

# Seroprevalence of Transfusion-transmitted Infections Among Multi-transfused Patients in Southwest Iran, Khuzestan Province

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## Abstract

**Background:** Transfusion-transmitted infections (TTIs) continue to be a problem in many parts of the world and multi-transfused patients are at a particularly increased risk for TTIs. The aim of this study was to determine the prevalence of Hepatitis C, Hepatitis B, and human immunodeficiency virus (HIV) infections among multi-transfused patients in Khuzestan Province.

**Materials and Methods:** A cross-sectional study was conducted on 349 multi-transfusion patients referred to the Hemoglobinopathy and Thalassemia Research Center from January 2007 to February 2008.

**Results:** Out of 349 patients, 205 (58.7%) and 144 (41.3%) were men and women, respectively. Mean ( $\pm$ SD) age of the participants was 18.70 $\pm$ 9.18 years. Of these 349 multi-transfused patients, 206 (59%) had thalassemia, 87 (24%) hemophilia, and 56 (16%) sickle cell anemia. The overall prevalence of HBsAg, anti-HCV, and anti-HIV were 0.6% (95% CI: 0-1.56), 28.4% (95% CI: 27.4-29.3), and 0.9% (95% CI: 0-1.86), respectively. The data indicate that anti-HCV positivity was significantly associated with an older age ( $P<0.001$ ), longer duration of transfusion ( $P<0.001$ ), and frequency of transfusion ( $P<0.001$ ).

**Conclusion:** Although it seems more sensitive screening tests and stringent donor selection procedures has reduced HCV infection, TTIs in multi-transfusion patients are still a serious risk for these patients. More stringent policy for blood product usage and continuous awareness programs for medical staff, general population, and patients are required to reduce the incidence of TTIs.

**Keywords:** Seroprevalence, Transfusion, Infection, Iran.

## Introduction

Transfusion-transmitted infections (TTIs) such as hepatitis B virus (HBV), Hepatitis C virus (HCV), and human immunodeficiency virus (HIV) continue to be a problem in many parts of the world, especially among multi-transfused patients. Regular blood or blood products transfusion in patients with thalassemia, hemophilia, and sickle cell anemia has improved their overall survival, but carries a definite risk of acquisition of blood-borne virus infections.<sup>1,2</sup> Improvement of the people's knowledge about TTI risk factors, blood screening strategies, and national HBV vaccination program since 1993 for all neonates have led to a dramatically decrease in prevalence of TTIs particularly HBV during the last decades.<sup>1,3</sup> However, post-transfusion transmission of HCV has still remained a major health concern in multi-transfused patients.<sup>4</sup>

Khuzestan Province located in the Southwest of Iran is a tropical area with an approximate population of 4.5 millions. It shares a land, river, and sea border with Iraq and Arabian countries along Persian Gulf. Khuzestan has suffered the heaviest damage among all Iranian provinces during a 28-year period including: the Iran-Iraq War (1980-1988), the Persian Gulf War (1990-1991), and the 18-year crisis in Iraq (1990-2008).<sup>5</sup> This geographical situation, mass immigration from Iraq, and frequent travels to Iraq and Arabian countries have all affected prevalence of TTIs in Khuzestan Province. Moreover, hemoglobinopathies (particularly thalassemia) are important health problems throughout Iran particularly in this region.

Due to the lack of sufficient reported data from our region, the current study, the first of its kind in

Southwest Iran, was conducted to investigate the prevalence of transfusion transmitted infections among multi-transfused patients in Khuzestan Province.

Material and Methods

Patients

This cross-sectional study was performed from January 2007 to February 2008 in Khuzestan Province on multi-transfused patients referred to Research Center of Thalassemia and Hemoglobinopathies (RCTH) in Khuzestan Province, southwest of Iran. The study protocol was approved by our institutional review board. A total of 349 whole blood samples were collected from the patients, after obtaining an informed consent. Serum samples were separated from the whole blood, aliquoted and stored at -20° C. Demographic data, such as age, duration, and number of blood transfusions were obtained from patient records.

Laboratory assays

All sera were screened using HBsAg, anti-HCV, and anti-HIV assays with commercial ELISA microplate kits (RADIM, Italy) according to the manufacturer’s instructions. Positive samples for anti-HCV and anti-HIV were confirmed using the second generation of recombinant immunoblot assay (RIBA) kits (HCV blot 3.0; Genelabs Diagnostics, Singapore) as a confirmatory test.

Statistical analysis

Prevalence and 95% confidence intervals (95%

CI) were calculated by SPSS software version 13.0 (SPSS Inc., Chicago, IL). Data comparisons were performed using the Chi-square test with Fisher’s exact and two-tailed t-test. The differences were considered significant if p-value<0.05.

Results

Three hundred and forty-nine multi-transfused patients were tested. There were 205 (58.7%) males and 144 (41.3%) females; their mean age (±SD) was 18.70±9.18 years (range 2–69 years) (table 1). Of these 349 multi-transfused patients, 206 (59%) had thalassemia, 87 (24%) were living with hemophilia and 56 (16%) had sickle cell anemia. Of thalassemia patients, 52.9% were female and 47.1% were male (table 2).

Ninety-nine patients were positive for HCV antibodies, for a prevalence rate of 28.4% (95% CI: 27.4-29.3). The prevalence in males was 33.2 % (95% CI: 31.9-34.4) and significantly higher than in females, 21.5% (95% CI: 20-23) (table 1). Hemophiliacs had the highest prevalence of anti-HCV, 54% (95% CI: 51.5-56.5) compared to 22.3% (95% CI: 21.4-23.1) among thalassemia patients, and 10.7% (95% CI: 7.92-13.48) among sickle-cell anemia patients (table 3). Two patients (0.6%, 95% CI: 0-1.56) were found to be HBsAg positive. One of them had hemophilia indicating a prevalence rate of 1.1% (95% CI: 0-3.6) and the other one had sickle cell showing a prevalence rate of 1.8% (95% CI: 0-4.58). Three patients (0.9%, 95% CI: 0-1.86) were found to be anti-HIV positive. All of them were hemophiliac for a prevalence rate of 3.4% (95% CI:

Table 1. Prevalence of TTIs’ serologic markers in multi-transfused patients by gender, age, duration of transfusion, and number of transfused units

Features	No.	HBsAg			TTI-Serologic Markers			Anti-HIV		
		%Negative (n=347)	%Positive (n=2)	P value	%Negative (n=250)	%Positive (n=99)	P value	%Negative (n=346)	%Positive (n=3)	P value
gender				0.5			<0.02			0.2
Male	205	99	1		66.8	33.2		98.5	1.5	
Female	144	100	0		78.5	21.5		100	0	
Age groups				0.5			<0.001			0.2
≤10	84	100	0		92.9	7.1		100	0	
11-21	180	99.4	0.6		80.6	19.4		99.4	0.6	
≥22	85	98.8	1.2		31.8	68.2		97.6	2.4	
Duration of transfusion (years)				0.1			<0.001			0.2
≤10	61	100	0		98.4	1.6		100	0	
10-20	175	100	0		79.4	20.6		99.4	0.6	
≥21	113	98.2	1.8		45.1	54.9		97.6	2.4	
No. of units transfused				0.3			0.001			0.9
≤100	60	100	0		85	15		100	0	
100-200	112	100	0		78.6	21.4		100	0	
>200	177	175	2		62.7	37.3		98.3	1.7	

These results indicate that in the male group of patients, 33.2% (68/205) were anti-HCV positive compared to 21.5% (31/144) in the female group, a difference that is statistically significant ( $p<0.02$ ).

In all diagnostic categories, anti-HCV positivity was correlated to the amount of transfused blood (table 4). In addition to the amount of transfused blood, the duration of transfusion, in patients with thalassemia, influenced the rate of anti-HCV positivity (table 4). The results indicate anti-HCV positivity was significantly associated with an older age ( $p<0.001$ ), longer duration of transfusion ( $p<0.001$ ), and frequency of transfusion ( $p<0.001$ ) (table 4).

## Discussion

This is the first study that incorporates a significant number of multi-transfused patients in Southwest Iran, Khuzestan province. We found that the prevalence of HBsAg, anti-HCV, and anti-HIV were 0.6% (2/349), 28.4% (99/349) and 0.9% (3/349), respectively.

Prevalence of HCV in blood donors among different provinces of Iran has been reported to be 0.3–0.97% (4.6-8), whereas in our study, HCV positivity was detected in 99 (28.4%) of the 349 multi-transfused patients. This rate is higher than blood donors in our region.

HCV infection was the most prevalent TTI among multi-transfused patients, and was especially common in patients with hemophilia (54%, 47/87). The prevalence of HCV infection in Iranian

hemophilia patients is from 15.65% in Fars Province, a southern district of Iran to 76.7% in northwest of Iran reported in different studies.<sup>4,9,10</sup> It has been reported that the prevalence of HCV antibody was directly related to the number of blood transfusions in multi-transfused patients.<sup>11,12</sup> Similarly, we found that the mean number of transfused blood units had statistically significant difference between anti-HCV positive patients (238.62) and negative patients (181.51) in the present study ( $p<0.001$ ).

When serologic tests for HBV and HCV became available, blood donor screening began to be performed in most countries. In Iran, mandatory anti-HCV screening was introduced to blood banks in 1996.<sup>4</sup> Our results show that 82.5% of multi-transfused patients included in this study had been transfused more than 10 years and thus had an increased risk of having received blood products which had not been tested for HCV. In our study HCV positive subjects had a significantly higher frequency of blood transfusion ( $p<0.001$ ).

There are more than 25,000 patients with thalassemia major in Iran.<sup>1</sup> It is an important health problem in Iran particularly in Khuzestan Province. The present study showed that the prevalence of HCV in thalassemia patients is 22.3%. In Iran, a recent report from northern part showed a prevalence of 63.8% anti-HCV positivity in thalassemia patients while the prevalence in blood donors was 0.5%. A confirmatory immunoblotting test was employed in HCV-positive patients, which showed that 92.6% of samples were positive.<sup>7</sup> In Shiraz, in south of Iran, It has been reported that

**Table 2.** Distribution of gender, age groups, duration of transfusion, and number of transfused units for each diagnostic category

Features	Diagnostic Category					
	Thalassemia		Hemophilia		Sickle cell anemia	
	n	%	n	%	n	%
gender						
Male	97	47.1	76	87.4	32	57.1
Female	109	52.9	11	12.6	24	42.9
Age groups						
≤10	41	19.9	13	14.9	8	14.3
11-21	121	58.7	33	37.9	21	37.5
≥22	44	21.4	41	47.1	27	48.2
Duration of transfusion (years)						
≤10	53	25.7	13	14.9	19	33.9
10-20	115	55.8	35	40.2	30	53.6
≥21	38	18.4	39	44.8	7	12.5
No. of units transfused						
≤100	40	19.4	9	10.3	11	19.6
100-200	67	32.5	23	26.4	12	21.4
>200	99	48.1	55	63.2	33	58.9

**Table 3.** TTIs' serologic markers for each diagnostic category

Diagnostics Category	TTI-Serologic Markers								
	HBsAg Positive			Anti-HCV Positive			Anti-HIV Positive		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
Thalassemia	0	0	-	46	22.3	21.4-23.1	0	0	-
Hemophilia	1	1.1	0.0-3.6	47	54	51.5-56.5	3	3.4	0.9-5.9
Sickle cell anemia	1	1.8	0.0-4.58	6	10.7	7.92-13.48	0	0	-

**Table 4.** HCV infection among diagnostics categories

Features	Thalassemia			Anti-HCV Hemophilia			Sickle cell anemia		
	Negative (n=16)	Positive (n=46)	P value	Negative (n=40)	Positive (n=47)	P value	Negative (n=50)	Positive (n=6)	P value
Duration of transfusion mean (year±SD)	13.27	18.37	<0.001	15.53	15.57	0.9	15.90	15.67	0.9
Duration of transfusion (years)			0.001			<0.001			0.01
≤10	90.6%	9.4%		100%	0		94.7%	5.3%	
10-20	78.3%	21.7%		77.1%	22.9%		93.3%	6.7%	
≥21	57.9%	42.1%		0	100%		57.1%	42.9%	
Mean of units transfused (No.±SD)	177.11	222.22	<0.003	186.78	255.68	<0.001	187.52	230.67	<0.006
No. of units transfused			<0.02			0.001			0.09
≤100	90%	10%		100%	0	<0.001	100%	0	
100-200	82.1%	17.9%		65.2%	34.8%		100%	0	
>200	69.7%	30.3%		29.1%	70.9%		81.8%	18.2%	

73 out of 466 thalassemia children with a history of multiple transfusions (15.7%) were positive for anti-HCV.<sup>13</sup> Results from another study on Iranian thalassemia patients revealed that 24.2% were anti-HCV positive.<sup>4</sup> Previous single-center studies on Iranian thalassemia patients revealed a wide range of 16 – 64% for prevalence of HCV infection.<sup>1,7,13</sup>

Studies from some neighboring Arabic countries reported an HCV infection rate of 33% in Kuwait and 40% in Bahrain which share sea boarder with Khuzestan Province.<sup>14,15</sup> In addition, the Iran-Iraq War of 1980-1988, has had a devastating impact on regional public health. Moreover, during a period of 18 years, due to poor security and living conditions, many Iraqi refugees have crossed over the Iraqi border to Iran, mainly to the southwestern regions.<sup>12</sup> A significantly higher prevalence of anti-HCV has been found among different populations in Iraq.<sup>16-18</sup>

In our study, HBsAg positivity was found to be 0.6% among the multi-transfused patients and none of the thalassemia patients were HBsAg positive. This rate was less than the rate among blood donors in Iran (0.6% vs. 3%).<sup>3</sup> This low rate may be due to national vaccination against HBV, especially in

patients with thalassemia. Hepatitis B vaccination in multi-transfused patients has decreased the carrier rate among young children significantly.<sup>3</sup> It seems that the average age of the infected individuals has increased. The epidemiology of infection is also changing from a vertical to horizontal route.<sup>3</sup>

In our study three multi-transfused patients were positive for HIV. All of whom were hemophiliacs. The prevalence of HIV infection in thalassemia patients was reported to be 8.9% in India,<sup>19</sup> while it was 1.6% in multi transfused patients in Bahrain.<sup>15</sup> In our study, the prevalence of HIV in multi-transfused patients was 0.9%, which is less than the prevalence found among the Iranian IV drug user population (0.9% vs. 23.2%).<sup>20</sup>

Fortunately, for the time being, HIV infection is not a health concern for multi-transfused population in Iran. This may be due to the relatively low prevalence of HIV infection among general population in Iran, as well as the fact that all donors are screened for HIV. Continued attention to the universal screening of blood products for TTIs as well as a more thorough screening and selection of potential blood donors is necessary to limit the number and rate of TTIs in our region in the future.

This study provides information that will assist in developing intervention guidelines to reduce the risk of acquiring TTIs, which continues to be a significant public health problem in Khuzestan Province.

## Conclusion

In conclusion, prevalence of HCV infection decreased after introduction of screening tests and stringent donor selection procedures, but TTIs in patients with thalassemia, hemophilia and sickle cell anemia are still serious risk for these patients.

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