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RESEARCH ARTICLE

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

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ABSTRACT

Background: Hepatic jaundice results from abnormal metabolism of bilirubin in the liver. The main hepatic jaundice causes are severe damage to hepatocytes due to autoimmune diseases, infectious diseases, drugs/ medication induced, or, less commonly, hereditary genetic diseases.

Aim: The aim of this study is to determine the prevalence of hepatitis B Virus (HBV), hepatitis A virus (HAV), and hepatitis C virus (HCV), in patients with hepatic jaundice as causes of acute viral hepatitis (AVH) in Sana'a city, Yemen.

Subjects 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 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 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 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 ($p<0.0001$).

Conclusion: 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.

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

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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 B (HBV), hepatitis C (HCV), hepatitis A (HAV), 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 death[7]. Clinical findings of viral hepatitis can range from subclinical to life-threatening infection[6,8,9]. HAV and HEV are spread by intake of contaminated food or water by human feces[10]; 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 products[11]. HAV and HEV typically have an effect on children and young adults correspondingly, and are endemic in numerous developing countries in Africa and Asia[12]; While HBV and HCV are mostly reported from adults and are found intermittently in North America, Western Europe, and other developed countries[13] 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 charge of these assays has limited evaluation in third world developing countries such as Yemen. The prevalence of hepatitis viruses in Yemen has been estimated to be high, but detailed information concerning 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 studies while there are no studies discusses the endemicity of HAV and HEV in Yemen[16-26]. The aim of this study is to clarify the prevalence of hepatitis B Virus (HBV), hepatitis A virus (HAV) and hepatitis C virus (HCV), in patients with hepatic jaundice as causes of acute viral hepatitis (AVH) in Sana'a city, Yemen.

SUBJECTS 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 the last 3 years in which the information provided was complete and clear. 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

Before inclusion in the study, approval was obtained on the condition that the names of the participants be confidential. From the Medical Research and Ethics Committee of the College of Medicine and Health Sciences, Sana'a University by document with reference number (223) dated 10 January 2021 the ethical approval was obtained to conduct the research.

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)

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 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 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 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 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 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 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 worldwide[29], 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].

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

Characteristics	HBC positive No (%)	*OR*	*CI 95%*	X^2	*p*
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)				

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 widespread in third world 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 cancer[30]. There are a number of hospital-based reports, sporadic cases and outbreaks of HAV in Yemen; but limited scholarly publication is presented on the Internet[31]. Only one published report detected hepatitis A virus antibodies indicating that 86% of the tested population had total IgG antibodies indicating previous exposure and immunity[31]. 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 immune[32]. 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.

The rate of HBV among patients with hepatic jaundice in the current study 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 etc[16-23]. Hepatitis B cases are still reported from different hospitals in Yemen, though the hepatitis B vaccine has been obtainable 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. The rate of HCV among patients with hepatic jaundice in the current study 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

Alteration the epidemiology and dynamics of hepatitis A-C viruses in Yemen is alarming and comprehensive study must be conducted to understand the real disease problem produced 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 produce a critical health problem in Yemen with a large population (about 30 millions). More accurate data on the on the whole prevalence of these viral infections may done by comprehensive studies, comprising 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. As well, standard quality control of the kit utilized in the blood bank will improve 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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