Sana'a University Journal of Medical and Health Sciences

Prevalence and Risk Factors of Blood-Borne Viral Infections among Multi-transfused Patients in Sana'a City, Yemen

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Abstract

Background: Blood-borne viruses (BBVs), like hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) among multi-transfused patients (MTPs), remain a major public health problem in Yemen. This study aimed to determine the seroprevalence of BBVs and associated risk factors among MTPs.
Methods: A cross-sectional study was conducted on MTPs at the Yemeni Society for Thalassemia, National Oncology Center, and Al Kuwait University Hospital in Sana'a City. Data were collected through face-to-face interviews using a predesigned questionnaire. Blood samples were drawn and tested for HBsAg, anti-HCV, and HIV-1,2 by using an electrochemiluminescence immunoassay technique.
Results: Among 361 MTPs, the overall seroprevalence of BBVs was 6.8%; seropositivity of HBsAg, anti-HCV, and anti-HIV-1,2 was 3.9%, 2.9%, and 0.0%, respectively. An increase in family size and low income were significantly associated factors with HBV infection. In addition, increases in age and blood transfusion units were found to be significant predictors for HCV ($p<0.05$).
Conclusion: Although the seroprevalence of BBVs is low, it remains a major problem among MTPs. The most frequent infection was HBV, followed by HCV, with a significantly higher rate among leukemia patients. Regular mentoring for viral markers and mandatory implementation of HCV antigen-antibodies testing as well as advanced technology in blood screening are highly recommended.

Article Info

Keywords:
Blood-borne viral infections, Multi-transfused patients, Yemen

Article History:
Received:24-September-2024 ,
Revised:4-October-2024 ,
Accepted:21-October-2024 ,
Available online:4-November-2024

1. INTRODUCTION

Blood-borne viruses (BBVs), like hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV), are most common during blood transfusion [1]. Mortality and morbidity resulting from the infected blood transfusion have far-reaching consequences not only for the recipients themselves but also for their families, communities, and the wider society [2]. Multi-transfused patients (MTPs) with conditions such as thalassemia, sickle cell anemia and leukemia are at higher risk of blood viral infections due to their frequent need for blood transfusion [3, 4]. Blood transfusion keeps lives and improves health, but many patients needing transfusion do not have timely access to safe blood. Adequate and safe blood providing should be integral to every country's national health care policy and infrastructure. All blood donations should be screened for infections prior to use according to WHO recommendations. HIV, HBV, HCV, and syphilis should be screening mandatory, and screening of blood should be performed according to quality system requirements [5]. Globally, WHO estimates that 254 and 50 million people were living with chronic HBV and HCV infection in 2022, with 1.2 and 1.0 million new infections each year, respectively. In addition, HBV resulted in an estimated 1.1 million deaths, and approximately 242,000 people died from HCV [6, 7]. By the end of 2023, 39.9 million people living with HIV,

65% of whom are in the African Region as well as an estimated 630, 000 people died from HIV-related causes [8]. The seroprevalence in Asia of HBV, HCV, and HIV or either one or two of these infections in thalassemic patients was range (2-55.73%), (0-6%) and (0-3.63%), respectively [9]. Previous studies conducted on Omani multiply transfused sickle cell disease (SCD) revealed the prevalence of HBV was 1.6%, 12.6% had anti-HCV, of whom 5.2% were HCV RNA positive, and none of the patients had positive serology for HIV [10]. In Yemen, hemoglobinopathies, including thalassemia and SCD are known to be prevalent inherited disorders in most Arab countries. A serious problem, affecting children in Yemen from an early age, therefore, there is a crucial need for an update on the prevalence rates of these common viral infections among MTPs. Although a reduction in the hepatitis prevalence is expected due to the updated infection control measures implemented in Yemen, it is believed that this prevalence is still high compared with developed countries. The prevalence of$\alpha-$ and $\beta-thalassemia$, sickle-cell trait and leukemia was 8.6%, 4.4%, 2.2% and 5.7% [11, 12]. There is no updated data on BBVs prevalence published from Yemen, especially in the last years and the previous studies have a limitation to identify associated risk factors. Therefore. This study was aimed to determine the seroprevalence of BBV infections and associated risk factors among MTPs which will help to understand the magnitude of the problem and guide evidence-based decision-making to improve screening practices against blood-borne infections.

2. MATERIALS AND METHODS

2.1. Study design

An analytical cross-sectional study was conducted on multi-transfused patients in Sana'a city from September 2023 to June 2024.

2.2. Study area and population

This study was conducted among attendants of the Yemeni Society for Thalassemia and Genetic Blood Disorders (YSTGBD), the National Oncology Center (NOC), and the Childhood of Leukemia unit at Al Kuwait University Hospital in Sana'a city. Known cases of sickle cell anemia, thalassemia, and leukemia, attending the medical centers who have received at least three units of blood or blood products and agreed to give their written consent were included in this study. In addition, patients who have been transfused less than three units of blood or received chemotherapy and who do not agree to give their written consent were excluded.

2.3. Sample size and sampling procedure

The sample size was calculated using Epi-info, assuming the population size of 6000 patients according to the last register, a margin of type I error of 5%, a confidence level of 95%, a sample proportion equal to 50%, and design effect 1. The sample size was calculated to be 361 participants. According to the data analysis results of NOC and the YSTGBD, the sample will be selected using the Population Propionate Sampling (PPS) technique with 53 thalassemia patients, 275 sickle cell anemia patients, and 33 leukemia patients chosen from the study population. Patients who were available during the data collection period were selected sequentially.

2.4. Data Collection and measurements

Data was collected through face-to-face interviews with patients aged above 18 years and from mothers or caregivers for patients below 18 years using a predesigned questionnaire. The questionnaire, which includes both closed and open-ended questions, covered demographic, socioeconomic characteristics and associated risk factors of blood-borne infections.

2.5. Sample collection and laboratory investigations

Three to five ml of whole blood samples were collected from each patient in a labeled plain tube with the unique identifier number. The samples were transported to the infectious disease department in the National Blood Transfusion and Research Center. The serum was separated and screened for HBV, HCV, and HIV markers by using a commercially available electrochemiluminescence immunoassay (ECLIA) (Roche technique).

2.6. Statistical analysis

Data was entered and analyzed by using Statistical Package for the Social Sciences (SPSS, version 26). Data was presented as frequencies and percentages. Cross-tabulation was used to identify associated factors with viral infections using the Chi-squared test for categorical. Estimation of the odds ratio (OR) was done at 95% confidence interval (CI), and P <0.05 is considered statistically significant.

2.7. Ethics consideration

The study was approved by the Research Medical Committee at the Faculty of Medicine and Health Sciences at Sana'a University. Permission of the centers and hospital was secured, and written consent was taken from patients and children's parents. Feedback regarding the

Table 1. Sociodemographic information with seropositivity HBsAg and anti-HCV of study MTPs, Sana'a City, Yemen,2024.

Characteristics	Total		HBsAg Positive		P-value	Anti-HCV Positive		P-value
	No	\%	No	\%		No	\%	
Gender								
Male	187	52	7	4	0.890	5	2.7	1.00
Female	174	48	7	3.7		5	2.9	
Age group Median = 14 (1-75)								
<20 years	266	74	11	4	0.872	5	1.9	0.03
20 - < 30 years	61	17	3	5		2	3.2	
>= 30 years	34	9	0	0.0		3	15	
Education Level								
Illiterate	15	4	0	0.0	1.00	0	0.0	1.00
Literate	346	96	14	4.1		10	2.90	
Marital Status								
Married	28	8	0	0.0	0.612	2	7.1	0.18
Single	333	92	14	4.2		8	2.8	
Occupation								
Student	252	82	14	5.6	0.847	7	2.8	0.68
Unemployed	10	3	0	0.0		0	0.0	
Housewife	28	9	0	0.0		2	7.1	
Labor/daily 'worker	11	4	0	0.0		0	0.0	
Employed	8	2	0	0.0		0	0.0	
Governorates Birthplace								
Taiz	97	26	5	5.1	0.664	5	5.2	0.29
Hajjah	64	17.7	1	1.6		0	0.0	
Dhamar	44	12.2	2	4.6		1	2.3	
Al Mahwit	27	7.5	2	7.4		0	0.0	
Al-Hodaida	27	7.5	0	0.0		0	0.0	
Amran	1	5.8	2	4.6		1	4.8	
Sana'a City	16	4.4	1	6.2		2	12.5	
Ibb	15	4.2	1	6.7		1	6.7	
Others	50	13.8	0	0.0		0	0.0	
Monthly income								
Low	190	52	11	5.8	0.04	6	3.2	0.64
High	171	48	3	1.8		4	2.3	

results of the study was given to the participants at the end of the study.

3. RESULTS

A total of 361 MTPs were included in this study. Amongst them, 52% were males, 48% were females, and the median age was 14 years (range: 1-75). The prevalence of HBsAg was found among male, age group between 20 and 30 years, literate, and low-income patients. Female, literate, housewives and who come from Taiz had the highest prevalence of anti-HCV. There was a significant difference in HBsAg seropositivity between low-income and high ($P < 0.05$). However, HCV seropositivity was highest among patients aged 30–40 years ($P < 0.05$) (Table 1).

The percentage of hepatitis B and C markers was found to be high among leukemia patients (15.2%), with significantly different compared to other diagnoses ($P = 0.013$ and $P = 0.001$), respectively. More than half of patients with O Rh positive blood group 59.3% and A Rh positive 26.3 have a predominate hepatitis infection and there is no significant association between hepatitis B and C markers and blood grouping types ($p > 0.05$) (Table 2).

The overall seroprevalence of BBV infections was 6.8%, and the most prevalent markers were HBsAg (3.9%), followed by anti-HCV (2.9%). All patients were HIV-1,2 negative. Four cases had co-infection of HBsAg and HCV (Figure 1). In the bivariate analysis of

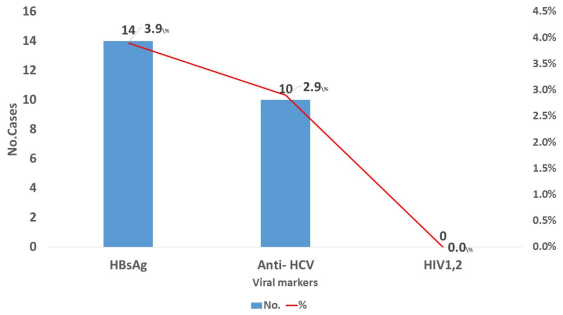

Figure 1. Seropostivity of blood-born viral markers among MTP, Sana'a city, 2024.

medical history factors associated with HBV and HCV, only patients who are receiving more than 30 blood units $(OR : 4.72; 95\% CI : 1.20 - 18.61; P = 0.035)$ were found

Table 2. Distribution of HBsAg and anti-HCV seropositivity by diseases and blood group types among MTPs, Sana'a city, 2024.

Category	Total		HBsAg – positive		*P*-Value	Anti-HCV-Positive		*P*-Value
	No.	\%	No.	\%		No.	\%	
Sickle cell anemia	275	76.2	8	2.9	0.013	5	1.8	0.001
Thalassemia	53	14.7	1	1.9		0	0.0	
Leukemia	33	9.1	5	15.2		5	15.2	
Blood group								
O RhD Positive	214	59.3	9	4.2	0.923	7	3.3	1.00
A RhD Positive	95	26.3	5	5.3		3	3.2	
B RhD Positive	22	6.1	0	0.0		0	0.0	
AB RhD Positive	7	1.9	0	0.0		0	0.0	
O RhD Negative	14	3.9	0	0.0		0	0.0	
A RhD Negative	7	1.9	0	0.0		0	0.0	
B RhD Negative	2	0.6	0	0.0		0	0.0	

to be significantly associated with HCV infection (Table (Table 3).

Regarding behavioral and other factors, only patients who live in crowded houses with family size more than seven persons $(OR : 4.81; 95\% CI : 1.32 - 17.567; P = 0.009)$ was found to be significantly associated with HBV infection (Table 4).

* Fisher-Exact

4. DISCUSSION

The risk of blood-borne viral infections in MTPs increases with time as the number of transfusions increases. The infections further complement the suffering of patients leading to increased morbidity. The use of advanced technology in blood screening, voluntary donations, donor selection, and asepsis during blood transfusion should be used to curtail the transmission [13]. Although improved techniques for viral infections in Yemen led a lowered prevalence rate of infections, the MTPs are not free of risk due to low viremia and mutant strains undetectable by different enzyme-linked immunosorbent assay (ELISA) techniques. Our study found that the overall prevalence of BBVs was 6.8% compared to 13.1% in a previous study conducted in Yemen [4], 24.5% in Syria [14] and 15.4% in India [15]. It was virtually similar to the study conducted in Nigeria, 7.7% [16] and lower than reported in Saudi Arabia, 4.6 [17]. The large differences in the seroprevalence of BBVs among MTPs in the different countries might be due to differences in prevalence in geographical locations, mean age of patients, sample size, and different screening techniques. In this study, we found that the prevalence of HBV and HCV among MTPs was 3.9% and 2.9%, respectively. Among thalassemia patients, the seroprevalence of HBsAg in in this study was 1.9 which is lower than the previous study conducted in (YSTGBD) 3.5% [18] and nearly similar to the study in Saudi Arabia 1.4% [17]. In addition, the seroprevalence of HBsAg among SCD was 2.9% which is lower than reported in Al-Hodeidah Governorate 35% [19]. This may be reflecting differences in the epidemiology HBV and differences in testing methodology, such as the rapid test that was used to detect HBsAg among blood donors in Hodeidah districts, which helps in the probability of viral transmission to MTPs. The seroprevalence of anti-HCV among thalassemia and sickle cell anemia patients was 0.0% and 1.8%, respectively. These findings are lower than studies reported in Sana'a city among thalassemia patients, 13.3% [20], and Saudi Arabia 2.9% and 3.7%, respectively [17]. Similar results of anti-HCV prevalence among SCD were reported in Nigeria: 1.6% and a higher HBsAg prevalence 6.1% [16]. The lower prevalence in our study is attributed to the most MTPs in Sana'a City can access the safe blood that was screened for HCV according to the criteria of the national blood transfusion guideline. Patients with leukemia have a greatly enhanced risk of contracting BBI due to immunosuppression secondary to chemotherapy and radiotherapy, frequent blood transfusions, bone and peripheral vein punctures, tissue damage and mucositis [21]. Our findings revealed the high and similar prevalence of HBsAg and anti-HCV leukemia cases 15.5% with a statistically significant association. Roughly similar to HBV prevalence of a previous study in Yemen, 14.3% [22]. However, lower than reported in India 39.4% [23] and in Iraq 32.3% [24]. In relation to HCV was 15.5%, which is slightly lower to 22% in Wasit Province-Iraq [25] but higher than reported from other studies in Yemen, 3.6% [16], Iraq 3.4% [24] and 4.7% in Sweden [26]. The high prevalence of hepatitis B and C infections among Leukemia patients compared to SCA and thalassemia, may be due to the fact that those patients are usually put on immunosuppressive drugs, repeated hospitalization, and frequent injections that may increase their susceptibility to these infections [24]. High seroprevalence of HBsAg and anti-HCV was found only in patients with O Rh positive and A Rh-positive blood grouping (4.2%, 5.3) and (3.3%, 3.2%), respectively. However, there is no significant association between ABO blood grouping and hepatitis viral infection. These findings agree with a study among blood donors in Yemen [27]. In contrast,

Table 3. Medical history factors associated with Hepatitis B and C markers among MTP, Sana'a, Yemen 2024.

Factors	HBsAg-positive N=14		OR (CI)	*P-Value*	Anti HCV-Positive N=10		OR (CI)	*P-Value*
	No.	\%			No.	\%		
Hospitalization due to other diseases								
Yes	10	3.5	0.656 (0.200-2.15)	0.485	6	2.1	0.388 (0.106-1.41)	0.137
No	4	5.9			4	5.2		
Surgical history								
Yes	3	3.2	0.767 (0.209-2.81)	0.688	2	2.1	0.703 (0.146-3.37)	1.00*
No	11	4.1			8	3		
Dental Visit								
Yes	4	3	0.66 (0.205-2.17)	0.499	5	3.7	1.72 (0.488-6.05)	0.509
No	10	4.4			5	2.2		
History of jaundice								
Yes	9	3.6	0.802 (0.262-2.45)	0.698	8	3.2	1.82 (0.384-8.73)	0.444
No	5	4.5			2	1.8		
Invasive diagnostic procedure								
Yes	1	2.5	0.990 (0.124-7.88)	0.993	2	7.7	3.40 (0.685-16.9)	0.157*
No	13	3.2			8	2.4		
Treatment by injection								
Yes	10	3.4	0.565 (0.171-1.86)	0.342	8	2.7	926 (0.192-4.46)	0.923
No	4	5.9			2	2.9		
Needle stick injuries								
Yes	4	2.8	0.605 (0.186-1.97)	0.400	6	4.2	2.37 (0.657-8.55)	0.200*
No	10	4.6			4	1.8		
Had acupuncture								
Yes	5	4.4	1.22 (0.402-3.75)	0.716	5	4.4	2.25 (0.638-7.93)	0.297*
No	9	3.6			5	2		
Number of blood unit transfusion								
<30	6	4.9	1.47 (0.499-4.34)	0.479	7	5.7	4.72 (1.20-18.61)	0.035
$\geq$30 unit	8	3.4			3	3		

* Fisher-Exact

Table 4. Behavioral and other factors associated with Hepatitis B and C markers among MTP, Sana'a, Yemen 2024.

Factors	**HBsAg-positive N=14**		**OR (CI)**	***P-Value***	**Anti HCV-Positive N=10**		**OR (CI)**	***P-Value***
	No.	**\%**			**No.**	**\%**		
Cupping								
Yes	0	0.0	—	0.519	0	0.0	—	1.00*
No	14	4			10	2.8		
Tattooing								
Yes	0	0.0	—	1.00	0	0.0	—	1.00*
No	14	4			10	2.8		
Smoking								
Yes	2	6.9	1.97 (0.420-9.284)	0.379	1	3.5	1.28	0.571*
No	12	3.6			9	2.7		
Qat Showing								
Yes	4	5.1	1.45 (0.442-4.75)	0.537	4	5.1	2.45 (0.674-8.91)	0.235*
No	10	3.6			6	2.1		
Traveled outside								
Yes	0	0.0	—	0.460	1	7.7	3.13(0.367-26.8)	0.310*
No	14	4.2			9	2.6		
Breastfeeding								
Yes	14	4	—	0.519	10	2.9	—	0.588
No	0	0.0			0	0.0		
Family size- persons								
> 7	11	6.8	4.81 (1.32-17.567)	0.009	6	3.7	1.89(0.526-6.83)	0.351
< 7	3	1.5			4	2		
* Fisher-Exact								

systematic review and meta-analysis performed by Jing, et al., showed a significant association between O blood type and HBV infection and the blood group B was associated with a lower risk of HBV infection. This association might be partly attributed to the regional factors, due to the high relevance between HBV endemic and regional health and economic development [28]. Furthermore, significant association was found among HBsAg patients who had low income and family size of more than seven people; these results are consistent with previous studies [29, 30]. In addition, we don't find significant association between HBV infection and the other predisposing factors such as history of cupping, tattoos, tooth extraction, frequency of blood transfusion, and surgical history. This may be attributed to an increase in awareness among younger age groups in the Yemeni population about HBV mod transfusion and mandatory testing of HBsAg and anti-HBc markers of blood donors in the last years. HCV infection is a serious complication for transfusion therapy in patients who received transfusions before the implementation of serological tests for detecting infection in blood donors in 1990 [31]. In the present study, significantly higher anti-HCV among patients with increase in age and received transfusions of more than 30 units. This finding is comparable to other studies carried out in Yemen and India [31, 13, 32]. This may be due to the reason that they have been receiving transfusions before 20 years, when screening for anti-HCV was routinely done by the chromatography method, and it became mandatory thereafter by the ELISA method for antibodies only. Regarding HIV seroprevalence, no patient was positive for anti-HIV1/2, this result agrees with findings in Oman and India [10, 32], This may be due to stringent and regular screening of blood for HIV as standard procedures in blood transfusion guidelines. Furthermore, the low HIV in our study also may reflect the low HIV prevalence among the Yemeni population.

5. CONCLUSION

Although the seroprevalence of BBVs is low compared with the previous findings reported from other regions, it remains an important problem among MTPs. The finding found that the most frequent infection among MTPs was HBV followed by HCV with a significantly higher rate among leukemia patients. Increase of family size and low income are significantly associated factors with HBV infection. An increase in age and blood transfusion units were found to be significant predictors for HCV infection. BBVs screening for MTPs should be strongly considered before initiating transfusion therapy as well as regular mentoring for viral markers and mandatory implementation of HCV antigen testing as well as, advanced technology in blood screening are highly recommended.

This study had a retrospective design and may have been affected by recall bias. In addition, the results of this study may not be generalizable to all governorates in Yemen as it was performed in a single governorate, so further study may be required.

ACKNOWLEDGMENTS

The authors acknowledge all patients enrolled in this study and staff in National Blood Transfusion Centers for their help in the sample testing. We would also like to thank the staff in the Yemeni Society for Thalassemia, National Oncology Center, and Childhood of Leukemia Unit at Al Kuwait Hospital for facilitating the collection of samples from patients.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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