SEROPREVALENCE OF HIV, SYPHILIS AND HIV/SYPHILIS COINFECTION IN MULTI TRANSFUSED PATIENTS: A CROSS SECTIONAL STUDY

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Author's Contribution:

I.N. and M.B.S. designed the model and the computational framework and analyzed the data. S.N. and M.W. carried out the implementation. I.N. performed the calculations. M.B.S. and S.N. wrote the manuscript with input from all authors. M.W. and I.N. conceived the study and were in charge of overall direction and planning.

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ABSTRACT:

Background:

Transfusion-transmissible infections (TTIs) such as human immunodeficiency virus (HIV) and Syphilis are among the documented dangers to blood safety for recipients. They are also the leading cause of mortality and morbidity in multi transfused patients.

Objective:

The aim of this study was to determine prevalence of HIV, Syphilis and HIV/Syphilis co infection in multi-transfused patients.

Methods:

This cross- sectional study was conducted from January 2020 to January 2021 at Baqai Medical University, Karachi; Fatima Hospital, Karachi and Muhammadi Laboratory and Diagnostic Centre, Numaish, Karachi. A total of 385 multi transfused patients comprising of transfusion dependent beta thalassemia, hemophilia, sickle cell anemia, aplastic anemia, leukemias, chronic renal failure and chronic liver failure of any age and gender were included. Electrochemiluminescence assay was carried out on Cobas e411 analyzer of Roche Diagnostics, Mannheim, Germany for detection of HIV and treponemal antibodies. Reactive samples of syphilis and HIV were confirmed on real time PCR.

Results:

Of all multi-transfused patients (N=385): 185 (48.1%), 15(3.9%), 40(10.4%), 32(8.3%),40(10.4%), 12(3.1%), 61(15.8%) were suffering from thalassemia, sickle cell anemia, hemophilia, leukemias, chronic liver disease, aplastic anemia and chronic renal failure. Overall, mean age of participants was 25.6 ± 2 years. The prevalence of TTIs, syphilis, HIV and HIV/syphilis co infection in our study population was 5.74%, 4.4%, 1.04%, and 0.3%, respectively. Out of 185/385 cases of thalassemia 7%, 1.1% and 0.5% were positive for syphilis, HIV, and HIV/syphilis coinfection. Among 40/385 cases of hemophilia 2 cases were HIV positive. while out of 61 cases of chronic renal failure 6.6% cases were seropositive for Syphilis. No TTIs were detected in sickle cell anemia, leukemias, chronic liver disease and aplastic anemia patients.

Conclusion:

Prevalence of TTIs was found to be high among multi-transfused patients especially in β-thalassemia cases. Most common type of TTI was Syphilis and documentation of HIV in 1.04% cases particularly in thalassemia and hemophilia in the present study is drawing attention towards alarming progress regarding spread of HIV in our region.

Keywords: HIV, Syphilis, HIV/Syphilis coinfection, multi-transfused patients

INTRODUCTION:

Transfusion-transmitted infections (TTIs) can be dangerous and have fatal consequences. Screening for transfusion-transmissible infections (TTIs) is a crucial part of the process of ensuring that transfusion is as safe as possible. The blood is routinely screened for five TTIs markers, i.e., Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human Immunodeficiency virus(HIV), malaria and Treponema Pallidum(Syphilis). Transfusion of blood and blood components are vital measures of the management of patients demanding repeated transfusion including hereditary hemolytic anemias especially thalassemia; hematological malignancies; chronic kidney disease; hemophilia [1].

Acquired immune deficiency syndrome (AIDS) is caused by Human immunodeficiency virus (HIV) which belongs to a subdivision of retrovirus called lentivirus. HIV is transmitted through unprotected sexual contact, contaminated needle stick injuries and tissue transplantation, and very rarely through transfusion of blood or blood components. With the invent of new screening tests the chance of getting HIV transmission is significantly reduce [2].

Syphilis is a systemic illness caused by Treponema pallidum which can be spread by sexual contact, contaminated blood and products and from mother to developing fetus. If untreated, it progresses through 4 stages: primary, secondary, latent and tertiary [3]. It can lead to permanent disability, including neurological and cardiovascular problems. Syphilis positive patients are more prone to HIV infection. It is therefore imperative that transfused blood is free of bacteria Treponema pallidum that causes syphilis. Syphilis spirochetes can survive blood bank's refrigerator temperature when kept between 72-120 hrs [3-5].

HIV and syphilis may affect similar patient groups and coinfection is common. It is recommended that all patients presenting with syphilis must be tested for HIV and all HIV-positive patients must be frequently screened for syphilis. Syphilis agent may expedites the spread of the HIV most likely through high incidence of genital ulcers [3]. Timely detection and treatment of syphilis can, thus, help to decrease HIV spread. In the HIV-positive patient Syphilis may shows with non-specific signs and symptoms: Primary syphilis may be uneventful and majority of HIV-positive patients present with secondary syphilis. Secondary infection may be more threating and there is a high rate of early neurological and eye diseases. Diagnosis is usually made with serological testing but there is risk of false-negative test in both primary and, less commonly, in secondary syphilis [4, 5].

Beta-thalassemia is an autosomal recessive disorder with worldwide distribution. In order to improve the quality of life and survival of transfusion dependent thalassemia patients, regular transfusion and iron chelation are the mainstay of traditional therapy from early childhood [6].

Thalassemia major patients have a high prevalence of transfusion-transmitted infections, primarily as a result of viral infections acquired viva blood transfusion. Conversely, blood transfusions endanger the patients to acquire transfusion-transmissible infections (TTIs). The chance of having TTIs is related to the number of transfusions; hence, the infection rate of TTIs increases with age in subsequent years [7].

In sickle cell disease blood transfusion is a supportive measure and has become an essential part of the therapeutic interventions in the management of patients in case of severe anemia due to hemolysis,

acute sequestration crises and aplastic crises, and multi-organ failure-strategies [8]. Hemophilia A is an X-linked recessive disorder characterized by lack of FVIII and repeated bleeding events, which may happen unexpectedly (as in severe hemophilia: FVIII <1%) or be triggered by trauma (in non-severe hemophilia: FVIII>1%) [9].

The chemotherapy induced anemia (CIA) and hemorrhage are the most common side-effects due to the chemotherapy. Up till now, multi transfusion is still the timely and prompt way in treating these complications. [10]. Bone marrow failure disorders include a heterogenous group of disorders, of which myelodysplastic syndrome (MDS), forms the largest subgroup. MDS is mainly a disease of the elderly, with many elderly people managed by supportive measures with regular transfusions to treat anemia [11]. Aplastic anemia is a disorder that results in a hypocellular bone marrow with pancytopenia. The incidence in Asia is higher, with estimates ranging from 3.9 to 7.4 per million per year [12]. Treatment is modified to the individual needs of the patient, but comprises a combination of supportive care for pancytopenia (red cell and platelet transfusions, prophylactic antimicrobials), immunosuppressive drugs, and bone marrow transplantation [11]. End-stage liver disease bleeding symptoms are accompanied with deranged laboratory investigation regarding blood coagulation. Use of blood and blood components such a fresh-frozen plasma and platelet concentrates is a common clinical practice to treat or prevent bleeding in these patients to secure hemostasis [13]. Chronic kidney disease which is a worldwide health concern, anemia is the most common complication. The requirement of RBC transfusion remains for patients who need an immediate increase in their RBC mass due to symptomatic anemia especially in patients on dialysis [14].

The aim of this study is to assess and evaluate the prevalence of syphilis, HIV and HIV/Syphilis coinfection in multi-transfused patients.

MATERIALS AND METHODS:

This cross- sectional study was conducted at Baqai Medical University, Karachi. Samples were taken from different thalassemia centers across Sind, Fatima Hospital, Karachi and Muhammadi Laboratory and Diagnostic Centre, Numaish, Karachi. A total of 385 multi transfused patients as: transfusion dependent beta thalassemia, hemophilia, sickle cell anemia, aplastic anemia, leukemias, chronic renal failure and chronic liver failure of any age and gender were included. These individuals were residing in different areas of Sindh belonging to different ethnic group. Individuals requiring sporadic transfusion or Occasional transfusion were excluded from this study. All participants were informed with details of study procedure before taking the written consents. The study was approved by the Ethics Committee of Baqai Medical University, Karachi & Board of Advanced Studies and Research (BASR), Baqai Medical University, Karachi. The research was conducted from January 2020 to January 2021 for a period of 1 year. The sample size for study population was (n=385) and calculated as under following:

$$n = \frac{z^2(p)(1-p)}{c^2}$$

Whereas z (level of confidence) = 1.96; p (%frequency of outcome) =0.5; c (standard error) = 0.05; n (sample size) =385

10 ml venous blood samples were collected in yellow-top (gel containing) vacutainers labelled with the participant's ID. Serum was extracted by centrifugation (2000 rpm for 10 min) and transferred to aliquots, stored at –70℃, within 1h of collection. Electrochemiluminescence assay was carried out on Cobas e411 analyzer of Roche Diagnostics, Mannheim, Germany for detection of treponemal antibodies and Elecsys HIV Combi PT for qualitative determination of HIV-1 p24 antigen and anti-HIV-1 & anti-HIV-2 antibodies. Reactive samples of syphilis and HIV were confirmed on real time PCR. Real line *Treponema pallidum Fla* – Format assay Kit by Bioron Diagnostic, Germany; for the qualitative detection of DNA for *Treponema Pallidum* and Artus HI Virus-1 RG RT-PCR Kit on Rotor-Gene Q, Qiagen Germany; for the quantitation of HIV-1 RNA in the serum were used. All the tests were run according to manufacturer guideline.

The statistical analysis was accomplished by using Statistical Package for Social Sciences (SPSS) version 25.0. This involved descriptive statistics and correlational analysis. Data was compiled as frequency (%). Association of parameters was determined by chi-square. P value of <0.05 was considered significant for all of the analyses.

RESULTS:

A total of 385 multi-transfused with a mean age of 25.6 ± 2 years were tested. Of all multi-transfused patients: 185 (48.1%), 15(3.9%), 40(10.4%), 32(8.3%), 40(10.4%), 12(3.1%), 61(15.8%) were suffering from thalassemia, sickle cell anemia, hemophilia, leukemia, chronic liver disease, aplastic anemia and chronic renal failure. The prevalence of TTIs, Syphilis, HIV, HIV/syphilis co infection in our study population was 5.74%, 4.4%, 1.04%, and 0.3%, respectively as shown in Table 1.

Table 1. Prevalence of Syphilis, HIV and HIV/Syphilis co-infection in multi-transfused patients.

DISORDERS	FREQUENCY	PERCENT
Syphilis	17	4.4
HIV	4	1.04
HIV/Syphilis	1	0.3
Non infectious	383	94.3
Total	**385**	**100.0**

There was no significant association between prevalence of TTI among different disorders (p>0.3). Out of 185/385 cases of thalassemia 13(7%), 2(1.1%) and 1(0.5%) were positive for syphilis, HIV, and HIV/syphilis co-infection, respectively. Among 40 cases of hemophilia (40/385) 2 case were HIV positive. while out of 61/385 cases of chronic renal failure 4(6.6%) cases were seropositive for Syphilis. No TTIs were detected in sickle cell anemia, leukemia, chronic liver disease and aplastic anemia patients as shown in Table 2.

Table 2. Disorders wise distribution of Syphilis, HIV and HIV/Syphilis co-infection in multi-transfused patients

		DISORDER / DISEASE							
TTIs		**THALASSEMIA**	**HEMOPHILIA**	**SICKLE CELL ANEMIA**	**APLASTIC ANEMIA**	**LEUKEMIA**	**CHRONIC LIVER DISEASE**	**CHRONIC LIVER FAILURE**	**TOTAL**
Syphilis	**Count**	13	0	0	0	0	0	4	17
	%Within disorders	7.0%	0.0%	0.0%	0.0%	0.0%	0.0%	6.6%	4.4%
HIV	**Count**	2	2	0	0	0	0	0	4
	%Within disorders	1.1%	5.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.0%
HIV/Syphilis	**Count**	1	0	0	0	0	0	0	1
	%Within disorders	0.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%
Non-reactive	**Count**	169	38	15	12	32	40	57	363
	%Within disorders	91.4%	95.0%	100.0%	100.0%	100.0%	100.0%	93.4%	94.3%
Total	**Count**	185	40	15	12	32	40	61	385
	%Within disorders	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

TTIs, Transfusion transmissible infections; Chi-square test for statistical difference in the distribution of TTIs within each group, (p >0.3)

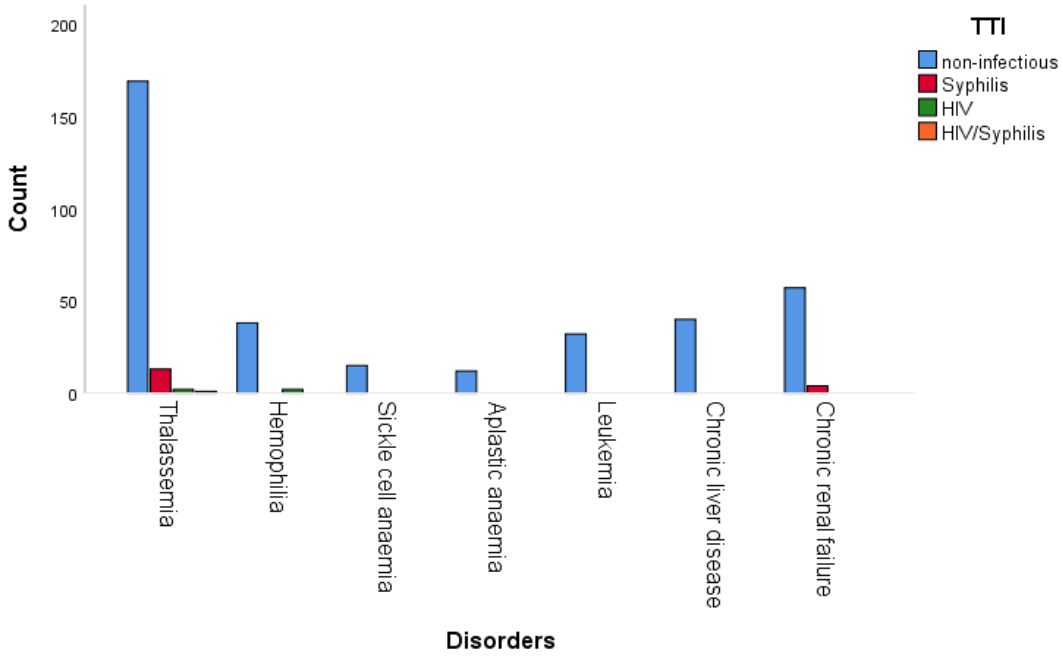

Figure 1. Prevalence of Transfusion transmissible infection among different categories of multi transfused patients.

DISCUSSION:

Blood transfusion is an integral part of routine clinical practice. Blood and blood components give exclusive and life-saving therapeutic supports to patients [1]. The major concern for both recipient and physician is for safe, prompt and good quality blood to be accessible when needed. It is well documented that discrepancies in blood transfusion practices can lead to fatal outcomes for the recipient in terms of morbidity and mortality [15]. Blood for transfusion is thought to be harmless when it is given by a cautiously selected, healthy donor; free from infectious agents that could be dangerous to the recipient; processed by reliable means of testing; transfused only upon requirement and for the patient's health and safety [1].

According to WHO report people suffering from HIV are 34 million in number, across the globe [16] and estimates that 5% to 10% of all HIV infections worldwide have been taken via infected blood and blood components transfusions. The risk of transfusion-associated HIV surpasses that of any other risk contacts, it is observed that 90% of recipients having HIV antibody-positive blood transfusion are found to be HIV infected at follow-up [17].

According to the WHO, every year 6.3 million new cases of syphilis occur, with high prevalence in low-income countries [18]. By 2009, Pakistan and National AIDS Control Program (UNAIDS) evaluated that in Pakistan approximately 130,000 HIV cases had been detected, with an overall prevalence of less than 0.05% in the general population. By applying the upgraded parameters of blood bank and by using worldwide approved kits to screen donor, the frequency of TTIs in multi-transfused patients will be decreased. Moreover, in blood banks the rigorous serological blood screening for TTIs before transfusion should be mandatory [7,15].

In our study we found prevalence of TTIs in 5.74% (21/385) multi-transfused patients. Out of which the frequency of syphilis, HIV and HIV/Syphilis co infection was 4.4%, 1.04%, and 0.3%, respectively. In multi transfused Beta thalassemia patients Syphilis, HIV and HIV/Syphilis co-infection was found. While in chronic renal failure only syphilis positivity (6.6%) detected and 2 cases of hemophilia were HIV positive. While in sickle cell anemia, aplastic anemia, chronic liver disease and leukemia patients the prevalence rate was 0%. There is scarcity of data regarding TTIs prevalence especially HIV, syphilis and HIV/syphilis co-infection in multi transfused patient related to leukemia, aplastic anemia, chronic liver failure and chronic liver disease. In Pakistan various studies conducted on prevalence of TTIs in multi-transfused patient were centered on transfusion dependent B thalassemia [7]. A comparison was done of our study with different studies conducted in our country and within other countries as shown in Table 3.

Table.3 Comparative analysis of prevalence of TTIs amongst multi transfused patients

AUTHORS	YEAR	COUNTRY	PROVINCE, CITY	SAMPLE SIZE	DISORDER	TTIS, HIV, SYPHILIS, AND HIV/SYPHILIS, RESPECTIVELY	REF
Batool et al.	2022	Pakistan	Bahawalpur,	1212	B- thalassemia	16.9 ,0.4, 1.7, *	19
Attaullah et al.	2022	Pakistan	TurbatKech Baluchistan	100	B- thalassemia	# ,4, #, #	20
Seck et al.	2022	Senegal	Dakar	235	SCD	#,0, #, #	21
Moghalles et al.	2022	Yemen	Sana'a	405	MTP (Leukemia)	13.1, 0.04, #, #	22
Ghafoor et al.	2021	Pakistan	Rahim Yar Khan	350	B- thalassemia	#,1.1,0, #	23
Bhuyan et al.	2021	Bangladesh	Dhaka	148	B- thalassemia	#,0, #, #	24
Shayo et al.	2021	Tanzania	-	385	SCD	*,1.8, #, #	25
Peng et al.	2020	China	North China	189	Hemophilia	*,1.1,0.5, *	26
Blatyta et al.	2020	Brazil	-	2779	SCD	5.2, 0.3,1.2, *	27
Mishra et al.	2020	India	Western India	196	B- thalassemia	*,3.1, #, #	28
Yasmeen and Hasnain,	2019	Pakistan	Lahore, Multan, Karachi and Peshawar	350	B- thalassemia	36.5, 0, #, #	29
Al-Moshary et al.	2019	Pakistan	Peshawar	431	B- thalassemia	29.3,1.39, #, #	30
Kansay et al.	2019	India	-	196	ERD	*,1.02, #, #	31
Mwanaut et al.	2019	DRC	Kinshasa	180	SCD	#,8.33, #, #	32
Mousavi et al.	2019	Afghanistan	-	80	Hemophilic	#,0, #, #	33
Kadhim &	2018	Iraq	Baghdad	639	Hemophilia	#,0.2, #, #	34

Lami,							
Junaid et al.	2017	Pakistan	Peshawar	396	Hemophilia	#,0, #, #	35
Atwa & Wahed,	2017	Egypt	-	121	B- thalassemia	#,0, #, #	36
Ahmed et al.	2016	Pakistan	Rawalpindi	1253	B- thalassemia	25.3, 0.5, #, #	37
Manisha et al.	2015	India	Central India	-	B thalassemia	#,1.5,0, #	38
Chen et al.	2012	China	Zhejiang	2	Leukemia	#,2, #, #	39
Borhany et al.	2011	Pakistan	Karachi	173	Hemophilia	#,0, #, #	40

TTIs, transfusion transmissible infections; MTP, multi transfused patients; SCD, sickle cell disease; ERD, end stage renal disease; *, not mentioned; # not determined; Ref, reference.

Studies in past on transfusion transmitted infections reported mainly prevalence of HCV, HBV, and HIV or their co infections on multi-transfused patients [25, 28, 31, 32]. There are few studies which documented prevalence of HIV, Syphilis and its co infection in multi transfused patients making it challenging to compare our results [19, 27]. Similarly, many studies conducted in different countries reported HIV prevalence 1.1% [23], 1.1% [26], 1.02% [31], 1.5% [38] that were comparable to our study results. Some studies reported high HIV prevalence than our study results [20,32]. Two recent studies conducted in our country but in different cities by Batool et al. and Attaullah et al. reported marked variability in the HIV prevalence in transfusion dependent B- thalassemia patients i.e., 0.4% [19] and 4% [20], respectively. The high prevalence of Syphilis (4.4%) in our study result is a threat to the multi transfused patients well-being. Similarly high HIV prevalence (1.04%) in multi-transfused patients especially transfusion dependent beta thalassemia and hemophilia, is very alarming situation. Unfortunately, there are many flaws in Pakistan's blood transfusion system which is already weak and conventional. In Pakistan, majority of health care facilities have their own blood banks, having unsatisfactory and unreliable system resulting in poor and insufficient transfusions and deadly consequences [16]. Inadequate surveillance statistics exists for HIV and syphilis in Pakistan. Rising burden of HIV demanded a well-organized inter-disciplinary and regional tactic to overcome the emerging danger of HIV. Syphilis seemed to have been controlled over the years, but now it is seemed to re-emerge as a major public health issue in communities. Incidence rate of these infections around the world have dropped due to awareness while Pakistan is still in a position to fight these deadly diseases [40].

CONCLUSION:

Transfusion dependent Beta thalassemia patients are more prone to develop TTIs. High prevalence of syphilis and of HIV in Beta thalassemia, chronic renal failure and hemophilia patients is an alarming situation. These patients should be discouraged from rapidly switching to multiple transfusion center for their blood and blood components. There is a need for rigorous donor screening along with screening of blood components the use of advanced molecular techniques for screening of blood units, and through community-based awareness programs will confidently aid in plummeting the problem statement.

CONFLICT OF INTEREST:

The authors reflect no conflict of interest.

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