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Hepatitis B and C among Multi-Transfused Pediatric Thalassemic Patients in Sana'a City, Yemen: A Single-Center Retrospective Study

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ABSTRACT

Objective: To determine the prevalence of hepatitis B and C infections and their association with repeated blood transfusions among thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders (YSTGBD) in Sana'a city, Yemen.

Methods: This retrospective cross-sectional study analyzed the medical records of 195 thalassemic children aged <18 years taken who were attending the YSTGBD from January 2008 to December 2018. Data about the gender and age of the child, time of thalassemia diagnosis, frequency of monthly blood transfusions, hepatitis B virus (HBV) vaccination status, hepatitis B infection and hepatitis C virus (HCV) seropositivity were retrieved from the records into a data collection sheet. Data were then analyzed and summarized as frequencies and proportions. The association between the independent variables and infection with hepatitis B and/or hepatitis C was tested using the chi-square test.

Results: The majority of thalassemic children attending the YSTGBD were males (58.5%), aged 8 years or older (81.0%), diagnosed with thalassemia at 6 months of age or older (71.8%, were receiving ≤500 ml of transfused blood per month (88.7%) and had been vaccinated against HBV (72.8%). Regarding the serostatus for viral hepatitis, 15.4% (30/195) of children were seropositive for the antibodies against HCV, 13.3% (26/195) were infected with hepatitis B as confirmed by HBsAg seropositivity, and 4.1% (8/195) were concomitantly seropositive for HBsAg and anti-HCV. Not getting vaccinated against HBV was significantly associated with infection with HBV (P <0.001), where 45.3% of unvaccinated children were seropositive compared to 1.4% of vaccinated children. In contrast, gender, age, age at thalassemia diagnosis and the quantity of monthly transfused blood were not significantly associated with infection with hepatitis B, anti-HCV seropositivity, or concomitant seropositivity for HBsAg and anti- HCV among thalassemic children.

Conclusions: Viral hepatitis is a major problem for thalassemic children seeking healthcare in institutions of concern in Yemen, but it is rather difficult to assess the status of hepatitis C infection because of the lack of confirmatory tests. On the other hand, vaccination against HBV is significantly associated with a lower prevalence of hepatitis B among thalassemic children, highlighting the need for vaccinating all thalassemic children before enrollment in specialized centers of care. Thalassemic children should be screened for blood-borne viruses, including hepatitis viruses, before the establishment of regular blood transfusions.

Keywords: Hepatitis B, Hepatitis C, Thalassemia, Yemen

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1. Introduction

Thalassemic patients are at a high risk of transfusion-related diseases, including hepatitis B and hepatitis C. Globally, approximately 60 thousand new infants are born with thalassemia every year.[1] The prevalence and distribution of thalassemia are changing worldwide due to migration rates and patterns. There are two types of thalassemia: α-thalassemia and β-thalassemia. Beta-thalassemia is the most prevalent type worldwide, particularly in malaria-prone societies such as Southeast Asia, the Middle East, Mediterranean and African countries and the Indian subconti- nent.[2–11] Both types of thalassemia have been re- ported in a number of Arab countries.[12–14]

Yemen is one of the poorest developing countries, where hereditary hemoglobinopathies are a major health problem. In 2009, thalassemia was reported to be prevalent among 13% of patients attending the outpatient clinics in Sana'a city, where β-thalassemia represented 4.4% and α-thalassemia represented 8.6% of cases.[15] Thalassemia is usually detected at an old age among Yemeni patients due to the low-level awareness of the Yemeni society about the disease and the low socioeconomic status along with the fewer facilities available for seeking medical advice.[16] Because thalassemia has been reported to be more prevalent in communities with a high rate of parent consanguinity,[17] it is expected to be highly prevalent among the Yemeni community. The rate of consanguineous marriage in Yemen is high, with first-degree relatives representing 64.2% of thalassemic patients in Yemen.[16]

Despite the high burden of thalassemia in Yemen, many centers do not adhere to the national policy for screening prior to blood transfusion, exposing children who receive multiple blood transfusions to the risk of transfusion-related infectious diseases. Viral infections with hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are among the most common infections associated with transfusion.[3] Other complications of repeated blood transfusions include iron overload that can lead to cardiac or hepatic disease, endocrinopathy and osteoporosis. Because blood transfusion is the main therapeutic intervention for thalassemic patients, blood-borne viral infections represent a challenge in the management of patients with thalassemia major worldwide. Viral hepatitis can cause significant morbidity and mortality among thalassemic patients, and it varies from one population to another from acute to chronic expressed as acute or chronic hepatitis, cirrhosis and hepatocellular carcinoma.[3] The prevalence of hepatitis B and C among thalassemic children in Yemen is unclear because no published studies have been found. Therefore, this study aims to determine the prevalence of hepatitis B infection and/or seropositivity for HCV among thalassemic children in Sana'a city and to study their association with the demographic characteristics and frequency of blood transfusions.

2. Subjects and methods

This retrospective cross-sectional study was conducted at the Yemen Society for Thalassemia and Genetic Blood Disorders (YSTGBD) in the period from January 2008 to December 2018. Data about the gender and age of the child, child's age at thalassemia diagnosis, monthly blood transfusions, vaccination status against HBV, hepatitis B surface antigen (HBsAg) and seropositivity for anti-HBV antibody were retrieved from 195 medical records of thalassemic children aged <18 years into a data collection sheet. Data were then analyzed using the IBM SPSS Statistics, Version 28 (IBM Corp., Armonk, NY, USA). Categorical data were presented as frequencies and proportions, and the chi-square test was used to test the association between the independent variables and infection with hepatitis B and/or seropositivity for anti- HCV at *P*-values <0.05.

3. Results

3.1. Characteristics of thalassemic children

Table (1) shows that the majority of thalassemic children were males (58.5%), aged 8 years or older (81.0%), diagnosed with thalassemia at 6 months of age or older (71.8%), were receiving ≤500 ml of transfused blood per month (88.7%) and had been vaccinated against HBV (72.8%).

Table 1. Characteristics of thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city, Yemen (2008-2018)*

Characteristics		*n*	(%)
Gender			
	Male	114	**(58.5)**
	Female	81	**(41.5)**
Age (years)			
	<8	37	**(19.0)**
	≥8	158	**(81.0)**
Age at thalassemia diagnosis (months)			
	<6	55	**(28.2)**
	≥6	140	**(71.8)**
Quantity of blood transfused (ml/month)			
	≤500	173	**(88.7)**
	>500	22	**(11.3)**
HBV vaccination status			
	Vaccinated	142	**(72.8)**
	Unvaccinated	53	**(27.2)**

* The total number of children was 195.

3.2. Prevalence of hepatitis B infection, anti-HCV seropositivity and concomitant seropositivity for HBsAg and anti-HCV among thalassemic children

Figure (1) shows that 15.4% (30/195) of children were seropositive for the antibodies against HCV, and 13.3% (26/195) of children were infected with hepatitis B as confirmed by HBsAg seropositivity. However, the concomitant seropositivity for HBsAg and anti-HCV was observed among 4.1% (8/195) of thalassemic children.

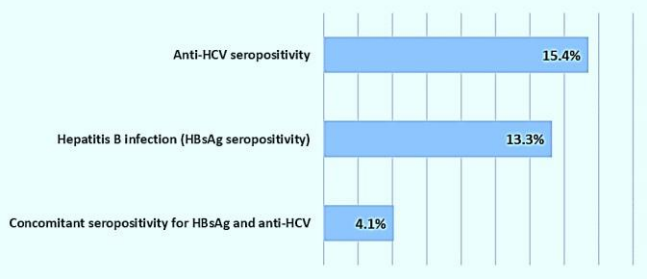

Fig 1. Serostatus of thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city (2008-2018) for HBsAg and anti-HCV

3.3. Factors associated with hepatitis B infection among thalassemic children

Table (2) shows that not getting vaccinated against HBV was significantly associated with in- fection with HBV (*P* <0.001) as confirmed by HBsAg seropositivity, where 45.3% of unvaccinat- ed children were seropositive compared to 1.4% for the vaccinated children. In contrast, no statistically significant association was observed between hepatitis B infection and gender (*P* =0.671), age (*P* = 0.790), age at thalassemia diagno- sis (*P* = 0.816), or the quantity of monthly trans- fused blood (*P* = 0.319).

Table 2. Association of demographic factors, HBV vaccination status, age at thalassemia diagnosis and quantity of transfused blood with HBsAg seropositivity among thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city (2008-2018)

Variable		*N*	HBsAg seropositivity *n* (%)	*P*-value
Gender				
	Male	114	14 **(12.3)**	0.671
	Female	81	12 **(14.8)**	
Age (years)				
	<8	37	4 **(10.8)**	0.790
	≥8	158	22 **(13.9)**	
HBV vaccination status				
	Vaccinated	142	2 **(1.4)**	<0.001
	Unvaccinated	53	24 **(45.3)**	
Age at thalassemia diagnosis (months)				
	<6	55	8 **(14.5)**	0.816
	≥6	140	18 **(12.9)**	
Quantity of transfused blood (ml/month)				
	≤500	173	25 **(14.5)**	0.319
	>500	22	1 **(4.5)**	

N, number examined; *n*, number positive for HBsAg; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen.

3.4. Factors associated with anti-HCV seropositivity among thalassemic children

Table (3) shows no statistically significant association between anti-HCV seropositivity and gender (P = 0.688), age (P = 0.213), age at thalassemia diagnosis (P = 0.275), or the quantity of monthly transfused blood (P = 0.117).

Table 3. Association of demographic factors, age at thalassemia diagnosis and quantity of transfused blood with anti-HCV seropositivity among thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city (2008-2018)

Variable		*N*	Anti-HCV seropositivity *n* (%)	*P*-value
Gender				
	Male	114	19 **(16.7)**	0.688
	Female	81	11 **(13.6)**	
Age (years)				
	<8	37	3 **(8.1)**	0.213
	≥8	158	27 **(17.1)**	
Age at thalassemia diagnosis (months)				
	<6	55	11 **(20.0)**	0.275
	≥6	140	19 **(13.6)**	
Quantity of transfused blood (ml/month)				
	≤500	173	24 **(13.9)**	0.117
	>500	22	6 **(27.3)**	

N, number examined; *n*, number positive for anti-HCV; HCV, hepatitis C virus.

3.5. Factors associated with concomitant seropositivity for HBsAg and anti-HCV among thalassemic children

Table (4) shows no statistically significant association between concomitant seropositivity for HBsAg and anti-HCV and gender (P = 0.472), age (P = 0.356), age at thalassemia diagnosis (P = 1.000), or the quantity of monthly transfused blood (P = 0.600).

Table 4. Association of demographic factors, age at thalassemia diagnosis and quantity of transfused blood with concomitant seropositivity for HBsAg and anti-HCV among thalassemic children attending the Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city (2008-2018)

Variable		*N*	HBsAg and anti-HCV seropositivity *n* (%)	*P*-value
Gender				
	Male	114	6 **(5.3)**	0.472
	Female	81	2 **(2.5)**	
Age (years)				
	<8	37	0 **(0.0)**	0.356
	≥8	158	8 **(5.1)**	
Age at thalassemia diagnosis (months)				
	<6	55	2 **(3.6)**	1.000
	≥6	140	6 **(4.3)**	
Quantity of transfused blood (ml/month)				
	≤500	173	8 **(4.6)**	0.600
	>500	22	0 **(0.0)**	

N, number examined; *n*, number positive for both HBsAg and anti-HCV; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus.

4. Discussion

The higher proportion of male thalassemic children as per the records of the YSTGBD is consistent with that reported elsewhere,[18–20] which could be explained by the more parental attention given to male children compared to females.[19] The finding that more than two-thirds of thalas- semic children in the present study had been di- agnosed at an age of six months or older is con- sistent with that reported for Indian thalassemic children,[21] where the majority (64%) presented before transfusion when younger than one year. In contrast, another study found that most Indian children had been diagnosed with thalassemia when they were younger than 6 months of age.[19] Such findings are supported by published evidence that most moderate-to-severe thalassemic children show signs and symptoms within their first two years of life.[22] It has also been confirmed that the symptoms of β-thalassemia major occur within 6-24 months of age.[23, 24]

The present study revealed that 13.3% of thalassemic children were infected with HBV as confirmed by HBsAg seropositivity. In contrast, higher prevalence rates of thalassemia were reported for

HBsAg among children in Egypt (29%) and India (56%).[26, 27] The lower proportion of Yemeni HBsAg-seropositive children in the present study could be due to the high coverage of HBV vaccination, where more than two-thirds of children had been vaccinated. On the other hand, lower prevalence rates of 5.7–6.6% for infection with HBV were reported for thalassemic children in India.[28,29] Such differences could be attributed to the variations in the epidemiology of hepatitis B infection across areas within the same countries and between different countries or regions.

The present study also revealed that 15.4% of thalassemic children showed seropositivity for anti-HCV, but such seropositivity had not been confirmed with more robust techniques. Accordingly, resolved infections or false positivity could not be ruled out. This prevalence rate is almost equal to that (15.7%) reported for anti-HCV seroprevalence among thalassemic children in Iran.[25] In contrast, higher anti-HCV prevalence rates of 40.5% and 42.1% were reported for thalassemic children in Egypt and Pakistan, respectively.[26,30] In thalassemic patients, the prevalence of HCV infection varies from one country to another worldwide. For instance, it ranges from low rates of 14% in Lebanon,[31] 16.7% in India,[32] and 22.4% in Malaysia[33] to high rates of 60% in Paki- stan,[34] 63% in Saudi Arabia,[35] and 85% in Ita- ly.[36] Such differences in the prevalence of HCV infection could be attributed to the variations in awareness about hepatitis C and other blood- borne diseases, showing more or less advancedblood safety.[26]

The significant association between the lack of HBV vaccination among thalassemic children and their seropositivity for HBsAg in the presentstudy. It is noteworthy that HBV vaccination was found to be significantly associated with a fourfoldincreased possibility of acquiring anti-HBsAg ti- ters compared to non-vaccination.[37] This finding is also supported by the fact that introducing effective vaccines against HBV reduces the prevalence of hepatitis B besides its health and economic impact.[38] Moreover, viral hepatitis has been significantly reduced by screening programs for viral hepatitis and HBV vaccination.[39]

The present study is limited by its retrospective nature and small sample size, besides the exclusion of a large number of records because of incomplete data. Therefore, its findings may not be generalizable to thalassemic children in the country. Nevertheless, it provides preliminary data about viral hepatitis among multi-transfused thalassemic children in Yemen. On the other hand, the laboratory of the YSTGBD tested children for anti-HCV only but did not confirm hepatitis C infection by PCR because of limited financial resources, making it difficult to decide on the infection (acute, chronic, or resolved) or false positivity for anti-HCV. In addition, there were no data about the serologic markers of hepatitis B and C before the intervention with regular blood transfusions.

5. Conclusions

Viral hepatitis is a major problem for thalassemic children seeking healthcare in institutions of concern in Yemen, but it is rather difficult to assess the status of hepatitis C infection because of the lack of confirmatory tests. On the other hand, vaccination against HBV is significantly associated with a lower prevalence of hepatitis B among thalassemic children, highlighting the need for vaccinating all thalassemic children before enrollment in specialized centers of care. Thalassemic children should be screened for blood-borne viruses, including hepatitis viruses, before the establishment of regular blood transfusions.

Viral hepatitis is a major concern in thalassemic patients in Yemen, highlighting the importance of hepatitis B vaccination. Accordingly, the national policy of blood component transfusion should be carefully followed, emphasizing the importance of hepatitis B vaccination.

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Ethical considerations

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine and Health Sciences, UST, Sana'a, Yemen (MECA No: EAC/UST219). In addition, permission was obtained from the administration of the YST-GBD.

Authors' contributions

ASH and AAS designed the study; AFS, FAB, IMA, MAA, MSH, OHA, WMA and YAA contributed to data collection, data analysis and interpretation of results. ASH, AAS and AASA drafted and revised the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests associated with this article.

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