Frequency and risk factors for Hepatitis C virus seropositivity in blood transfusion-dependent thalassemic patients in Qena hospitals

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Abstract

Background: Beta-thalassemia major (BTM) is still mostly treated with routine blood transfusions. One of the most prevalent transfusion-transmitted infections (TTI) of clinical significance is the hepatitis C virus (HCV).

Objectives: To estimate the prevalence of HCV infection among thalassemic patients in Qena hospitals, and to identify the possible risk factors associated with HCV infection.

Patients and methods: a cross-sectional study involving 400 thalassemic patients with an age ranging from 1.5 to 29 years, a mean age of 12.8 ±7.3 years, 176 (44%) were male and 224 (56%) were female, and 75.5% were from rural areas. All are reviewed by a structured questionnaire**.**

Results: The study revealed that the prevalence of HCV infection in the studied thalassemic patients was 9.5%. The most important risk factors were the duration of blood transfusion for more than 15 years, previous surgery, dental procedure, and splenectomy (P<0.001), followed by patient age of more than 18 years (P = 0.001), urban population, and a positive family history of thalassemia (P = 0.001), and frequency of blood transfusion (P = 0.054).

Conclusion: The most important risk factors were the duration of blood transfusion for more than 15 years, previous surgery, dental procedure, and splenectomy. Thalassemic patients with older age were at higher risk for HCV infection. The risk increased with patients aged more than 18 years old. A family history of thalassemia was a risk factor for HCV infection.

Keywords: Beta-thalassemia major; Blood transfusion; HCV.

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Introduction

A genetic defect in the synthesis of beta-globin chains causes a set of hereditary illnesses known as beta-thalassemia, which results in chronic hemolytic anaemia and calls for long-term transfusion therapy and iron chelation therapy **(Origa, 2017).**

Despite improvements in the treatment of thalassemia, long-term transfusion therapy still carries a risk of increased iron compartmentalization in a number of organs, including the liver, heart, endocrine glands like the pituitary, pancreas, ovaries, testicles, thyroid, and parathyroid, as well as the adrenals, which can result in life-threatening complications **(De Sanctis et al., 2018).**

Since it accounts for 85% of hereditary hemoglobinopathies, -thalassemia poses a serious health concern in Egypt as well as several other Mediterranean nations **(De Sanctis et al., 2017).** The high incidence of HCV infection among thalassemia patients exacerbates the damaging effects of iron overload on the liver **(Elalfy et al., 2018).**

The prevalence of HCV among thalassemic patients reached over 85% before Egypt made HCV screening at blood banks mandatory **(Said et al., 2013).** A recent study revealed that 37% of Egyptians with thalassemia have HCV infection, despite the existing rigorous regulations on HCV screening in blood banks **(Ragab et al., 2010).**

Interfamilial and iatrogenic HCV transmission are significant HCV transmission routes among thalassemic patients in Egypt due to the high incidence of HCV there **(Said et al., 2013).** The primary causes of severe liver fibrosis and cirrhosis in Egyptian multi-transfused thalassemia patients are concurrent HCV infection and iron overload **(Borgna-Pignatti et al., 2004).**

Patient and methods

Participants and Study Design: A cross-sectional study was conducted to determine the prevalence and risk factors of HCV infection among thalassemic patients in Qena hospitals. Data were collected during the period from 20 June 2021 to 30 December 2022 Informed written consent was taken from the caregivers. The current study had been approved by the ethics committee of the Faculty of Medicine, SVU, Qena, Egypt and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethical approval code is:SVU-MED-COM009-2-21-4-182.

Data Collections: Clinical Assessment of the patients involved as follow: A thorough medical history, including the patient's age, sex, place of residence, mother's education, and consanguinity, was obtained from the patients or their mothers. In addition, questions regarding the length, quantity, and frequency of blood transfusions were posed to the participants. Previous surgical, dental, and splenectomy histories.

Statitical analysis

Data management and statistical analysis: SPSS version 26 was used for the statistical analysis. While qualitative data were given as means SD, quantitative data were presented as figures and percentages. Descriptive statistics and logistic regressions were used for the analysis. Frequencies were generated and the study variables were described using descriptive statistics. In order to assess dichotomous variables, the

current study used bivariate analyses with chi-square tests. The last phase is, a multivariate analysis using logistic regression to determine the variables affecting HCV infection. P-values were considered statistically significant when P < 0.05.

Results

Demographic and Clinical Data

A total of 400 thalassemic patients were included in this study, their ages ranged from 1.5 to 29 years, with a mean age of 12.8 ±7.3 years, 176 (44%) of them were male and 224 (56%) were female, 302(75.5%) were from rural areas, and positive consanguinity present in 314(78.5%) of cases, **(Table .1).**

Table 1. Thalassemic patients' socio-demographic characteristics

Characteristics		**Number**	**Percent %**
Age groups (years)	Less than 9 years	106	26.5%
	9-18 years	210	52.5%
	More than 18 years	84	21%
Age (years)	Mean ± SD	12.8525 ±7.2939	
	Median (range)	11 (1.5-29)	
Gender	Male	176	44%
	Female	224	56%
Residence	Rural Urban	302 98	75.5% 24.5%
Maternal education Level	Illiterate	105	26.3%
	Primary	107	26.8%
	Intermediate	160	40%
	High	28	7%
Consanguinity	Positive	314	78.5%
	Negative	86	21.5%

Effect of demographic characteristics of the studied thalassemic patients on the frequency of HCV Infection

The mean age in thalassemic patients with HCV was older (19.76 ± 6.637) years than those without (12.4 ± 6.987).Twenty (9.5%) of thalassemic patients with HCV aged between nine and eighteen years compared to 90.5% of those without. Eighteen (21.4%) of thalassemic patients with HCV aged more than eighteen years compared to 78.6% of those without**.**

Residence, there is a statistically significant difference (P = 0.001) between thalassemic patients with HCV and those without: 6.6% of rural patients had HCV, while 18.4% of urban patients had HCV.

Maternal education, there is a

statistically significant difference (P = 0.002) between thalassemic patients with HCV and those without 1.9% of patients whose mothers were not educated had HCV, 15% of patients whose mothers had primary education had HCV, and 12.5% of patients whose mothers had intermediate education had HCV, **(Table. 2).**

Table 2. Effect of Demographic characteristics of the studied thalassemic patients on the frequency of HCV infection

Characteristics		Thalassemic patients with HCV (N=38)		Thalassemic patients without HCV (N=362)		P value
		Number	%	Number	%	
Gender	Male	12	6.8%	164	93.2%	0.105
	Female	26	11.6%	198	88.4%	
Age groups (years)	Less than 9	0	0%	106	100%	<0.001*
	9-18	20	9.5%	190	90.5%	
	More than 18	18	21.4%	66	78.6%	
Residence	Rural	20	6.6%	282	93.4%	0.001*
	Urban	18	18.4%	80	81.6%	
Maternal education	Illiterate	2	1.9%	103	98.1%	0.002*
	Primary	16	15%	91	85%	
	Intermediate	20	12.5%	140	87.5%	
	High	0	0%	28	100%	
Consanguinity	Positive	20	6.4%	294	93.6%	<0.001*
	Negative	18	20.9%	68	79.1%	
Age	Mean ± SD	19.7105± 6.637		12.1325± 6.987		<0.001**

*Chi square test - **student's t test

Prevalence of HCV among the studied thalassemic patients

The prevalence of HCV among the studied thalassemic patients was 38(9.5%), (**Table. 3**).

Table 3: Frequency of HCV in the studied thalassemic patients

Group	Number	Percent %
Thalassemic patients with HCV	38	9.5%
Thalassemic patients without HCV	362	90.5%

Healthcare characteristics of the studied thalassemic patients concerning HCV infection (N=400)

34.2% (13 patients) of the 38 thalassemia cases with HCV antibodies had received the HBV vaccine, compared to 26.2% (95 patients) of those without the virus, however, this difference was not statistically significant (P = 0.293).

The difference between thalassemia patients with HCV antibodies and those without in terms of thalassemia family history was statistically significant (P 0.001), with 37 (97.4%) of thalassemic patients with HCV antibodies having a positive family history of thalassemia as opposed to 207 (57.2%) of those without.

Thirty-sex (94.7%) of thalassemia patients with HCV antibodies had undergone previous surgery, compared to 143(39.5%) in those without. There was a statistically significant difference (P< 0.001).

Eighteen (47.7%) of thalassemia patients with HCV antibodies had undergone previous dental procedures, compared to 41(11.3%) of those without, (P< 0.001). Thirty- five (92.1%) of thalassemic patients with HCV had splenectomy compared to 27.6% in those without, (**Table. 4**).

Table 4. Health care characteristics of the studied thalassemic patients concerning HCV infection

Characteristics		Thalassemic patients with HCV (N=38)		Thalassemic patients without HCV (N=362)		P-value
	Total	Number	%	Number	%	
HBV vaccine						
Received	108	13	34.2%	95	26.2%	**0.293**
Not received	292	25	65.8%	267	73.8%	
Family history of thalassemia						
Positive	245	37	97.4%	207	57.2%	**<0.001***
Negative	155	1	2.6%	155	42.8%	
History of surgery						
Yes	181	36	94.7%	143	39.5%	**<0.001***
No	219	2	5.3%	219	60.5%	
History of dental procedure						
Yes	59	18	47.4%	41	11.3%	**<0.001***
No	341	20	52.6%	321	88.7%	
History of tattooing						
Yes	10	0	0%	10	2.8%	**0.299**
No	390	38	100%	352	97.2%	
History of hepatomegaly						
Yes	27	8	21.1%	69	19.1%	**0.767**
No	323	30	78.9%	293	80.9%	
History of splenomegaly						
Yes	300	38	100%	262	72.4%	**0.001***
No	100	0	0%	100	27.6%	
Splenectomy						
Yes	135	35	92.1%	100	27.6%	**<0.001***
No	265	3	7.9%	262	72.4%	

Blood transfusion

In comparison to 93.9% of those without HCV, 100% of thalassemic patients with HCV received one unit of blood. The difference is insignificant (P = 0.486). Accordingly, 68.4% of thalassemic patients with HCV received blood more than once a month compared to 32.9% of those without HCV, 21.1% of thalassemic patients with HCV received blood once a month compared to 52.2% of those without, and 10.5% received blood twice a month compared to 14.9% of those without. Prior to blood transfusion, all thalassemic patients with HCV (38 patients) had hemoglobin levels between 6 and less than 8 g/dl, compared to 67.1% of those without HCV.

The duration of blood transfusion was significantly (P<0.001) longer in thalassemic patients with HCV (17.132 ± 4.822) years than those without HCV (8.6878 ± 5.702) years,(**Table. 5**).

Table 5. The relationship between HCV and blood transfusion of the studied thalassemic patients

Characteristics		**Thalassemic patients with HCV (N=38)**		**Thalassemic patients without HCV (N=362)**		**P value**
	Total	**Number**	**%**	**Number**	**%**	
Number of transfused units (whole blood) (bag)						
0.3	4	0	0%	4	1.1%	**0.486**
0.5	4	0	0%	4	1.1%	
1	378	38	100%	340	93.9%	
2	14	0	0%	14	3.9%	
Frequency of blood transfusion						
Twice per month	58	4	10.5%	54	14.9%	**<0.001***
Once per month	197	8	21.1%	189	52.2%	
More than one month	145	26	68.4%	119	32.9%	
Switch between centers						
Yes	78	4	10.5%	74	20.4%	**0.142**
No	322	34	89.5%	288	79.6%	
Hemoglobin level pretransfusion (g/dl)						
Less than 6	111	0	0%	111	30.7 %	**<0.001***
6 to less than 8	281	38	100%	243	67.1%	
8 or more	8	0	0 %	8	2.2 %	
Duration of receiving blood transfusion (years)		**Mean**	**SD**	**Mean**	**SD**	**<0.001****
		17.132	4.822	8.6878	5.702	

*Chi square test - **student's t test

Iron chelating agents

97.4% of thalassemic patients with HCV received iron chelating agents, compared to 64.4% of those without HCV. There is a statistically significant difference (P <0.001). Also, all thalassemic patients with HCV received it orally, compared to 96.6% of those without. The difference is not statistically significant (P = 0.246). 89.2% of thalassemic patients with HCV received iron chelating agents regularly, compared to 84.5% of those without. The difference is not statistically significant (P = 0.427). Regarding the frequency of measuring ferritin, 78.9% of thalassemic patients with HCV measured it every 3 months, compared to 44.5% of those without HCV, and 21.1% of those with HCV measured ferritin every 6 months, compared to 49.2% of those without HCV. The distinction is statistically significant (P< 0.001),(**Table. 6**).

Table 6. The relationship between HCV and iron chelating agents in the studied thalassemic patients

Characteristics		**Thalassemic patients with HCV (N=38)**		**Thalassemic patients without HCV (N=362)**		**P value**
	Total	**Number**	**%**	**Number**	**%**	
Iron chelating agents						
Receiving	270	37	97.4%	233	64.4%	**<0.001***
Not receiving	130	1	2.6%	129	35.6%	
Route of administration (N=270)						
Oral	262	37	100%	225	96.6%	**0.253**
Subcutaneous	8	0	0%	8	3.4%	
Regularity of receiving iron chelating agents (N=270)						
Regular	230	33	89.2%	194	84.5%	**0.461**
Unregular	40	4	10.8%	36	15.5%	
Frequency of measuring ferritin						
Every 3 months	191	30	78.9%	161	44.5%	**<0.001***
Every 6 months	186	8	21.1%	178	49.2%	
Every year	23	0	0%	23	6.4%	
Age at start of iron chelating agents (years)		**Mean**	**SD**	**Mean**	**SD**	**0.069(#)**
		9.8919	8.96	7.05	5.66975	

*Chi square test – (#)student's t test

Multivariable logistic regression analysis for risk factors of HCV among the studied thalassemic patients

(Table.7) shows logistic regression analysis of HCV among the studied thalassemic patients. There were twelve risk factors for HCV among thalassemic patients. The most important factors were duration of blood

transfusion for more than 15 years, previous surgery and dental procedures, and splenectomy (P< 0.001), followed by patient age of more than 18 years (P = 0.001), urban population and a positive family history of thalassemia (P = 0.001), receiving iron chelating agents (P = 0.003), primary maternal education (P = 0.004), intermediate maternal education (P= 0.008) and splenomegaly (P = 0.009), age between 9 and 18 years, and frequency of blood transfusion (P = 0.054).

Table7. Multivariable logistic regression analysis for risk factors of HCV among the studied thalassemic patients

Variable		Odds ratio OR	95% CI		P value
			Lower	Upper	
Longer Duration of blood transfusion	15 years or more	3.489	2.584	4.710	**<0.001**
Dental procedure	Yes	4.182	2.688	6.507	**<0.001**
Splenectomy	Yes	3.334	2.755	4.036	**<0.001**
Previous surgery	Yes	2.398	2.069	2.780	**<0.001**
Age (years)	9-18	1.480	1.297	1.688	**0.022**
	More than 18	2.469	1.987	3.067	**0.001**
Residence	Urban	2.143	1.456	3.156	**0.001**
Family history of thalassemia	Positive	1.703	1.536	1.888	**0.001**
Iron chelating agents	Receiving	1.513	1.379	1.660	**0.003**
Maternal education	Primary	1.895	1.518	2.365	**0.004**
	Intermediate	1.578	1.330	1.871	**0.008**
Splenomegaly	Yes	1.345	1.239	1.461	**0.009**
Frequency of blood transfusion	Every more than one month	1.260	1.060	1.497	**0.054**

Discussion

In more than 60 nations around the world, thalassemia is the most common single-gene illness. The only other option, except bone marrow transplantation (BMT), is routine transfusion. The need for blood transfusions and, thus, the likelihood of acquiring TTIs have been steadily rising due to ineffective thalassemia prevention **(Saeed et al., 2015).**

According to **Reker and Islam (2014),** the world's highest recorded prevalence of HCV antibodies is found in Egypt. According **to El-Zanaty and Way (2006),** 15% of people in the 15- to 59-year-old age group have antibodies to the HCV virus. According to **Jimenez et al. (2010),** the main cause of HCV transmission in Egypt is insufficient infection management during medical treatment.This study aimed to estimate the prevalence of hepatitis C virus infection in β-thalassemia patients and its correlated risk factors in the Qena

governorate.

In our study, the Prevalence rate of HCV among the studied thalassemic patients was 9.5%. In our study, there was an insignificant difference between thalassemic patients with HCV and those without regarding gender. Moreover; the mean age for positive HCV thalassemic patients was significantly greater (19.76 ± 6.63) years than for negative HCV patients (12.4 ± 6.98).

Our results are in agreement with **Atwa and Wahed (2017)** who reported the prevalence of HCV infection in thalassemic patients in the Fayoum governorate in Egypt was 20.7%. Also, they reported several risk factors such as age, residency in rural areas, and mother education are an important predictor for HCV infection in endemic areas in the Fayoum governorate. Their study revealed that the mean age of HCV-infected cases was significantly greater than that of non-HCV-infected cases. An age ≥10 years was a significant predictor for HCV infection.

In a study done in Mansoura governorate in Egypt, involving two hundred thalassemic patients, 111 (55.5%) males and 89(44.5%) females. The median age was 13 years (ranging from 11 months to 19 years). Out of the 200 patients, 81(40.5%.) were anti-HCV positive by ELISA. This is a relatively high percentage, keeping in mind that all donated blood is regularly screened for HCV at all thalassemic centers in Egypt **(Mansour et al., 2012).**

Another study was conducted in Upper Egypt, involving a total of 97 thalassemic children from both El-Minia, and Sohag governorates, 36.08% of patients were female, and 63.92% were male. The mean age at the time of the study was 8.89 (5.07) years (range: 6-18 years)**.** A total of 36 patients (37.11%) were found to have anti-HCV antibody positive **(Mahmoud et al., 2016).**

Another study conducted in the El-Minia governorate in Egypt revealed a prevalence rate of 38.5% of HCV infection in thalassemic patients. Out of 200 patients, there were 77(38.5 %) were positive for anti-HCV- antibodies. The remaining 123(61.5%) were seronegative **(El-Fouly et al., 2019)**.

Another study in Ismalia-Egypt included 25 cases with transfusion-dependent Beta thalassemia, 9 males and 16 females with a mean age of 10.56 ± 3.96 years and the age range of 5-18 years. 16(64%) of the studied thalassemic patients use Desferroxamine while only 7(28%) use oral chelating agents, 16(64%) have frequent blood transfusions every month, 9(36%) have frequent blood transfusions every 2 months, a splenectomy was performed in 12(48%) of them, HCV-Ab was positive in 8(32%) of thalassemia cases, and ferritin was found to be elevated more than 1000µg/l in 15(60%) of cases **(Ibrahim et al., 2011).**

The prevalence rate of HCV in thalassemic patients in Egypt is high when compared with the prevalence rate in Iraq, as the infection percentage of HCV in thalassemia patients was reported to be 3.8% in a study by **(Jallab and Easa, 2020)** who evaluated 80 thalassemic patients regularly visit the thalassemia center in AD-diwaniyah for transfusion therapy (at least once monthly).

Our study was partially consistent with the findings of **Al-Moshary et al. (2019)** in a study conducted in Pakistan. A total of 431 patients were included in this study. The age of patients ranged from five years to 23 years with the mean age of patients being 11.54 ± 3.6 years, with a high proportion of HCV in males 71 (27.95%) compared to the female 31 (17.51%) patients; however, this difference was not statistically significant (p = 0.31). A total of 254 (58.93%) were male and the rest were female with a male-to-female ratio of 1.43:1. Other previous studies showed similar figures; a study in the Middle East and North Africa showed an average age of 11.5 ± 5.2 years in β-thalassemia patients **(Harfouche et al., 2017).** However, the study by **Ansari et al. (2012)** reported an estimated average age of 8.5 ± 6.42 years.

In different parts of the world, the prevalence of HCV infection in thalassemic patients differs: A study done in the south of Iran revealed a prevalence rate of 17.6% of HCV-positive thalassemic patients. Serum samples were obtained from 125 patients with β-thalassemia major. Of the 125 thalassemia patients, 22 cases were positive for anti-HCV antibodies **(Farshadpour and Taherkhani, 2022)**.

However, Another study conducted in Pakistan found a prevalence rate of HCV of 28.1% in thalassemic patients. Out of the total 224 Thalassemia patients, 123 (54.9%) were male and 101 (45.1%) were female. In this study, the mean age of patients was calculated to be 7.51± 4.67 years, ranging from 1-18 years **(Mahmood et al., 2022).**

In terms of thalassemia family history, in our study, there is a statistically significant (P < 0.001) difference between thalassemic patients with HCV and those without**.** In the study conducted in Pakistan, 91(42.3%) of thalassemic patients with HCV had a positive family history of thalassemia and 52(44.1%) of them did not have a family history while the rest of them did not know **(Yasmeen and Hasnain, 2019)**.

In our study, 36 (94.7%) of thalassemic patients with HCV had previous surgery compared to 39.5% of those without. This does not agree with the study conducted in the Fayoum governorate where 9(40.9%) of thalassemic patients with HCV had a history of previous surgery compared to 34(34.4%) in those without HCV **(Atwa and Wahed, 2017).**

In our study, thirty-eight (100%) of thalassemic patients with HCV had splenomegaly compared to 262 (72.4%) in those without. The difference is statistically significant (P= 0.001).

In a study conducted in Pakistan, 22(52.4%) of thalassemic patients with HCV had splenomegaly compared to 20 (47.6%) in those without. The difference was statistically insignificant (p=0.04) **(Yasmeen and Hasnain, 2019)**.

In our study, eight (21.1%) of thalassemic patients with HCV had hepatomegaly compared to 69(19.1%) in those without. The difference is statistically significant (p=0.001).

In the study conducted in Pakistan, eight (72.7%) of thalassemic patients with HCV had hepatomegaly compared to 3(27.3%) in those without. The difference was statistically insignificant (p=0.04) **(Yasmeen and Hasnain, 2019)**.

In our study, thirty-five (92.1%) of thalassemic patients with HCV had splenectomy compared to 100(27.6%) in those without. The difference was statistically significant (p<0.001).

In the study conducted in Pakistan, ten (66.7%) of thalassemic patients with HCV had splenectomy compared to 5(33.3%) those without. The difference was statistically insignificant.

Conclusion

The prevalence of HCV infection in the studied thalassemic patients was 9.5%. The most important risk factors for HCV infection were duration of blood transfusion for more than 15 years, previous surgery, dental procedure, and splenectomy. Older patients were at higher risk for HCV infection. The risk increased with patients aged more than 18 years old. A family history of thalassemia was a risk factor for HCV infection.

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