

PREVALENCE OF HEPATITIS A VIRUS, HEPATITIS B VIRUS, AND HEPATITIS C VIRUS, AMONG PATIENTS WITH HEPATIC JAUNDICE IN SANA'A CITY, YEMEN: A HOSPITAL BASED STUDY

ABSTRACT

Background: Hepatic jaundice results from abnormal metabolism of bilirubin in the liver. The main causes of hepatic jaundice are severe damage to hepatocytes due to infectious diseases, drugs/medication induced, autoimmune diseases or, less commonly, hereditary genetic diseases. **Aim:** The aim of this study is to determine the prevalence of hepatitis A virus (HAV) and hepatitis B Virus (HBV), and hepatitis C virus (HCV), in patients with hepatic jaundice as causes of acute viral hepatitis (AVH) in Sana'a city, Yemen. **Materials and Methods:** Data of patients with hepatic jaundice tested for hepatitis B surface antigen, total anti-HCV antibody, and anti-HAV immunoglobulin M (IgM) by enzyme-linked immunosorbent assay were collected from Class I Viral Diagnostic Laboratories in Sana'a (Department of Laboratories, University of Science and Technology Hospital, Al-Olagi Private Laboratory, and the National Center for Public Health Laboratories in Sana'a, Ministry of Health and Population) for 3 years. Then the statistical analysis of the data was used where the descriptive analysis was calculated: frequency and percentage, as well as the association of infection with sex and age group by means of detection odds ratio, 95% CI and X^2 more than 3.9 and $P < 0.05$ were considered statistically significant. **Results:** The study included 644 males (43.8%) and 826 females (56.2%), while most patients were less than 21 years old. The rate of Hepatitis viruses positive was 27.6% positive. Hepatitis A virus infection was the most common virus diagnosed among patients with jaundice accounting for 259 cases (17.6% of the total), while HBV was less common with 104 (7.1%) and HCV only 42 cases (2.9%). The highest incidence of hepatitis A was in 2-10 years patients (44.4%), with an associated OR 19.3 ($p < 0.0001$). While the rates of hepatitis A virus infection in the older age groups were very low and ranged between 0 and 6.8%. The highest incidence of hepatitis B was in 11-20 years patients (18.2%), with an associated OR 9.3 ($p < 0.0001$). The highest incidence of hepatitis C was in 31-40 years patients (7.3%), with an associated OR 3.3 ($p < 0.0001$). While the rates of hepatitis C virus infection in younger age group (2-10 years) was 0%. **Conclusions:** Alarmingly changing the epidemiology and dynamics of hepatitis A-C viruses in Yemen, a detailed study is required to understand the definite disease problem caused by these viruses. It is noticeable in this study the high prevalence of hepatitis A virus and hepatitis B virus in the Yemeni population with hepatic jaundice. Also, to our knowledge, this study is the first to report epidemiological transformation of hepatitis A virus in Sana'a, Yemen.

Key words: Hepatic jaundice, Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, prevalence, Sana'a, viral hepatitis, Yemen

INTRODUCTION

Hepatic jaundice results from abnormal metabolism of bilirubin in the liver. The main causes of hepatic jaundice are severe damage to the liver cells due to infectious agents such as viral hepatitis and leptospirosis, drug/drug-induced hepatitis, autoimmune etiologies or, less commonly, due to hereditary genetic diseases such as Gilbert's syndrome, Crigler-Najjar syndrome, type I and Crigler-Najjar syndrome type II^{1,2}. Liver disease caused by hepatitis virus is a major global public health problem influence millions of people worldwide^{3,4}. A distinctive group of hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis E (HEV), hepatitis D virus (HDV), and newly classified hepatitis viruses such as hepatitis G (HGV) are responsible for liver disease. The whole of these viruses are connected with considerable mortality and morbidity in developed and developing countries^{5,6}. In 2015, the World Health Organization expected 1.34 million deaths from viral hepatitis with hepatitis B, and HCV being a leading cause of death⁷. Clinical findings of viral hepatitis can range from subclinical to life-threatening infection^{6,8,9}. HAV and HEV are transmitted by ingestion of contaminated food or water by human feces¹⁰; While hepatitis B virus and HCV are transmitted mainly by perinatal route, including saliva exchange; by sexual contact, from mother to offspring by vertical transmission, and exposure to infected blood products¹¹. HAV and HEV typically have an effect on children and young adults correspondingly, and are endemic in numerous developing countries in Africa and Asia¹²; While

HBV and HCV are mostly reported from adults and are found intermittently in North America, Western Europe, and other developed countries¹³ HAV and HEV most cases are undetectable clinically or self-healing; while 70-80% of acutely infected with hepatitis B and HCV develop chronic hepatitis^{14, 15}. Only recently, there were few reliable commercial assays (sensitive and specific) for the detection of hepatitis viruses (HAV, HEV, HCV, and HBV) antigens and antibodies that could be used for routine diagnosis. Even though newly new assays have been developed that demonstrate high sensitivity and specificity, make available for more perfect detection/diagnosis of hospital cases. On the other hand, the high cost of these assays has limited evaluation in developing countries such as Yemen.

The prevalence of hepatitis viruses in Yemen has been estimated to be high, but detailed information regarding the current status of infection due to hepatitis viruses in Yemen is still insufficient to understand the burden of hepatitis disease due to the limitation of these studies in which only HBV, HCV and HGV were studied while there are no studies discuss the endemicity of HAV and HEV in Yemen¹⁶⁻²⁶. The aim of this study is to determine the prevalence of hepatitis A virus (HAV) and hepatitis B Virus (HBV), and hepatitis C virus (HCV), in patients with hepatic jaundice as causes of acute viral hepatitis (AVH) in Sana'a city, Yemen.

MATERIALS AND METHODS

Data collection:

Data of patients with hepatic jaundice tested for hepatitis B surface antigen, total anti-HCV antibody, and anti-HAV immunoglobulin M (IgM) by enzyme-linked immunosorbent assay were collected from Class I Viral Diagnostic Laboratories in Sana'a (Department of Laboratories, University of Science and Technology Hospital, Al-Olagi Private Laboratory, and the viral department in the National Center for Public Health Laboratories in Sana'a, Ministry of Health and Population) for 3 years. Then the statistical analysis of the data was used where the descriptive analysis was calculated: frequency and percentage, as well as the association of infection with sex and age group by means of detection odds ratio, 95% CI and X^2 more than 3.9 and $P < 0.05$ were considered statistically significant.

Ethical approval

Approval was obtained from the participants prior to including in the study. Ethical approval was obtained from the Medical Research and Ethics Committee of the Faculty of Medicine and Health Sciences, Sana'a University with reference number (223) on 10/01/2021.

RESULTS

Table 1 presents the demographic data of jaundice patients screened for hepatitis A, B and C viruses in the main laboratories in Sana'a city for a period of 3 years. It included 644 males (43.8%) and 826 females (56.2%), while most patients were less than 21 years old (2-10 years old 33.7% and 11-20 years old 29.9%), while patients over 40 years old only 5.4% of total patients. Hepatitis viruses (HAV + HBV + HCV) were 405 (27.6%) positive, while 1065 (72.4%) patients with jaundice were negative for HAV, HBV and HCV. When considering sex, the positive rates of the three viruses were approximately equal in males (27.8%) and females (27.4%). Table 2 shows the distribution of different hepatitis viruses among male and female jaundice patients. Hepatitis A virus infection was the most common virus diagnosed among patients with jaundice accounting for 259 cases (17.6% of the total), while HBV was less common with 104 (7.1%) and HCV only 42 cases (2.9%). Table 3 shows the distribution of the age groups of patients infected with hepatitis A virus. The highest incidence of hepatitis A at 2-10 years jaundice patients was 220 cases (44.4%), with an associated OR 19.3, with a 95% CI equal to 13.3-77.6 and this correlation was highly significant with X^2 being 364, $p < 0.0001$. While the rates of hepatitis A virus infection in the older age groups were very low and ranged between 0 and 6.8%. Table 4 shows the distribution of the age groups of patients infected with hepatitis B virus. The highest incidence of hepatitis B at 11-20 years jaundice patients was 89 cases (18.2%), with an associated OR 9.3, with a 95% CI equal to 5.8-14.9 and this correlation was highly significant with X^2 being 118, $p < 0.0001$. While the rates of hepatitis B virus infection in younger age group (2-10 years) was 0.2%, and in other older age groups were ranged from 2.5% to 6.7%. Table 5 shows the distribution of the age groups of patients infected with hepatitis C virus. The highest incidence of hepatitis C at 31-40 years jaundice patients was 7.3%, with an associated OR 3.3, with a 95% CI equal to 1.6- 6.6 and this correlation was highly significant with X^2 being 13, $p < 0.0001$. While the rates of hepatitis c virus infection in younger age group (2-10 years) was 0%, and in other age groups were ranged from 3.8% to 6.3%.

DISCUSSION

The causes of hepatitis can be divided into the following main categories: metabolic, ischemic, infectious, genetic, autoimmune, and others more. Metabolic causes include prescription drugs, toxins (especially alcohol), and nonalcoholic fatty liver disease. Autoimmune and genetic causes of hepatitis include a genetic predisposition and tend to affect distinct populations. In the current study, hepatitis viruses (HAV + HBV + HCV) were positive in 405 (27.6%) patients with hepatitis (hepatic jaundice) while the remaining 1065 (72.4%) jaundiced patients were negative for HAV and HBV and HCV (Table 1). This result indicated that the majority of cases in the current study may be infected with other infectious agents including viruses, bacteria, and parasites or suffer from other previously mentioned causes of hepatitis^{27, 28}. Viral hepatitis is the most common type of hepatitis worldwide²⁹, and this fact differs from the current study in that 72.4% of patients with hepatitis may have other causes. These results can be explained by the fact that other viral hepatitis was not investigated in the current study and only 3 viruses were examined. Viral hepatitis is caused by five different viruses (hepatitis A, B, C, D, and E)³⁰.

Hepatitis A virus infection was the most common virus diagnosed among patients with jaundice accounting for 259 cases (17.6% of the total) (Table 2). Therefore, hepatitis A, which is transmitted through fecal-oral, is more common in developing countries, and with its high prevalence, it is a self-limiting disease that does not lead to chronic hepatitis and its complications as liver cancer³⁰. There are a number of hospital-based reports, sporadic cases and outbreaks of HAV in Yemen; but limited scholarly publication is available on the Internet³¹. Only one published report detected hepatitis A virus antibodies indicating that 86% of the tested population had total IgG antibodies indicating previous exposure and immunity³¹. While the results of the current study showed 17.6% of the tested patients had active infection (IgM positive) among children and adults. In the current study the highest incidence of hepatitis A was in children (2-10 years) (44.4%), with an associated OR 19.3, with a 95% CI equal to 13.3-77.6 ($p < 0.0001$) (Table 3). The current finding is similar to that in developing countries where they have higher circulating levels of HAV and most cases are reported in children while most adolescents and adults in developing countries have already contracted the disease and are thus immune³². On the other hand, we found that active infection with hepatitis A virus is present in adults in the current study, therefore, it is necessary to examine the immune status of adults and children in Yemen and to vaccinate non-immune children and people at risk of infection with the virus, as well as people suffering from other liver diseases in which active Hepatitis A infection might lead to liver failure^{33,34}. Hepatitis A virus (HAV) infection is mostly associated with poor hygiene and spreads through the oral and fecal route. Although the HAV vaccine is available in the immunization programs of many countries of the world; However, this vaccine is not available at all in Yemen.

In the current study, the rate of HBV among patients with hepatic jaundice was 7.1%, and the highest rate was in 11-20 years of patients (18.2%). The prevalence of hepatitis B virus in previous studies in Yemen ranged from 1% among the general population to 20% among high-risk groups such as health care workers, dialysis patients etc¹⁶⁻²³. Hepatitis B cases are still reported from different hospitals in Yemen, although the hepatitis B vaccine has been available for about 22 years in the country, there are still many people in Yemen who do not benefit from the protection available for this successful vaccine. This is due to its high cost and its low priority for the decision-maker at the governmental level, in addition to the ongoing war in Yemen over the past seven years.

In the current study, the rate of HCV among patients with hepatic jaundice was 2.9%, and the highest incidence of hepatitis C was in the 31-40 year old patients with jaundice (7.3%), with an associated odds ratio of 3.3 ($p < 0.0001$). While the infection rates of hepatitis C virus in the younger age group (2-10 years) were 0% (Table 5). The prevalence of hepatitis C virus in previous studies in Yemen ranged from 0.1% among the general population and blood donors to 19% among high-risk groups such as public health center cleaners, health care workers and dialysis patients^{16,17,23, 24}. Although the exact reasons for the spread of HCV in this population remain unclear; Blood transfusion without proper screening, and the use of non-sterile syringes may be one of the factors for the spread of hepatitis C virus in Yemen. A detailed study should be done in the future because hepatitis C is one of the main causes of cirrhosis and hepatocellular carcinoma in chronic patients^{16,17}.

Even though the hospital-based data obtainable in this study will not characterize the entire country, the burden of disease from this viral infection appears to be alarming these days and relevant authorities should prioritize overcoming viral hepatitis in the country.

CONCLUSION AND RECOMMENDATION

Changing epidemiology and dynamics of hepatitis A-C viruses in Yemen is alarming and detailed study must be conducted to understand the actual disease burden caused by these viruses. This study, which was conducted on hospitals, noted the high prevalence of hepatitis A virus and hepatitis B virus in the Yemeni population with hepatic jaundice and elevated liver enzymes. The study found HAV is a major causative agent for hepatic Jaundice followed by HBV and HCV, indicating that group of hepatitis virus to cause a serious health problem in Yemen with a large population (about 30 millions). More accurate information on the overall prevalence of these viral infections may done by detailed studies, including well-designed systematic surveillance with random selection of people. We believe that an urgent standard public health approach should be followed in implementation such as provision of clean water, appropriate disposal of wastewater and improved hygiene of persons through health education and application of the HAV vaccine that may help control HAV infection in the future. Also, mass vaccination of hepatitis B virus should be started which should reach all rural and urban areas in Yemen to prevent future infection with hepatitis B virus because vaccination against hepatitis B virus has not been achieved by the Yemeni government as expected. This may be unaware of this vaccine or the financial district due to the high cost of the vaccine. In addition, regular quality control of the kit used in the blood bank will help prevent transfusion of hepatitis B and HCV-infected blood to the recipient. Since the hepatitis C vaccine is not available, raising awareness of the handling of blood and its derivatives may help reduce the spread of hepatitis C infection in Yemen

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CONFLICT OF INTEREST

No conflict of interest associated with this work.

AUTHOR'S CONTRIBUTIONS

All authors co-wrote the articles and reviewed the results.

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Review

Table 1: Demographic Data of Jaundice Patients Screened for Hepatitis A, B, and C Viruses in major Laboratories in Sana'a city for a Period of 3 Years

Characteristics	Hepatitis viruses positive HAV+HBV+HCV		Hepatitis viruses negative HAV+HBV+HCV		Total tested	
	No	%	No	%	No	%
Age groups						
2-10 years	221	44.6	274	55.4	495	33.7
11-20 years	124	28.2	315	71.8	439	29.9
21-30 years	27	9.3	264	90.7	291	19.8
31-40 years	25	15.2	140	84.8	165	11.2
>40 years	8	10	72	90	80	5.4
Gender						
Male	179	27.8	465	72.2	644	43.8
Female	226	27.4	600	72.6	826	56.2
Total	405	27.6	1065	72.4	1470	100

Table 2: Distribution of different hepatitis viruses among male and female jaundice patients

Characteristics	HAV positive		HBV positive		HCV positive		Total positive	
	No	%	No	%	No	%	No	%
Male	111	42.9	43	41.3	25	59.5	179	12.2
Female	148	57.1	61	58.7	17	40.5	226	15.3
Total	259	17.6	104	7.1	42	2.9	405	27.6

Table 3: Age groups distribution of patients infected with hepatitis A virus

Characteristics	HAV positive		OR	CI 95%	X ²	P
	No	%				
2-10 years n=495	220	44.4	19.3	13.3-77.6	364	<0.0001
11-20 years n=439	30	6.8	0.25	0.17-0.3	50	<0.0001
21-30 years n=291	6	2.1	0.07	0.03-0.17	60.4	<0.0001
31-40 years n=165	3	1.8	0.07	0.02-0.2	31.9	<0.0001
>40 years n=80	0	0	0	0-0.16	18	<0.0001
Total n=1470	259	17.6				

Table 4: The distribution of the age groups of patients infected with hepatitis B virus.

Characteristics	HBV positive		OR	CI 95%	X ²	P
	No	%				
2-10 years n=495	1	0.2	0.01	0.002-0.1	53	<0.0001
11-20 years n=439	80	18.2	9.3	5.8-14.9	118	<0.0001
21-30 years n=291	10	3.4	0.4	0.2-0.7	7.3	0.006
31-40 years n=165	11	6.7	0.9	0.4-1.7	0.04	0.82
>40 years n=80	2	2.5	0.32	0.07-1.3	2.6	0.10
Total n=1470	104	7.1				

Table 5: The distribution of the age groups of patients infected with hepatitis C virus

Characteristics	HBC positive		OR	CI 95%	X ²	P
	No	%				
2-10 years n=495	0	0	0	0-0.1	21.9	<0.0001
11-20 years n=439	14	3.2	1.1	0.6-2.2	0.24	0.61
21-30 years n=291	11	3.8	1.45	0.7-2.9	1.1	0.29
31-40 years n=165	12	7.3	3.3	1.6-6.6	13	<0.0001
>40 years n=80	5	6.3	2.4	0.9-6.2	3.5	0.06
Total n=1470	42	2.9				

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