HTLV-I/II Seroprevalence and Cost-Effectiveness of Blood Donor Screening in Saudi Arabia a focus on the Eastern province "A Retrospective Study"

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Abstract

Human T-lymphotropic virus type I and II (HTLV-I/II) infections pose significant public health concerns due to their association with severe diseases such as adult T-cell leukemia/lymphoma (ATLL) and HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP). However, limited data exist on the prevalence and confirmation of HTLV infection among blood donors in the Eastern Province of Saudi Arabia. This study aims to determine the seroprevalence and cost-effectiveness of HTLV-I/II screening among blood donors in the Eastern Province of Saudi Arabia. This retrospective study was conducted at the Dammam Regional Laboratory and Blood Bank from January 2020 to December 2023. Data were obtained from the donor database, including all blood donors during the study period. Screening for HTLV antibodies was performed using chemiluminescence microparticle immunoassay (CMIA), followed by confirmatory testing with Western blot analysis. Among 101,821 blood donors, 56 donations were initially reactive for HTLV antibodies. Confirmatory testing identified one case of HTLV infection, resulting in an overall seroprevalence of 0.0009%. The findings suggest a minimal risk of HTLV transmission among blood donors in this region. Continued surveillance and stringent screening protocols are essential for maintaining blood safety and minimizing the risk of HTLV transmission in the region. Further research is needed to understand the epidemiology and clinical implications of HTLV infection in this population. Replicated studies in different regions of Saudi Arabia may indicate the necessity of revising current HTLV screening recommendations, potentially customizing HTLV testing for specific populations rather than all donors. Conservative protocols might be adopted.

Keywords: HTLV-I, HTLV-II, seroprevalence, confirmation, blood donors, Dammam, Saudi Arabia, retrospective study

Human T-lymphotropic virus types I and II (HTLV-I/II) are retroviruses belonging to the family Retroviridae, known for their tropism towards T cells and association with severe

diseases such as adult T-cell leukemia/lymphoma (ATLL) and HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP). These viruses are significant public health concerns worldwide due to their potential long-term consequences and transmission modes including; sexual contact, mother to child mainly by breastfeeding, and blood transfusions (Nicolás et al., 2015) (Williams, 2018).

Although HTLV infections are relatively rare compared to other blood-borne viruses such as HIV and hepatitis viruses, they pose substantial public health risks due to their potential long-term consequences. ATLL, associated with HTLV-I infection, carries a poor prognosis with limited treatment options contributing to significant morbidity and mortality. Similarly, HAM/TSP characterized by progressive neurological impairment imposes a substantial burden on affected individuals and healthcare systems (Legrand et al., 2022)

HTLV-1 is endemic in certain regions, primarily tropical and subtropical areas. The highest prevalence rate reported in southwestern Japan, the Caribbean, parts of sub-Saharan Africa, and South America. It infects at least 5 to 10 million people worldwide, although this figure is likely underestimated due to a lack of data from many countries, most of the epidemiological data are derived from blood banks and antenatal clinics which may add to the underestimation issue (Legrand et al., 2022).

Despite the global concern regarding HTLV infections, there remains a paucity of data on their prevalence in regions like Middle East. This study designed to explore the epidemiological prevalence of HTLV in the Eastern province of Saudi Arabia. This region is a crucial hub for healthcare services and experiences a considerable influx of blood donors. However, limited research has been conducted to understand the epidemiology of HTLV infection in this area, leaving gaps in our knowledge regarding the prevalence and associated risk factors (Hindawi et al., 2017) (Al-Mozain et al., 2023).

Blood transfusions represent a potential route of HTLV transmission, highlighting the importance of rigorous screening measures. Health authorities in Saudi Arabia currently mandate screening all blood donors for HTLV-I and HTLV-II through antibody detection methods. However, the prevalence of HTLV infection among blood donors in the kingdom and specially Eastern Province remains poorly understood, necessitating comprehensive studies to assess the seroprevalence status of HTLV infection in this population (Al-Mozain et al., 2023) (Mujeeb & Mehmood, 1996).

Dammam regional laboratory is one of the main diagnostic laboratories in the Kingdom. The lab serve the Eastern province and it provides the main supply of blood donations. The annual blood donation supply by this lab is around 25,000 donations. Saudi and non-Saudi donors are voluntarily donate blood. All blood donations are screened routinely for blood born infections including HTLV-I and HTLV-II.

This study aims to investigate the seroprevalence of HTLV-I/II infection among blood donors in the Eastern Province of Saudi Arabia and to evaluate the costs associated with this practice. By elucidating the prevalence and risk factors of HTLV infection among blood donors at the Dammam Regional Laboratory.

Methods

A retrospective study was conducted at the Dammam Regional Laboratory and Blood Bank from January 2020 to December 2023. Blood samples were received n from four donor centers in the Eastern Province: Dammam Regional Laboratory (DRL), Qatif Central Hospital, Khafgi hospital and Jubail Central Hospital, with all samples analyzed at Dammam Regional Laboratory (DRL). Ethical approval was obtained with IRB number MD-LM-01.

Data for this retrospective analysis were retrieved from the donor database at DRL. All

individuals who donated blood between January 1, 2020, and December 31, 2023, were included in the study. All samples were analyzed anonymously after donation with no further testing during data collection and analysis period.

Before being eligible to donate blood, individuals underwent a thorough screening process, which included filling out a donor questionnaire, undergoing an interview, and a brief physical examination. All donors signed informed consent. All donations included in this study underwent routine testing at DRL for blood born infectious diseases, including syphilis, malaria, HBV, HCV, HIVI/II, and HTLV I/II

The chemiluminescence microparticle immunoassay (CMIA, Abbott ALINITY S) was used for anti-HTLV I/II testing. Samples with a sample/cutoff ratio (S/CO) of ≥1.00 were initially considered reactive and were repeat-tested in duplicate using the same assay. The sensitivity of the CMIA test for HTLV detection is reported as 100%, with a specificity among blood donors of ≥99.5%, as declared by the manufacturer (Guiraud V;Crémoux F;Leroy I;Cohier J;Hernandez P;Mansaly S;Gautheret-Dejean A;) .

Samples that were reactive during serology screening were subjected to duplicate testing. Repeatedly reactive samples for HTLV underwent confirmation through Western blot analysis (INNO-LIA HTLV I/II) using the same samples.

Results

Over the study period from January 2020 to December 2023, a total of 101,821 individuals donated blood at the Dammam Regional Laboratory and Blood Bank.

During the initial serology screening utilizing the chemiluminescence microparticle immunoassay (CMIA), 56 donations exhibited reactivity for anti-HTLV 1 and/or anti-HTLV 2 antibodies, representing 0.055% of the total donors, as shown in Table 1. Subsequent duplicate testing retained all 56 samples with persistent HTLV reactivity.

Confirmatory Western blot analysis was performed on the 56 repeatedly reactive samples, resulting in 1 confirmed case of HTLV infection. Additionally, 6 samples were classified as HTLV-1/2 indeterminate by INNO-LIA.

The overall seroprevalence of HTLV infection among blood donors in the Eastern Province of Saudi Arabia during the study period was calculated to be 0.0009%. The positive case exhibited elevated signal-to-cutoff (S/CO) ratios in CLIA titer antibody assessments. Notably, the positive case was a non-Saudi donor.

Discussion

The findings of this retrospective study provides a valuable insight into the seroprevalence and confirmation of HTLV infection among blood donors in the Eastern Province of Saudi Arabia. Our results revealed an overall HTLV seroprevalence of 0.0009% among blood donors during the study period. Although this prevalence rate is very low, it underscores the importance of continued vigilance in blood safety measures, given the potential long-term consequences associated with HTLV infection (Ji et al., 2020).

Importance of Confirmatory Testing

The confirmation of HTLV infection in one donor highlights the critical role of confirmatory testing, especially in regions where HTLV prevalence is very low. Confirmatory tests such as Western blot analysis are crucial for distinguishing true positive cases from false positives, ensuring accurate diagnosis and appropriate management. This step is vital to prevent unnecessary alarm and potential exclusion of donors based on false positive results, which can have significant public health and economic implications (Ji et al., 2020) (Youn et al., 2015).

In our study, 56 initially reactive samples were identified through the chemiluminescence microparticle immunoassay (CMIA), of which 1

case was confirmed positive for HTLV infection through Western blot analysis. Additionally, 6 samples were classified as indeterminate by the Western blot test, indicating that these samples did not meet the criteria for a definitive positive or negative result. These indeterminate results highlight the complexities and challenges in HTLV diagnostics, underscoring the need for robust confirmatory testing and follow-up (Youn et al., 2015). Furthermore, the indeterminate result remain a source of confusion to the pathologist, which necessitate the need for robust testing, and the need for advanced PCR, genetic testing is a must with regards to this era.

Risk Factors and Transmission Dynamics

Our findings also underscore the need to investigate potential risk factors associated with HTLV infection among blood donors. Identifying and understanding these factors can help in developing targeted interventions to reduce the risk of HTLV transmission. In our study, the confirmed HTLV-positive case was a non-Saudi donor, suggesting the possibility of geographic or demographic variations in HTLV prevalence. Further investigation into these factors is warranted to better understand the dynamics of HTLV transmission in the region. This includes assessing the impact of variables such as donor origin, travel history, sexual behavior, and previous blood transfusions (Percher et al., 2016) (Gallo et al., 2016).

Diagnostic Limitations and Antibody Responses

The elevated signal-to-cutoff (S/CO) ratios observed in the confirmed case indicate robust antibody responses, further validating our findings. However, it is essential to acknowledge the limitations of serological testing alone in diagnosing HTLV infection. Seropositivity does not necessarily imply active viral replication or clinical disease. Thus, relying solely on serological tests may not provide a complete picture of HTLV prevalence. Longitudinal studies examining the clinical outcomes and disease progression in HTLV-positive individuals are needed to elucidate the impact of HTLV infection on public health in the Eastern Province of Saudi Arabia (Gallo et al., 2016).

Cost-Effectiveness of Screening Strategies

Our study come in accordance with previous findings from different studies in Saudi Arabia, indicating a very low prevalence of HTLV infection in the country. Considering the high cost of HTLV testing, which is approximately $5.30 per sample, further research is needed to assess the cost-effectiveness of different screening strategies.

Potential strategies include testing only first-time donors, screening all donors from endemic areas or with possible risk factors, or selectively screening at-risk donors. Each approach has its own merits and limitations, and comprehensive cost-benefit analyses are required to determine the most effective and economical strategy.

Testing only first-time donors is a strategy that has been adopted in several countries with low HTLV prevalence, such as Norway and the UK. This approach balances the need for safety with cost-efficiency, ensuring that resources are allocated where they are most needed while maintaining a high level of blood safety (Crowder et al., 2023) (Piron et al., 2022).

Given the cost of $5.30 per sample for HTLV screening, a balance must be struck between maintaining high safety standards and managing the financial burden on blood banks and healthcare systems. This cost consideration is particularly pertinent in regions with low prevalence rates, where the cost of screening might outweigh the benefits (Piron et al., 2022).

Universal Leukodepletion

While universal leukodepletion has been proposed as a strategy to reduce the transmission of HTLV and other infections, recent studies suggest it may not be completely effective. Leukodepletion involves the removal of white blood cells from donated blood, which can harbor viruses like HTLV. However, the effectiveness of this intervention in preventing HTLV transmission remains inconclusive. Further studies are required to evaluate the efficacy and cost-effectiveness of such

interventions in the context of HTLV and other blood-borne pathogens (O'Brien et al., 2018) (Al-Hababi et al., 2020).

Conclusion

The seroprevalence of HTLV-I/II among blood donors in Dammam, Eastern Province of Saudi Arabia, highlights the importance of routine screening and surveillance efforts to ensure blood safety and prevent HTLV transmission through blood transfusions. Targeted interventions are needed to raise awareness about HTLV infection and promote preventive measures in the population. Further research is warranted to elucidate the factors driving HTLV transmission and inform the development of effective prevention and control measures.

Our study offers valuable epidemiological insights into HTLV infection among blood donors in the Eastern Province of Saudi Arabia. Continuous surveillance and stringent screening protocols are crucial for maintaining blood safety and minimizing the risk of HTLV transmission, with a focus on testing only first-time donors. Future research on risk factors, clinical outcomes, and the effectiveness of intervention strategies will enhance our understanding of HTLV infection and guide public health efforts to mitigate its impact.

This study might give an insight to the need for reviewing protocols of HTLV testing in blood donor screening. Region with low prevalence rate have their own protocols of testing. Similar conservative protocol might be adopted. More conserved testing strategies might be implemented.

Table 1: Annual Distribution of Donor Screening Results from the Eastern Province (2020–2023).

Year	Total Donors	Positive Screening by CMIA	Negative by INNO-LIA	Indeterminate by INNO-LIA	Confirmed Positive by INNO-LIA
2020	17,480	12	11	0	1
2021	23,540	17	15	2	0
2022	24,722	9	7	2	0
2023	36,079	18	16	2	0
Total	101,821	56 (0.05%)	49	6	1 (0.0009%)

This table summarizes the yearly donor counts and the outcomes of CMIA screening and INNO-LIA confirmatory tests, including the number of positive, negative, indeterminate, and confirmed positive cases, along with relevant percentages.

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