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The prevalence of hepatitis B virus, human T-lymphotropic virus and human immunodeficiency virus in patients receiving blood transfusions in South Africa.

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Willemse, Reynier Grobler, Christa Murphy, Edward <u>et al.</u>

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THE PREVALENCE OF HBV, HTLV, HIV IN PATIENTS RECEIVING BLOOD TRANSFUSIONS IN SOUTH AFRICA

Reynier J. Willemse^{1,2}, Christa J. Grobler², Edward L. Murphy^{3,4}, Nareg Roubinian^{3,5}, Charl Colemen¹, Solly Machaba¹, Marion Vermeulen^{1,6}

¹South African National Blood Service, Johannesburg, SA

²Vaal University of Technology (VUT), Vereeniging, SA

³University of California San Francisco (UCSF), San Francisco, CA, USA

⁴Vitalant Research Institute, San Francisco, CA, USA

⁵Kaiser Permanente Northern California, Oakland CA, USA

⁶University of the Free State, Bloemfontein, SA

Abstract

BACKGROUND: South Africa has a high prevalence of Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) and to a lesser extent Human T-lymphotropic Virus (HTLV). Each of these agents is transfusion-transmissible but deciding whether to implement preventive screening depends upon knowledge of background prevalence in transfused patients. We determined the prevalence of HIV, HBV, and HTLV I/II among blood transfusion recipients in South African hospitals.

METHODS: We obtained identity-unlinked samples used for blood crossmatching at 634 South African hospitals served by the South African National Blood Service (SANBS). The ABBOTT Alinity S[®] Immunochemiluminescent system measured HIV, HBV, and HTLV-I/II antibodies. Repeatedly reactive samples were confirmed using the Roche Cobas[®] 8000. Logistic regression was performed to investigate the determinants of associations for HIV, HBV, and HTLV infections.

RESULTS: The overall prevalences of HIV, HBV, and HTLV were 37.8%, 7.4%, and 0.6% respectively. The HIV prevalence in blood recipients was twice as high as general population estimates. Public hospital patients had a significantly higher prevalence compared to private hospital patients for HIV and HBV. HIV prevalence was significantly higher in females, and HBV prevalence was significantly higher in males, excluding the unknown gender results.

CONCLUSION: Patients receiving blood transfusions in South Africa have high rates of HIV and HBV infection that should be taken into consideration when determining donor screening strategies for other viral infections. Measurable prevalence of HTLV indicates endemicity of this infection in South Africa.

Corresponding Authers: Reynier Willemse, Barney Molokwane str, Highveld Mediclinic, SANBS, Trichardt, 2300, Reynier.Willemse@sanbs.org.za, Marion Vermeulen, 1 Constancia Boulevard, SANBS, Constancia Kloof, 1709, Marion.Vermeulen@sanbs.org.za.

Introduction

South Africa is the country most affected by the ongoing HIV epidemic in the world, with 18% of adults living with HIV, accounting for 15% of new global infections and 11% of global AIDS-related deaths [1].

For HBV infection, Spearman and Sonderup [2] suggested that an estimated 65 million people in Africa are chronically infected and 2.5 million of them are in South Africa. According to Schweitzer et al. [3], the HBsAg seroprevalence was estimated at 6.7%, pointing to high intermediate endemicity with an estimated 3.5 million individuals chronically HBV infected in South Africa.

There is a paucity of data on HTLV prevalence in the South African general population. One study done by Bhigjee et al. [4], showed a seroprevalence of HTLV among patients in KwaZulu Natal to be 2.6%.

In this environment, the South African National Blood Service (SANBS) collects and tests blood donations. The prevalence of HIV in first-time blood donors was 1.13% [5], and the incidence in repeat donors was estimated at between 1.56 and 1.94 per 1000 personyears between 2012 and 2016 [6]. The hepatitis B virus prevalence in the first-time donor population was found to be 0.66%, which is significantly lower compared to other studies in the general population [5], A 2013 cross-sectional study of HTLV prevalence among 46,752 South African blood donors confirmed that HTLV prevalence was 0.16% in Black donors, 0.02% in both White and Coloured donors, and 0% in South African Asian donors, for an overall prevalence of 0.062% extrapolated to the 2013 blood donor population [7]. The South African healthcare system consists of two sectors: public and private. Transfusion events across both sectors are predominantly distributed in the following clinical disciplines: Medical (30.4%), Gynecology/Obstetrics (18.1%), Intensive Care Unit (ICU) (13.8%), General Surgery (11.6%), Pediatrics (7.7%), and Hematology/Oncology (5.5%) [8].

The problem of HIV/HTLV coinfection and its potential pathologic effects has been debated for the past 20 years [9]. It is estimated that rates of HTLV or HTLV-2 co-infections in HIV-infected hospital patients are at least 100 to 500 times greater than in the general population [10]. HTLV may be detrimental to the HIV-infected individual with increased risk for the development of neurologic complications including HTLV-1–associated myelopathy / tropical spastic paraparesis (HAM/TSP), leukaemia, and lymphoma [10].

Currently, there is little data available on the HIV, HBV, and HTLV prevalence in transfused hospital patients in South Africa. This information is essential for understanding the disease burden in the transfusion recipient population. Receipt of an infectious unit may have lower consequences in a patient already infected with the virus [11]. On the other hand, co-infection with a different virus may be deleterious. Currently the SANBS have implemented screening strategies for HIV, HCV and HBV which reduces the possibility of TTI from these viruses, whereas SANBS does not test for HTLV and HTLV screening is not mandated by the WHO or regulatory bodies within South Africa. Vermeulen et al. [12], estimate that without implementing HTLV screening, 3.55 symptomatic cases of transfusion transmitted HTLV would occur annually.

This study investigated the prevalence of HIV, HBV, HTLV, and co-infections thereof in patients requiring blood transfusion.

Methods

An unlinked cross-sectional study was conducted on 6983 transfused patients in hospitals across South Africa except for the area served by the Western Cape Blood Service.

SANBS has 85 blood transfusion crossmatch laboratories in 8 of the 9 provinces serving 90% of the country's hospitals. These provinces have been divided into 7 operational zones, namely, Eastern Cape, Egoli, KwaZulu Natal, Mpumalanga, Northern, Vaal, Free-state, and Northern Cape. Two-thirds of transfused patients within these zones are from provincial hospitals, and the remaining patients are from private hospitals [8]. To represent the overall transfused population, the collection of samples was stratified by hospital based on the percentage of blood transfusion requisitions received annually per hospital.

Residual crossmatch plasma samples were collected from all blood transfusion laboratories proportionally based on historical blood and blood product usage data. After demographic and geographic data were retained, identifying codes were removed. Specimens were centrifuged at 3000 rpm, and the plasma was separated from the red cells. The plasma was stored frozen (-18°C and below) until all sampling for the hospital was complete. The samples were sent to the central donation testing laboratory where they were stored frozen for two months before analysis.

The specimens collected were tested for antibodies and/or antigens for HIV, HBV, and HTLV on the Alinity S[®] (Abbott Diagnostics, Delkenheim, Germany) immunochemiluminescent autoanalyzer using the Alinity S[®] HIV Ag/Ab Combo (antigen-antibody-antigen), HBsAg, and HTLV I/II assays. All samples that tested initially reactive were repeated in duplicate on the Alinity. Confirmation of repeat reactive samples was performed on the cobas[®] E801 (Roche Diagnostics, Rotkreuz, Switzerland) electrochemiluminescent autoanalyzer using the cobas[®] Elecsys HIV Duo (antigen-antibody-antigen), HBsAg II for HIV and HBV respectively. HTLV confirmation was performed on the cobas[®] E411 (Roche Diagnostics, Rotkreuz, Switzerland) electrochemiluminescent autoanalyzer using the HTLV I/II assays.

We calculated frequencies and descriptive statistics and performed bivariate analyses using the chi-square test and separate multivariable logistic regression models to assess the association of patient demographics characteristics with HIV, HBV, and HTLV infection. Due to sample quality and sample volume, , 894 repeat-reactive patient samples tested with the Abbott Alinity S[®] assay could not be confirmed using the Roche Cobas[®] E801 To address the missing results for HIV, HBV, and HTLV, we impute d the data using the survey impute function in SAS University Edition (SAS Institute, North Carolina, USA) with the Hot-deck method [13]. This method employs a set of cells and randomly selects one as the donor to impute the recipient cell [13]. Prevalence was calculated both as an unadjusted proportion and after standardization by age and sex to the South African general population using the direct method. Statistical analyses were conducted with SPSS[®] version

25 (IBM, Chicago, Illinois) software and SAS university edition (SAS Institute, North Carolina, USA).

Research ethics approvals were obtained from the Medical Research Council / VUT and the SANBS human research ethics committee (2017/13).

Results

Study population.

We analyzed results from 6983 specimens collected from 634 hospitals distributed across 8 out of the 9 South African provinces. All age groups were represented with fewer sample numbers in the 0 to 10-year-old and 81 years and older (Table 1) excluding the unknown age group. Patients below the ages of 20 made up 5.8% of the sample, 10.3% of the patients were above the age of 70 and 26.1% of the patients' age group was unknown. Females made up two-thirds of the transfused patient population excluding the unknown gender. Most blood transfusion recipients were from the Egoli zone (25.2%) followed by the Northern zone (24.2%) and KwaZulu Natal zone (17.7%); Mpumalanga and Free State and Northern Cape zones comprised the fewest (6.1%). Provincial hospital patients were the biggest contributors to the sample (63.6%). (table 1)

Prevalence.

Out of the 2,763 Abbott Alinity S repeat-reactive patient samples for HIV, 708 could not be confirmed using the Roche Cobas® E801 and thus were imputed. Among these, 675 samples were inputted as positive and 33 as negative. Similarly, for HBV, of the 531 Abbott Alinity S repeat-reactive patient samples, 455 could not be confirmed using the Roche Cobas[®] E801 and were imputed, with 444 imputed as positive and 11 as negative. For HTLV, of the 49 Abbott Alinity S repeat-reactive patient samples, 17 could not be confirmed with the Roche Cobas® E801. Among these, 13 samples were imputed as positive and four as negative. Including the imputed results, the overall pre-transfusion prevalence of HIV, HBV, and HTLV in transfused recipients was 37.40%, 7.40%, and 0.60%, respectively. After standardizing to the age- and sex-distribution of the South African population, HIV, HBV and HTLV prevalence were 33.04%, 7.14% and 0.56% respectively, excluding the unknown gender and age results. Figure 1 shows the breakdown of coinfections, with the majority being coinfected with HIV and HBV (329), followed by coinfections with HIV and HTLV (21). There were only 2 (0.02%) concurrent infections between all three viruses (HIV, HTLV, and HBV). Prevalence by demographic for each marker can be seen in Tables 2, 3 and 4. All associations seen in the bivariate analysis remained significant in the multivariable analyses described below, excluding all unknown variables (age, blood group and gender).

Multivariable logistic regression.

In the multivariable analyses females had an adjusted odds ratio (aOR) of 1.3 (CI 1.17–1.44) for having an HIV infection and in contrast an aOR 0.73 (Cl 0.61–0.88) having an HBV infection, both compared with males this result excluded the unknown gender. When compared to the Free State / Northern Cape zone, transfused patients in the Mpumalanga

zone had an aOR of 2.4 (Cl 1.82–3.24) and 2.0 (Cl 1.13–3.5) for HIV and HBV infection respectively followed by the KwaZulu Natal zone (aOR of 1.5 (Cl 1.22–1.97) and 1.9 (1.19–3.20)) respectively. The Vaal zone had an odds of HIV infection of 1.4 (Cl 1.17–1.92) and the Eastern Cape zone had double the odds of HBV infection (aOR 1.78 (Cl 1.04–3.15)), both compared to the Free State / Northern Cape zone. Provincial hospital transfusion recipients were more likely to be HIV and HBV positive with odds of 1.5 (Cl 1.17–1.92) and 1.35 (Cl 1.11–1.64) respectively compared to private hospital patients. There was no significant difference in HIV and HBV prevalence across the patients' blood groups, results excluded the unknown blood.

In the multivariable analysis for HTLV-positive patients, female patients had an odds of 2.05 (CI 1.02–2.59) for HTLV infection compared to male patients these results excluded the unknown gender. There was no significant difference in HTLV infection between zones, age groups, blood groups, or hospital class in either the bivariate or multivariable analysis with the exclusion of unknown gender, age and blood group results.

Discussion

In this study of blood transfusion recipients, we found a very high HIV, intermediate HBV and detectable but low HTLV infection among transfused patients in SA. Demographic and geographic associations with these viral infections were similar to those previously reported in SA general population [2, 4, 6, 7, 9, 10]. Co-infections were mostly observed for HIV and HBV.

Because we were surprised by the high HIV prevalence in our patients, we wanted to compare them to the general South African population after accounting for differences in age and sex by statistical standardization. According to Stats SA [14], the 2018 estimated HIV prevalence in the general South African population is approximately 13,1%. The total number of people living with HIV is estimated at approximately 7.52 million in 2018. After standardizing our results by age and sex to the South African general population, we found an HIV prevalence in pre-transfused patients of 33.04%, almost three times higher than population estimates when excluding the unknown gender and age results. Age and sex-specific prevalence in transfused patients was also at least twice as high as the general population in most age/sex categories, excluding the unknown gender and age results [15].

Differences in prevalence between subgroups observed in this study align with findings documented in other research publications [16]. The regions of Mpumalanga, KwaZulu-Natal, and Vaal geographical regions in South Africa are the most affected by HIV compared to the general population [17]. Both this study and our own found that similar results were observed in this study for gender HIV infection, showing that females had a higher HIV prevalence than males [17]. Women are disproportionately affected by HIV in South Africa due to a combination of biological, social, and economic factors [17].

According to Parikh and Veenstra [17], an HIV prevalence of 25.7% was found among patients visiting primary health care facilities across four South African provinces which is slightly below what was found in the hospitalized patients included in this study.

Finding is likely due to Berksonian bias, also called admission rate bias which was first described in 1946 [18]. This bias results from the fact that patients with the disease or condition are more likely to be hospitalised than patients without the disease or condition. This certainly applies to HIV which causes several conditions which might results in medical care or hospitalisation [18]. HIV infection poses complex challenges, especially in managing hematologic complications like anemia, thrombocytopenia, and coagulopathies, which significantly affect patient well-being and prognosis [16]. Blood transfusions are crucial to addressing these issues, requiring careful attention and specialized care [16]. Parikh and Veenstra reported HIV prevalences of 34% and 36% in two primary health care facilities clinics, in line with the findings within this study [17].

According to Schweitzer et al. [3], the HBsAg seroprevalence was estimated at 6.7% in South Africa, pointing to high intermediate endemicity with an estimated 3.5 million individuals chronically HBV infected. After standardizing for age and sex we found an HBV prevalence of 7.17% which is similar to the estimated population prevalence of 6.7%, suggesting little bias related to hospitalization for HBV, once again this standardization excluded the unknow age and gender results. With the introduction of the universal HBV vaccination in 1995 [19], it was expected that there would be a noticeable decrease in HBV prevalence in the younger age groups (20 years and below) compared to older age groups (31 years and above) which was not the case within this study. Interesting to note is that there seems to be less admission rate bias for HBV, perhaps because most HBV infection remain asymptomatic for much longer periods [19]. The patient population trends in this study align with findings well-documented in Moonsamy et al. research publications [20]. The regions of Mpumalanga, KwaZulu-Natal, and Vaal geographical regions in South Africa are the most affected by HBV comparing the general population [20]. The higher prevalence of HBV among males in South Africa can be attributed to several factors. Men are more likely to engage in high-risk behaviors such as unprotected sex and intravenous drug use, which increase the likelihood of HBV transmission. Additionally, cultural practices and societal norms might lead to lower healthcare-seeking behavior among men, resulting in reduced vaccination rates and lower access to preventative measures [20].

Anyanwu et al. [21] estimated the HTLV prevalence in South Africa to be 1%, which is slightly higher than the observed (0.60%) or age- and sex-standardized (0.56%) prevalence found in this study. According to Vermeulen et al. [22], the prevalence of HTLV in South African blood donors was 0.062% with 0.16% in Black donors, both of which are lower than previously reported prevalence in the general population and the results of this recipient study. In contrast to Berksonian bias, this could be due to the healthy donor effect whereby blood donors are selected for better health compared to the general population [11]. The prevalence of HTLV was highest in the Mpumalanga and KwaZulu-Natal regions and among female patients, which aligns with previously published results [22].

Currently, HTLV screening of blood donors is not mandated by the WHO or by regulatory standards in South Africa and SANBS does not test for HTLV. However, SANBS uses both buffy coat and filter based leukoreduced red blood cell products which has been shown to reduce transfusion transmission to 1% [23]. In the Vermeulen *et al.* publication, SANBS assumed an HTLV-transfusion-transmitted efficiency of 10% and a clinical manifestation

of 6%, estimating that unscreened blood would result in 3.55 clinical cases of transfusiontransmitted HTLV disease annually. There could therefore be a very small risk of transfusion transmission of HTLV to HIV-infected transfusion recipients occurring within South Africa [12]. Assessments of whether or not to test for a specific TTI are complex and nuanced, especially in a resource-constrained setting such as South Africa. The underlying and not insignificant HTLV prevalence from non-transfusion routes found in this study and no reported cases of TT-HTLV in the independent-hemovigilance program in the past ten years provides corroboration in the decision not to test donors for HTLV in South Africa at this time [24].

There are some limitations in this study. Patient race was not recorded on the request forms for blood transfusion recipients and could not be used in data analysis. Due to sample quality and sample volume 708 samples for HIV, 455 samples for HBV and 17 samples for HTLV could not be confirmed using the Roche assays, although we did impute these data. The lack of statistical significance for the association of HTLV with demographic variables is probably due to the small number of HTLV positive samples in this study. Finally, we only included three TTI in the study and specifically did not study the hepatitis C virus, which comparatively has a low prevalence in South African donors [25].

In conclusion, this study provides estimates of HIV, HBV and HTLV prevalence in hospitalized transfusion recipients and offers useful public health information for understanding the burden on the health and/or social care system. It also provides data for determining blood donor screening strategies for other viral infections and for patient blood management. Finally, it confirms that HTLV is endemic at a low prevalence in South Africa.

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RJ performed the research, acquired, analyzed the data, and wrote the first draft of the manuscript; CJ, EL, and MV supervised the research, helped with statistical analysis, reviewed and edited the manuscript. NR helped with the design, review, and editing of the research study. C. and S. helped with expert guidance on essential reagents or tools and managing of these reagents and tools.

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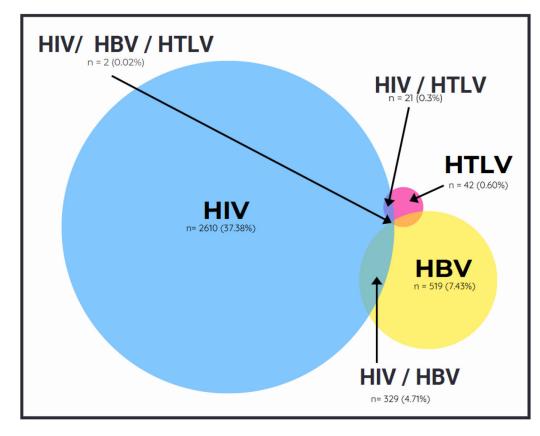


Figure 1.

Concurrent Infections of blood transfusion patient from May 2017 to May 2018

Table 1.

Blood transfusion patient characteristics from May 2017 to May 2018 (N = 6983).

	N (%)
Gender	
Female	4379 (62.7)
Male	2591 (37.1)
Unknown	13 (0.2)
Age Group	
0–10	107 (1.5)
11–20	303 (4.3)
21–30	849 (12.2)
31-40	984 (14.1)
41–50	769 (11.0)
51-60	702 (10.1)
61–70	726 (10.4)
71-80	489 (7.0)
80+	231 (3.3)
Unknown	1823 (26.1)
Blood Group	
A	1881 (26.9)
В	1191 (17.1)
AB	294 (4.2)
0	2962 (42.4)
Unknown	655 (9.4)
Zone	
Egoli	1761 (25.2)
Northern	1693 (24.2)
KwaZulu Natal	1235 (17.7)
Vaal	927 (13.3)
Eastern Cape	516 (7.4)
Free State / North Cape	428 (6.1)
Mpumalanga	423 (6.1)
Hospital Class	
Hospital Class Provincial Hospital	4441 (63.6)

Private Hospital

2542 (36.4)

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Table 2.

Prevalence and demographic associations of HIV seropositivity in transfused hospital patients, May 2017 to May 2018. Crude and adjusted odds ratios (OR) were derived from logistic regression models.

Demographic Data	Total N	HIV Reactive N (%)	Crude	e OR (95% CI)	Adjusted OR (95% CI)		
Total	6983	2610 (37.4)					
Gender							
Female	4379	1773 (40.5)	1.44	(1.30–1.60)	1.30	(1.17–1.44)	
Male	2591	833 (32.2)			1.00		
Unknown	13	4 (30.8)	0.94	(0.29–3.06)	0.68	(0.18–2.11)	
Age							
0–10	107	15 (14.0)	0.40	(0.22–0.70)	0.73	(0.46–1.14)	
11–20	303	73 (24.1)	0.77	(0.57-1.05	0.98	(0.78–1.19)	
21-30	849	370 (43.6)	1.87	(1.52–2.32)	0.96	(0.78–1.19)	
31-40	984	589 (59.9)	3.62	(2.94–4.45)	0.99	(0.80–1.21)	
41-50	769	406 (52.8)	2.71	(2.19–3.36)	0.92	(0.74–1.14)	
51-60	702	205 (29.2)	1.00		1.00		
61+	1446	123 (8.5)	0.23	(0.18–0.29)	0.86	(0.71–1.05)	
Unknown	1823	829 (45.5)	2.02	(1.68–2.44)	1.28	(1.07–1.54)	
Blood Group							
А	1881	660 (35.1)	0.93	(0.82–1.05)	0.98	(0.86–1.11)	
В	1191	473 (39.7)	1.14	(0.99–1.31)	1.13	(0.98–1.30)	
AB	294	104 (35.4)	0.94	(0.74–1.21)	0.97	(0.75–1.25)	
0	2962	1087 (36.7)			1.00		
Unknown	655	286 (43.7)	1.34	(1.13–1.59)	1.41	(1.18–1.69)	
Zone / Region							
Egoli	1761	605 (34.4)	1.16	(0.93–1.46)	1.13	(0.90–1.43)	
Northern	1693	580 (34.3)	1.16	(0.92–1.452)	1.12	(0.89–1.42)	
KwaZulu Natal	1235	511 (41.4)	1.57	(1.24–1.98)	1.55	(1.22–1.97)	
Vaal	927	357 (38.5)	1.39	(1.09–1.77)	1.50	(1.17–1.93)	
Eastern Cape	516	205 (39.7)	1.46	(1.12–1.92)	1.30	(0.99–1.72)	
Free State / North Cape	428	133 (31.1)			1.00		
Mpumalanga	423	219 (51.8)	2.38	(1.80–3.15)	2.43	(1.82–3.25)	
Hospital Class							
Provincial	4441	2053 (46.3)	2.22	(2.00–2.46)	1.50	(1.17–1.93)	
Private	2542	710 (27.9)			1.00		

Table 3.

Prevalence and demographic associations of HBV seropositivity in transfused hospital patients, May 2017 to May 2018. Crude and adjusted odds ratios (OR) were derived from logistic regression models.

Demographic Data	Total N	HBV Reactive N (%)	Crude	e OR (95% CI)	Adjusted OR (95% CI)		
Total	6983	519 (7.4)					
Gender							
Female	4379	295 (6.5)	0.77	(0.64–0.92)	0.73	(0.61–0.88)	
Male	2591	223 (8.8)			1.00		
Unknown	13	1 (7.7)	0.89	(0.12-6.84)	0.75	(0.04–3.89)	
Age							
0–10	108	4 (3.7)	0.55	(0.20–1.57)	1.14	(0.51–2.28)	
11-20	304	26 (8.9)	1.34	(0.81–2.21)	0.88	(0.50–1.47)	
21-30	852	59 (7.2)	1.07	(0.72–1.59)	0.95	(0.65–1.39)	
31-40	993	90 (9.4)	1.43	(0.99–2.07)	0.98	(0.68–1.42)	
41-50	772	58 (7.6)	1.17	(0.78–1.74)	0.71	(0.46–1.07)	
51-60	706	46 (6.5)			1.00		
61+	1448	72 (5.0)	0.75	(0.51–1.10)	0.90	(0.64–1.28)	
Unknown	1832	164 (9.1)	1.41	(1.01–1.98)	1.20	(0.87–1.67)	
Blood Group							
А	1881	134 (7.1)	1.01	(0.80–1.26)	1.01	(0.81–1.27)	
В	1191	94 (7.9)	1.12	(0.871.45)	1.11	(0.85–1.42)	
AB	655	25 (3.8)	0.52	(0.34–0.79)	1.21	(0.77–1.84)	
0	2962	210(7.1)			1.00		
Unknown	655	56 (8.6)	1.23	(0.90–1.67)	1.21	(0.88–1.64)	
Zone / Region							
Egoli	1761	122 (6.9)	1.52	(0.94–2.47)	1.43	(0.89–2.40)	
Northern	1693	120 (7.1)	1.56	(0.96–2.53)	1.52	(0.95–2.54)	
KwaZulu Natal	1235	109 (8.8)	1.98	(1.21–3.22)	1.91	(1.19–3.20)	
Vaal	927	67 (7.2)	1.59	(0.95–2.66)	1.58	(0.96–2.71)	
Eastern Cape	516	43 (8.3)	1.86	(1.07–3.20)	1.78	(1.04–3.15)	
Free State / North Cape	428	20 (4.7)			1.00		
Mpumalanga	423	38 (9.0)	2.01	(1.15–3.52)	1.96	(1.13–3.50)	
Hospital Class							
Provincial	4463	357 (8.0)	1.28	(1.0–1.56)	1.35	(1.11–1.64)	
Private	2552	162 (6.3)			1.00		

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Table 4.

Prevalence and demographic associations of HTLV seropositivity in transfused hospital patients, May 2017 to May 2018. Crude and adjusted odds ratios (OR) were derived from logistic regression models.

Demographic Data	Total N	HTLV Reactive N (%)	Crude OR (95% CI)		Adjusted OR (95% CI)	
Total	6983	42 (0.6)				
Gender						
Female	4379	33 (0.8)	2.18	(1.04–4.56)	2.05	(1.02–4.59)
Male	2591	9 (0.4)			1.00	
Unknown	13	0 (0)	0	0	0.00	0
Age						
0–30	1252	7 (0.6)	0.91	(0.37–2.24)	0.87	(0.36–1.94)
31-60	2440	15 (0.6)			1.00	
61+	1439	7 (0.5)	0.79	(0.32–1.94)	0.66	(0.26–1.53)
Unknown	1810	13 (0.7)	1.17	(0.56–2.46)	0.67	(0.29–1.46)
Blood Group						
A	1881	13 (0.7)	1.21	(0.58–2.49)	1.25	(0.59–2.57)
В	1191	7 (0.6)	1.02	(0.42–2.48)	1.01	(0.39–2.36)
AB	294	0 (0)	0	0	0.00	0
0	2962	17 (0.6)			1.00	
Unknown	655	5 (0.8)	1.33	(0.49–3.63)	1.42	(0.46–3.63)
Zone / Region						
Egoli, Vaal and Northern	4360	21 (0.5)	0.64	(0.27–1.52)	0.81	(0.35-2.23)
Mpumalanga and KwaZulu Natal	1644	14 (0.9)	1.14	(0.46–2.84)	1.24	(0.50–3.53)
Eastern, North Cape and Free state	937	7 (0.8)			1.00	
Hospital Class						
Provincial	4441	31 (0.7)	1.62	(0.81-3.22)	1.41	(0.72–2.98)
Private	2542	11 (0.4)			1.00	

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