Prevalence of Hepatitis C Virus Infection in Children with Hemoglobinopathies: A Retrospective Study at the Center for Hereditary Blood Diseases – Basrah, Southern Iraq

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***Abstract*:** Hepatitis C virus (HCV) infection remains a major global health challenge, particularly for children with hereditary hemoglobinopathies who require lifelong transfusion support. This retrospective, registry-based study examined all 1,140 patients aged 6–18 years with hemoglobinopathies registered at the Basra Center for Hereditary Blood Diseases between 1 January 2017 and 31 December 2021 to determine HCV prevalence and associated risk factors. Annual HCV seropositivity ranged from 9.12 % in 2017 to a peak of 10.78 % in 2019; screening volume was highest in 2019 (n = 408) and lowest in 2021 (n = 54). Sickle-cell disease (SCD) constituted the largest diagnostic category. In 2021 HCV rates were 5.55 % in SCD and 3.70 % in transfusion-dependent thalassemia (TDT). Across the five-year period, multivariable analysis demonstrated significant associations between HCV seropositivity and older age, TDT diagnosis, frequent transfusion (≥12 units /year), prior splenectomy and use of deferoxamine infusion pumps (all $p < 0.05$). No significant relationship was observed with gender, urban versus rural residence, or history of dental procedures. Although the center's overall HCV prevalence remains higher than that reported for the Iraqi general population, it is comparable to figures from the same institution in 2013–2014 and lower than rates published by other hereditary-blood-disease centers in Iraq and neighboring countries. These findings suggest gradual improvement in transfusion safety and infection-control practices but underscore the ongoing vulnerability of transfusion-dependent children. Continued efforts to enhance donor-blood screening, enforce strict transfusion protocols and educate families about HCV transmission are recommended to further reduce infection risk. Routine virological monitoring and early antiviral therapy should also be incorporated into comprehensive care pathways for children with hemoglobinopathies in Basra.

***Index Terms*:** Hepatitis C virus, hemoglobinopathy, thalassemia, sickle cell disease, blood transfusion

INTRODUCTION

Hepatitis C virus (HCV) is an enveloped, single-stranded RNA virus from the Flaviviridae family, first detected in 1989 [1]. It has seven genotypes, with genotype 1 being the most prevalent globally [1]. HCV is a major cause of morbidity and mortality and is the most commonly reported bloodborne infection worldwide, particularly impacting the Eastern Mediterranean region [2–4]. It affects around 170 million individuals globally—five times more prevalent than HIV [4]. In Egypt, HCV prevalence is 10% in adults and 0.4% in children [5], while in Iraq it's 3.2% among healthy individuals and 67.3% among multitransfused thalassemia patients [6–7]. In Basra, the prevalence was 2% in 2018 [8]. Transmission primarily occurs through percutaneous blood exposure [2, 9].

HCV is the leading cause of post-transfusion hepatitis [10]. Patients with hereditary hemoglobinopathies, especially thalassemia and sickle cell anemia (SCA), are particularly vulnerable due to frequent transfusions [11–13]. Thalassemia prevalence in Iraq rose from 33.5 to 37.1 per 100,000 between 2010 and 2015 [13]. Blood screening in Iraq is still based on serology, which cannot detect infections in the window period [14]. Developed countries have adopted Nucleic Acid Amplification Testing (NAT), which provides earlier detection [15].

Risk factors for HCV include transfusions, contaminated drug equipment, vertical transmission, and tattooing [2]. Clinically, HCV is often asymptomatic in its acute phase, though symptoms

like jaundice or abdominal pain can occur [2, 9]. Chronic infection develops in over 50% of cases [2], defined by the persistence of HCV RNA beyond six months [2, 12]. Several host factors influence progression [12–13].

Diagnosis starts with HCV antibody testing (EIA), followed by confirmatory HCV RNA PCR [2, 16–18]. Detection of viral RNA within 2–3 weeks of exposure allows for early diagnosis, especially during the seronegative window period [19]. Monitoring frequency depends on transfusion dependency [20].

Treatment aims at achieving a sustained virologic response (SVR12 or SVR24), effectively curing the infection [2, 16, 18, 21]. DAA therapies are recommended for all patients ≥3 years [16, 21]. Regimens and dosing differ by age, weight, and HCV genotype [16, 21].

Complications include liver cirrhosis, hepatic failure, and hepatocellular carcinoma [1, 22].

Hemoglobinopathies, including thalassemia and structural hemoglobin variants, are autosomal recessive disorders of hemoglobin production or structure [23–25]. They are highly prevalent in the Middle East, including Iraq [24]. Globally, around 300,000–400,000 infants are born annually with hemoglobinopathies [25].

Thalassemia results from impaired globin chain synthesis, leading to ineffective erythropoiesis [26–27]. Alpha thalassemia involves deletion of α-globin genes and varies from silent carriers to fatal Hb Bart's hydrops fetalis [27]. Beta thalassemia arises from defective β-globin synthesis and ranges from trait to major forms [27]. SCD results from a mutation in the β-globin chain (HbS), leading to red cell sickling and complications [28–30].

Other hemoglobin variants include HbC, HbE, and HbD. HbE disorders range from asymptomatic to transfusion-dependent thalassemia, with over a million affected worldwide [31–33]. HbD variants are mostly mild but clinically relevant when co-inherited with HbS or β-thalassemia [33–34].

Diagnosis involves neonatal and premarital screening, hematological tests, electrophoresis, and DNA analysis [35–37].

Complications of hemoglobinopathies include infections due to immunologic dysfunction and transfusion-related risks (e.g., HBV, HCV, HIV) [38–41], acute splenic sequestration [42], aplastic crisis [43], acute chest syndrome [44–45], stroke [46–47], vaso-occlusive crises [48], cholelithiasis [49], renal complications [50–51], and growth and endocrine disorders [52–55].

Management strategies include transfusions, classified as transfusion-dependent (TDT) or non-transfusion dependent (NTDT) [17, 27, 56–57]. Hydroxyurea to increase HbF and reduce crises [26, 58–59]. Iron chelation therapy to manage transfusion-induced iron overload [33]. Splenectomy in cases of hypersplenism or recurrent sequestration [60–61]. Hematopoietic stem cell transplantation as a potential cure [33, 62]. Pain management during vaso-occlusive episodes [63]. Prophylactic antibiotics like penicillin for children with SCA [33, 64–65].

This study aims to determine the prevalence of hepatitis C virus infection among patients with hemoglobinopathy in Basra from 2017–2021, investigate its association with selected risk factors, and describe key sociodemographic characteristics of the affected population.

METHODS

This study was a descriptive, retrospective, registry-based analysis conducted to determine the prevalence of hepatitis C virus (HCV) among patients with hemoglobinopathy registered at the Basra Center for Hereditary Blood Diseases over a five-year period, from January 1, 2017, to December 31, 2021. Prevalence was calculated as the proportion of individuals in the population who had HCV at a specific point or over a defined period. It included both newly diagnosed and pre-existing cases.

The study population consisted of 1,140 patients aged 6 to 18 years, including 608 males and 532 females. Information collected included date of birth, gender, residence, diagnosis, frequency of blood transfusions, history of splenectomy or dental interventions, and the use of deferoxamine infusion pump for iron chelation therapy. Based on their diagnosis, patients were categorized into three groups: transfusion-dependent thalassemia (TDT), non-transfusion-dependent thalassemia (NTDT), and sickle cell disease (SCD). The TDT group included patients with β-thalassemia major (β-TM), severe Hemoglobin E/β-thalassemia, and α-thalassemia major (Hemoglobin Bart's). The NTDT group included β-thalassemia intermedia (β-TI), mild to moderate HbE/β-thalassemia, and α-thalassemia intermedia (HbH disease). The SCD group included sickle cell anemia (SCA), sickle/β-thalassemia, HbSC disease, and HbSD disease [17, 56, 57, 67].

The frequency of blood transfusion was classified into three categories: patients with no history of blood transfusion; those who received transfusions according to disease-specific guidelines; and those who received frequent transfusions, defined as more than the usual requirement due to complications such as

heart failure, stroke, splenic sequestration, or pulmonary hypertension [56, 57, 68].

Patients were screened for HCV infection every 6 to 12 months using enzyme-linked immunosorbent assay (ELISA) to detect anti-HCV antibodies. For those who tested positive, a blood sample was collected for further analysis of HCV RNA viral load and genotyping using real-time polymerase chain reaction (PCR) [17].

Ethical and administrative approval for the study was obtained from the Basra Health Directorate, under the authority of the Iraq Ministry of Health, to access and review the medical records of patients at the Basra Center for Hereditary Blood Diseases.

To identify potential issues in data collection, a pre-test was conducted on 20 cases. As a result, some initially intended variables, such as the educational level of patients and their parents, were excluded due to lack of documentation in the medical records. Patient data such as date of birth, gender, diagnosis, deferoxamine use, and HCV screening results were obtained from electronic records. However, other variables—including place of residence, blood transfusion frequency, history of splenectomy, and dental interventions—required manual review of individual files, which posed challenges to including all registered patients in the study.

Some limitations were encountered during the study, including poor documentation in older patient files and incomplete records of dental history. These limitations may have impacted the completeness of the data.

Data analysis was performed using SPSS version 26. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD). Student's t-test was used to compare means between two groups. The chi-square test and Fisher's exact test were used to evaluate the association between categorical variables. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Figure (1) shows that HCV prevalence were close results from 2018-2020 (10.35%, 10.78% &10.08%) respectively but decreased to 9.9%in 2021.

Figure (1) :HCV prevalence in five-year period of the study

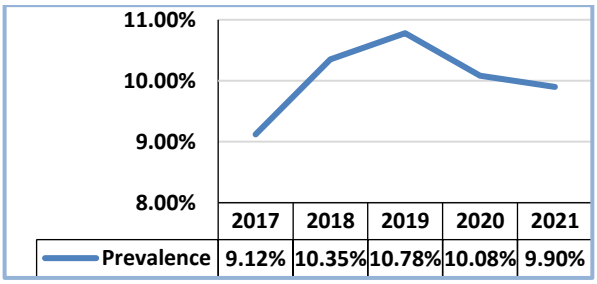

Table (1) shows that from a total of (1140) screened cases for 5 years period, majority of cases (782) were SCD, followed by (272) cases TDT. Higher number of screened cases were (408) in 2019 followed by (390) case in 2018 while the lowest number of screened cases were 54 cases in 2021.

Table (1): Distribution of cases of hemoglobinopathy in relation to type of disease and year of screening

Years Vs. Diagnosis	2017	2018	2019	2020	2021	Total
SCD	75	259	277	131	40	782
TDT	32	100	107	20	13	272
NTDT	11	31	24	19	1	86
Total	118	390	408	170	54	1140

Table (2) shows total number of positive HCV cases (49) during the five-year period, (25) were patients with SCD and (24) were patient with TDT, there were no cases of HCV among patients with NTDT

Table (2) Distribution of cases of hepatitis C according to the type of disease

Result of HCV screening	SCD	TDT	NTDT	Total
HCV positive	25	24	0	49
HCV negative	757	248	86	1041
Total	782	272	86	1140

Figure (2) shows that the higher frequency of HCV seropositivity in all types of disease were 9.25%in 2021 while the lowest frequency 1.69%in 2017.Regard the type of the disease, the higher frequency was in SCD (4.11%, 5.55%) in 2020 &2021 respectively followed by 3.7% in TDT in 2021 while the lowest percentage during the whole study period were in NTDT which equal to 0%.

Figure (2): The frequency of HCV seropositivity in relation to type of disease and year of screening.

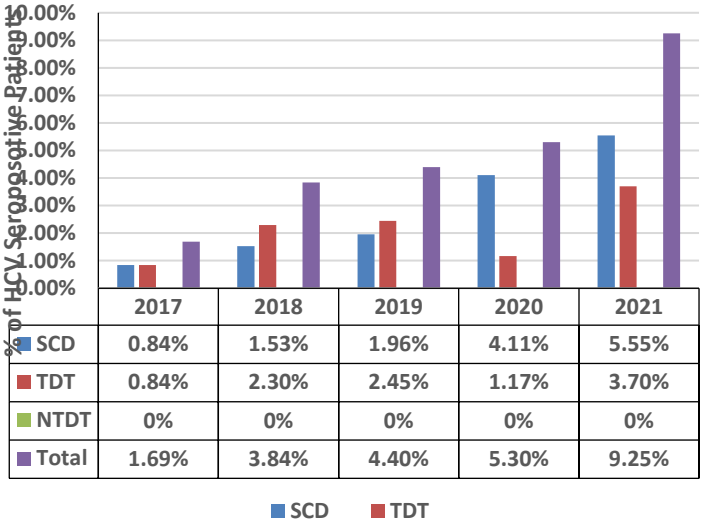

Table (3) shows that from total of 1140 case, 53.3% were male while 46.7% female, there is no statistically significant difference between the two age groups regarded HCV seropositivity with P-value 0.226.

Table (3): Hepatitis C seropositivity in relation to gender

Sex	HCV Ab		Total	P-value
	Positive	Negative		
Male	22 (44.9)	586 (53.7)	608 (53.3)	0.226
Female	27 (55.1)	505 (46.3)	532 (46.7)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (4) shows that the majority of cases enrolled in the study were from 10-18years old (60.4%), there is statistically significant differences between the two-age groups with P-value 0.0001.

Table (4): Hepatitis C seropositivity in relation to age

Age groups	HCV Ab		Total	P-value
	Positive	Negative		
<10years	2 (4.1)	450 (41.2)	452 (39.6)	0.0001
10-18years	47 (95.9)	641 (58.8)	688 (60.4)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (6) shows that in 61.9% of cases from periphery of Basra province, there is no statistically significant difference in HCV seropositivity between center & periphery with P-value 0.641.

Table (6): Hepatitis C seropositivity in relation to residence of patients

Residence	HCV Ab		Total	P-value
	Positive	Negative		
Centre	12 (24.5)	422 (38.7)	434 (38.1)	0.641
Peripheries	37 (75.5)	669 (61.3)	706 (61.9)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (7) shows that majority of patients who lived in periphery of Basra province were from Abi Al Khaseeb 23.4% followed by 14.9% from Al Medina & the majority of HCV infected were from Shatt AL Arab 21.6% while the lowest percentage were from Om Qesir 0%.

Table (7): Distribution of patients according to their residence in periphery of Basra province

Peripheries	HCV Ab		Total
	Positive	Negative	
Shatt AL Arab	8 (21.6)	98 (14.6)	106 (15)
Al Zubair	7 (18.9)	96 (14.4)	103 (14.6)
Al Mdeina	6 (16.2)	99 (14.8)	105 (14.9)
Al kerma	5 (13.5)	77 (11.5)	82 (11.65)
Abi Al Khaseeb	4 (10.8)	161 (24.1)	165 (23.4)
Al Qurna	3 (8.2)	45 (6.7)	48 (6.8)
Al Hartha	2 (5.4)	42 (6.3)	44 (6.2)
Al Faw	1 (2.7)	21 (3.1)	22 (3.1)
Al Deir	1 (2.7)	24 (3.6)	25 (3.5)
Om Qesir	0 (0)	6 (0.9)	6 (0.9)
Total	37 (5.2)	669 (94.8)	706 (100)

Table (8) shows that HCV seropositivity was higher in patients with TDT and there is a statistically significant difference among the three groups of disease types with P-value 0.0001.

Table (8): Hepatitis C seropositivity in relation to type of disease

Diagnosis	HCV Ab		Total	P-value
	Positive	Negative		
Sickle cell disease	25 (51)	757 (69.4)	782 (68.6)	0.0001
Transfusion dependent thalassemia	24 (49)	248 (22.7)	272 (23.9)	
Non-transfusion dependent thalassemia	0 (0)	86 (7.9)	86 (7.5)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (9) shows that 34.7% of HCV infections were among splenectomies patients and there is statistically significant difference between splenectomies and non-splenectomies patients with P-value 0.0001.

Table (9): Hepatitis C seropositivity in relation to splenectomy

Splenectomy	HCV Ab		Total	P-value
	Positive	Negative		
Yes	17 (34.7)	92 (8.4)	109 (9.6)	0.0001
No	32 (65.3)	999 (91.6)	103 (90.4)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (10) shows that the higher seropositivity of HCV infection was among patients on deferoxamine infusion pump, there is statistically significant difference between the two groups with P-value 0.003.

Table (10): Hepatitis C seropositivity in relation to the use of deferoxamine infusion pump

Deferoxamine infusion pump	HCV Ab		Total	p-value
	Positive	Negative		
Yes	4 (8.2)	10 (0.9)	14 (1.2)	0.003
No	45 (91.8)	1081 (99.1)	1126 (98.8)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (11) shows that frequent blood transfusion is a risk factor for HCV infection and there is a statistically significant difference among the three groups with P-value 0.001.

Table (11): Hepatitis C seropositivity in relation to the frequency of blood transfusion

Frequency of blood transfusions	HCV Ab		Total	P-value
	Positive	Negative		
No history of blood transfusion	3 (6.1)	415 (38.1)	418 (36.7)	0.0001
Frequent blood transfusion	35 (71.4)	369 (33.8)	404 (35.4)	
Blood transfusion according to type of diseases guideline	11 (22.5)	307 (28.1)	318 (27.9)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

Table (12) shows that there was no statistically significant difference between patient with and without history of dental intervention with P-value 0.833.

Table (12): Hepatitis C seropositivity in relation to dental intervention

Dental intervention	HCV Ab		Total	P-value
	Positive	Negative		
Yes	6 (12.2)	145 (13.3)	151 (13.2)	0.833
No	43 (87.8)	946 (86.7)	989 (86.8)	
Total	49 (4.3)	1091 (95.7)	1140 (100)	

DISCUSSION

Repeated blood transfusion is essential for the survival of patients with thalassemia and sickle cell disease (SCD). However, multi-transfused patients with these conditions are at higher risk for transfusion-associated infections such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) [7].

The overall HCV seroprevalence in this five-year study is comparable to the findings of a previous study conducted at the same center in 2013–2014, which reported rates of 10.8% and 9.2%, respectively [17]. However, the rates observed in our study are lower than those reported by Yazaji et al. (11.23%) among multi-transfused hemoglobinopathy patients in Syria [42], and higher than those reported by Al Noomani et al. (3.5%) among patients with hereditary hemoglobinopathies in Saudi Arabia [3].

Out of 1,140 patients included in this study, 272 (23%) were diagnosed with transfusion-dependent thalassemia (TDT). The annual HCV seropositivity rates among TDT patients from 2017 to 2021 were 0.48%, 2.3%, 2.4%, 1.1%, and 3.7%, respectively. In all years, these rates were lower than those reported by Khaled et al. (10.4%) in Nineveh Governorate, Iraq [xx], Albakaa et al. (7.86%) in Al-Najaf [xx], and Jallab et al. (3.8%) in Al-Diwaniyah [xx]. When compared internationally, our findings are also lower than those of Behzadifar et al. (19%) in Iran [xx], Akhtar et al. (36.21%) in Pakistan [xx], and Mansour et al. (19.5%) in Egypt [xx].

Among the study population, 782 patients (68%) had SCD. The annual HCV seropositivity in this group was 0.84%, 1.53%, 1.96%, 4.11%, and 5.55%, respectively. These rates were consistently lower than those reported by Mousa et al. (23%) among Egyptian children with SCD [xx], Alkindi et al. (12.6%) in Oman [xx], and Master et al. (5.4%) in the United States [xx], except in 2021 when the rate (5.55%) slightly exceeded that reported by Master et al.

Eighty-six patients were diagnosed with non-transfusion-dependent thalassemia (NTDT), and their HCV seropositivity remained 0% throughout the five-year period. This is lower than the 3.7% rate reported by Najim et al. in Basra [17].

The observed reduction in HCV seropositivity among all three groups may be attributed to a combination of factors. These include adherence to updated blood transfusion guidelines based on the recommendations of the Thalassemia International Federation, and increased patient and family awareness regarding hydroxyurea therapy—especially for patients with SCD and NTDT. Hydroxyurea helps reduce disease complications and improve hemoglobin levels, decreasing the need for frequent transfusions and, in turn, reducing the risk of transfusion-related infections such as HCV.

When combining HCV seropositivity across all patient groups (TDT, NTDT, and SCD) for each year, the rates were 1.69%, 3.84%, 4.40%, 5.30%, and 9.25% from 2017 to 2021, respectively. This variation may be attributed to differences in the number of patients screened each year, variation in new patient registrations, inconsistent outpatient follow-up, and the impact of COVID-19 restrictions prior to 2021.

Analysis of sociodemographic factors revealed a statistically significant association between increasing age and HCV seropositivity (P = 0.0001), which is consistent with findings by Bhavsar et al. in Gujarat [xx] and Akhtar et al. in Pakistan [73]. This may reflect the cumulative effect of transfusions over time. No significant association was found between gender and HCV seropositivity (P = 0.226), consistent with Akhtar et al. [73] but contradicting the findings of Yazaji et al. in Syria [42]. Additionally, no significant association was observed between place of residence (urban vs. peripheral) and HCV seropositivity (P = 0.641).

In developed countries, the implementation of mandatory screening for blood products in the early 1990s led to a significant decrease in HCV prevalence. For example, in Japan the rate declined from 4.9% to 1.9%, and in the United States from 3.84% to 0.57% [xx].

This study also showed a significant association between HCV seropositivity and the frequency of blood transfusion (P = 0.0001), consistent with findings reported by Al Noomani et al. in Saudi Arabia [3], Mansour et al. in Egypt [74], and Alkindi et al. in Oman [76]. However, this finding contrasts with those of Najim et al. in Basra [17] and Yazaji et al. in Syria [42].

A significant association was also found between disease type and HCV seropositivity (P = 0.0001), with the highest rates observed among TDT patients. This is in agreement with Najim et al. [17] and likely reflects the frequent transfusion requirements in TDT, which increase the risk of HCV exposure.

Furthermore, HCV seropositivity was significantly associated with both a history of splenectomy (P = 0.0001) and use of a deferoxamine infusion pump (P = 0.003). The association with splenectomy may be due to the increased transfusion needs in patients with hypersplenism, or to the possibility of HCV transmission during the window period prior to detection. It is unlikely to be due to surgical contamination, as hospitals follow strict infection control protocols. The association with deferoxamine pumps may be explained by shared use among family members or improper injection practices, especially in cases of device malfunction. Najim et al. in Basra also reported an association between HCV and deferoxamine pump use but not splenectomy [17], whereas Al-Sweedan et al. in Jordan found the reverse—an association with splenectomy but not with pump use [xx].

In contrast, no significant association was found between HCV seropositivity and history of dental interventions. This may reflect the stringent precautionary protocols followed in dental settings and the pre-procedure screening practices in place. No published studies were found to confirm or refute this observation.

CONCLUSIONS AND RECOMMENDATIONS

The seroprevalence of HCV among patients with hemoglobinopathy remains higher than in the general population but is comparable to rates reported in a previous study conducted at the same center in 2013–2014. HCV prevalence among TDT and SCD patients was lower than that reported in other centers across Iraq and neighboring countries. Significant associations were found between HCV seropositivity and TDT, increasing age, frequency of blood transfusion, splenectomy, and use of deferoxamine infusion pumps, while no significant associations were observed with gender, residence, or dental intervention. To reduce HCV transmission, it is recommended to enhance public and high-risk group awareness about transmission routes and preventive measures and to improve blood donor screening using nucleic acid amplification techniques to detect infections during the window period.

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The study funded by the researchers.

DATA CONFIDENTIALITY AND STORAGE

The data will be processed with a higher degree of confidentiality and privacy.

CONFLICTS OF INTEREST

The researchers did not report any conflicts of interest.

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