

Original Article

# Transfusion-Transmissible Infections: A Comprehensive Review of Prevalence, Diagnostic Technologies, and Barriers to Blood Safety

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## Article History

Submitted: 17/06/2026; Accepted: 24/06/2026; Published: 28/06/2026

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## ABSTRACT

Blood transfusion is a life-saving therapeutic intervention, yet the transmission of transfusion-transmissible infections (TTIs) such as HIV, Hepatitis B (HBV), Hepatitis C (HCV), and syphilis remain a formidable global public health challenge. While high-income nations have achieved near-zero residual risks through advanced donor screening and surveillance, low- and middle-income countries (LMICs)—particularly in sub-Saharan Africa—continue to bear a disproportionate burden of TTIs. This review synthesizes global scholarly literature to evaluate the epidemiology, transmission mechanisms, diagnostic technologies, and systemic barriers influencing blood safety.

**Keywords:** Blood Safety, Haemovigilance, Nucleic Acid Testing, Seroprevalence, Transfusion-Transmissible Infections, Voluntary Non-Remunerated Donation

## INTRODUCTION

Blood transfusion remains one of the most vital therapeutic interventions in modern medicine worldwide, playing a crucial role in the management of trauma, surgical procedures, obstetrics complications, haematological disorders, and other chronic illnesses.<sup>1,2</sup> Since the ABO blood group system was discovered by Karl Landsteiner in 1901,<sup>3</sup> Blood transfusion has continued to evolve remarkably, leading to the development of well-organized blood banking systems and transfusion services across the globe. In spite of advances in blood screening methods, the safety of blood and blood products remains a major public health concern, particularly in developing countries where healthcare infrastructure and screening technologies may be inadequate. The transmission of infections through blood and blood products continues to complicate blood transfusion practice globally.<sup>1,4</sup>

These infections are called transfusion transmissible infections (TTIs).

### Definition of TTIs

Transfusion-transmissible infections (TTIs) are infections that can be passed from a donor to a recipient through transfusion of contaminated blood and/or blood products<sup>4,5</sup>. They constitute one of the most significant risks associated with blood transfusion and remain a major public health concern worldwide, particularly in developing countries where screening systems may be inadequate. TTIs continue to pose a serious challenge because infected donors may be asymptomatic and can evade routine screening procedures during the window period<sup>6</sup>.

### Evolution of Blood Screening Practices

Blood screening technologies have advanced significantly over the past decades in response to the

### Article Access



Website: [www.wjmb.site](http://www.wjmb.site)

 10.5281/zenodo.21047000

### How to cite this article

Okoli RO, Osunde I, Mke A. Transfusion-Transmissible Infections: A Comprehensive Review of Prevalence, Diagnostic Technologies, and Barriers to Blood Safety. *West J Med & Biomed Sci.* 2026;7(2):316-330. DOI:10.5281/zenodo.21047000.

growing burden of transfusion-transmissible infections (TTIs)<sup>2,7</sup>. Earlier transfusion practices relied mainly on donor history and physical examination, with little or no laboratory testing. The emergence of Human Immunodeficiency Virus (HIV) and viral hepatitis in the late 1970s and early 1980s accelerated the development of more sensitive and reliable screening techniques<sup>8,9</sup>. Contemporary blood screening now integrates serological, molecular, and pathogen-reduction methods, all aimed at minimizing transfusion risk and enhancing transfusion safety worldwide.

### **MAJOR TRANSFUSION-TRANSMISSIBLE INFECTIONS (TTIS): CLASSIFICATION AND OVERVIEW**

Clinically significant transfusion-transmissible infections are generally grouped into viral, bacterial, parasitic, and other infectious agents. Viral infections constitute the most common and clinically important group<sup>5,10</sup> and include Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human T-cell Lymphotropic Virus (HTLV) and Cytomegalovirus (CMV).

Bacterial infections typically arise from contamination of blood or blood products during collection, transportation, storage, or transfusion. Commonly implicated bacterial pathogens include *Staphylococcus aureus* and *Yersinia enterocolitica*.

Parasitic infections may also be transmitted through blood transfusion and include *Plasmodium* species (malaria), *Trypanosoma cruzi* (the causative agent of Chagas disease), and *Babesia* species.

In addition, Emerging pathogens such as Zika virus, West Nile virus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have further heightened concerns regarding transfusion safety<sup>11,12,13</sup> in recent times.

#### **Viral TTIs**

Viral infections constitute the most significant group of transfusion transmissible infections because of their high prevalence, chronicity, associated complications and ability to survive in blood products. Major viral TTIs include HIV, HBV, HCV, HTLV, and CMV<sup>5,10</sup>.

#### **Human Immunodeficiency Virus (HIV)**

HIV is an enveloped RNA retrovirus that targets CD4+ T lymphocytes<sup>14</sup>, causing progressive immune

suppression and acquired immunodeficiency syndrome (AIDS). Transmission occurs through transfusion of infected blood and/or blood products. Because of the high viral load during early infection, transfusion is one of the most efficient routes of HIV transmission. The introduction of enzyme-linked immunosorbent assay (ELISA), rapid antibody tests, antigen detection, and nucleic acid testing (NAT) has significantly reduced transfusion-related HIV transmission<sup>15,16</sup>. However, residual risk persists because of window period infections, occult infections, laboratory errors and inadequate screening systems particularly in low-resource settings.

#### **Hepatitis B Virus (HBV)**

HBV is a DNA virus that infects hepatocytes causing acute or chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma<sup>17</sup>. Chronic hepatitis B virus (HBV) infection remains endemic in much of the developing world. The detection of HBV DNA in the circulation of individuals who test negative for hepatitis B surface antigen (HBsAg) represents a substantial threat to the safety of the blood supply. Additionally, window period infections further undermine donor screening, as individuals can be highly infectious before conventional HBV markers become detectable in blood<sup>18,19</sup>.

#### **Hepatitis C Virus (HCV)**

Hepatitis C virus (HCV) is an RNA virus that can be efficiently transmitted via transfusion of contaminated blood or blood products. It is a major contributor to the global burden of chronic liver disease. An estimated 70–85% of those infected progress to chronic infection, with a substantial proportion ultimately developing cirrhosis and hepatocellular carcinoma<sup>20</sup>. Screening with highly sensitive nucleic acid testing (NAT) has markedly reduced transfusion-associated HCV transmission. Nonetheless, HCV continues to pose a significant threat in settings with inadequate blood safety infrastructure, a problem compounded by the absence of an effective vaccine against the virus<sup>15,21</sup>.

#### **Human T-cell Lymphotropic Virus (HTLV)**

HTLV types I and II are retroviruses associated with adult T-cell leukemia lymphoma and neurological disorders, including tropical spastic paraparesis. Transmission occurs via infected lymphocytes present in blood components. Routine screening for

HTLV has been implemented in several high-income countries but remains uncommon in many resource-limited settings.

### **Cytomegalovirus (CMV)**

Cytomegalovirus (CMV) is a herpesvirus that establishes lifelong latency following primary infection. While infection is typically asymptomatic in immunocompetent individuals, CMV can cause severe morbidity in neonates, transplant recipients, and other immunocompromised patients. In the transfusion setting, transmission occurs predominantly via leukocyte-containing blood components<sup>23</sup>. Leucodepletion and selection of CMV-seronegative donors help to reduce transmission risk of CMV<sup>24</sup>.

### **Bacterial TTIs**

Bacterial TTIs most often arise from contamination of blood at the stages of collection, processing, storage, or transfusion. Bacteria may be introduced from the donor's skin flora, contaminated equipment, or improper handling of blood and blood components. Platelet concentrates are especially prone to bacterial transmission because they are stored at room temperature<sup>25,26</sup>, which promotes bacterial proliferation and growth. Common bacterial pathogens implicated in transfusion-related infections include *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Yersinia enterocolitica* and *Bacillus* species. Clinical manifestations range from mild fever to severe septic shock and death<sup>26,26</sup>. Adherence to strict aseptic technique, together with optimized conditions for the transport and storage of blood components, is critical for the prevention of bacterial transfusion-transmissible infections.

### **Parasitic TTIs**

#### **Malaria**

Malaria represents one of the most clinically significant parasitic TTIs in endemic regions. Transfusion-transmitted malaria occurs when blood from an infected donor containing *Plasmodium* parasites is administered to a recipient<sup>27</sup>.

#### **Trypanosomiasis**

American Trypanosomiasis, particularly Chagas disease caused by *Trypanosoma cruzi*, is a significant TTI in America<sup>28</sup>.

#### **Babesiosis**

Babesiosis, caused by *Babesia* species and

transmitted via infected red blood cells, is increasingly recognized in North America. It can lead to haemolytic anaemia and other severe, potentially life-threatening complications, particularly in immunocompromised individuals<sup>29</sup>.

#### **Leishmaniasis**

Leishmaniasis is caused by *Leishmania* parasites and has been reported as a rare transfusion-transmitted infection, particularly in endemic regions<sup>30</sup>.

#### **Toxoplasmosis**

*Toxoplasma gondii* may occasionally be transmitted through blood transfusion, particularly in immunosuppressed recipients. Although such events are rare, they may result in severe complications in vulnerable individuals<sup>31</sup>.

#### **Fungal and Prion Transmission**

Fungal TTIs are uncommon but can occur when blood products become contaminated during collection, processing, or storage. Opportunistic fungi, particularly *Candida* species, have been implicated in rare cases of transfusion-associated infection<sup>32,33</sup>.

Prion diseases, most notably variant Creutzfeldt–Jakob disease (vCJD), constitute rare yet serious transfusion-related hazards. Prions are aberrant infectious proteins that are highly resistant to standard sterilization procedures.<sup>32,33</sup>

### **MECHANISMS OF TRANSMISSION OF TTIS**

Transmission of TTIs arises when a recipient is exposed to infectious agents present in transfused blood or blood components, such as packed red cells, platelets, plasma, or clotting factor concentrates<sup>6</sup>. While several factors may contribute to the transfusion-transmission process, one key determinant is the “window period,” which refers to the interval between acquisition of infection and the point at which the pathogen becomes detectable by available laboratory screening techniques<sup>6,15</sup>. Other contributory factors include suboptimal donor selection, inadequate screening methodologies, unsafe transfusion practices, and the absence of robust quality assurance systems, all of which amplify the risk of TTIs. In addition, heavy reliance on remunerated or family replacement donors who may be more likely to withhold relevant risk information compared with truly voluntary, non-

remunerated donors, substantially contributes to the burden of TTIs in certain regions.

### **EPIDEMIOLOGY OF TRANSFUSION TRANSMISSIBLE INFECTIONS (TTIs)**

TTIs remain a very important aspect of transfusion medicine because it provides information on disease burden, donor safety and the effectiveness of blood screening services<sup>1,34</sup>. Transfusion-transmissible infections (TTIs) make a substantial contribution to the global burden of infectious disease. Seroprevalence studies are widely employed to characterize the distribution of TTIs among blood donors and to monitor trends in the transmission of major pathogens, including Human Immunodeficiency Virus (HIV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), syphilis, and malaria. Each year, millions of blood donations are collected worldwide, yet, despite improvements in screening technologies and services, TTIs remain highly prevalent in many low- and middle-income countries. The African subregion, in particular, carries a disproportionate burden of TTIs, reflecting both the high background prevalence of HIV, HBV, and HCV in the general population and the persistent limitations in infrastructure required to ensure comprehensive blood screening and transfusion safety<sup>34</sup>. The prevalence of TTIs varies across regions depending as a result of socioeconomic conditions, healthcare infrastructure, stringent donor selection criteria as well as cultural practices.

### **Prevalence and Global Burden of Transfusion Transmissible Infections (TTIs)**

Transfusion-transmissible infections constitute a major global health challenge. According to the World Health Organization (WHO), millions of blood donations are collected each year, yet marked disparities in donor selection practices and the quality of laboratory screening result in substantial regional differences in the safety of transfusion services<sup>1, 34, 35</sup>. Developing countries, particularly those in sub-Saharan Africa, bear a disproportionately high burden of TTIs due to the elevated prevalence of blood-borne pathogens in the general population, limited access to high-quality screening services, and continued reliance on replacement and/or paid blood donors. Seroprevalence studies consistently demonstrate marked differences in TTI prevalence between high-income and low- and middle-income settings.

Whereas high-income countries report very low rates of HIV, HBV, and HCV among blood donors, many low- and middle-income countries continue to document comparatively high seroprevalence levels. Globally, hepatitis B virus (HBV) remains the most prevalent TTI. HIV seroprevalence among blood donors is substantially higher in Africa than in Europe or North America. Data from several African countries indicate HBV prevalence rates of approximately 5–15% among donors, with HCV seroprevalence ranging from about 1% to 8%. In contrast, prevalence rates in developed countries are considerably lower, largely owing to the widespread adoption of advanced screening modalities such as nucleic acid testing (NAT). Europe has some of the lowest documented TTI prevalence rates worldwide, supported by strong health systems, stringent blood safety regulations, and well-established haemovigilance and transfusion surveillance programs. Most European nations perform comprehensive screening for HIV, HBV, HCV, and syphilis using highly sensitive assays. Similarly, North American countries, particularly the United States and Canada, employ sophisticated donor-selection strategies and advanced technologies, including NAT and pathogen-reduction methods, resulting in a very low residual risk of TTIs. The systematic recruitment of voluntary, non-remunerated blood donors and the implementation of national surveillance initiatives have substantially reduced transfusion-related transmission of HIV and viral hepatitis in these settings<sup>34,35</sup>.

Emerging and re-emerging pathogens nonetheless continue to jeopardize the safety of blood transfusion worldwide. Despite major advances in donor screening and transfusion services, TTIs remain a substantial public health and clinical problem. Ongoing emergence of novel agents, together with weak or poorly coordinated transfusion-surveillance systems, continues to erode gains in blood safety. In many developing countries, deficiencies in donor recruitment strategies, limited laboratory screening capacity, and under-resourced surveillance frameworks further heighten the risk of transfusion-associated infections<sup>34,35</sup>.

### **Socioeconomic, Cultural Determinants and Donor Demographics as risks for TTIs<sup>36,37</sup>**

Socioeconomic and cultural factors play an important role in the prevalence and spread of TTIs.

Poverty restricts access to healthcare services and key preventive interventions, including vaccination against blood-borne pathogens. Individuals of lower socioeconomic status are also more likely to engage in high-risk behaviours such as unprotected sex, multiple sexual partnerships, tattooing and scarification, excessive alcohol use, and injection drug use, all of which increase the likelihood of TTIs among prospective blood donors<sup>36,37</sup>.

Cultural beliefs, myths and misconceptions surrounding blood donation affect the availability of safe voluntary blood donors. In some communities, individuals hold onto myths that donating blood can weaken the body, result to infertility, death or spiritual consequences. Such beliefs discourage voluntary, non-remunerated donation and foster dependence on family-replacement and paid donors, who generally carry a higher TTI risk profile<sup>36,37</sup>.

Low literacy levels and inadequate public awareness campaigns also undermine blood safety initiatives. In many developing countries, knowledge of TTIs, their modes of transmission, and available preventive measures remains grossly insufficient, limiting the effectiveness of donor education and risk-reduction strategies<sup>36,37</sup>.

Other demographics like age and sex are important determinants of prevalence of TTIs. Young adults between 18 and 35 years constitute the majority of blood donors in many countries and may exhibit higher prevalence of HIV due to risky sexual behaviors when compared to general population, while older donors may demonstrate higher HBV or HCV prevalence due to cumulative lifetime exposures<sup>36, 37</sup>. Male donors predominate in blood donation worldwide, reflecting a combination of cultural, physiological, and social influences. Numerous studies have documented a higher prevalence of TTIs among male donors. This pattern is partly attributable to the greater frequency of donation among men, but may also indicate a higher level of engagement in high-risk behaviours compared with women. Occupation also impacts exposure to TTIs as commercial drivers, the military, migrant workers and informal laborers tend to have increased risk of infection because of mobility, poor access to healthcare, and engagement in risky social

behaviors<sup>36,37</sup>.

### Regional Epidemiology and Distribution of Transfusion-Transmissible Infections

In Asia<sup>38</sup> the prevalence of TTIs vary significantly across countries. While Southern Asian countries continue to battle substantial burdens of HBV and HCV infections, developed nations of Japan and South Korea have achieved improvement in blood transfusion safety through advanced screening technologies and stringent donor-selection policies. In contrast, in countries such as India, Pakistan, Bangladesh, and parts of China, hepatitis B and C remain among the most important transfusion-related infections. High population density, constrained health-care infrastructure, and unsafe medical practices continue to sustain transmission in these settings. Nevertheless, the gradual expansion of nucleic acid testing (NAT), together with improved donor education and the increased recruitment of lower-risk voluntary donors, has contributed to progressive reductions in TTI prevalence across many Asian countries<sup>38</sup>.

Latin America<sup>28, 39</sup> on the other hand presents an intermediate burden of TTIs. Although many countries in the region have strengthened blood transfusion services and implemented more rigorous screening programmes, marked disparities persist between urban and rural healthcare systems. Hepatitis B, hepatitis C, HIV, and Chagas disease remain major transfusion-related concerns. Chagas disease, caused by *Trypanosoma cruzi*, is particularly highly endemic in several Latin American countries and represents a distinctive parasitic TTI challenge. Improvements in voluntary blood donation and mandatory screening policies have reduced transmission rates in many countries in the last few decades<sup>28,39</sup>.

Sub-Saharan Africa bears the highest global burden of TTIs, driven by limited laboratory capacity, inconsistent blood-screening practices, recurrent reagent shortages, and heavy reliance on family-replacement and paid donors, all of which substantially increase transfusion-related infection risk. According to WHO estimates, low-income countries report markedly higher TTI prevalence among donated blood than high-income settings;

HIV prevalence among blood donations in these countries is around 0.7%, while HBV prevalence exceeds 2.8%. Meanwhile, the high burden of infections in Africa increases the demand for blood transfusion, further worsening challenges in maintaining safe blood supplies<sup>41,42,43,44</sup>.

Benue State continues to experience an alarmingly high burden of transfusion-transmissible infections (TTIs), particularly HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis. This high prevalence is likely driven by a combination of pervasive poverty, weak health-care infrastructure, inadequate blood-screening capacity, and a heavy reliance on paid and family-replacement donors. Studies conducted among blood donors in the State have consistently documented higher seroprevalence rates of HBV and HIV compared with many other Nigerian states. The persistence of unsafe transfusion practices, together with a profound shortage of voluntary, non-remunerated blood donors, further amplifies the risk of TTIs in Benue State<sup>43,44</sup>.

#### **OVERVIEW OF GLOBAL SCHOLARLY LITERATURE ON THE PREVALENCE OF TRANSFUSION-TRANSMISSIBLE INFECTIONS**

Transfusion-transmissible infections have continued to attract considerable attention from researchers worldwide. In response, numerous studies have investigated this scourge with the aim of accurately defining its true burden and characterising its impact on blood safety and public health.

In India, Das M et al<sup>45</sup> conducted a research titled Prevalence and trends of transfusion transmitted infections among blood donors in a tertiary care hospital of Assam. The overall prevalence of TTIs in their study was found to be 3.1%, with HCV having the highest prevalence (1.14%), followed by syphilis (1.0%), HBV (0.54%), HIV (0.41%), and malaria (0.01%). This finding was slightly above the Indian value of 1.58%, which the researchers blamed on lack of public awareness, insufficient knowledge, and inadequate counselling within the studied population. They noted a significant positive association between donors lacking ABO

antigens and TTI positivity ( $p < 0.05$ ). Additionally, they found out that donors with Rh-negative blood groups had a lower likelihood of TTIs compared to Rh-positive donors<sup>45</sup>.

In another study, Thakur SK et al<sup>46</sup> investigated Prevalence of TTI among Indian blood donors. A total of 345 (2.038%) blood donors were positive for TTIs. Prevalence of HBV, HCV, HIV-I/II, syphilis and MP were 188(1.111%), 73(0.431%), 34(0.201%), 49(0.29%) and 1(0.006%) respectively. Their result also showed a trend of decrease in prevalence of TTIs; 2.267%, 2.111% and 1.614% between the year 2020, 2021 and 2022 respectively. A significant association of syphilis infection ( $P=0.036$ ) and HCV infection ( $P=0.012$ ) with ABO blood group antigen was observed. Blood group O donors were found to be 1.81 times more infected with syphilis compared to donor having A and B antigen. Donors having blood group antigen B were 1.80 times more infected with HCV compared to donor not having B antigen. The study results show ABO blood group has an association with HCV and VDRL infection<sup>46</sup>.

Furthermore, Golia S et al<sup>47</sup> conducted a systemic review and meta-analysis titled Seroprevalence of transfusion-transmitted infections among blood donors in India: A systematic review and meta-analysis. The analysis included 41 studies with 1,860,594 blood donors. The pooled prevalence rates for HIV, HBV, HCV, syphilis and malaria among Indian blood donors were 0.12%, 0.91%, 0.28%, 0.14% and 0.01%, respectively. Males, replacement donors and first-time donors had a higher prevalence compared to females, voluntary donors and repeat donors, respectively. HIV (0.18%) and HCV (0.83%) were most prevalent in the North-east, HBV (1.57%) in the Central, syphilis (0.48%) in the North and malaria (0.04%) in the East zone. Their review highlighted the influence of donor demographics and testing methodologies on TTI prevalence, emphasizing zonal disparities, with findings laying the groundwork for policy development and future research to improve blood supply reliability<sup>47</sup>.

In Pakistan, a five years hospital-based retrospective study, the estimated overall prevalence of Hepatitis

B surface antigen (HBsAg), HCV, HIV, and syphilis was found to be 1.30%, 0.26%, 0.25%, and 0.28%, respectively<sup>48</sup>.

In another study among blood donors, the prevalence of HIV, HBV, HCV, Syphilis, and Malaria was found to be 0.04%, 1.84%, 1.7%, 2.1%, and 0.07%, respectively<sup>49</sup>.

In Ghana, Charwudzi A et al<sup>50</sup> looked at Prevalence and predictors of transfusion-transmitted infections among blood donor types at a teaching hospital in Ghana: Implications for haemovigilance. The overall prevalence of TTIs (infection with at least one tested pathogen) was 16.5% (95% CI: 15.80-17.20; N = 1,675), with syphilis 8.4% (95% CI: 7.83-8.91; N = 850) being the most common. Voluntary donors had a lower TTI prevalence than replacement donors (10.6% vs 19.9%,  $p < 0.001$ ). Repeat donors exhibited reduced risk of HBV (aOR: 0.254, 95% CI: 0.206-0.313,  $p < 0.001$ ), HCV (aOR: 0.734, 95% CI: 0.568-0.949,  $p = 0.018$ ), and syphilis (aOR: 0.486, 95% CI: 0.417-0.567,  $p < 0.001$ ). However, donor type itself was not a significant predictor of TTIs after adjusting for sociodemographic variables. ELISA testing identified an additional 7.3% (95% CI: 6.67-8.01; N = 422/5,754) TTI cases among RDT non-reactive fixed-site donors<sup>50</sup>. In another work done in Uganda and titled Prevalence and Factors Associated with transfusion-transmissible infections among blood donors in Arua regional blood bank, Uganda, Cwinyai N et al<sup>51</sup> reported that majority of the blood donors were male (80.1%), and the median donor age was 23 years (IQR = 8 years). The overall prevalence of TTIs was found to be 13.8% (95%CI: 12.0-15.6%), with specific prevalences of 1.9% for HIV, 4.1% for HBV, 6.6% for HCV and 2.8% for *Treponema pallidum*. Male sex (AOR = 2.10, 95%CI: 1.32–3.36,  $p$ -value = 0.002) and lapsed donor type compared to new donor type (AOR = 0.34, 95%CI: 0.13–0.87,  $p$ -value = 0.025) were found to be associated with TTIs<sup>51</sup>. In Cameroon, Ngomtcho SCH et al<sup>52</sup> examined Trends in immunological markers of transfusion transmissible infections among blood donors in Mamfe District Hospital, Southwest Cameroon. A hundred and sixty-five donors were enrolled in the study with a male preponderance giving a male-female sex ratio of 22.5 and a mean age of

32.23 ± 8.60 years. The majority (75.2%) of the donors were of the O-positive blood type, repeat donors (69.1%) and were mainly family replacement and paid donors as against the voluntary blood donors (39.4% and 37.0% vs. 23.6% respectively). overall TTIs prevalence was 18.78% (31/165), with HBsAg being the most predominant marker at 12.12% (20/165) followed by *Treponema pallidum*, HCV and HIV antibodies at 4.85 (8/165), 1.21%(2/165), 0.60% (1/165) respectively. Except for the HBV, The prevalence of TTIs was higher when using a single RDT than the ELISA test, and the difference was significant ( $p < 0.05$ )<sup>52</sup>.

More so, Mangala C et al<sup>53</sup> observed the prevalence and factors associated with transfusion-transmissible infections (HIV, HBV, HCV and Syphilis) among blood donors in Gabon. A total of 175,140 blood donors from the nine eligible studies were admitted to this study. The combined prevalence of HIV, HBV, HCV and syphilis obtained in the random effects model was 3.0%, 6.0%, 4.0% and 3.0%, respectively. Moreover, being a male blood donor and aged between 25 and 44 years was significantly associated with HBV infection and being a female blood donor and aged 35 years and over was significantly associated with HIV infection. Family or replacement blood donors had a high infection burden for all four TTIs of study<sup>53</sup>.

In South west Nigeria, Tijani BA et al<sup>54</sup> investigated the Prevalence of transfusion-transmissible infections among blood donors in a tertiary health institution in South-west, Nigeria: a three-year retrospective study. A total of 11,386 blood donor records were retrieved across the three-year period. Above quarter, 25.5% were from 2020, 36.4% from 2021, and 38.1% from 2022. The mean age of the donors was 33.09 ± 8.66 years. More males, 81.2%, constituted the donors, while females represented 18.8%. Most of the donations were family/replacement-based, 90.3% compared to 9.7% of voluntary blood donations. TTIs were prevalent among the age group of 25–34 years. Among all donors tested for the various TTIs, 761 (8.0%) tested positive for Hepatitis B, 358 (4.1%) for Hepatitis C, 235 (2.7%) for Syphilis, 94 (1.1%) for HIV. Over the years, Hepatitis B, recorded the

highest prevalence in 2021 with 296 (8.6%), Hepatitis C on the other hand was highest in 2020 at 110 (4.7%), Syphilis recorded the highest prevalence at 80 (3.5%) in 2020 and HIV was highest in 2021 and 2022 with 38 (1.2%) cases<sup>54</sup>.

In Northern Nigeria, Habibu I et al<sup>55</sup> reported the seroprevalence of HIV, HBV, HCV and Syphilis among blood donors in a Nigerian tertiary medical centre. Of the total blood donors, 17.00% (68/400) tested positive for at least one TTIs. The presence of HIV, HBV, HCV, and syphilis was identified in 2.8% (11/400), 8.3% (33/400), 1.8% (7/400), and 4.3% (17/400) of the donors, respectively. Multivariate analysis, after adjustments with various variables, indicates only commercial blood donors [Adjusted Odds Ratio (AOR) (95% CI): 14.63 (1.76-121.27)] and multiple sexual partners [AOR (95% CI): 5.40 (1.28-22.70)] were associated with HIV, while blood transfusion and piercing or tattoo were associated with HBV. Multiple sexual partners and a history of STDs were associated with syphilis infection<sup>55</sup>.

In Ekiti state of Nigeria, the overall prevalence of TTIs was 11.3% and Hepatitis B virus (HBV) (4.4%) was the most prevalent. Family donors have a significantly highest proportion of hepatitis B surface antigen, 17 (9.9%), and human immunodeficiency virus, 5 (3.0%), with  $P < 0.001$  and  $P < 0.046$ , respectively. Age below 26 years of age (adjusted odds ratio [AOR] = 1.491; 95% confidence interval [CI] = 1.249–1.781,  $P < 0.001$ ), female donors (AOR = 1.358; 95% CI = 1.081–1.705,  $P = 0.008$ ), being a family donor (AOR = 2.471, 95% CI = 1.851–3.297,  $P < 0.001$ ), and voluntary donor (AOR = 1.461; 95% CI = 1.267–1.707,  $P < 0.001$ ) were predictive of unfit to donate blood<sup>56</sup>.

In Benue state North central Nigeria, Nwannadi AI et al<sup>57</sup> conducted a study titled Risk of Transfusion Transmissible Infections: Our Experience in a Tertiary Health Care Facility in North-central, Nigeria to test the comparative advantage of ELISA over RDT. Five hundred and forty (540) donors negative to the RDT for HBV, HCV, HIV, Syphilis were subsequently screened with Enzyme linked immunosorbent assay (ELISA). A total of 72 (13.3%) prospective donors that tested negative to

RDT for the TTIs tested positive to the ELISA technique. Further analysis showed that twenty-three (4.3%) donors were positive to HIV, 23 (4.3%) to hepatitis B, 20 (3.7%) to hepatitis C and 6 (1.1%) to VDRL. Three donors (0.6%) were found to be positive to both HIV/HBV, 3(0.6%) to HIV/ HCV, 2 (0.4%) each to HIV/VDRL, HBV/ HCV and HBV/VDRL. They concluded that the risk of transfusing infected blood using rapid diagnostic test (RDT) technique is high and this can be significantly reduced by using ELISA testing techniques<sup>57</sup>.

The reviewed literature demonstrates substantial variation in the reported seroprevalence of TTIs across studies and regions. These discrepancies likely reflect differences in the diagnostic modalities used for donor screening, as well as variations in the sociodemographic characteristics of donor populations worldwide. Overall, ELISA consistently outperforms RDTs in terms of sensitivity and reliability. It is also noteworthy that voluntary, non-remunerated donors exhibit lower TTI prevalence than family-replacement and paid donors. This pattern strongly supports the preferential reliance on voluntary donors over replacement and commercial donors as a key strategy for reducing the risk of TTIs.

## DIAGNOSTIC AND SCREENING TECHNOLOGIES IN TRANSFUSION TRANSMISSIBLE INFECTIONS (TTIS)

### Serological Screening Methods

Serological assays remain the cornerstone of blood-donor screening in many countries, largely because they are relatively inexpensive, technically straightforward, and feasible to implement at scale.

### Rapid Diagnostic Tests (RDTs)

Rapid diagnostic tests (RDTs) yield results within a short time frame and are widely used in low-resource settings where laboratory infrastructure is limited. They are simple to perform, inexpensive, and require minimal technical expertise. However, despite their utility, RDTs generally exhibit lower sensitivity than ELISA and molecular diagnostic methods<sup>58</sup>.

### ELISA

The Enzyme-Linked Immunosorbent Assay (ELISA) is one of the most widely used screening modalities for detecting antibodies or antigens associated with infections such as HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV). ELISA offers superior sensitivity and specificity compared with RDTs and is well suited for large-scale blood-donor screening. Nevertheless, it may still fail to identify infections during the diagnostic window period<sup>59</sup>.

### Chemiluminescence Assays

Chemiluminescence immunoassays (CLIA) are advanced automated serological techniques that use light-emitting reactions to detect infectious markers. They offer improved sensitivity, faster turnaround times, and reduced human error. CLIA systems are increasingly used in modern blood banks because of their high throughput and automation capabilities<sup>60</sup>.

### Molecular Testing

#### Nucleic Acid Testing (NAT)

Nucleic acid testing (NAT) detects the genetic material of a pathogen directly, rather than relying on antibody or antigen detection. By markedly shortening the diagnostic window period, NAT substantially reduces the risk of transfusion-transmitted infections. Consequently, it has become an integral component of routine blood-screening algorithms in many developed countries<sup>15,61</sup>.

#### PCR Technologies

Polymerase chain reaction (PCR)-based technologies amplify minute quantities of pathogen nucleic acids, allowing very early and highly sensitive detection of infection. These methods are particularly valuable for confirming infection status and identifying occult infections that may not be detected by conventional serological assays<sup>62</sup>.

#### Multiplex Assays

Multiplex molecular assays enable the simultaneous detection of multiple pathogens within a single reaction. This approach enhances diagnostic efficiency, shortens turnaround time, and conserves laboratory resources. Such multiplex platforms are increasingly important for screening emerging infectious agents and have the potential to

significantly strengthen blood-safety practices<sup>63</sup>.

### Pathogen Reduction Technologies

Pathogen-reduction technologies (PRTs) are specifically designed to inactivate a broad range of infectious agents in blood components. Most platforms combine ultraviolet light with photosensitising chemicals such as riboflavin or psoralen derivatives. PRTs are particularly valuable for platelet and plasma products, which carry a higher risk of bacterial contamination. However, their high cost and substantial technical and infrastructure requirements have limited widespread adoption in many developing countries, despite their demonstrated effectiveness<sup>64,65</sup>.

## COMPARATIVE PERFORMANCE OF SCREENING METHODS AND COST EFFECTIVENESS

**Sensitivity:** Molecular methods such as NAT and PCR demonstrate the highest sensitivity because they detect infections during the early stages before antibody production. ELISA and CLIA also provide high sensitivity, while rapid diagnostic tests are generally less sensitive.

**Specificity:** Chemiluminescence assays and molecular techniques exhibit excellent specificity, reducing false-positive results.

**Cost-Effectiveness:** Serological methods, particularly ELISA and RDTs, remain more affordable and feasible in low-and-middle income countries. Although, molecular technologies provide superior safety, they are expensive and require sophisticated infrastructure and are not affordable by many developing

### Measures for Prevention and Control of Transfusion-Transmissible Infections (TTIs)

The prevention and control of TTIs are fundamental to achieving safe blood transfusion. Advances in donor recruitment strategies, screening technologies, vaccination programmes, and haemovigilance systems have substantially reduced the transmission of infectious agents through blood and blood components. Nonetheless, continuous refinement and rigorous implementation of these preventive measures remain indispensable to maintaining and further improving transfusion

safety.

### **Use of Voluntary Non-Remunerated Blood Donation**

Voluntary non-remunerated blood donors are widely regarded as the safest source of blood for transfusion. These donors give blood willingly without financial incentive and, as a group, exhibit lower prevalences of TTIs than family-replacement or commercial donors. They are also more likely to disclose relevant information about their medical history and lifestyle and to comply with donor-eligibility criteria. Rigorous donor selection is a cornerstone of TTI prevention. Careful donor recruitment, incorporating detailed medical history taking and focused physical examination, facilitates the identification of individuals with possible or overt infections, while high-risk donors are appropriately deferred to minimise the likelihood of collecting infected blood<sup>66,67</sup>.

### **Improved Screening Technologies**

Although advances in blood-screening technologies have markedly improved transfusion safety, conventional serological assays—including RDTs, ELISA, and chemiluminescence immunoassays—still have important limitations in detecting TTIs, particularly during early infection. Integration of molecular techniques, especially nucleic acid testing (NAT), into screening algorithms can substantially enhance diagnostic sensitivity and specificity, thereby shortening the window period and further reducing the risk of transfusion-transmitted infections.

### **Vaccination Strategies**

Vaccination remains an effective measure to prevent TTIs. Universal HBV vaccination programs will significantly reduce HBV prevalence globally, especially among younger populations<sup>68</sup>.

### **Public Health Education**

Educational campaigns should be implemented to promote voluntary blood donation, encourage safe sexual practices, discourage behaviours that undermine transfusion safety, and strengthen understanding of infection-prevention measures. Well-designed public awareness programmes can also help dispel misconceptions and reduce the

stigma associated with blood donation and infectious diseases.

### **Strengthening National Blood Services**

Robust national blood transfusion services are essential for maintaining a safe and sufficient blood supply. Governments should establish centralised blood transfusion agencies to standardise, coordinate, and regulate transfusion policies and practices. In addition, sustainable funding, adequately equipped laboratory infrastructure, a well-trained workforce, and reliable supply chains for reagents and equipment are all critical prerequisites for effective control of TTIs.

### **Haemovigilance and Surveillance**

Haemovigilance entails continuous monitoring of the entire transfusion chain—from donor venepuncture to recipient follow-up—with the objective of identifying, reporting, and preventing adverse transfusion events. Such systems generate critical data for the early detection of emerging infectious threats and provide an evidence base for formulating and refining policies aimed at controlling TTIs<sup>69,70</sup>.

### **FUTURE PREVENTIVE INNOVATIONS**

Future strategies for preventing TTIs should prioritise enhancing diagnostic sensitivity, reducing costs, and effectively addressing emerging pathogens. Advances in genomic sequencing, biosensor technology, and next-generation molecular assays have the potential to facilitate earlier and more accurate pathogen detection, thereby further improving transfusion safety. In parallel, research into synthetic blood substitutes and the development of effective vaccines against key transfusion-relevant pathogens holds considerable promise for strengthening blood safety in the coming years.

### **Barriers to Effective Control of Transfusion-Transmissible Infections (TTIs)**

Control of transfusion-transmissible infections (TTIs) remains a major public-health challenge worldwide, particularly in settings where health-care systems are under-resourced and blood transfusion services are weak. Despite substantial advances in diagnostic modalities and

donor-screening technologies, multiple systemic, technical, and operational constraints continue to compromise blood safety and sustain the risk of infection transmission through transfusion<sup>6,15</sup>.

### **Window Period Infections**

One of the principal challenges in controlling TTIs is the occurrence of window-period infections—the interval between acquisition of infection and the appearance of detectable antibodies or antigens in the bloodstream. During this phase, infected donors may test seronegative yet remain capable of transmitting infection. This window period therefore constitutes an important source of residual transfusion risk. Although nucleic acid testing (NAT) has substantially shortened the window period in settings where it is implemented, many low-resource countries continue to depend primarily on less sensitive serological assays, thereby maintaining a higher likelihood of undetected infections entering the blood supply<sup>6,15</sup>.

### **Inadequate Funding**

Inadequate funding remains a critical barrier to the effective control of TTIs. Blood transfusion services require substantial and sustained financial investment for the procurement of screening reagents, purchase and maintenance of equipment, staff training, and the implementation of comprehensive quality-assurance systems. In many low-resource countries, limited government support and heavy dependence on external donor agencies constrain access to advanced screening technologies such as NAT and pathogen-reduction systems. As a result, numerous health-care facilities continue to rely on outdated or less sensitive diagnostic methods, thereby perpetuating a higher residual risk of transfusion-transmitted infections<sup>1,35</sup>.

### **Human Resource Limitations in Blood Transfusion Services**

Shortages of skilled professionals significantly compromise the safety and quality of blood transfusion services. Many laboratories lack adequately trained personnel capable of performing advanced diagnostic procedures and maintaining rigorous quality standards. In addition, excessive workload, poor remuneration, and limited

opportunities for continuing professional development contribute to reduced efficiency and a higher incidence of laboratory errors. In some rural settings, blood transfusion services are overseen by minimally trained staff, resulting in suboptimal screening and unsafe transfusion practices<sup>71</sup>.

### **Inadequate Laboratory Infrastructure**

Inadequate laboratory infrastructure remains a major challenge in many developing countries. Blood banks frequently contend with unreliable electricity supply, disrupted cold-chain systems, insufficient storage facilities, and recurrent shortages of essential laboratory consumables. These constraints undermine the integrity of blood collection, processing, and testing, and ultimately compromise transfusion safety<sup>71</sup>.

### **Unsafe Practices in Blood Donation and Collection**

Unsafe blood donation practices contribute substantially to the persistence of TTIs. In many countries, blood services continue to depend heavily on family-replacement and commercial donors rather than voluntary, non-remunerated donors. Such donors may conceal relevant risk information in order to obtain financial compensation or meet family obligations. Inadequate donor-selection procedures and insufficient pre-donation counselling further undermine blood safety and increase the likelihood of collecting infected units<sup>71</sup>.

### **Gaps in Data and Transfusion Surveillance Systems**

Effective control of TTIs requires robust transfusion-surveillance systems and reliable epidemiological data. However, in many countries, major data gaps arise from poor record-keeping, inadequate reporting mechanisms, and limited research capacity. Weak surveillance systems hinder early outbreak detection, tracking of infection trends, and evaluation of blood-safety interventions. The absence of national donor databases and weak coordination among healthcare institutions further contributes to fragmented and ineffective transfusion-safety programmes. Addressing these challenges necessitates increased funding, strengthened laboratory infrastructure,

implementation of strong haemovigilance systems, sustained public enlightenment,

active promotion of voluntary blood donation, and wider adoption of advanced screening technologies to ensure safer transfusion practices<sup>69,70</sup>.

## CONCLUSION

Transfusion-transmissible infections (TTIs) remain a major global public-health concern and continue to pose significant challenges to blood safety and transfusion medicine. Despite substantial advances in donor screening, laboratory technology, vaccination programmes, and haemovigilance systems, the risk of transmitting infectious agents through transfusion has not been completely eliminated. This risk is particularly pronounced in developing countries, where health-care systems are weakened by inadequate funding, poor laboratory infrastructure, shortages of skilled personnel, window-period infections, weak transfusion-surveillance systems, the emergence of new pathogens, and continued reliance on replacement or commercial blood donors. In addition, sociocultural barriers and increasing population mobility facilitate the emergence and spread of novel infectious threats, further compromising blood safety. Recent advances in molecular diagnostics, including nucleic acid testing (NAT), as well as the digitalisation and strengthening of haemovigilance systems, offer important opportunities to enhance transfusion safety. However, access to these technologies remains highly unequal and continues to represent a major challenge for many developing nations

## Recommendations

1. Healthcare institutions should ensure strict adherence to standardised blood transfusion guidelines and infection-prevention protocols as specified by national blood transfusion services and regulatory authorities
2. Donor screening and recruitment should encompass a detailed medical history, thorough physical examination, and appropriate laboratory testing. Where feasible, blood banks should incorporate highly sensitive screening modalities, such as NAT, to further reduce the risk

of TTIs

3. Policies that promote voluntary, non-remunerated blood donation should be prioritised, while commercial and family-replacement donation practices should be progressively discouraged.
4. Governments should strengthen national blood transfusion agencies through increased funding, stronger regulation, and effective implementation of evidence-based policies
5. Public health education and awareness campaigns should be scaled up to improve knowledge of TTIs, safe blood donation practices, and preventive health behaviours
6. Tackling misconceptions, myths, stigma, and sociocultural barriers surrounding blood donation is essential for improving donor participation and enhancing the overall safety of the blood supply.

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