

SJMLS - 9(2) - 008**Transmissibility of Human T-Lymphotropic Viruses through Blood Transfusion in Africa: A Public Health Challenge**

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Summary

Human T-lymphotropic viruses (HTLV) types 1 and 2 are retroviruses primarily transmitted through close contact with infected bodily fluids. While blood transfusion is a significant route of HTLV transmission, improved screening measures can drastically reduce this risk. This review examines the historical context of HTLV transmission through blood transfusion, the current state of screening and risk mitigation strategies, and ongoing research efforts.

Keywords: Transfusion, safety, TTIs, HTLV

Introduction

Human T-lymphotropic viruses (HTLV) types 1 and 2 pose a significant public health threat due to their unique characteristics and the severity of associated diseases. Unlike many viruses, HTLV-1 and HTLV-2 are classified as slow viruses, meaning they exhibit a prolonged latency period following infection. This extended period, which can span decades (Lewis *et al.*, 2021), can elude detection and complicate efforts to prevent transmission. Despite establishing lifelong infection in the host, only a small percentage of individuals infected with HTLV-1 develop clinical HTLV-1-associated diseases (Melo *et al.*, 2020). However, when they do emerge, these diseases are often highly aggressive and debilitating.

The primary concern associated with HTLV-1 infection is adult T-cell leukemia/lymphoma (ATL). ATL is an aggressive malignancy of T-lymphocytes, a critical component of the immune system (Uchiyama *et al.*, 1998). The

disease is characterized by uncontrolled proliferation of abnormal T-cells, leading to a compromised immune response and a poor prognosis for patients (Uchida *et al.*, 2019). In addition to ATL, HTLV-1 infection is also associated with HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), a chronic inflammatory condition affecting the central nervous system (CNS) (Gallo, 2020). Symptoms of HAM/TSP include progressive weakness, spasticity, and difficulty walking, significantly impacting a patient's quality of life (Gallo, 2020).

While HTLV-2 shares some similarities with HTLV-1 in terms of transmission and integration into the host genome, it is considered less pathogenic. The risk of developing ATL or HAM/TSP is significantly lower for individuals infected with HTLV-2 compared to HTLV-1 (Lewis *et al.*, 2021). This highlights the importance of differentiating between HTLV-1 and HTLV-2 in clinical settings, as the disease burden and treatment approaches may differ.

Given the severity of HTLV-1-associated diseases and the ongoing challenges in prevention and treatment, a comprehensive review of the current understanding of HTLV-1 is warranted. This review aims to explore the latest advancements in our understanding of HTLV-1 transmission, viral pathogenesis, and disease development. We will examine the current diagnostic landscape and available treatment options for HTLV-1-associated diseases. Furthermore, we will discuss ongoing research efforts aimed at developing effective

vaccines and therapeutic strategies to combat HTLV-1 infection and its associated pathologies.

The primary modes of HTLV transmission

Human T-lymphotropic viruses (HTLV) types 1 and 2 as retroviruses that target the human immune system are transmissible primarily through the modes highlighted here-under. Understanding modes of HTLV transmission is crucial for preventing the spread of these life-threatening conditions in our society.

Cell-to-Cell Transmission

The primary mode of HTLV transmission is through infected T-lymphocytes coming into direct contact with uninfected T-cells (Jones *et al.*, 2020). This intimate cell-to-cell contact allows the HTLV virus to transfer its genetic material to the recipient cell, establishing a lifelong infection. This mode of transmission is particularly relevant in the context of sexual activity, where infected T-cells in the blood or genital secretions can come into contact with mucosal tissues of an uninfected partner (Barbosa *et al.*, 2018).

Blood Transfusion and Organ Transplantation

Prior to the implementation of routine HTLV screening in the 1980s in the United States, blood transfusions were a major route of HTLV transmission (Mann *et al.*, 1980). This resulted in a significant number of iatrogenic HTLV infections, particularly in regions with high HTLV prevalence. The development and implementation of sensitive serological assays for HTLV-1 and HTLV-2 antibodies was a consequence of the reported cases (Ciesielski *et al.*, 2017). These assays significantly reduced the risk of HTLV transmission through blood transfusions.

While blood screening practices have significantly reduced the risk of HTLV transmission through blood transfusions, residual risks remain (Tokunaga *et al.*, 2018). This underscores the importance of continued vigilance in donor screening procedures and the potential benefits of implementing more sensitive HTLV testing methods. Similarly, organ transplantation carries a low but finite risk of HTLV transmission, highlighting the need for

careful donor selection and recipient education (Ciesielski *et al.*, 2017).

Mother-to-Child Transmission

Vertical transmission of HTLV from mother to child can occur during pregnancy, breastfeeding, or a combination of both. The risk of mother-to-child transmission varies depending on factors like the mother's viral load and breastfeeding practices. Recent studies suggest that prolonged breastfeeding might be associated with a higher risk of transmission (Lewis *et al.*, 2021). However, the benefits of breastfeeding for child health necessitate a careful risk-benefit analysis on a case-by-case basis.

Other Potential Routes

The possibility of HTLV transmission through other routes, such as sharing needles or close household contact, is a subject of ongoing investigation. While some studies suggest a potential role for these routes (Castelli *et al.*, 2018), more robust evidence is needed to establish a definitive link. Research efforts exploring the precise mechanisms of HTLV transmission in these scenarios are crucial for informing public health recommendations.

Prevalence of HTLV in Africa

Africa is considered the largest endemic area for HTLV-1 infection globally (Tefera *et al.*, 2020; Motoshima *et al.*, 2020). However, prevalence varies considerably across the continent, ranging from 0.11% in Zimbabwe to 4.2% in Gabon (Motoshima *et al.*, 2020). This underscores the need for region-specific data to guide blood safety strategies. Data on HTLV-1 prevalence among blood donors in Nigeria is scarce and inconclusive. A study in Ibadan reported no HTLV-1 cases among 300 donors (Oyelami *et al.*, 2015). However, the limited sample size restricts generalizability. In Osogbo, a study conducted using stringent ELISA technique reported a seroprevalence of HTLV was 3.6% among blood donors, bulk of whom are not voluntary blood donors (Alli *et al.*, 2011).

Similarly, studies from Central Africa paint a concerning picture regarding HTLV-1 prevalence among blood donors. Research by Mbosso *et al.* (2018) in Gabon identified an

overall prevalence of HTLV-1 at 0.74% among blood donors, with some areas exceeding 1% (Motoshima *et al.*, 2020). This is significantly higher than the global average for blood donors, which is estimated to be around 0.1% (Tsallas *et al.*, 2010). Also, Njouokeu *et al.* (2013) reported a seroprevalence of HTLV-1/HTLV-2 (which includes HTLV-1) of 5.7% among blood donors in Yaoundé, Cameroon. This highlights a critical public health concern in these regions, where blood transfusions could potentially transmit HTLV-1 to recipients and pose a significant risk for developing severe illnesses like Adult T-cell leukemia/lymphoma (ATLL) and HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP). However, studies from Gabon and Cameroon report a significantly higher HTLV-1 prevalence among blood donors (Njouokeu *et al.*, 2013; Mbosso *et al.*, 2018). Such variations may arise from distinct epidemiological patterns, population dynamics, or healthcare practices in different regions (Anyanwu *et al.*, 2019).

HTLV transmission through blood transfusion and screening practices

Having examined critically the primary mode of HTLV transmission, it was established that blood transfusion historically played a significant role in HTLV transmission. Screening blood donors for HTLV, where prevalence data support such policy, will be of impact on the public health and transfusion safety. In regions with a high prevalence of HTLV-1, such as parts of Africa and Latin America, stronger arguments exist for incorporating HTLV testing into blood safety protocols (Tefera *et al.*, 2020).

Some of the impacts are discussed below.

Improved Blood Safety Measures

Blood transfusions are a lifesaving medical intervention, but they also carry a small risk of transmitting infectious diseases. Human T-lymphotropic virus (HTLV) is a retrovirus that can be transmitted through blood products, potentially leading to severe conditions like Adult T-cell leukemia/lymphoma (ATLL) and HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP) in recipients (Motoshima *et al.*, 2020). Implementing HTLV screening in blood donation programs plays a crucial role in enhancing blood safety measures.

Reduced Risk of HTLV Transmission

HTLV can be transmitted through cellular blood components like red blood cells, platelets, and whole blood (Motoshima *et al.*, 2020). Screening blood donations for HTLV antibodies identifies infected individuals, allowing their blood to be excluded from the transfusion pool. This significantly reduces the risk of HTLV transmission to recipients, protecting them from developing potentially life-threatening conditions.

Strengthening Blood Donor Selection

HTLV screening can be combined with existing blood donor selection criteria to further enhance safety. Studies suggest a higher prevalence of HTLV among first-time blood donors compared to repeat donors (Motoshima *et al.*, 2020). Implementing HTLV testing alongside existing risk factor questionnaires could help identify individuals with a higher risk of HTLV infection, even if they don't disclose relevant risk factors during questioning.

Improved Public Health Surveillance

Routine HTLV screening of blood donors provides valuable data on the prevalence of the virus within a population. This data can be used for public health surveillance purposes, allowing health authorities to monitor trends in HTLV infection and identify areas with a higher burden (Tsallas *et al.*, 2010). This information can then be used to develop targeted public health interventions aimed at raising awareness and promoting prevention strategies.

Cost-Effectiveness Considerations

The cost-effectiveness of implementing HTLV screening in blood banks needs to be carefully evaluated. While the initial cost of testing kits might be a concern, the potential savings from preventing HTLV transmission through blood transfusions can be significant. Additionally, early detection of HTLV in infected individuals allows for better disease management and potentially reduces healthcare costs associated with advanced stages of HTLV-related diseases.

Current Screening Practices and Residual Risks

Modern blood screening algorithms for HTLV typically employ enzyme-linked immunosorbent assays (ELISA) followed by confirmation with Western blot or a more

specific confirmatory assay (Bak *et al.*, 2019). These methods offer high sensitivity and specificity for detecting HTLV infection. However, residual risks remain due to limitations inherent to any screening test. The window period between HTLV infection and seroconversion, where an individual is infected but does not yet test positive, poses a challenge (Tokunaga *et al.*, 2018). Additionally, the possibility of false-negative results due to technical limitations or rare viral variants necessitates continued vigilance.

Emerging Technologies and the Future of Blood Safety

Advancements in nucleic acid testing (NAT) offer the potential for further enhancing blood safety regarding HTLV transmission. NAT can detect the presence of HTLV viral RNA, potentially reducing the window period and offering greater sensitivity compared to traditional antibody-based assays (Lee *et al.*, 2020). However, the high cost and logistical considerations associated with implementing routine NAT for HTLV screening require further evaluation and cost-effectiveness analysis.

Regional Variations and Resource Constraints

The effectiveness of blood safety measures related to HTLV transmission can vary significantly across different regions. Resource-limited settings might face challenges in implementing the latest screening technologies due to cost constraints. International collaboration and knowledge sharing are crucial for ensuring equitable access to advanced screening methods and promoting consistent blood safety practices globally (World Health Organization, 2023).

Challenges and Considerations

Despite the advancements in HTLV screening, some challenges remain. These include:

Window Period: Antibody tests may not detect recent HTLV infections during the window period when antibodies haven't yet developed. NAT testing could potentially address this gap but requires further evaluation for cost-effectiveness and implementation feasibility (Lee *et al.*, 2020).

Emerging Endemic Regions: The rise of HTLV prevalence in certain regions not previously considered highly endemic necessitates ongoing vigilance and adaptation of screening strategies (Bak *et al.*, 2019).

Blood Product Sharing in Resource-limited Settings: In low-resource settings, limited access to screening tests and lack of infrastructure for blood product safety measures can pose a higher risk of HTLV transmission through transfusion (Motoshima *et al.*, 2020).

Recommendations

Based on this research, our recommendations regarding blood transfusion safety vis a vis HTLV transmission are elucidated as follows:

Blood Donor Selection and Deferral Strategies

Blood donor selection criteria play a crucial role in minimizing the risk of HTLV transmission. Deferring individuals from blood donation who engage in high-risk behaviors associated with HTLV transmission, such as unprotected sexual intercourse with high-risk partners or intravenous drug use, remains an important strategy.

Donor Education

Donor education regarding HTLV risk factors and encouraging self-deferral of individuals at potential risk can further contribute to safer blood supplies. This applies where voluntary blood donation practice is religiously embraced.

Public Awareness

Beyond donors' population, the public can benefit from health campaigns designed to raise awareness about HTLV transmission and prevention strategies.

Nationwide Prevalence Studies

Literature reveals that most Africa countries, including Nigeria, has no adequate data on prevalence and spread of HTLV on national scale. Hence, large-scale studies are needed to establish a more accurate picture of HTLV prevalence and review blood transfusion policy, as situation may dictate.

Pilot Implementation of HTLV Testing

Pilot testing as an intervention can be implemented as programs of Government and her partners, to assess feasibility and cost-effectiveness.

Strengthen Blood Donor Screening Protocols

There should be regular review and update of national guidelines and standards to facilitate the potential inclusion of HTLV screening testing by Governments and their regulatory agencies. Support for blood establishments through capacity building and provision of certain consumables at the commencement of new policy on HTLV screening, will ensure blood safety.

Development of More Sensitive and Specific Assays

Newer assays with higher sensitivity and specificity for HTLV detection should be developed and validated for clinical use. These assays might improve the ability to identify infected individuals, particularly during the window period.

Point-of-Care Testing

The development of rapid and reliable point-of-care (POC) tests for HTLV would be particularly valuable in resource-limited settings. POC tests would enable faster decision-making regarding blood product use and potentially improve blood safety in these regions.

Vaccines

Although no licensed vaccines are currently available for HTLV, efforts should be in that direction. Developing a safe and effective vaccine would be a significant breakthrough in preventing HTLV transmission through all routes, including blood transfusion.

Conclusion

Limited data hinders effective public health interventions regarding HTLV among blood donors in Africa. Concerted efforts are needed to improve data collection, raise public awareness, and potentially implement HTLV screening in blood banks based on cost-effectiveness analyses. This will ensure a safer blood supply and protect recipients from HTLV transmission risks.

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