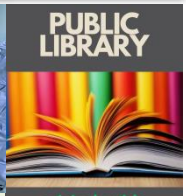

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SEROPREVALENCE AND INCIDENCE OF INFECTIONS TRANSMITTED BY BLOOD TRANSFUSION AMONG BLOOD DONORS FROM DIFFERENT COUNTRIES AROUND THE WORLD: A LITERATURE REVIEW

CARYL CALEB YOUMBI MENOUGONG[1*]
Catholic University of Central Africa

ETIENNE KIMESSOUKIÉ OMOLOMO[2]
Faculty of Medicine and Biomedical Sciences

DORA MBANYA[3]
National Blood Transfusion Service of Cameroon

***Corresponding Author:** **Caryl Caleb Youmbi Menougong**

ABSTRACT.
Blood transfusion is an act that saves human lives, through compatible and safe blood donations from a donor to a recipient. This transfused blood, if not properly screened, is capable of transmitting infections, such as hepatitis B, C and HIV viruses, from one individual to another. This is why the World Health Organization recommends that low-risk donors be selected for blood collection. The objective of this literature review is to determine the seroprevalence and incidence of infections transmissible by blood transfusion in health facilities among blood donors from different countries of the world. Data were collected from the Hinari, Pubmed/Medline and Google Scholar databases. The articles were selected over a period of ten years, from 2012 to 2022. The thematic analysis was done on the basis of 21 articles selected from the databases. The results confirm that HIV, HBV, HCV and syphilis are pathogens sometimes found in blood products. Other pathogens equally dangerous to human health are also found, such as dengue virus, hepatitis E, and human T-lymphotropic virus type 1 and 2 (HTLV-1/2). The results of this literature review also show that blood collected from previous and first-time donors does not always have the same characteristics. First-time donors show higher trends (prevalences and incidences) than regular donors. Incidence measurement is important for monitoring and maintaining the safety of the blood supply. However, it has also been observed that centrifugation of samples at high speed can reduce the rate of false positives for the Hepatitis B surface antigen, which is why good professional practices must be adopted in blood banks. In another setting, the test positivity rate decreased when considering results confirmed by nucleic acid amplification testing. For this, each government should facilitate the implementation of this test, and set an affordable price, so that patients can benefit from it. These various measures must also be closely monitored, because the lack of application of the principles of blood safety remains a public health problem in Africa, due to the supply of unsafe blood, which has considerable impacts in terms of mortality and morbidity.

Keywords: Seroprevalence and incidence, blood safety, blood transfusion.

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RESUME
La transfusion sanguine est un acte qui permet de sauver des vies humaines, au travers des dons de sang compatibles et sécurisés d'un donneur à un receveur. Il y a eu une augmentation de la demande en sang dans le monde entre 2008 et 2018, soit 10,7 millions de dons de sang, provenant des donneurs volontaires non rémunérés. Ce sang transfusé est susceptible de transmettre des infections, comme les virus de l'hépatite B, C et le VIH, d'un individu à un autre. L'acte transfusionnel se heurte au problème de transmission d'infections du donneur au receveur, c'est pourquoi l'Organisation Mondiale de la Santé recommande que les donneurs soient sélectionnés. L'objectif de cette recension des écrits est de déterminer la séroprévalence et l'incidence des infections transmissibles par transfusion sanguine dans les formations sanitaires parmi différents donneurs de sang de divers pays à travers le monde. Les résultats obtenus lors de cette étude proviennent des bases de données (Hinari, Pubmed/Medline et Google Scholar). Les articles ont été sélectionnés sur une période de dix ans, c'est-à-dire de 2012 à 2022. L'analyse thématique s'est faite sur la base de 21 articles sélectionnés des bases de données. Il en ressort que le VIH, le VHB, le VHC et la syphilis sont des agents pathogènes parfois retrouvés dans les produits sanguins. D'autres agents pathogènes tout aussi dangereux pour la santé humaine sont aussi retrouvés, à l'instar du virus de la dengue, de l'hépatite E, le virus T- lymphotrope humain de type 1 et 2 (HTLV-1/2). Les résultats de cette recension d'écrits montrent aussi que le sang prélevé chez les anciens et les nouveaux donneurs ne présentent pas toujours les mêmes caractéristiques. Les anciens donneurs présentent des tendances (prévalences et incidences) plus élevées que les nouveaux donneurs. La mesure de l'incidence est importante pour surveiller et maintenir la sécurité de l'approvisionnement en sang. Toutefois, il a aussi été remarqué que la centrifugation des échantillons à grande vitesse peut réduire le taux de faux positifs de l'antigène HBs, c'est pourquoi des pratiques professionnelles de qualité doivent être adoptées dans les banques de sang. Dans un autre contexte, le taux de positivité des tests diminuait lorsque l'on considérait les résultats confirmés par le test d'amplification d'acide nucléique. Pour cela, chaque gouvernement devrait faciliter la mise en place de ce test, et y fixer un prix abordable, afin que les patients puissent en bénéficier. Ces différentes mesures devraient aussi être surveillées de près, car le manque d'application des principes de la sécurité transfusionnelle demeure un problème de santé publique en Afrique, à cause de l'approvisionnement de sang non sécurisé, ce qui engendre des impacts considérables en termes de mortalité et de morbidité.

Mots clés : Séroprévalence et incidence, sécurité transfusionnelle, transfusion sanguine.

INTRODUCTION
Blood transfusion is an act that saves human lives, through the use of good quality blood and verified compatibility between donors and recipients. Demand for blood transfusions has continued to increase in recent years worldwide, particularly between 2008 and 2018, these demands were met in the majority by voluntary unpaid donors, the blood donations made by them accounted for nearly 10.7 million (WHO, 2022). The application of the principles of transfusion safety in blood banks takes into account many elements, ranging from the recruitment of low-risk blood donors to the administration of blood bags. It is for this reason that it is necessary to understand the demographic characteristics of blood donors, in order to guide their recruitment, as well as the different strategies that would allow their retention (Elsafi, 2020).

In addition to knowing the characteristics of donors, safety standards should also be put in place to ensure the safety of recipients. However, there is a lack of standardization of transfusion practices to guarantee the reduction of the infectious risk for recipients, in particular with regard to hepatitis B and C viruses, syphilis and HIV (Ehsan et al., 2020). Several infections can be transmitted by blood donation through various infectious agents. A blood-transmissible infection is any infection that is transmitted through the donation of blood or blood derivatives, the magnitude of which varies from country to country (Mohammed & Bekele, 2016). The human immunodeficiency virus (HIV), hepatitis B virus (HBV) and syphilis are infectious agents that are dangerous for blood safety (Abate & Wolde, 2016).
Other pathogens can also constitute a danger for transfusion safety, in particular: the hepatitis E virus, the dengue virus, the different types of plasmodium, etc. This is how microorganisms, including viruses and bacteria, constitute the greatest threats to the transfusion safety of the blood recipient (Kengne et al., 2018). To ensure the safety of blood recipients, one of the recommendations of the World Health Organization (WHO) is the procurement of blood from voluntary and unpaid blood donors, due to their markedly reduced chances to harbor and transmit infections, but these are unfortunately few in number (Aneke & Okocha, 2017). In sub-Saharan Africa, many donors are excluded from blood donations because they do not meet the eligibility conditions. To this end, it would therefore be wise to transform family donors into voluntary donors, because they meet all the criteria for blood donation and are ready to become voluntary donors and renew the donation (Allain & Sibinga, 2016). But, it has been proven that altruism (voluntary donation) is not yet generally accepted in developing countries, this being related to the cultural and psychological aspects, because people are more able to donate blood when a person is in need (Allain & Sibinga, 2016; Aneke & Okocha, 2017).

This situation has created three types of blood donors in Nigeria: voluntary (unpaid), replacement (family/friends) donors, and commercial (paid) donors (Aneke & Okocha, 2017). In addition to the difficulty that exists in retaining donors, there is also a real infectious problem associated with blood transfusion. During blood transfusion, several types of microorganisms can be transmitted, including: viruses and bacteria which are among the greatest threats to transfusion safety in blood recipient (Kengne et al, 2018). Faced with all these difficulties that blood transfusion faces, and particularly transfusion safety, it is relevant to question the seroprevalence and incidence of infections transmissible by blood transfusion among blood donors.

This article aims to determine the seroprevalence and incidence of infections transmitted by blood transfusion among blood donors in health facilities in different countries all around the world. To achieve this objective, a thematic review of the literature was made around 21 articles in English and French. These articles were identified from different databases including Pubmed/Medline, Google Scholar and Hinari. This work focuses on the review of the literature or the review of the writings. Apart from the introduction and the conclusion, it consists of three main parts. The first part is devoted to the methodological anchoring which defines the type of review, as well as the inclusion and exclusion criteria, and also the research methods. The second part is related to the results of the documentary research, and the last part is reserved for the discussion of the results.

METHODOLOGY

To conduct this literature review, it was a question of consulting scientific databases with the aim of highlighting the elements relating to blood transfusion, particularly seroprevalence and the incidence of infections transmissible by blood transfusion. The literature review was done over a ten-year interval, specifically studies that were published from 2012 until 2022. To perform this successfully, the integrative review method was used. First of all, it was a question of grouping together the studies on the seroprevalence and incidence of infections transmissible by blood transfusion in the different regions of the world, of carrying out a content analysis of these, and finally of carrying out a categorization of these different studies. This review mainly includes quantitative studies.

With regard to the inclusion criteria for this study, two languages were chosen for this research, French and English. The documentary research was carried out over a period of ten years, specifically from 2012 to 2022. The studies that were excluded from this search are those that had no relation to the objectives of the study. To extract the information collected from the various studies listed, these were entered into a Word document called “Reading sheet”. This document included the following information: names of authors, title of the study, objectives, methodology, results and limitations. These documents were selected from three databases which are: Hinari, pubmed/medline and Google scholar. Then, it was a question of proceeding to a first reading in order to retain the studies which are in line with the research objective. After that, a second reading of the articles was made in order to definitively select the articles necessary for this documentary research. In the end, twenty-one articles were selected.

RESULTS

Several threats pose a risk to the safety of recipients, among them human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and *Trepanoma pallidum* which are among the major threats to these. Blood is therefore a major vector for the transmission of infections (Alharazi et al., 2022; Noubiap et al., 2013). The seroprevalence and varying incidence of infections transmitted by blood transfusion varies from place to place. In Ethiopia, two studies carried out during two different years whose titles were: “Sero-prevalence of Human Immunodeficiency Virus, Hepatitis B Virus, Hepatitis C Virus, and Syphilis among Blood Donors at Jigjiga Blood Bank, Eastern” and “Sero-prevalence of transfusion transmittable infections: HIV, Hepatitis B, C and Treponema pallidum and associated factors among blood donors in Ethiopia: A retrospective study”. These report respective prevalence rates of HIV, HBV, HCV and the syphilis virus (3.16% and 0.4%; 9.48% and 2.4%; 0.73% and 0.4%; 0.73% and 0.9%) (Abate & Wolde, 2016; Abdella et al., 2020). However, there was a considerable discrepancy between the sizes of the populations of these studies, for Abdella et al. (2020) the study population was 554,954 donors, while Abate & Wolde (2016) the study population was 6827 donors.

The prevalence and incidence can also vary from one infection to another; this is how we can have a prevalence and an incidence that are many times higher than those of other infections. This situation can be illustrated by a study carried out in Burkina-Faso where the seroprevalence of HBV (8.56%), was twice that of HCV, likewise that of HCV (4.40%), which was almost four times that of HIV (1.80%). A similar result was obtained in South Africa where the incidence of HIV among new donors was almost double that of those giving blood for the first time (3.32 and 3.81 per 1000 people/year for new donors; for former donors it was 1.56 and 1.94 per 1000 people/year (Vermeulen et al., 2021; Yooda et al., 2019). These different cases show that repeat and first-time

donors do not always have the same characteristics. This is why measuring incidence is important to monitor and maintain the safety of the blood supply. In addition to this, blood collected from repeat donors allows these to be tracked over time and also helps in estimating the incidence of viral infections (Vermeulen et al., 2021).
It is very important for hospitals to have quality screening tests, as many infections can be transmitted to recipients of blood products. Several retrospective studies have shown the importance of quality screening tests for the detection of infections transmitted by blood transfusion. Some studies such as Wang et al. (2022), as well as Nkansah et al. (2022) report high prevalences of infections. At Jinling Hospital Nanjing University, seropositivity rates were 86.67% for HBV; 35.09% for HCV; 20.75% for HIV and 100% for *Treponema pallidum*, it is also worth noting that the authors results showed that centrifugation of samples at high speed can reduce the rate of false positives for HBs antigen (Wang et al., 2022). Nkansah et al. (2022) showed that over a nine-year period, the prevalence of HIV and syphilis among blood donors was 10.9% (95% C.I (0.098-0.120)). However, prospectively, women were less infected by *Treponema pallidum* than males (OR 0.511, [0.340 – 0.769]) (Nkansah et al, 2022).

Added to this, the results are also influenced by the types of tests performed as stated by some authors, during a study done in Mexico, when they show that: the test positivity rate decreased when considering the results confirmed by nucleic acid amplification test (Guerrero-García et al., 2021). Using this type of test could be useful for Ghana and China, because it could help to reduce the number of infections transmitted by transfusion in those countries. However, before the implementation of this test, the government should facilitate its implementation, and the cost should not be a barrier (Jain et al., 2012). Other authors have also highlighted a variation in infectious trends over the years. Vermeulen et al. (2021) found that HBV prevalence among blood donors decreased in South Africa from 0.84% in 2011 to 0.66% in 2019, following the implementation of a program to fight against hepatitis B. Similarly, among donors in southern Iran, the seroprevalences of HBV, HCV and HIV were respectively 0.15%; 0.1% and 0.004%, with HIV infection showing a slight decrease (Farshadpour et al., 2016). The authors also report that these infections were more common in poorly educated men who were first-time donors. The results of these different studies make it possible to make a difference between the characteristics of new and old blood donors, as mentioned above.

The trends indicate that first-time blood donors are more infected than repeat donors, these present trends (prevalences and incidences) with regard to HBV, HCV, HIV and syphilis much higher than the repeat donors (M'baya et al ., 2019; Nagalo et al., 2012; Vermeulen et al., 2021; Yooda et al., 2019). Replacement donors also have high burdens of HBV, HCV and HIV infections (Mulugeta et al., 2019). It should also be mentioned that several donors had co-infections. Noubiap et al. (2013) who reported 26 co-infections, the most common of which were HBV-HCV and HBV-HIV. Tigabu et al. (2019) also showed that 58 donors (0.96%) had multiple infections and that the prevalence of HIV, HBV and HCV was respectively equal to 2.5%; 4.1% and 1.6% out of a population of 5983 donors. Other researchers like Yang et al. (2016), also highlighted the fact that seropositivity increased considerably among blood donors (OR = 1.54, $P < 0.001$) and farmers (OR = 1.70, $P < 0.001$).

Some authors have presented overall prevalence results above 10%. These include Mohammed et al. (2016) in Ethiopia, as well as Okoroiwu et al. (2018) in Nigeria. These respectively reported prevalence rates for syphilis, HIV, HBV and HCV between 11.5% and 14.96%; with respective populations of 4224 and 24979 donors. In addition, paid donors were more infected than unpaid donors (Okoroiwu et al., 2018). These infections are also linked to risk factors such as having multiple sexual partners, a low level of education, as well as marital status, with married people being more infected (Bartonjo et al., 2019). Although the minimum WHO-recommended infections most often screened for in blood transfusion are HIV, HBV, HCV and syphilis, other infections also constitute a danger for blood transfusion safety (Ramassamy et al., 2020). In particular, the dengue virus, hepatitis E, human T-lymphotropic virus type 1 and 2 (HTLV-1/2) … (Ramassamy et al., 2020). The African continent is considered to be the most endemic continent for HTLV-1, with several million people affected (Ramassamy et al., 2020). It is thought that blood transfusion screening tests in these regions, should include anti-HTLV-1/2 tests (Kengne et al., 2018).

The human T-lymphotropic virus type 1 and 2 therefore constitutes a danger to public health, particularly for transfusion safety. Kengne et al. (2018) showed in their study carried out in Cameroon, that 4 participants, or 5.2% of the participants, had a double infection with HTLV-1/2. In Gabon, out of 3123 donors, 132 were positive for HTLV-1/2 (4.2%), while the prevalence of human T-lymphotropic virus type 1 was 0.74%; 1% for those who donated blood for the first time, and 0.5% for regular donors (Ramassamy et al., 2020). In addition, the dengue virus is found in asymptomatic donors, this disease is endemic in sub-Saharan Africa, particularly in Cameroon (Tchuandom et al., 2020). Asymptomatic potential donors with respect to dengue fever in Cameroon and Saudi Arabia tested positive for anti-DENV IgM and IgG antibodies (Ashshi et al., 2017; Tchuandom et al.,

2020). Anti-DENV IgM antibody seropositivity reflects an ongoing asymptomatic viraemic stage during the donation period, while anti-DENV IgG seropositivity reflects the high dengue endemicity in Saudi Arabia (Ashshi et al., 2017).

The majority of hepatitis E infections worldwide are caused by water, as well as food, but cases of this disease have also been reported among infections transmitted by blood transfusion (Bi et al., 2020). These also showed that overall anti-HEV IgG antibody levels in blood donors in Europe ranged from 4.7% to 52.5%; 6% in Australia, between 14.3% to 21.48% and 16% in the United States. In the Middle East and North Africa region, the prevalence of HEV from the year 2000 to the year 2014 ranged from 2% to 37.5%; this seroprevalence was higher in men than in women (Yazbek et al., 2016).

Certain infections of parasitic origin such as microfilariae can also hamper transfusion safety. Some authors report the prevalence of these in Nigeria, they were 1.3% for *Loa Loa*; 15.6% for *Mansonella Perstans* and 0.2% co-infections of *Loa Loa* and *Mansonella. Perstans* (Bloch et al., 2012). In the same country, the prevalence rates reach 18%, 23% and 12.3% for HIV, HBV and HCV respectively (Aneke & Okocha, 2017). Thus, guaranteeing the availability and safety of blood requires the recruitment of voluntary non-remunerated donors, and the prevention of infections transmitted by blood transfusion (Kanagasabai et al., 2018). In addition, there is still a lack of information related to the number of infections encountered in blood transfusions, in several countries, such as Yemen. This lack of information is due to the non-existence of hospital studies or national reports. (Alharazi et al., 2022).

DISCUSSION

In this section it has been a question of highlighting the extent of infections transmissible through blood transfusion in different parts of the world. These various studies were based on serological tests carried out in laboratories and blood banks. These tests are important because screening has public health benefits, not only at the level of the recipients, but also of the community (Mulugeta et al., 2019). From this section, it appears that several infections can affect transfusion safety. Several studies measured the impact of HIV, HCV, HBV and syphilis on blood transfusion, others spoke of infections such as dengue virus, HTLV-1/2, hepatitis E virus… It should also be noted that the incidence and prevalence of these infections vary considerably from one region of the world to another.

For example, in two retrospective studies carried out in Ethiopia, Abate & Wolde (2016), and Abdella et al. (2020), the seroprevalences of HIV, HBV, HCV and syphilis in a population of 6827 donors were respectively: 3.16%; 9.48%; 0.73% and 0.73%, and were respectively: 0.4%; 2.4%; 0.4%; 0.9% in the 554,954 donors analysed by Abdella et al. (2020). These differences can be explained by the difference in the sizes of the study populations, and also because these studies were not done during the same years. Apart from the fact that the size of the study population can greatly influence the measurement of seroprevalence and incidence of infections, other factors can also considerably influence these measurements. One of these limitations is the fact that many of these studies measure data retrospectively. The studies of Abate & Wolde (2016), and Abdella et al. (2020), these studies measure prevalence at a given time, but do not allow for an estimate of the actual incidence (appearance of new cases).

It was also noticed that infections transmissible by blood transfusion were more numerous among first-time donors, compared to repeat ones, confirmed by Vermeulen et al. (2021) and Yooda et al. (2019). A similar result was found in Eritrea, the prevalence of transfusion-transmissible infections was 10.8% among first-time blood donors, compared with 0.16% among second-time donors and even lower among regular donors (Siraj et al., 2018). These results confirm the need to ensure a blood supply from voluntary non-remunerated donors, as recommended by the World Health Organization, due to their reduced chances of harboring and transmitting infections, but there are unfortunately fewer in number than replacement donors (Aneke & Okocha, 2017).

However, without longitudinal monitoring of these donors, it is impossible to detect infections occurring after donation or to assess the residual risk. Tagny et al. (2018) also shown that the increase of voluntary donors is able to reduce the number of infections transmitted by blood transfusion. Indeed, these authors had shown that there had been an increase in the number of voluntary blood donors of 20% (between 2012 and 2016) in eleven French-speaking African countries, and a decrease in the seroprevalence of infections which are transmitted by blood transfusion by 7% (between 2009 and 2016). This increase in voluntary blood donors could be associated with improved communication strategies implemented in these countries to encourage blood donation. However, an increase in the number of voluntary or first-time donors does not always lead to a reduction in transfusion-transmissible infections. For example, a study conducted in Ethiopia reported that the prevalence of HIV among blood donors was 2.5% (Siraj et al., 2018).

For this reason, incidence measurement is necessary to monitor and maintain the blood supply, as well as for the follow-up of past donors to estimate the incidence of viral infections (Vermeulen et al., 2021). Some authors in China and Ghana report very high prevalence rates of infection by at least 20% for each of these infections (HBV, HIV, HCV and *Treponema pallidum*) (Wang et al., 2022). Furthermore, the cumulative seroprevalence of HIV and Treponema pallidum was 19.1% in the "Offinso-North District" health facility in Ghana, during a retrospective study carried out over the period from January 2010 to December 2018 (Nkansah et al., 2022).

In Africa, it would be better to express some reservations regarding this type of result, in particular because of the limited access to confirmatory tests or advanced techniques such as NAT. These studies have some limitations. Among these, there is first of all the retrospective approach (the data having already been collected, the researcher therefore has no control over its quality, completeness or accuracy). Secondly, Secondly, these studies do not describe the causes of the infections; they are limited to describing the results without exploring their underlying causes. However, these results show the extent of blood transmissible infections in blood banks, and the importance of using adequate testing strategies. Since centrifugation of samples at high speed can reduce the rate of false positives for HBs antigen (Wang et al., 2022), several blood donors in blood banks may have been declared positive for HBV due to centrifugation.

It should also be noted that in another context, the test positivity rate decreased when considering the results confirmed by the nucleic acid amplification test (Guerrero-García et al., 2021). Although very costly, it will be an effective test where the government can facilitate its use. Several studies reported prevalence rates above 10% for HIV, HBV and HCV (Mohammed & Bekele, 2016; Okoroiwu et al., 2018). These rates could have been influenced by the quality of the tests used, or even because these are retrospective studies that take into consideration a large population over several years. These high prevalences could also be explained by certain risk factors such as multiple sexual partners, a low level of education (Bartonjo et al., 2019). It would therefore be important to find strategies to limit the spread of infections among potential blood donors with a low level of education, as well as to raise awareness among those who have many sexual partners.

Other infections such as dengue virus, HTLV-1/2, and other infections have been mentioned as constituting a danger to for blood safety. HTLV-1/2 as well as dengue virus have been cited as being endemic in Africa, and may be dengue virus may be present in asymptomatic donors. These different results all indicate that systematic screening for these infections must be established blood banks in sub-Saharan Africa, because several potential donors may be affected. This is why while waiting for a vaccine, measures must be taken to secure blood products in areas endemic and not endemic to dengue virus, moreover the attention put on this virus could help prevent other unknown viruses, but dangerous for blood transfusion (Pozzetto et al., 2015). In addition to these infections which have been discussed above, other microorganisms such as microfilariae also impact blood safety in Africa. These different infections must also be closely monitored, because the lack of application of the principles of transfusion safety remains a public health problem in Africa, due to the unsafe blood supply, which has considerable impacts in terms of mortality and morbidity (Bloch et al., 2012).

CONCLUSION

This review highlights the high prevalences of transfusion-transmissible infections in first-time donors, compared to voluntary and repeat donors. It shows the need for implementation of the World Health Organization recommendation that voluntary blood donors should be prioritized for blood transfusion over family/replacement or even paid donors. The results of this review further highlight the infectious risks associated with blood transfusion and the need to intensify screening strategies for blood-borne infections, particularly in low-and middle-income countries, including sub-Saharan African countries, which have high prevalence and incidence rates for these infections.

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