Serological Analyzes of 263 Case

Masoud Salehi and Batol Sharifi

In the present study determined the relative importance of recognized etiologic agents of AVH and to compare the clinical, biochemical and demographic factors of AVH in Zahedan the capital city of the Sistan and Baluchestan province. Blood samples as well as demographic and clinical data were collected from 263 consecutive patients with AVH who were seen at Zahedan hepatitis clinic and Bu-Ali and Ali-Asghar Hospitals. Patients were tested for HbsAg, IgM Anti HAV, IgM antiHBc, IgM Anti HDV and HCV as needed. Hepatitis E was not investigated as relevant diagnostic kits were not available. A total of 263 patients with AVH were studied. 188 (75.5%) had hepatitis A, 47 (17.9%) hepatitis B, 6(2.3%) hepatitis C, 5(1.9%) hepatitis D and 17(6.6%) had hepatitis non A-D. Hepatitis A occurred most frequently in young children and patients with hepatitis B, C and D occurred generally in young adults. Mean age of patients affected by hepatitis A, were (6.1, CI 95%:5.4-6.9) B, (20.6, CI 95%:17.5-23.7) C, (20.2, CI 95%:5.7-34.7) D, (26.2, CI 95%:16.2-36.2) and Non A-D (18.7, CI 95%: 10.9-26.4). Hepatitis A patients presented to hospital or clinic earlier (p=0.01) and had lower initial serum bilirubin, ALT and AST, but had higher Alkaline Phosphatase (ALP). Who had parenterally transmitted hepatitis were more likely to have excoriation, however patients with hepatitis A were more likely to have anorexia, vomiting, fever, chill, abdominal pain and prodromal symptoms. Nearly all cases of AVH in children were due to hepatitis A, whereas hepatitis B, C and D generally occur in adults and there is some difference in clinical and laboratory findings across the etiology of AVH.

Key words: Viral hepatitis, hepatitis A, hepatitis B, hepatitis C, hepatitis D, etiology

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INTRODUCTION

Acute Viral Hepatitis (AVH) is an important cause of morbidity and mortality worldwide. However, its incidence varies, being low in much developed countries but high in parts of South America, Africa and Asia including the Middle East. Classic acute viral hepatitis is currently consisted of hepatitis A, B, C, D and E. The relative importance of these five agents differs dramatically with the geographically region. For instance, in the United States, hepatitis A, B and C account for 97% of acute viral hepatitis[1]. In regions such as Senegal, Tunisia and Ethiopia about 20% of acute hepatitis is composed of hepatitis C[2], whereas, in Northern parts of India china and Pakistan, hepatitis C is the rare cause of non A non B hepatitis and hepatitis E has a wide prevalence[3,4]. In view of dissimilar prognosis of different types of hepatitis and elementary difference between measures for epidemiological investigations and control programs, the determination of etiology of AVH is crucially important for the patients, their families and community[5].

There is no report on the etiology of acute viral hepatitis in Sistan and Baluchestan province, southeast of Iran. Therefore, we decided to determine the relative importance of recognized etiologic agents of acute viral hepatitis and to compare the clinical, biochemical and demographic factors associated with each type of AVH in Zahedan the capital city of the province. The situation in Sistan and Baluchestan province is special in that it is the border of Iran with Pakistan and Afghanistan, there is a large Afghan refugee and the province has the highest rate of hepatitis infection in the country. Therefore the results of this study provide useful information for health policy makers and physicians.

MATERIALS AND METHODS

Blood samples as well as demographic and clinical data were collected from 262 consecutive patients with sporadic AVH who were seen at Zahedan hepatitis clinic and Bu-Ali and Ali-Asghar Hospitals. These two hospitals are the only ones that have infectious diseases departments. Since patients in whom AVH is suspected are almost always referred to one these facilities for diagnosis and management, our subjects represented most of the clinically apparent cases of AVH in Zahedan during the study.

The infectious disease specialists at the hospitals and the hepatitis clinic made the clinical diagnosis of AVH. The diagnosis was based upon an illness of <1 month's duration with symptoms compatible with acute hepatitis, an initial serum level of alanine aminotransferase (ALT) that was more than 5 times the upper limit of normal and the exclusion of the other potential non-viral causes of hepatocellular injuries and rule out alcoholic hepatitis, chronic liver disease, anoxic hepatitis, drug hepatitis and systemic diseases such as malaria, typhoid and brucellosis by conventional clinical and laboratory studies.

For each suspected case of sporadic AVH presenting to the hepatitis clinic and the hospitals an initial blood sample was drawn and tested for serum bilirubin and serum liver enzyme levels. On the basis of clinical and biochemical findings, the infectious diseases specialist made the clinical diagnosis of AVH as described above.

All 263 patients with AVH following physical examination completed a detailed questionnaire in a 10 to 15 min interview and provide a blood sample, which was sent to the Zahedan Blood Transfusion Organization laboratory. The questionnaire included demographic information, data on risk factors for hepatitis during the previous 6 months and symptoms and signs.

Each serological test was performed without knowledge of the results of other serological tests. The sera were tested by EIA for IgM antibody to HAV, for hepatitis B surface antigen (HbsAg), for antibody to HbsAg (anti-HBs) and for IgM antibody to hepatitis B core antigen (anti-HBc). All HBs-Ag-positive sera, with or without IgM anti-HBc, were tested by EIA for antibody to HDV (anti-HDV).

Acute hepatitis A was diagnosed if the serum sample was positive for IgM anti-HAV. Acute hepatitis B was diagnosed if the serum sample was positive for IgM anti-HBc. Patients with HbsAg and anti-HDV who were lacking IgM anti-HBc were diagnosed as having hepatitis D superinfection. Hepatitis C was diagnosed if the serum was positive for anti-HCV or HCV RNA at initial visit or 3 month later. AVH type nonA-nonD was defined by the absence of serological markers of recent infection with HAV HBV HCV and HDV. Hepatitis E was not investigated because pertinent diagnostic kits were not available.

Frequency distributions were compared with the chi-square test. The t-student test was used for the comparison of mean values in two independent groups and one-way analysis of variance (ANOVA) for comparison of mean values of numerical variables across the different etiologic types of AVH. F test were used for the evaluation of significance. All values are expressed as mean±SD. A p-value of <0.5 was considered significant.

RESULTS

Of the 263 cases of AVH 93.5% were attributed to one the four investigated hepatitis viruses. HAV was the most frequent etiologic agent, accounting for 188 cases (71.5%, CI 95%= 65.9-77.1). Next were HBV, accounting for 47 cases (17.9%, CI 95%=13.2-22.6); HCV was the etiologic

Table 1: The characteristics of patients

	Hepatitis					
Variable	Hepatitis A (n=188)	Hepatitis B (n=47)	Hepatitis C (n=6)	Hepatitis D (n=5)	Hepatitis non A-D (n=17)	p-value
Male sex (%)	97(52)	30(64)	4(67)	3(60)	5(19)	0.15
Age						
Mean (CI 95%)	6.1	20.6	20.2	26.2	18.7	
	5.4-6.9	17.5-23.7	5.7-34.7	16.2-36.2	10.9-26.4	
0-4 years (%)	86(47)	2(5)	0(0)	0(0)	3(18)	0.000
5-14 years (%)	88(48)	15(32)	2(33)	0(0)	3(18)	
15-65 years (%)	11(6)	30(64)	4(67)	5(100)	11(65)	
Outpatient (%)	176(94)	33(77)	5(83)	3(60)	15(88)	0.2
Duration of illness						
before presentation	7.3 (6.2-7.8)	11.2 (9.5-12.8)	14 (7.6-19.5)	13.4 (8.5-18.3)	10.9 (8.7-8.9)	0.000
ALT	825	1049	926	1317	916	0.18
Mean (CI 95%)	(730-919)	814-1284	376-1475	424-2210	632-1201	
AST	808	1219	1128	1665	1267	0.001
Mean (CI 95%)	721-893	871-1567	487-1769	21-3308	696-1837	
Total bilirubin	6.1	10.7	8.5	25	13.9	0.000
Mean (CI 95%)	5.7-6.6	8.8-12.6	5.9-11	5.6-44.4	8.3-19.5	
ALP	663	332	493	288	389	0.000
Mean (CI 95%)	608-817	281-384	360-627	115-461	308-469	

Table 2: Sign and symptoms of patients

Sign and symptoms	Hepatitis A n (%)	Parentally transmitted hepatitis* n (%)	Odds ratio (CI 95%)
Hepatomegaly	17(9)	9(15)	0.5(0.2-1.4)
Splenomegaly	10(6)	5(8)	0.6(0.2-2.1)
Fever*	149(79)	34(61)	2.5(1.2-4.9)
Anorexia*	180(96)	41(71)	9.3(3.5-25.5)
Nausea	124(66)	39(70)	0.8(0.4-1.7)
Vomiting*	95(51)	17(30)	2.3(1.2-4.7)
Dark urine	182(98)	55(98)	0.8(0.6-1.5)
Chill*	34(18.1)	3(5.2)	4.0(1.1-17.2)
RUQ pain	47(27)	16(28)	0.9(0.5-1.9)
Coryza*	40(24)	3(6)	5.4(1.5-23)
Cough*	35(21)	3(6)	4.6(1.3-19.5)
Throat pain	12(7)	1(2)	4.1(0.5-87.1)
Diarrhea	33(20)	7(13)	1.6(0.6-4.3)
Constipation	30(18)	16(29)	0.6(0.3-1.2)
Excoriation*	28(17)	19(35)	0.4(0.2-0.8)
Abdominal pain*	131(79)	33(60)	2.6(1.3-5.2)

*: Hepatitis B, C and D; **: significant difference

agent in only 6 cases (2.3%, CI 95%=0.5-4.1) and HDV in only 5 cases (1.9%, CI 95%=0.2-3.6) All of the HDV cases were diagnosed as superinfection of HBV carriers. The exact cause of acute hepatitis was not diagnosed in 17 patients (6.5%); they might be due to hepatitis E, or other viral hepatitis, autoimmune hepatitis or other causes.

One hundred and thirty nine (52.9%) of all patients were male. The relative frequency of Hepatitis A in both gender had no difference, however, the relative frequency of Hepatitis B, C and D in male was more than female (Table 1). They were aged in a range of 1 to 65 years with a mean of 10.1 years old. Hepatitis A occurred most frequently in young children and patients with hepatitis B, C and D occurred generally in young adults. Mean age of patients affected by hepatitis A, were 6.1, (CI 95%; 5.4-6.9) B, 20.6 (CI 95%:17.5-23.7) C, 20.2(CI 95%:5.7-34.7) D, 26.2 (CI 95%:16.2-36.2) and Non A-D 18.7 (CI 95%: 10.9-26.4). Hepatitis A patients presented to hospital or clinic earlier (p=0.01) and had lower initial serum bilirubin, ALT and AST, but had higher Alkaline Phosphatase (ALP). The outpatient cases comprise 94.1% of hepatitis A and 66.7% of hepatitis B patients. All but one hepatitis C cases were among the outpatients. Patients with hepatitis D consisted of 3 outpatient and 2 inpatients.

Who had parenterally transmitted hepatitis were more likely to have excoriation, however patients with hepatitis A were more likely to have anorexia, vomiting, fever, chill, abdominal pain and prodromal symptoms (coryza, cough, throat pain). Since jaundice and dark urine were components of the case definition, almost all patients with AVH had these signs (Table 2).

DISCUSSION

It was found that the most common cause for acute viral hepatitis in Zahedan is hepatitis A (75.5%). It was followed by hepatitis B (14.7%). Hepatitis A was the most common cause of AVH in children, but hepatitis B was the most common in adults. This study is one the first to provide an analysis of the etiology of AVH in the Iran where all type of AVH is medically important.

In developing countries the infection with hepatitis A takes place in the first years of life and 90% of children have acquired the infection of hepatitis A before 10[6]. A Study in Sistan and Baluchestan province showed 89% of fewer than 5 year old children were affected by hepatitis A infection[7]. On the other hand it is known that the infection of hepatitis A in young children is often asymptomatic. In spite of the asymptomatic clinical

feature of hepatitis A in children, we have found that it was the main cause of clinical AVH in children in the city of Zahedan and in adults, hepatitis A was a rare cause of acute hepatitis. This seems to be due to the high incidence of hepatitis A infection in childhood and this early acquisition of infection prevents further infection later in life. It is similar to the results of studies conducted in the Middle East and developing countries[4,9-13].

Although the infection of hepatitis B is prevalent in most developing countries, its prevalence differs in some countries. In Iran about 20% of populations have been infected with hepatitis B[14]. A study in Zahedan showed a ratio of hepatitis B infection 34%[15]. Therefore, the infection of Hepatitis B and, as a result of it, acute hepatitis B is prevalent in the city of Zahedan; however it is the cause for only 14.3% of acute viral hepatitis. This low ratio can be due to a high share of acute hepatitis A in one hand and universal vaccination of neonate against hepatitis B since 1993, in the other hand. In united state of America incidence of HBV infection decreased in recent two decade following HBV vaccination[1,16]. In the same way it is predicted that HBV infection continuously decreased in Iran.

Acute hepatitis D superinfection was diagnosed n 9 cases. HDV is endemic in the Mediterranean area and the Middle East and has been reported to cause acute and chronic liver disease in those regions[9]. In Iran 3-14% of chronic hepatitis B carriers, are also carriers for chronic hepatitis D[14]. In the present study, 1.8% of acute viral hepatitis was due to hepatitis D and in fact 11% of acute hepatitis B was along with hepatitis D. Similarly in Saudi Arabia 10% of acute hepatitis B cases had hepatitis D infection[17].

HCV appears a rare but important cause of AVH in the region, although, the differentiation of acute from chronic infection is problematic. We know that at present HCV infection in general population of Iran is very low. Studies conducted in Fars Sistan and Balochistan provinces showed only 0.1-0.2% of population infected by HCV viruses[18,19].

Seventeen cases (6.7%) of AVH could not diagnose as having been caused by the hepatitis A, B, C and D viruses, probably some of them were due to hepatitis E, nevertheless we can conclude that hepatitis E is not prevalent as hepatitis A and B in this region. There is no any report about sero-epidemiology of hepatitis E from Iran.

Contrary to some previous reports[5,9], in this study clinical and laboratory factors were useful in predicting the diagnosis of AVH in individual cases, those with hepatitis A had lower serum lever of bilirubin ALT and AST. A Spanish study[20] showed that fatigue, anorexia, fever, chills and lymphadenopathy where more common in hepatitis A. Bilirubin levels where higher in patients with hepatitis B (10.3) and C (9.7) compared with hepatitis A (6.7). Alamine-Aminotransferase (ALT) levels where higher in patients with hepatitis B. However it may be an age related issue, in the present study patients with hepatitis A were significantly younger than patients with other types of hepatitis and it is known that severity of AVH has a converse relationship with age[21]. Cholestatic hepatitis is a clinical presentation of acute hepatitis A especially in children and this can explain the higher serum level of ALP in hepatitis A patients[22].

There are limited records about etiology of AVH in Iran, by conducting the similar studies around the country we will have evidently data about this issue; particularly we must try to achieve the importance of hepatitis E virus in AVH etiology.

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