

Prevention strategies of transfusion-transmitted parasitic infections (TTPIs): Strengths and challenges of current approaches, and evaluation of the strategies implemented in Iran

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ABSTRACT

Background: Several strategies are being implemented in blood transfusion centers of the world to prevent the transfusion-transmitted parasitic infections (TTPIs). The objective of this study was to determine and describe the strategies to minimize the transmission risk of parasitic agents via blood transfusion in Iran.

Methods: This study was conducted in the Iranian blood transfusion organization (IBTO). The data were extracted from the latest version of the “medical interview” standard operating procedure (SOP).

Results: The donor selection is the first and only step to reduce the risk of TTPIs in endemic and non-endemic areas of Iran. In all blood transfusion centers of the IBTO, the blood donation volunteers with a previous history of malaria, Chagas disease, visceral leishmaniasis (VL), mucocutaneous leishmaniasis and babesiosis, as well as those with clinical toxoplasmosis, cutaneous leishmaniasis (CL) and with a history of residence in, or travel to, malaria-endemic areas are permanently or temporarily deferred from the blood donation.

Conclusions: Since malaria, toxoplasmosis and VL are endemic in parts of Iran, as well as the increasing travels to endemic areas and immigrations from endemic to non-endemic areas of parasitic infections, the extensive use of blood and blood components and the asymptomatic occurrence of most parasitic infections in blood donors, the donor selection strategy is not sufficient to prevent the TTPIs. Therefore, the changing of donor selection process and the use of other common preventive strategies are recommended to reduce the risk of TTPIs, especially for high-risk groups of toxoplasmosis and VL.

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1. Introduction

Blood transfusion can be a lifesaving procedure for patients in need, but it may also lead to infectious and non-infectious complications in recipients (Cheesbrough, 1998). Parasitic infections are one of the most important adverse effects of blood transfusion.

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sion which should be considered (Carson et al., 2012). To be transmitted through transfusion, parasitic agents must: (1) be present in the bloodstream of donors for long period or in a sufficient load to a susceptible recipient; (2) cause infection without clinical symptoms; (3) survive in the storage duration of blood and blood components; and (4) have a relatively long incubation period (Reesink and Engelfriet, 2004).

So far, the transmission of six parasitic infections and diseases via blood and blood components transfusion has been reported, including malaria, toxoplasmosis, American trypanosomiasis (Chagas disease), visceral leishmaniasis (VL), babesiosis and filariasis (Dod, 1998). With the exception of filariasis, which is a helminthic infection, the causative agent of the rest of the infections is protozoa. The protozoal parasitic infections are often transmitted through the transfusion of cellular blood components (Reesink, 2005). Although the incidence of transfusion-transmitted parasitic infections (TTPIs) is lower compared to viral and bacterial infections, they can cause serious outcomes, especially in people with a weakened or suppressed immune system (Garraud, 2006).

In Iran, malaria is endemic in the southeast of country consists of Sistan and Baluchestan, Hormozgan and Kerman provinces (Fig. 1) (Piroozi et al., 2019). According to the global report of the WHO, 939 malaria cases were reported in 2017, of which 57 (6.07%) were autochthonous cases (World Health Organization, 2018). Toxoplasmosis has been reported in all areas of Iran and the performed studies showed a high seroprevalence among the general population (Daryani et al., 2014; Foroutan et al., 2018). Visceral leishmaniasis is endemic in some parts of Iran and 100–300 new cases are reported every year (Mohebbi, 2013; Shokri et al., 2017). As TTPI, of these diseases, only malaria has been reported in Iran (Mardani et al., 2016).



Fig. 1. Map of Iran and geographical situation of malaria endemic areas of this country namely Sistan and Baluchestan, Hormozgan and Kerman provinces, as well as two main foci of visceral leishmaniasis (VL): one in Fars Province and the other in Ardabil Province.

Prevention strategies of TTPIs are different in endemic and non-endemic areas (World Health Organization, 2012). There are multiple strategies to prevent the transmission of parasitic agents via blood transfusion, including donor selection and deferral (permanent or temporary), testing of blood donation and the use of leukoreduction filters and pathogen inactivation techniques (World Health Organization, 2012; Pan American Health Organization, 2009; Aché and Matos, 2001; Wendel Neto, 1995). In Europe and the United States of America (USA), the main strategy for preventing TTPIs is donor selection by interviewing (Reesink, 2005).

The aim of this study was to determine and describe the strategies to prevent the transfusion-transmitted parasitic infections (TTPIs) in Iran.

2. Materials and methods

The present study was performed in the Iranian blood transfusion organization (IBTO) from November 2018 to February 2019. In this study, the latest version of the "medical interview" standard operating procedure (SOP) was fully reviewed and the data on parasites and parasitic infections or diseases were extracted.

It is worth noting that all physicians must complete the training courses associated with this document before they start working in the section of donor selection of the IBTO. The most important training courses are how to register and accept blood donation volunteers, medical interview and examination and how to implement a confidential self-exclusion system, as well as identification and recording of adverse reactions caused by blood donation.

3. Results

In all blood transfusion centers of the IBTO, donor selection or screening of blood donors through interviewing is the first and only step in the prevention of TTPIs in endemic and non-endemic areas that is performed by a trained physician. In this prevention strategy, the potential blood donors with a previous history of malaria, Chagas disease, visceral leishmaniasis (VL) or kala-azar, muco-cutaneous leishmaniasis and babesiosis are permanently deferred from donating blood.

The blood donation volunteers with a history of residence in, or travel to, malaria-endemic areas are deferred for three years after departure and one year after return from a malarious area, respectively. Based on the SOP of IBTO, the volunteers who are temporarily deferred for living or traveling in malaria-endemic areas can be accepted as blood donor if they were symptom-free during the deferral period (Fig. 2).

The blood donation volunteers with clinical toxoplasmosis and cutaneous leishmaniasis (CL) are deferred from the blood donation for up to 6 months and one year after treatment and complete recovery, respectively.

4. Discussion

The main task of the IBTO is to supply a sufficient and safe blood and its components to patients (Pourfathollah et al., 2015; Cheraghali, 2012). In blood transfusion centers of Iran, all the donated blood is screened for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis, as well as in some centers for human T-lymphotropic virus (HTLV) type 1 and type 2 (Pourfathollah et al., 2015; Cheraghali, 2012; Abolghasemi et al., 2009). The laboratory screening of donated blood for TTPIs is not routinely performed in most countries of the world, including Iran (World Health Organization, 2017a). Therefore, the selection of blood donors through interviewing is the only way of prevention the transmission of parasitic infections via transfusion (Polizzotto et al., 2008; Newman, 2001). Prevention strategies of TTPIs and the current status of transmissible parasitic infections via blood transfusion in Iran and the world are discussed separately in the following sections.

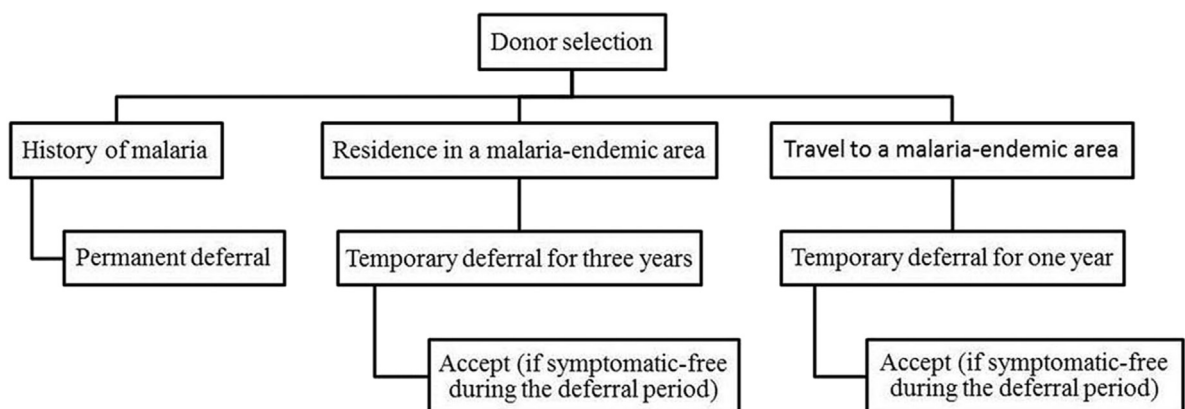


Fig. 2. Algorithm of blood donor selection and deferral for malaria in Iran.

4.1. Malaria

Malaria is a vector-borne disease caused by five *Plasmodium* species in humans (Antinori et al., 2012). Globally, 219 million cases were reported from 90 countries with 435,000 deaths in 2017 (World Health Organization, 2018). Malaria is one of the first reported transfusion-transmitted infections (TTIs) (Kitchen and Chiodini, 2006) and more than 3000 cases of transfusion-transmitted malaria (TTM), totally, were reported worldwide (Mardani et al., 2016). Two main strategies are being implemented to prevent the TTM in endemic and non-endemic areas including donor selection and laboratory screening (Kitchen and Chiodini, 2006). Furthermore, the leukoreduction by filtration of whole blood (WB) and/or red blood cells (RBCs) units could be a suitable and cost-effective policy to reduce the risk of TTM (Jimenez-Marco and Girona-Llobera, 2019; Cardo et al., 2009). According to the WHO recommendations, if possible, all donated blood should be screened for malaria (World Health Organization, 2010; Okwa, 2003). On the other hand, there has been no reliable test available for universal screening of malaria in blood donors (Seed et al., 2005; Singh and Sehgal, 2010). In many countries, however, donor selection or blood donors screening through interviewing is the only step of preventing of TTM (Slinger et al., 2001). The ideal strategy to minimize the transmission risk of malaria via blood transfusion is a combination of appropriate donor selection and laboratory screening in non-endemic and endemic areas (Kitchen and Chiodini, 2006; Kitchen et al., 2005; Fugikaha et al., 2007).

In Iran, the blood donation volunteers with a history of malaria are permanently deferred (Fig. 2), like in Canada (O'Brien et al., 2015). These individuals are accepted under conditions as blood donor in Australia, England, France and the USA (O'Brien et al., 2015). The blood donation volunteers who were lived or resided for a while in a malaria-endemic area are deferred for three years in several countries including Brazil, Canada, Estonia, Italy, Spain and the USA (Reesink and Engelfriet, 2004; Reesink, 2005). In Australia, England and France, this deferral time is four, six and four months, respectively (O'Brien et al., 2015). A history of living or staying in an endemic area of malaria results in permanent deferral in Ireland (Reesink and Engelfriet, 2004; Reesink, 2005). The visitors to malaria-endemic areas are accepted six months after their return in Estonia, Italy and Spain (Reesink and Engelfriet, 2004; Reesink, 2005), as well as three years in Australia (O'Brien et al., 2015). In Canada, England and the USA, the blood donation volunteers with a history of travel to an endemic area of malaria are deferred for 12 months (one year) after return (Reesink, 2005; O'Brien et al., 2015). A deferral time of four months is applied for traveling to malaria-endemic areas in France (Reesink and Engelfriet, 2004; Reesink, 2005). In Iran, a history of staying in and traveling to endemic areas of malaria leads to a deferral for three years and one year, respectively (Fig. 2).

So far, five studies have been conducted on blood donors in Iran. The laboratory testing results were negative by microscopic examination of Giemsa-stained blood smears and rapid diagnostic test (RDT) methods, as well as the seroprevalence of malaria infection was 13.98% (91/651) and 4.69% (18/384) using indirect immunofluorescence assay (IFA) and enzyme linked immunosorbent assay (ELISA) methods, respectively (Mardani et al., 2016). According to study performed by Mardani et al. (2016), 344 cases of TTM were reported during 1963–1983 from Iran. From 1984 to 2018, no case of TTM has been reported in Iran which may be due to the effectiveness of the donor selection strategy in blood transfusion centers, but there are other reasons that should not be ignored: (1) Extreme decrease of malaria incidence in the recent three decades (Piroozzi et al., 2019; Hemami et al., 2013; Norouzinejad et al., n.d.); (2) Carelessness to the occurrence of malaria in non-endemic areas; and (3) Lack of recording and reporting of TTM cases. On the other hand, malaria is endemic in regions of Iran and in neighboring countries including Pakistan and Afghanistan with high prevalence (World Health Organization, 2018), as well as due to the increasing need to blood and blood components and the travel and migration from malaria-endemic to non-endemic areas, the transmission of malaria through blood transfusion is possible. Therefore, in malaria-endemic areas, all donated blood should be screened with a test based on antigen detection. In non-endemic areas of malaria in addition to the implementation of donor selection and deferral strategies, the blood donation volunteers with a history of residence in and travel to malaria-endemic areas should be screened after the deferral period with a test based on antigen and antibody detection, respectively. According to the WHO report, the laboratory screening of all or part of blood donations is performed for malaria infection in 55 countries by microscopic examination of blood smears, immunodiagnostic or molecular methods (World Health Organization, 2017a; World Health Organization, 2017b). Since the clinical symptoms of malaria is similar to many diseases, such as influenza (Bartoloni and Zammarchi, 2012), the acceptance of temporarily malaria-deferred volunteers due to staying and traveling to endemic areas of malaria based on not having clinical symptoms should be changed and performed on the basis of laboratory testing. It is important to note that the unnecessary deferral is discouraging and most malaria-deferred volunteers never return to donate blood (Dodd, 2007).

4.2. Chagas disease

Chagas disease (CD), or American trypanosomiasis, a zoonosis caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*) is endemic in Latin American countries (Rassi et al., 2012). In non-endemic countries, the transfusion of blood and its products is one of the main routes of CD transmission (Angheben et al., 2015). The total number of transfusion-transmitted chagas disease (TT-CD) is not exactly clear, although it is estimated to be between 300 and 800 in the past decades (Wendel, 1998; Hernández-Becerril et al., 2005). Strategies to prevent the TT-CD are different in endemic and non-endemic regions. All blood donations should be tested in the endemic areas for anti-*T. cruzi* antibodies (Schmunis, 2007). Donor selection and deferral through interviewing and laboratory screening of donations from at-risk individuals (selective testing) are two strategies that are being implemented in non-endemic countries including Australia, Belgium, Canada, France, Japan, Luxembourg, New Zealand, Norway, Spain, Sweden, Switzerland, the UK (United Kingdom) and the USA (World Health Organization, 2017a; Angheben et al., 2015). In

non-endemic areas, individuals with at least one of the following conditions are identified as those at-risk for Chagas disease: birth in, stay in an endemic area for at least 6 months; having mother or maternal grandmother born in endemic countries; Receiving blood and/or its components or organ transplantation in endemic areas; Traveling for at least 28 days in the villages of endemic regions. These individuals should be permanently deferred unless a valid serological test is available, which may be accepted six months after the last exposure if the test result is negative (Castro, 2009; O'Brien et al., 2008). According to recommendations of the American association of blood banks (AABB), council of Europe (CoE), Caribbean regional standards (CRS) and pan American health organization (PAHO), individuals with a history of CD should be permanently deferred from the blood donation (Pan American Health Organization, 2009). In addition to these strategies, leukoreduction filters and pathogen inactivation systems have been studied to improve the safety of blood components such as platelet and plasma, which needs to be further investigated (Angheben et al., 2015).

CD and TT-CD have not been reported in Iran. The permanent deferral of individuals with a history of CD is the only policy to prevent the TT-CD in blood transfusion centers of the IBTO. Due to increasing migrations from endemic areas and travels to endemic areas of CD, it is imperative to adopt and implement a suitable strategy for screening of at-risk donors for CD (having at least one of the above-mentioned conditions).

4.3. Babesiosis

Babesiosis is the most prevalent TTPIs after malaria and endemic in parts of the North America continent (McQuiston et al., 2000; Pantanowitz et al., 2002). This disease is caused by the intraerythrocytic protozoan parasites of the genus *Babesia* (Vannier et al., 2015). The actual rate of transfusion-transmitted babesiosis (TTB) is unclear in the world, but more than 200 cases have been reported only in the USA (Moritz et al., 2016; Moritz et al., 2017; Herwaldt et al., 2011; Fang and McCullough, 2016). For individuals with a history of babesiosis, the AABB, CoE, CRS and PAHO recommend that they should be deferred indefinitely from donating blood (Pan American Health Organization, 2009; American Association of Blood Banks, 2018). Since the babesial infection is often without clinical symptoms in individuals with normal immune system, the donor selection strategy cannot effectively identify asymptomatic and undiagnosed cases (Wudhikarn et al., 2011; Krause et al., 1998). Although the food and drug administration (FDA) of the USA has licensed the arrayed fluorescent immunoassay (AFIA) and the nucleic acid test (NAT) to screen blood donations for the detection of specific antibodies and DNA of *Babesia microti*, respectively (Food and Drug Administration, 2018), there is currently no approved test for babesiosis screening (Okwa, 2003; Krause et al., 1998) and the laboratory testing of blood donations is not routinely performed even in blood transfusion centers of endemic areas. Other preventive strategies of TTB, including leukoreduction filter and pathogen inactivation systems, are not generally applicable or effective and access to them is difficult (Wudhikarn et al., 2011).

In Iran, there is no documented report of human babesiosis and TTB, as well as individuals with a history of babesiosis are permanently deferred from donating blood. Since most cases of babesiosis are asymptomatic, the donor selection strategy cannot effectively prevent the TTB (Wudhikarn et al., 2011; Krause et al., 1998). On the other hand, this infection has been reported with relatively high prevalence in domestic herbivores from different regions of Iran and may be a potential life-threatening for inhabitants particularly farmers and ranchers (Haghi et al., 2017). Therefore, an appropriate strategy should be adopted and implemented for screening of at-risk donors for babesiosis, as well as this disease consider in the differential diagnosis of unknown hemolytic anemia after blood transfusion with or without fever (Herwaldt et al., 2011).

4.4. Toxoplasmosis

Toxoplasmosis is a zoonotic disease caused by *Toxoplasma gondii* (*T. gondii*), an obligate intracellular protozoan parasite (Sundar et al., 2007). The parasite infects a wide range of warm-blooded animals and humans in different parts of the world (Robert-Gangneux and Dardé, 2012). It is estimated that up to one-third of the world's human population is infected with this parasite (Robert-Gangneux and Dardé, 2012). The seroprevalence of *Toxoplasma gondii* infection varies from less than 10% to more than 90% in different countries (Robert-Gangneux and Dardé, 2012). The infection is often without clinical symptoms (asymptomatic) in immunocompetent individuals (Hoseini et al., 2014). Severe infections usually occur in hosts with immune deficiency such as cancer patients, HIV-positive individuals and organ transplant recipients (Robert-Gangneux and Dardé, 2012; Ahmadpour et al., 2014). In addition, pregnant women, neonates and children are the high-risk groups for toxoplasmosis (Daryani et al., 2014; Ahmadpour et al., 2014; Foroutan-Rad et al., 2016a).

Most blood and blood components recipients are immunocompromised individuals who are prone to transfusion-transmitted toxoplasmosis (TTT) (Shaddel et al., 2014; Zainodini et al., 2014). The occurrence of TTT is rare and only the transmission in four definite cases through granulocyte concentrates transfusion, as well as one possible case via platelet transfusion, has been reported (American Association of Blood Banks, 2009). According to studies conducted in different countries, the overall rate of *T. gondii* infection seroprevalence was 33% in healthy blood donors (Foroutan-Rad et al., 2016b). The presence of anti-*Toxoplasma* antibodies is long-lasting and does not mean active infection (Mansouri et al., 2017; Montoya, 2002).

Given the high seroprevalence of *T. gondii* infection in blood donors (Foroutan-Rad et al., 2016b) and the lack of a reliable approved laboratory test for toxoplasmosis screening (Okwa, 2003; Karimi et al., 2016), prevention of TTT is not possible through donor selection and serological screening strategies (Channon et al., 2000). Moreover, discarding blood donations based on positive serology test results heavily endangers blood availability, especially in countries with a high prevalence of infection (Channon et al., 2000). Due to the ability of *T. gondii* to survive and replicate in leukocytes (Channon et al., 2000), the use of

leukoreduction filters may reduce the risk of TTT (Okwa, 2003; Spencer, 2016). AABB, Australian Red Cross (ARC), CoE, and CRS do not have a specific requirement for preventing toxoplasmosis via blood transfusion. PAHO recommends preparation of anti-*T. gondii* negative blood and blood components for at-risk groups (Pan American Health Organization, 2009).

Based on performed studies, the *T. gondii* seroprevalence was 43%, 26% and 34.4% in the Iranian general population, animal intermediate hosts and blood donors, respectively (Foroutan et al., 2018; Mansouri et al., 2017). TTT has not been reported in Iran. The deferral for up to 6 months after potential treatment and complete recovery is the only strategy to prevent the TTT in blood transfusion centers of the IBTO. Many studies have been conducted in blood donors in Iran (Mansouri et al., 2017), most of which emphasize the necessity of laboratory testing to prevent toxoplasmosis by blood transfusion. For several reasons, the universal screening of blood donations is not feasible:

- (1) Given the high seroprevalence of *T. gondii* infection in Iranian blood donors, the discarding blood donations based on a positive serology test result leads to reduce blood supply.
- (2) Currently, there is no licensed laboratory test for toxoplasmosis screening in blood donors.
- (3) The laboratory screening of blood donations for TTT is not routinely carried out in the world.
- (4) A positive serology test result does not mean active toxoplasma infection.

Therefore, the use of leukocyte-reduced (filtered) blood components and also preparation of anti-*Toxoplasma gondii* negative blood and its products for high-risk groups is recommended to reduce the risk of TTT in Iran.

4.5. Visceral leishmaniasis

Visceral leishmaniasis (VL), also known as “kala-azar”, is the most serious clinical type of leishmaniasis, which, if left untreated, leads to death in almost 100% of cases (Herwaldt, 1999; Thornton et al., 2010). This disease is caused by *Leishmania donovani* (*L. donovani*) complex (Chappuis et al., 2007) including *L. donovani*, the causative agent of anthroponotic VL (AVL) in the Indian subcontinent and Eastern Africa, and *L. infantum*, the causative agent of zoonotic VL (ZVL) in the Mediterranean basin, Middle East, West Africa and South America (Sarkari et al., 2012; Quinnell and Courtenay, 2009). In 2017, 94% (20,792) of new cases of VL occurred in seven countries: Brazil, Ethiopia, India, Kenya, Somalia, South Sudan and Sudan (World Health Organization, 2019). More than 95% of *L. donovani* and *L. infantum* infections are asymptomatic in immunocompetent individuals (Engwerda et al., 2004; Cardo, 2006; Dey and Singh, 2006). On the other hand, the immunocompromised patients, pregnant women and infants are at-risk of transmitting VL through blood transfusion as the high-risk groups. Therefore, *Leishmania*-infected blood donors in VL-endemic areas can be a potential source of risk and transmit infection to blood and blood components recipients (Dod, 1998; Cardo, 2006; Jimenez-Marco et al., 2016; Michel et al., 2011).

The transmission of leishmaniasis by blood transfusion is relatively rare (Dod, 1998) and only 14 cases of transfusion-transmitted leishmaniasis (TTL) with controversial evidences have been reported in the world (Jimenez-Marco et al., 2016). Based on performed studies in different regions, the prevalence of VL was 7% among healthy blood donors using serological methods (Asfaram et al., 2017a). Due to the lack of valid and available laboratory test (Okwa, 2003; Jimenez-Marco et al., 2012), VL screening is not routinely implemented in blood transfusion centers around the world (Jimenez-Marco et al., 2016). Additionally, most individuals infected with the etiologic agents of VL are without clinical symptoms (Engwerda et al., 2004; Cardo, 2006; Dey and Singh, 2006; Jimenez-Marco et al., 2016), as well as a positive result by serology test does not indicate active infection (Fakhar et al., 2012; Riera et al., 2008). The prevention TTL, therefore, is not feasible only by the donor selection and serological screening strategies. Since the species of *Leishmania* are obligate intracellular parasites (Alexander and Russell, 1992) and able to survive and proliferate in the macrophages (Antoine et al., 1998), the filtration of leukocytes at the time of blood collection or at the patient's bedside can decrease the risk of TTL (Mansueto et al., 2014; Cardo et al., 2006a). The use of pathogens inactivation techniques has demonstrated different results in reducing the load of *Leishmania* parasites in various blood components (Jimenez-Marco et al., 2012; Mansueto et al., 2014; Eastman et al., 2005; Cardo et al., 2006b; Tonnetti et al., 2015; Shulman, 1994; Wagner et al., 2006). The CoE and PAHO require the permanent deferral of individuals with a history of VL. According to recommendation of the PAHO, individuals with a history of travel to, or transfusion in, an endemic area of VL should be deferred for two years from the blood donation (Pan American Health Organization, 2009). For individuals with a history of extended stay in VL-endemic areas, the WHO recommends that they should be deferred for at least one year since their last return (World Health Organization, 2012). In most European countries, there are no specific measures to prevent the TTL. In Ireland and the USA, the blood donation volunteers with a history of travel to Iraq are deferred for one year, as well as in Israel these visitors are permanently deferred from the blood donation (Reesink, 2005). It seems that the use of leukoreduction filters is the most efficient policy to reduce the transmission risk of leishmaniasis through blood transfusion (Cardo, 2006; Riera et al., 2008).

In Iran, *L. infantum* is the causative agent of VL (Sarkari et al., 2012). This disease is endemic in at least eight provinces with an annual incidence rate of around 100–300 cases (Mohebbali, 2013; Shokri et al., 2017). Up to now, TTL have not been reported in Iran and only two studies were executed on healthy blood donors in two main foci of VL: one in Fars Province (Fig. 1) by Sarkari et al. (2015) and the other in Ardabil Province (Fig. 1) by Asfaram et al. (2017b). The results of these studies showed that the prevalence of *Leishmania* infection was 1.4% (28/2003) and 3.8% (23/600) by direct agglutination test (DAT), respectively. In Iran, the blood donation volunteers with a history of VL are permanently deferred and this is the only strategy to prevent the TTL. According to studies performed in VL-endemic areas of Iran, the seroprevalence of this disease was relatively high among healthy blood donors (Sarkari et al., 2015; Asfaram et al., 2017b). Moreover, *Leishmania*-infected blood donation volunteers are often asymptomatic (Engwerda et al., 2004; Cardo, 2006; Dey and Singh, 2006; Jimenez-Marco et al., 2016), as well as the

universal screening of blood donors for VL is not routinely carried out in the world (Jimenez-Marco et al., 2016) due to the lack of licensed laboratory test (Okwa, 2003; Jimenez-Marco et al., 2012). To prevent the occurrence of TTL in Iran, in addition to the donor selection and deferral strategies, the use of leukoreduced blood components is recommended for high-risk groups, especially in VL-endemic regions.

4.6. Filariasis

Filariasis is the general name for a group of diseases caused by parasitic roundworms or nematodes (Hotez and Kamath, 2009; Chandy et al., 2011) and endemic in the tropical regions of Africa, Southern America and Asia (Arora and Arora, 2005). This life-threatening disease is transmitted by the bite of infected hematophagous vectors (Sasa, 1979). Only eight species of the several hundred of known filarial parasitic worms are responsible for human infections: *Wuchereria bancrofti*, *Onchocerca volvulus*, *Brugia malayi*, *Brugia timori*, *Loa loa*, *Mansonella streptocerca*, *Mansonella perstans* and *Mansonella ozzardi* (McConnaughey, 2014). In addition to these species, zoonotic filarial parasites of the genus *Dirofilaria* (*D. immitis* and *D. repens*) infect humans and are prevalent in the Mediterranean basin (Tahir et al., 2019). Since arthropod vectors play an evolutionary role in the life cycle of filarial worms (Wendel Neto, 1995), the transmitted microfilaria via blood transfusion do not develop into adult worm (Choudhury et al., 2003; Weller et al., 1978). In microfilaria-infected blood recipients, allergic reactions might often occur that are self-limited and disappear after a certain period of time depending on the parasite species (Wendel Neto, 1995; Choudhury et al., 2003; Bregani et al., 2003).

The transmission of filariasis through transfusion is possible (Choudhury et al., 2003; Ojo-bola et al., 2014; Viroj, 2009) and a serious threat to blood and its components recipients (Ojo-bola et al., 2014; Bolaji et al., 2014). Despite the potential for transmission, the reported cases of transfusion-transmitted filariasis (TTF) are very low (Viroj, 2009; Bloch et al., 2012). According to studies carried out mainly in endemic countries, the prevalence of anti-filarial antibodies and microfilaraemia was high among healthy blood donors (Choudhury et al., 2003; Weller et al., 1978; Bregani et al., 2003; Ojo-bola et al., 2014; Bolaji et al., 2014; Emeribe and Ejezie, 1989; Akinboye and Ogunrinade, 1987; Mabayoje et al., 2006; Adediran et al., 2005; Hira and Husein, 1979). Although the screening of blood donors for filariasis is not routinely done in the world, the laboratory testing of all donated blood with a test based on filarial antigen detection in endemic areas and permanent deferral from donating blood for individuals with a history of filariasis particularly in non-endemic areas has been recommended to reduce the risk of TTF (Okwa, 2003; Choudhury et al., 2003; Viroj, 2009; Bolaji et al., 2014).

To date, filariasis and TTF have not been reported from Iran. IBTO does not implement any strategies to prevent the transmission of filariasis through blood transfusion and blood donation volunteers are not questioned for filarial infection risk. Given the increasing migrations from endemic areas and travels to endemic areas of TTF, the permanent deferral for individuals with a history of filariasis, as well as the adoption of an appropriate strategy for travelers to filariasis-endemic countries is recommended to prevent the occurrence of TTF in Iran.

As mentioned, most TTPIs are zoonotic. Therefore, knowledge of the prevalence of these infections in key animal hosts is important information and has an essential role in the adoption of prevention and control strategies.

5. Conclusions

Addressing parasites as one group of transmissible pathogens by blood transfusion, reporting any cases of TTPIs detected and evaluation of the strategies implemented in different countries of the world, as well as the use of new prevention techniques could be effective for improving blood safety. Since malaria, toxoplasmosis and VL are endemic in parts of Iran, as well as the increasing travels to endemic areas and immigrations from endemic to non-endemic areas of parasitic infections, the extensive use of blood and blood components, especially in immunocompromised patients and the asymptomatic occurrence of most parasitic infections in blood donors, the prevention of TTPIs is not possible only by implementing a donor selection strategy and the current policies to prevent the TTPIs in Iran are not sufficient. Therefore, the laboratory screening of all donated blood with a test based on antigen detection in malaria-endemic areas, the adoption and implementation of a suitable strategy for screening of at-risk donors for CD, the preparation of anti-*T. gondii* negative blood for high-risk groups and the use of leukoreduced blood components for high-risk groups of toxoplasmosis and VL, as well as the permanent deferral for individuals with a history of filariasis and the adoption of an appropriate strategy for travelers to filariasis-endemic countries are recommended to reduce the risk of TTPIs in Iran.

Declaration of competing interest

The author has no conflict of interest.

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