

PREVALENCE OF HEPATITIS C VIRUS INFECTION IN B- THALASSEMIA PATIENTS

Sahar Kareem Raheem^{1*}, Seveem Omran Jasim² and Ayser Fathi Abdurraheem³

¹Family Medicine Specialist, Al Salam University College, Baghdad, Iraq.

²Medical City, Baghdad, Iraq.

³Fathi Abdurraheem, Baghdad Al-Rusafa Health Directorate, Baghdad, Iraq.

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*Corresponding Author: Sahar Kareem Raheem

Family Medicine Specialist, Al Salam University College, Baghdad, Iraq.

ABSTRACT

Background: The incidence of transfusion-associated hepatitis has decreased significantly with donor screening for HCV antibodies. However, thalassemia patients still face high liver disease rates due to transfusion-related iron overload and infections from blood-borne agents. HCV is the primary cause of post-transfusion non-A-non-B hepatitis in patients with β -thalassemia major. **Method:** The prevalence of blood-borne viral infections in multi-transfused patients correlates with community virus prevalence. A cross-sectional study conducted from December 1, 2008, to May 31, 2009, examined the prevalence and epidemiological changes of HCV infection in 513 thalassemic patients at Al-Karamah Teaching Hospital. Data were collected using a questionnaire, direct patient interviews, and hospital case reports. **Results:** The study found a male-to-female ratio of 1.3:1, with the most affected age group being 15-19 years (42.7%). A high proportion had low education levels and lived in Baghdad (26%), with family origins from other governorates (29.6%). Most were unemployed (27.3%), diagnosed with thalassemia at one year or older (23.5%), and first received blood between 6 months to one year of age (28.8%). Positive cases often had consanguineous parents (26.6%), no family history of HCV (27.4%), and received desferrioxamine (27.8%). Clinically, 27.5% were pale, 36.7% had jaundice, 37.5% had hepatosplenomegaly, and 43.5% had elevated liver function tests. **Conclusion:** It is recommended to implement a national survey of blood-borne infections, particularly HCV, among thalassemia patients. An effective health education program should discourage consanguineous marriages, especially among families with a history of thalassemia. Community engagement is crucial in preventing thalassemia syndromes.

KEYWORDS: Prevalence, Hepatitis c virus, B thalassemia.

INTRODUCTION

Thalassemia, the most common monogenic disease, was first recognized in 1925 by Thomas B. Cooley. It encompasses a heterogeneous group of genetic disorders characterized by reduced synthesis of alpha (α) or beta (β) polypeptide chains, forming normal adult hemoglobin (Hb) molecules, leading to decreased Hb content in red blood cells (RBCs)^[1] Thalassemia results in underproduction of normal globin proteins, often due to mutations in regulatory genes.^[2] The disease is particularly prevalent among Mediterranean populations, hence its name: "Thalassa" (Greek for sea) and "Haema" (Greek for blood), and is inherited as an autosomal recessive trait. Thalassemia causes anemia with hypochromia and microcytosis, leading to ineffective erythropoiesis and hemolysis. Clinical manifestations range from asymptomatic microcytosis to severe anemia, which can be fatal in utero.^[3] Thalassemias are prevalent in populations from humid climates and affect all races,

particularly Arabs, people of Mediterranean origin, and Asians.^[4] According to WHO (1994), 3% of the Iraqi population carries β -thalassemia, with higher prevalence in Misaan, Diyala, Baghdad, and Mosul.^[5,6] Types of thalassemia include alpha (α) thalassemia, involving genes HBA1 & HBA2, and beta (β) thalassemia, resulting from over 150 mutations in the HBB gene on chromosome 11, leading to subtypes such as β thalassemia minor, β thalassemia major, and thalassemia intermedia.^[1,3] Clinical features of thalassemia include craniofacial abnormalities, hepatosplenomegaly, iron overload, osteoporosis, infections, skin darkening, and complications like gallstones, secondary gout, and bleeding disorders.^[7] Consanguineous marriages, common in the Eastern Mediterranean region, increase the risk of recessive inherited disorders, including thalassemia.^[1] Modern therapy has significantly improved the prognosis and quality of life for patients with β -thalassemia major, preventing severe skeletal

changes and cosmetic abnormalities. Prognosis depends on therapy compliance, with childhood or early second-decade deaths often due to inadequate transfusions, severe anemia, infections (mainly HCV), and hypersplenism.^[1] The thalassemia program in Iraq, established in 1989 by the Ministry of Health in collaboration with WHO, provides comprehensive medical services, including blood supply, medical services, staff training, family planning, health education, carrier identification, premarital screening, and prenatal diagnosis.^[1,8] Hepatitis C Virus (HCV) infection, first identified in 1989, is a major global health problem, with an estimated 170 million chronically infected individuals worldwide.^[9,10] Prevalence is highest in Africa and Asia, with Egypt reporting up to 22%, and lowest in industrialized countries like Germany (0.6%).^[11] HCV, a single-stranded RNA virus, causes over 80% of post-transfusion hepatitis cases and many sporadic hepatitis cases.^[12] The incubation period averages 2 weeks to 6 months, with clinical illness often mild or asymptomatic.^[9] About 15-25% of infected individuals recover spontaneously, while 10-20% develop cirrhosis, and 1-5% develop hepatocellular carcinoma.^[13] HCV diagnosis before the 1990s relied on enzyme immunoassays, with confirmation by recombinant immunoblot assay (RIBA).^[14] No vaccine is available, and treatment for chronic HCV is costly. Reducing HCV transmission through safe blood transfusions, sterilized medical procedures, and reducing high-risk behaviors is crucial. Up to 13 million units of the global blood supply are not adequately screened for transfusion-transmissible infections, underscoring the need for reliable, affordable diagnostic tests.^[15] Interferon-alpha (IFN- α) monotherapy is the first-line treatment for HCV in transfusion-dependent thalassemic patients. Hemolytic complications of ribavirin restrict its combination with IFN to investigational settings.^[16] Advances in treatment include pegylated interferon (PEG-IFN), which has improved HCV management.^[17,18] The current study aimed to: (1) provide information on the prevalence of HCV infection among thalassemic patients, and (2) monitor changes in the epidemiology, including the frequency and characteristics, of HCV infection.

METHOD

A descriptive cross-sectional study was conducted at the Haemoglobinopathy Center in AL-Karamah Teaching Hospital, a consultant clinic with an in-patient ward. The diagnosis of thalassemia was confirmed by a specialized doctor. Data collection spanned six months, from December 1, 2008, to May 31, 2009, with regular visits three times a week. The study included all transfusion-dependent β -thalassemia patients (major and intermediate) attending the center. Exclusion criteria were thalassemia minor patients, sickle cell disease and other hemoglobinopathies, alpha thalassemia cases, patients who did not attend the center for six months for unknown reasons, those transferred to other centers, and deceased patients. Pilot study cases were also excluded.

Data were collected through direct interviews using a well-designed questionnaire (Appendix 1) and from hospital records. The questionnaire covered:

1. **Demographic Information:** Name, age, sex, address, family origin, occupation, and education level.
2. **Risk Factors:** Age at first diagnosis, age at first blood transfusion, parental relation (consanguinity), family history of thalassemia, associated diseases, compliance to therapy, monthly blood transfusion frequency, family knowledge about HCV infection and transmission, and history of injectable drug use.
3. **General Examination:** Assessment for weakness, pallor, jaundice, hepatosplenomegaly, and splenectomy.
4. **Investigations:** Blood group and Rh, liver function tests, and anti-HCV antibody.

A pilot study was conducted two weeks prior to the main study on 20 cases to determine the average time required for file review, physical examination, and patient interviews. This led to adjustments in the questionnaire.

Inclusion and Exclusion Criteria

Inclusion Criteria

1. All age groups and both sexes.
2. Transfusion-dependent thalassemia major and intermediate.

Exclusion Criteria

- Thalassemia minor patients.
- Sickle cell disease and other hemoglobinopathies.
- Alpha thalassemia cases.
- Patients not attending the center for six months.
- Patients transferred to other centers and deceased patients.
- Pilot study cases.

Statistical Analysis

Data analysis was performed using SPSS version 15. The analysis included:

- Frequency distribution for selected variables.
- Mean \pm standard deviation (min-max) for quantitative data.
- Pearson chi-squared test for the significance of association between categorical variables.
- T-test for the significance of difference between two independent means.
- Statistical significance was set at $P \leq 0.05$.

RESULTS

Table 1: Association of HCV positive cases according to sex, age, address and family origin, association of HCV positive cases according to sex shows that mainly among males (88; 30.3%), and it was more in age group 15-19 years (50; 42.7%), that means it was more among adolescent, it was significant statistically ($p=0.0001$), most patients were living in Baghdad center (67; 26%), and who were their family origin was from other

governorate (66; 29.6%). Table 2: Association of HCV +ve cases according to occupation, education, marital state, family size and socio economic status, Most cases were not worker (133; 27.3%), and had level of education mainly those between primary and secondary it was significant at (p=0.021), and distributed between

single (79; 38.2%) and child (57; 19.3%), it was significant (p= 0.0001), family size mainly those of 6 (41; 25.2%) and the rest was distributed among others (>=8, 7, 5 and 4) regarding socio economic status the infection was mainly between medium and low (table2).

Table 1: Association of HCV positive cases according to sex, age, address, family origin.

	Total		HC Post		Chi	d.f.	p
	No	%	No	%			
Sex Male	290	56.5	88	30.3	3.137	1	0.077
Female	223	43.5	52	23.3			
Age (years) 1--4	16	3.1	-	-	42.02	5	0.0001*
5--9	113	22.0	8	7.1			
10--14	150	29.2	44	29.3			
15--19	117	22.8	50	42.7			
20--24	69	13.5	24	34.8			
25--29	32	6.2	12	37.5			
=>30	16	3.1	2	12.5			
Current address Baghdad=center	258	50.3	67	26.0	1.275	2	0.529
Baghdad=peripheral	130	25.3	34	26.2			
Other governorates	125	24.4	39	31.2			
Origin of the family Baghdad=center	169	32.9	47	27.8	2.131	2	0.345
Baghdad=peripheral	121	23.6	27	22.3			
Other governorates	223	43.5	66	29.6			

* The Pearson chi-square statistic is significant at the 0.05 level.

Table 2: Association of HCV +ve cases according to occupation, education, marital state, family size, socio economic state.

		No	%	No	%	Chi	d.f.	P
		Occupation	Yes	25	4.9			
	No	488	95.1	133	27.3			
Level of education	Baby	31	6.0	-	-	11.59	4	0.021*
	Illiterate	10	1.9	3	30.0			
	1-6	295	57.5	73	24.7			
	7-12	125	24.4	51	40.8			
	>12	42	8.2	11	26.2			
	Higher education	10	1.9	2	20.0			
Marital status	Child	296	57.7	57	19.3	22.776	2	0.0001*
	Single	207	40.4	79	38.2			
	Married	10	1.9	4	40.0			
Family size	3	7	1.4	-	-	7.97	4	0.093
	4	38	7.4	10	26.3			
	5	81	15.8	21	25.9			
	6	163	31.8	41	25.2			
	7	83	16.2	33	39.8			
	=>8	141	27.5	35	24.8			
Socio economic state	Low	224	43.7	68	30.4	1.88	1	0.170
	Medium	288	56.1	72	25.0			
	High	1	0.2	-	-			

* The Pearson chi-square statistic is significant at the 0.05 level.

The association of HCV positive cases showed that patients diagnosed with thalassemia at age one year or older and those diagnosed between 6 months to one year were mainly thalassemia major cases, with a statistically

significant rate of 29% (p=0.009). More HCV-infected cases were found among patients from consanguineous marriages and those with a family history of thalassemia, at rates of 26.6% and 28.8% respectively. Most HCV

positive patients had no associated medical history (21.1%), while others had conditions like heart failure or cardiomyopathy (43.2%), with a significance level of $p=0.0001$. Higher HCV cases were seen in patients who

started blood transfusions at 6 months to one year (28.8%). A high proportion of cases took 2 pints of blood per month (27.2%), also significant at $p=0.0001$. as show in table 3 and 4.

Table 3: Association of HCV +ve cases according to (age of first diagnosis. and type of thalassaemia).

	Total		HC Post		Chi	d.f.	P
	No	%	No	%			
Age first diagnosed 1 month	6	1.2	1	16.7	6.390	6	0.381
2 months	17	3.3	8	47.1			
3 months	59	11.5	19	32.2			
4 months	25	4.9	8	32.0			
5 months	16	3.1	5	31.3			
6 months - <1 year	177	34.5	49	27.7			
1 year and more	213	41.5	50	23.5			
Type of thalassaemia Major	462	90.1	134	29.0	6.879	1	0.009*
Intermediate	51	9.9	6	11.8			

* The Pearson chi-square statistic is significant at the 0.05 level.

Table 4: Association of HCV +ve cases according to relative, family history, medical history, age and date when took first pint of blood, regularity and compliance of management and number of pints per month.

	Total		HC Post		Chi	d.f.	P
	No	%	No	%			
Are parents relatives Yes	398	77.6	106	26.6	0.387	1	0.534
No	115	22.4	34	29.6			
Family history of thalassaemia Yes	316	61.6	91	28.8	0.942	1	0.332
No	197	38.4	49	24.9			
Associated medical history Hypertension	2	0.4	-	-	25.50	2	0.0001*
Diabetes mellitus	7	1.4	3	42.9			
Others	139	27.1	60	43.2			
No	365	71.2	77	21.1			
Age when took first pint of blood 1 month	6	1.2	1	16.7	7.910	6	0.245
2 months	16	3.1	8	50.0			
3 months	59	11.5	20	33.9			
4 months	27	5.3	7	25.9			
5 months	13	2.5	3	23.1			
6 months - <1 year	177	34.5	51	28.8			
1 year and more	215	41.9	50	23.3			
When took first pint of blood <1980	10	1.9	2	20.0	48.85	5	0.0001*
1980--1984	25	4.9	9	36.0			
1985--1989	60	11.7	22	36.7			
1990--1994	112	21.8	50	44.6			
1994--1999	126	24.6	39	31.0			
2000-2004	144	28.1	18	12.5			
2005-2009	36	7.0	-	-			
Regular visit Yes	435	84.8	115	26.4	1.051	1	0.305
No	78	15.2	25	32.1			
Compliance Yes	323	63.0	84	26.0	0.725	1	0.395
No	190	37.0	56	29.5			
How many blood pints/month 1	155	30.2	59	38.1	24.468	3	0.0001*
2	254	49.5	69	27.2			
3	66	12.9	11	16.7			
4	38	7.4	1	2.6			

• The Pearson chi-square statistic is significant at the 0.05 level.

Table 5: Clinical and Behavioral Associations

- **Site of Blood Transfusion:** 32.1% of HCV positive cases received blood transfusions outside the center (p=0.013).
- **Knowledge of HCV Transmission:** 37.3% of positive cases had information about HCV transmission (p=0.0001).
- **Family History and Drug Use:** Most positive cases had no family history of HCV and no history of drug injection. All positive cases received desferrioxamine injections (27.8%).
- **Clinical Examination:**
 - 26.2% of cases showed no weakness (p=0.029).

- 27.5% had pallor.
- 36.7% had jaundice (p=0.0001).
- 37.5% had hepatosplenomegaly (p=0.0001).
- 22.7% did not have a splenectomy (p=0.0001).

Table 6: Blood Group and Liver Function Test Associations

- **Blood Group and Rh:** HCV positive cases were mainly in blood groups O and A, and Rh positive.
- **Liver Function Tests:** 43.5% of cases had elevated liver enzymes (p=0.0001).

Table 5: Association of HCV +ve cases according to (history of site of blood taken, knowledge, history of HCV, history of drug injection, alcohol, tattoo and to clinical examination.)

		Total		HC Post		Chi	d.f.	P
		No	%	No	%			
Is the patient took blood from other side than the center	Yes	251	48.9	81	32.3	6.144	1	0.013*
	No	262	51.1	59	22.5			
Knowledge of family and patient about HCV infection mode of transmission	Yes	260	50.7	97	37.3	26.660	1	0.0001*
	No	253	49.3	43	17.0			
Family history HCV	Yes	17	3.3	4	23.5	0.125	1	0.723
	No	496	96.7	136	27.4			
That taken by injection	Yes	25	4.9	10	40.0	2.139	1	0.144
	No	488	95.1	130	26.6			
Desferrioxamin injection	Yes	504	98.2	140	27.8	-		-
	No	9	1.8	-	-			
Alcohol consumption	Yes	1	0.2	-	-	-		-
	No	512	99.8	140	27.3			
Tattooing	Yes	3	0.6	1	33.3	0.056	1	0.814
	No	510	99.4	139	27.3			
Weakness	Yes	29	5.7	13	44.8	4.764	1	0.029*
	No	484	94.3	127	26.2			
Pallor	Yes	509	99.2	140	27.5	-		-
	No	4	0.8	-	-			
Jaundice	Yes	237	46.2	87	36.7	19.693	1	0.0001*
	No	276	53.8	53	19.2			
Hepatosplenomegaly	Yes	317	61.8	119	37.5	43.922	1	0.0001*
	No	196	38.2	21	10.7			
Splenectomy history	Yes	104	20.3	47	45.2	21.068	1	0.0001*
	No	409	79.7	93	22.7			

The Pearson chi-square statistic is significant at the 0.05 level.

Table 6: Association of HCV +ve cases according to blood group & Rh, Liver Function Test.

	Total		HC Post		Chi	d.f.	P
	No	%	No	%			
Blood group A	149	29.0	39	26.2	1.423	3	0.700
AB	30	5.9	7	23.3			
B	142	27.7	36	25.4			
O	192	37.4	58	30.2			
Rh Rh positive	472	92.2	132	28.0	1.178	1	0.278
Rh négative	40	7.8	8	20.0			
Liver fonction test Normal	214	41.7	10	4.7	94.656	1	0.0001*
Elevâtes	299	58.3	130	43.5			

*The Pearson chi-square statistic is significant at the 0.05 level.

Table 7: [Mean \pm SD (Min-Max)]. Of thalassemia patients with HCV positive and negative cases, relation to age, the mean age of diagnosis of HCV infection +ve was (17.06 \pm 6.64) 6y – 60 years *Significant at (p=0.0001), the mean age months when first diagnosed

as thalassemia (13.72 \pm 16.33) 1 –72 months, the mean age months when took first pint of blood (13.82 \pm 16.40) 1 –72 months, according to whole blood pints' number (197.63 \pm 111.25) 24 –846.

Table 7: Profile of thalassemia patients [Mean \pm SD (Min-Max)].

	Total	Anti HC Ab positive	Anti HC Ab negative	Z-value	d.f.	P value
Age (years)	14.88 \pm 7.77 (6m-67y)	17.06 \pm 6.64 (6y-60y)	14.06 \pm 8.01 (6m-67y)	3.941	511	0.0001*
Age (months) when first diagnosed as thalassemia	19.16 \pm 43.52 (1-660)	13.72 \pm 16.33 (1-72)	21.20 \pm 49.92 (1-660)	1.737	511	0.083
Age (months) when took first pint of blood	19.25 \pm 46.08 (1-696)	13.82 \pm 16.40 (1-72)	21.29 \pm 52.98 (1-696)	1.637	511	0.102
Blood pint	-	197.63 \pm 111.25 (24-846)	-	-	-	-

*Significant at 0.05 level of significance using Z- value for two independent mean.

DISCUSSION

This cross-sectional study identified a higher prevalence rate of HCV in thalassemic Iraqi patients compared to previous reports. In Iraq, the HCV-antibody seroprevalence among pregnant women in 2002 was recorded at 3.2%, reflecting the seroprevalence among the general population.^[19] The age range of thalassemia patients with HCV infection in this study was 6-60 years, with a prevalence of 27.29% among β -thalassemia patients. Among the age group 1-9 years, the HCV infection rate was 7.1% (129 patients), lower than the 67.3% reported in a 1998 Baghdad study with a larger sample of 559 patients.^[8] For the age group 5-29 years, the current study showed a 28.6% infection rate among 481 patients, compared to 37.4% in a 2005 study conducted in Baghdad with 1800 patients.^[1] In the 5-9 years age group, 7.1% of 113 patients were infected, significantly lower than the 12.5% reported in a 2003 study in Bangladesh with 152 patients.^[20] For patients aged 1-24 years, the current study found a 27% infection rate among 465 patients, lower than the 60% reported in a 2005 Delhi study with 50 patients.^[21] The 35.1% infection rate among 336 patients aged 10-24 years in the current study was lower than the 80% reported in a 1999 multi-center study with 48 samples.^[22] The overall prevalence of 27.29% among 513 patients was also lower than the 47.1% reported in a 1999 Lebanese study with 17 patients^[23] and the 35% reported among 100 Pakistani patients in 1999.^[24] In comparison, the infection rate in this study was significantly lower than the 55.5% and 46.7% reported in a 2000 Myanmar-Japan cooperation study at the Yangon General and Children's Hospitals with 102 patients.^[25] The 27.29% prevalence was also lower than the 35% found in a 2000-2003 Rawalpindi survey with 40 patients^[26], and the 63.8% reported in a 2001 North Iran study.^[27] A study in Bari in 1998 reported a 22% infection rate among patients aged 5 months to 3 years, while the current study found no positive cases in that age group.^[28] The 27.29% prevalence was comparable to an Indian study of 39 patients followed up from 1993-1995, which showed a gradual increase in positivity from 23% to 35.9% over

three years.^[29] The current study's rate was slightly higher than the 22.4% reported in a 1998 Malaysian study with 85 patients.^[30] An Indian study in 2002 with 50 patients aged 5-15 years reported a 30% infection rate, compared to 36.4% among 263 patients in the same age group in the current study.^[31] The present study's results were higher than the 17.1% reported in a 1998 Indian study^[32] and the 14.8% in a multi-center prospective study with 1481 thalassemics in 31 centers.^[33] The current study's rate was also higher than the 5.1% reported in a 2007 study in Markazi province, Iran.^[34] Household contact is significant for HCV transmission, as a 1999 Karachi study found that 20.5% of household contacts of HCV-positive thalassemic children were also positive for anti-HCV antibodies.^[35]

CONCLUSION

Hepatitis C virus infection is slightly more common among thalassemia patients in Iraq, particularly affecting males and those aged 15-19. A high proportion of cases had low education levels, and about one-third were of blood group O and Rh+ve. Less than half of the positive cases had elevated liver enzymes, with β -thalassemia major being the predominant type, and increasing cases linked to consanguineous marriages.

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