The Most Common Causes of Transfusion-Transmitted Diseases among Blood Donors in the Middle Eastern States

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Author’s contribution

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ABSTRACT

The need for blood is essential, but there is no timely access to safe blood for millions of individuals who need a transfusion. Additionally, blood transfusions can also be the fastest and simplest form of checking for the existence of transfusion-transmitted diseases to the recipients. Blood safety concerns are an issue of great concern in Middle Eastern Countries in which the inaccessibility or provision of unsafe blood has an adverse effect on morbidity and mortality in the region. Additionally, many organizations and safety procedures of blood transfusion in this region need to be updated. Articles containing the key phrases Middle Eastern Countries, Blood, blood donor, blood transfusion, transfusion safety, transfusion-transmitted infections, and transfusion guidelines published from 2003 to 2020 in MEDLINE, PubMed, Scopus, and Google Scholar. Therefore, to determine the most prevalent causes of transfusion-transmitted disease among blood donors in the Middle East countries, this literature review was intended for research. Based on the data gathered were potentially related to HBsAg and HCV prevalence in blood donors from most of the middle eastern countries. While no positive cases of either HIV Ag-Ab or syphilis antibodies have been recorded especially among the blood donated from Egypt and Saudi

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1. INTRODUCTION

Blood donation is recognized as an effective life-saving procedure in medicine and, most prominently, in medical emergencies [1]. Yearly, public health often faces challenges of blood safety due to transfusion-transmissible infections (TTIs). This has become higher, especially within risk groups such as children and pregnant women with Malaria, hemorrhage, or pregnancy anemia [2].

Based on the WHO's Global database, at least 92 million blood donations are collected from 164 different countries annually [3]. Forty-one low-income countries were unable to screen for the Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV), and syphilis in blood donations. In developed countries, only 47% of blood donors were screened [4]. At least 13 million donors were also deferred because of TTI infection that could be spread by blood, including HIV, HBV, HCV and syphilis, a pre-existing medical condition or anemia [3].

The Middle East is an unclearly defined geographical area of Africa-Eurasia; it historically includes Southwest Asia and some North Africa parts [5]. The Regional Office for the Eastern Mediterranean is one of WHO's six regional offices, comprising 22 Member States with 605 million [6].

According to a WHO report, many nations do not have access to sufficient supplies of safe blood for transfusion. In the Middle East, only Iran and Turkey rely totally on unpaid voluntary blood donations. In the 1940s, Iran had a non-centralized, fragmented, and intermittent supervised blood transfusion service. Until almost 40 years ago, blood was mainly supplied by commercial organizations and professional blood donors. In 1947, the Iranian Blood Transfusion Organization was established to coordinate blood transfusion activities nationwide. However, similar services in other Middle Eastern countries developed more slowly.

In Egypt, for example, blood transfusion services were fragmented until 1997 [7]. Therefore, to determine the most prevalent causes of transfusion-transmitted disease among blood donors in the Middle East countries, this literature review was intended for research.

2. STUDY DESIGN

An electronic literature search was carried out and it contained the following keywords in titles and abstracts Middle Eastern Countries, Blood, blood donor, blood transfusion, transfusion-transmitted infections, transfusion safety, and transfusion guidelines published from 2003 to 2020 MEDLINE, PubMed, Scopus, and Google Scholar. According to WHO classification, EMR countries include: (Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Pakistan, Palestine, Oman, Qatar, Saudi Arabia, Somalia, Syria, Tunisia, Turkey, United Arab Emirates (UAE) and Yemen) these countries in the Middle Eastern region were included in the keywords. Research articles in English and Arabic were considered if they met the following requirements, such as cross-sectional studies. Overall, the published reports recorded positive TTI cases among safe blood donors from Middle Eastern countries. Then studies that record confusing information and studies with less than 1,000 samples were the excluded. The author's name or journal-title did not affect the option to exclude or include an article.

2.1 Blood Donation and Blood Safety in the Middle East Countries

Middle East countries have different economies, populations, and medical care [5]. However, they all express similar concerns about the protection of blood [8]. Based on WHO data, 112.5 units of blood are collected annually worldwide, half of which come from countries in the low- and middle-income nations. About 80 percent of the world population receives blood. The levels of donors in low-income and middle-

Keywords: Transmitted diseases; blood donors; SARS-CoV-2; HIV.
income countries are average 11.7 and 4.6 per 1000 person, respectively, compared to the high-income countries that stand at 33.1. Also, blood collection rates in 6 out of 21 EMR nations are below 10 per 1000 residents, and more than half of the collected blood in countries of low incomes is used by children less than five years old [9].

In 2004, 17 countries collected around two million blood units. The amount of blood obtained through a voluntary donation in these countries has fallen significantly, ranging from 3-100 %. Rates of donation ranging from 0.2% in Syria to 2.7% in Kuwait [10].

Despite recent advances in blood safety in the Middle East, concerns related to blood transfusion are still prevalent in rising TTIs [11]. Therefore, WHO suggests that all countries ensure blood donors' safety by promoting safe blood donation, promoting quality assurance, and ensuring blood products safety [4]. The prevalence of TTIs in blood donors is significantly lower in those who donate voluntarily. Even so, more nations also rely on voluntary contributions or alternative donors; the patients were unrelated/unknown and had come to the center to donate blood to replace the patients needed. [12].

Blood safety policies apply throughout Egypt to screen blood donated for hepatitis B, hepatitis C, HIV, and syphilis. From 2008 to 2009, 52 positive HIV blood bags were identified and removed. In 2009, 1,280,000 blood units were checked and 44 HIV-positive blood bags were found and discarded [4,13]. The prevalence of hepatitis C infection in thalassemia patients has been recently assessed in the EMR. Patients with thalassemia are, for example, among the most prone to TTIs. Therefore, infectious agents' prevalence in this community of patients may provide valuable information about the blood safety index [14]. Over the years, Pakistan's blood transfusion situation has remained far from reasonable [15–17]. Blood transfusion services in Pakistan are largely hospital-based, and most blood donors pay and direct the donors. HIV, HCV, and HBV are not assertively tested for commercial blood donors in Pakistan [18]. The study reviews the serological testing of HBV, HCV, HIV, and syphilis in blood donors from 1996 to 2005 in Lahore. Serological marker frequency ranged from 1.46–2.99% for HBV, with a steady decline for HCV (from 3.01 to 4.99 %), for HIV (from 0 to 0.06%) and for syphilis (from 0.19 to 0.57%) [17].

2.2 Transfusion-Transmitted Diseases (TTDs)

The safe procedure of blood transfusion saves millions of lives every year worldwide. Whole blood can be transfused to one patient, or blood-derived products can be separated so that multiple patients can use them. However, it has been established that blood transfusion can present a risk of spreading certain diseases [19,20]. These infections are referred to as transfusion-transmissible infections (Table 1) that occur when blood products are supplied to people without proper blood-borne infection screening. Allowing unsafe transfusion can lead to several negative outcomes, as it can cause an acute clinical sickness, be passed on to the receiver as a carrier, or cause asymptomatic infection [21].

Four things are needed for an infectious agent to cause TTS. First, the agent must be present in the donor’s blood, and the donor must be qualified to donate, healthy and feeling well on the day of donation, and must pass our screening board and consenting interview. Secondly, sensitive cells must be located in which to invade and proliferate by the agent. Finally, it must render the receiver sick to be a TTD. Viral, bacterial, parasite and prion infections are included [22,23]. The increasing rate of these infectious diseases raises blood safety risk, especially in middle and low-income countries [24]. HIV, HBV and HCV, due to their high prevalence rates, are the most common among these [23]. Other agents are Dengue Viruses, bacterial and Malaria [19].

2.3 Viral

2.3.1 Human immunodeficiency virus (HIV)

In the 1990s, one of the main ways to be infected with HIV in the Middle east was blood transfusion [25]. The average number of AIDS cases reported from countries in the region was 3,745 by the end of 1995. Despite major improvements in transfusion safety in the region, the main route of HIV transmission remains blood transfusion. The relevant information was available in 3,461 diagnosed cases (92.4%). Of those who received blood or blood products, 368 cases were, and the majority of these were reported in Saudi Arabia, Iran, Egypt, Iraq, and Morocco. For example, subsequent studies proved that most HIV infections were not due to Iranian products, but rather due to imported coagulation factors.
Sexual contact is the most common way (71%) in Egypt to transmit HIV. Until recently and collectively, blood and blood products were contaminated in 5% of Iran’s cases [13].

In the study of voluntary student blood donors at Mansoura University, El-Gilany and El-Fedawy reported no HIV cases among donors [27]. From 2000 to 2005, a retrospective study analyzing the history of 99,757 donors at the National Cancer Institute Blood Bank confirmed that no HIV positivity was found compared to two cases five years before [28]. During the five years 2010-2014, Senosy et al. examined the prevalence of HIV across blood donors in the Blood Bank of Beni-Suef University Hospital, Egypt. 93.5% of the blood donors were male and 6.5% were female. The HIV prevalence was 0.1%; 92.9% male donors and 7.1% female donor were among them, but this difference was not statistically significant. HIV-HCV coinfections have occurred in two donors (14.3%) [29]. Recent study by Kamel and Rafeh estimated the seroprevalence of HBV, HCV, HIV, and T. Pallidum antibodies among blood donors in a Suez Canal university blood bank from 2015-2019. In blood donors, the prevalence of HCV Ab and HBsAg are about 1.87% and 0.97%. No positive cases of either HIV Ag-Ab or syphilis antibodies has been recorded among the blood donated from this duration [24]. Research have been published throughout the world to determine the prevalence of HIV in blood donors. For example, seroprevalence of HIV is 0.004% in Iran [30], 0.002% in Turkey [31], and 0.06% in Iraq [32] among blood donors.

2.3.2 Hepatitis virus

Information collected from blood tests of over 211,772 people from Egypt showed hepatitis B surface antigen (HBsAg) and HCV antibodies prevalence are 1.65% and 9.02%, respectively. There is a significantly higher prevalence of anti-HCV than HBsAg; there is a significantly greater incidence of these in rural versus urban donors (11.3% and 2.27%, respectively) [33].

The only blood and blood components provider in Kuwait is Kuwait's central blood bank, which performs collected, processed, tested, distributed, and transfused services for any hospital. A study conducted in 2002 showed that 51.2% of blood donors in Kuwait are Kuwaiti nationals, and 48.8% of blood donors are non-Kuwait Arabs. Out of the first-time national and non-Kuwait Arab donors, prevalence rates of anti-HCV were 0.8 and 5.4%. In these age groups, the prevalence of HBsAg was 1.1% and 3.5%. These data illustrated that Kuwait’s heterogeneous population and the reliance on blood donations from replacement donors might affect the incidence of hepatitis infection between blood donors [34].

Several studies have been conducted in the Middle East and Eastern Mediterranean Regions concerning HBsAg positivity in blood donors. Below is a summary of the findings. HBsAg prevalence assessed between 1998 and 2007 among blood donors in Iran [35]. During the ten years in Maghsudlu et al. were collected 14,599,783 donations. Due to improvements in the recruitment, selection of donors, import of automatic supply and the implementation of transfusions services, and the potentially decreasing HBV prevalence in all populations, the total HBsAg rates decreased from 1.79% to 0.41% [35]. Another study also examined the viral screening in 15 million Iranian blood donors for syphilis, HBV, HCV, and HIV from 2004 to 2007 [36]. They reported that about 1% of blood donors were HBsAg positive, and the prevalence decreased over the study period [37]. Mohammadali and Pourfathollah conducted another large-scale study for over six years. They showed that only 0.5% of Iran’s blood donors were HBsAg positive [38]. Gurol et al. reported the prevalence of HBsAg 1.5% in Turkish blood donors [39]. In addition, a study conducted by Tigen et al. on 6 million Turkish blood donors stated that HBsAg was positive for over 4 percent of the population [40]. The prevalence increases in Djibodit’s blood donors [41] and Pakistan [42], with 10% and 6%, respectively.

The Blood Donor Unit collected 78,428 blood units from Qatar’s multinational donors from 1994 to 2001. Out of the 10,382 units, 13% were positive for at least one tested hepatitis markers. Seven hundred sixty-nine units were positive for HBsAg, 516 units were positive for HbcAb, and 976 units were positive for HCV Abs. The positivity rate for HBsAg was similar among Qataris and those from other countries. A striking finding was that 11.2% of Egyptian donations have antibodies for HCV [43].
Table 1. Pathogen, Clinical Manifestation, Screening Methods, Blood donor seroprevalence from published studies in Middle East countries

| Pathogen                          | Clinical Manifestation | Screening Methods                  | Blood donor seroprevalence from published studies |
|-----------------------------------|------------------------|-------------------------------------|--------------------------------------------------|
| **Viral**                         |                        |                                     |                                                  |
| Human Immunodeficiency Virus (HIV)| AIDS                   | Serology anti-HIV                   | Egypt: 2000 - 2005 (0% HIV positivity) [29]. 2006 (0% HIV) [27]. 2010-2014 (HIV infection 0.01%) and (HIV-HCV coinfection 14.3%) [29]. 2015-2019 (0% HIV positivity) [23] |
|                                   |                        |                                     | Iraq: (2017-2018) HIV 0.06%. The seropositive donors 1.8% HIV [32]. Iran (2004-2007) 0.004% [30].   |
|                                   |                        |                                     | Turkey: anti-HIV 0.002% [31]. Saudi Arabia; (1984-2009) 15,157 positive HIV cases [98,99]. (2000-2002) [99], and 2001 [123] (0% HIV), 1985-2010 (HIV-HCV and HBV coinfection 10% and 20%, retrospective) [100]. 2017-2019 (0% HIV) [124]. |
| Hepatitis virus                   | Viral hepatitis        | Serology anti-HBsAg, anti-HCV       | Turkey: (2004-2010) 1.31% HBsAg and HCV 0.38% [31]. Iraq: (2017-2018) HBV 3% and HCV 0.5%. The seropositive donors: HBV 84.3% and 13.9% HCV [32]. Saudi Arabia: (1985-2010) HBsAg 3% [100]. (2015-2017) 0.33% HBsAg; 0.40% HCV; 0.13% HIV Ab/Ag; 9.81% HBCAb; and 7.80%; HBsAbs. 0.53% syphilis. No samples were positive for malaria [125]. |
|                                   |                        |                                     | Kuwait: prevalence rates of anti-HCV were 0.8 and 5.4 %, The prevalence of HBsAg was 1.1 % and 3.6 % [34]. |
| Severe acute respiratory syndrome | COVID-19               | enzyme-linked immunosorbent assay (ELISA) | Saudi Arabia: 19.31% [121]. |
| coronavirus 2 (SARS-CoV-2)        |                        |                                     |                                                  |
| Middle East respiratory syndrome  | Middle East respiratory | Immunofluorescence assay, ELISA and confirmed by testing for neutralizing Abs (nAbs) | Saudi Arabia: 0% [118]. (2011 – 2016) 0.23 % [126]. |
| coronavirus (MERS-CoV)            |                       |                                     |                                                  |
| Dengue virus                      | Dengue fever           | ELISA                              | Saudi Arabia: 3.2% primary infections and 2.3% secondary infections [122]. |
| Bacterial                         | Syphilis               | VDRL/TPHA                          | Iran: 0% seroprevalence syphilis cases [53]. Egypt: 0% seroprevalence syphilis cases [52,53]. Turkey: 0.02% [54]. Pakistan: 0.75% [55]. Saudi Arabia: (2006-2015) 0.044 % syphilis positive cases [58]. |
| T. pallidum                       |                        |                                     |                                                  |
| Protozoa                          | Malaria                | Donor history questionnaire; blood smear microscopy | Saudi Arabia: (2006 – 2015) 79% Saudis, and 13 % non-Saudis [58], antibody 7.6 % and antigen 0.17 % [110]. |
| P. falciparum                     |                        |                                     |                                                  |
| T. gondii                         | Toxoplasmosis          | Donor history questionnaire; blood smear microscopy | Jordan: 47.1% [67]. Egypt: 72.6% [69], 59.6% anti-T. gondii IgG [71]. Saudi Arabia: 37.5 and 52.1 % [112,113]. |
Siddiqui and his colleagues' study aimed to establish the various TTIs in blood donors in Islamabad. This study was conducted at a blood bank from 2016 to 2017. Almost 847 prospective donors' samples were screened for the TTIs. They reported that 32 (3.72%) of the blood donors had TTIs. The prevalence of HBV, HCV, Malaria, Syphilis, and HIV was found to be 11 (1.29%), 15 (1.77%), 01 (0.11%), 03 (0.35%) and 02 (0.023%), respectively. They determine that TTIs were significantly lower among voluntary blood donors [2].

2.4 Bacterial Infections

2.4.1 Bacteria contamination

Blood transfusion can lead to immunosuppression, which may increase an individual's risk of acquiring an infection. Bacterial infection is the greatest threat posed by the transfusion of blood products. One of the most common causes of blood contamination is direct effect through blood products' processing, but increasing attention is now being paid to an indirect effect [44]. Bacterial contamination of blood products can include bacteria found on the skin and the environment, such as Yersinia, Pseudomonas, Proteus, Escherichia coli, Klebsiella, Acinetobacter, and Serratia [45].

Nevertheless, Transfusion Transmissible Bacterial Infections remain a major source of blood-borne infections leading to high morbidity and mortality rate, especially through platelets concentrates in hospitalized patients. Bacterial sepsis is more common when platelets that have been contaminated with bacteria are transfused. Approximately 18% of all transfusion-related deaths are due to bacteria's presence in platelet donations [46,47].

2.4.2 Syphilis

Syphilis is a transmissible venereal disease due to a spirochete called Treponema pallidum. The bacteria mix with the blood of a blood donor and infects the blood of a recipient. Syphilis is still a very prevalent public health problem in the world. Fordyce was the first person to report transmission of syphilis via transfusions. Many people have suffered from syphilis in different countries, including the United States (US) and Great Britain [48]. Syphilis can be passed from sexual contact, transfusions, and a pregnant woman during childbirth to her fetus [49]. Moreover, the number of cases of syphilis transmitted through transfusions has decreased across the world. Within the past 35 years, only three cases of syphilis transmission by blood transfusion were recorded in literature and the last one occurred more than 40 years ago in the US [50]. However, blood transfusion plays a minor role because many blood-testing methods are sensitive, and routine blood screening for syphilis is performed. Screening for syphilis is required before receiving routine blood transfusions, as well as blood donations. Despite its prevalence in developing countries, syphilis has re-emerged as a widespread health concern in many nations in recent decades [51]. Interestingly, there were 0% seroprevalence syphilis cases among Iranian and Egyptian blood donors [52,53], 0.02% in Turkey [54], and 0.75% in Pakistan [55].

2.5 Malaria and Protozoa

Bacteria, viruses and other bloodborne pathogens can be transmitted through blood transfusion. Parasitic infections through blood transfusions are generally rare. However, Malaria is a major cause of TTIs in tropical countries [56]. In addition to malaria transmission through mosquito bites, there have been rare malaria reports occurring through transfusion. The condition occurs because the donors' parasite load is very low, and no symptoms may be seen during donation. Also, some Plasmodium species do not cause symptoms in their hosts, and those who may have acquired immunity to the parasite may still carry a low level of infectious parasitemia [57]. Blood from asymptomatic donors or blood from imported malaria cases is becoming increasingly available due to travel and demand for transfusions [58]. Transmission of malaria has been reported mostly from single-donor products such as red cells, platelets or white cell concentrates, cryoprecipitate, and red cells after thawing and washing [59]. Because the parasites are stable for at least 18 days at +4°C in plasma and whole blood, they are also stable in the frozen state for more extended periods [59,60].

Toxoplasma gondii (T. gondii) was first discovered a century ago in North Africa by scientists investigating Leishmania [61]. Toxoplasma gondii, an obligate intracellular parasite, is a generally successful microorganism that globally infects around 30% of the human population and may be transmitted via whole blood [62–64]. The Middle East's total infection rate is around 30%-50%, making it the highest in the global regions [65,66]. Several studies across
the Middle East countries reported higher *T. gondii* rates in pregnant women in Jordan 47.1% [67] and Egypt 72.6% [68].

A cross-sectional study was performed at six blood donation centers in Iran. A total of 491 serum samples were collected from 2014 to 2015. Totally, 200 (40.7%) samples were seropositive for anti-*T. gondii* antibodies; 184 (37.5%) donors tested seropositive for only IgG antibody, 8 (1.6%) tested seropositive for both IgM and IgG and 8 (1.6%) were positive for IgM antibody alone. Therefore, appropriate screening programs should set up to prevent the spread of transfusion-transmitted toxoplasmosis [64]. Many studies have reported *T. gondii* seropositivity in southeastern Iran’s blood donors [69,70]. However, a cross-sectional study was conducted to evaluate the seroprevalence of *Toxoplasma gondii* antibodies among 260 blood donors who attended blood banks at Mansoura University Hospital, Egypt. Multivariate logistic regression analysis showed a significant association between *T. gondii* seropositivity and eating meat by-products or being non-educated. These findings highlight that *T. gondii* is prevalent among blood donors in Egypt [71]. This difference in *T. gondii* seropositivity among the blood donors worldwide could be associated with geographical and environmental factors, sociocultural habits, transmission routes, and sample size in the studied population [64].

### 2.6 Specific Agents of Recent Concern

#### 2.6.1 Middle East respiratory syndrome (MERS)

The disease first appeared in the Middle East and spread to many countries around the world. [72,73]. However, the exact way in which MERS transmission is unknown. The main concern with blood transfusion is the possibility of its transmission to a recipient by blood. Since the MERS-causing virus is a coronavirus similar to the one that causes severe respiratory distress syndrome (SARS), the focus should be on the transmission via blood transfusion. The possibility of transmission through blood transfusion is confirmed, emphasizing SARS, and the inactivation of the virus in infected blood is the subject of current research [74,75]. However, there is still no case report of MERS transmitted by blood transfusion until now.

#### 2.6.2 Dengue virus

The Dengue virus is the world's most widespread viral arthropod-borne infection, attributed to millions of individuals. A dengue virus with four main serotypes is a single-stranded RNA virus. The predominant transmission route is through the mosquito vector of *Aedes aegypti*, but dengue also spread through blood transfusion and organ transplantation. [76].

In endemic areas where the vector is widespread, it could be difficult to differentiate a small number of transfusion transmission reports between non-mosquito transmission and mosquito-borne infection. Many infections can also lead to mild or asymptomatic diseases that are not recognized as transfusion-acquired infections, and many endemic countries also do not have diagnostic laboratories to record infections and their origins [77].

There are only two reported cases of blood transfusion transmission. As a consequence of a blood transfusion in Hong Kong, a patient developed fever three days after the transfusion, with severe thrombocytopenia, moderate neutropenia, and hypotension. At the time of donation, the donor was asymptomatic, but dengue fever occurred one day later. The sample also tested positive for dengue virus by Real-Time PCR [78].

The second case involved dengue transmission from a blood donor who became sick the day after blood donation. They completed further investigation and found evidence of dengue infection in the recipients of this blood donation. Two recipients experienced fever with some capillary leak-evidence, while the third recipient experienced no fever. A stored serum sample from the donation tested positive [79].

#### 2.6.3 Coronavirus disease (COVID-19)

With the outbreak of the new coronavirus, *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2) in Wuhan, China, in 2019, a new coronavirus gained the attention of the world [80]. Several published studies indicate that SARS-CoV-2 RNA is found in the blood, plasma, and serum of infected people [81–83]. Unsurprisingly, some of these reports include RNA detection in blood donors[84,85]. Researchers identified traces of RNA of the virus in a SARS patient’s blood nine days after the appearance of the symptoms. The viral plasma was low [86]. Investigators were able to identify SARS-CoV RNA in plasma specimens when the load of the virus reached 190 copies/mL. The investigators did not identify RNA in the plasma from two contacts, although only one sputum
specimen was positive in three or four different PCR assays, and the viral load was as high as six million copies/mL [86]. Based on this study’s findings and others, WHO [87] and the Food and Drug Administration (FDA) [88] implemented suggestions as a precautionary measure against the spread of the SARS via blood transfusion. They suggested some preventative values with regards to deferring blood donations from areas with recent local transmission. Blood donors diagnosed as confirmed or suspected patients with SARS must also alert collection agencies. In such circumstances, efforts will be made to identify receivers and recollect any blood donations that are not transfused.

To date, few studies have addressed the pandemic’s impact on blood donation. When completing the questionnaire, 505,000 confirmed cases existed, ranging from 122 in Syria to 148,950 in Iran's Islamic Republic [89]. The drop in blood supplies within the reporting nations was variable during the first months and probably reflected the virus's degree of spread by the community and governmental steps in the reporting countries. The magnitude of the shift in supply depends on the blood supply system’s organizational structure and the blood sources, which differ between the region's countries. Different factors can adversely affect the number of blood donors during a viral pandemic [90].

Kwon et al. observed that none of the transfusion recipients exhibited signs of COVID-19-related disease from SARS-CoV2, and none of them tested positive for SARS-CoV-2 infection. Therefore, transfusion transmission of SARS-CoV-2 to recipients did not occur. Although transfusion to recipients all occurred before COVID-19 diagnosis in donors, blood services should receive the details of all COVID-19 cases from their health authorities and not solely rely on post-donation information provided by blood donors [91].

2.7 The prevalence of transfusion-transmitted diseases in Saudi Arabia among blood donors

Generally, in Saudi Arabia, blood donation is performed in hospitals and blood collected from relatives and colleagues of concerned patients (replacement donors) and volunteer donors. Also, in Saudi Arabia, most blood is obtained from replacement donors [92,93].

According to the Joint United Nations Program on HIV/acquired immune deficiency syndrome (AIDS) (UNAIDS), about 34 million people are infected with HIV worldwide [94]. There is not a lot of HIV prevalence data available for the Middle East. AIDS was first discovered and reported in Saudi Arabia in 1984 [95]. The data on HIV prevalence in Saudi Arabia comes mostly from surveys of high-risk groups, facility-based surveillance, and mandatory screening programs [96]. The UNAIDS estimate of 2011 put the endemic rate at about 0.02%. From 1984 through 2009, 15,157 HIV cases were reported in Saudi Arabia, with 4003 cases occurring among Saudis and 11,194 occurring among foreign residents [97,98].

Serological markers of HBV, HCV, HIV 1, 2 and HTLV-I/II were examined in 20423 Saudi and 3750 non-Saudi blood donors at King Khalid University Hospital, Riyadh, using commercially available kits from 2000-2002. The prevalence rates of HIV, HBV, and HCV infections were 0%, 1.5%, and 0.4%, respectively. The prevalence in males was not significantly greater than in female donors, but was significantly higher in non-Saudi donors relative to Saudi donors [99].

Data were collected and reported on all HIV-positive individuals over 18 years of age between 1985 and 2010 at King Faisal Specialist Hospital and Research Centre in Riyadh, Saudi Arabia. In the study of over 341 HIV-infected patients, HCV was found in over 41 patients. The most common risk factor for HCV and HIV infection was blood/blood product transfusion in 24 (60%) of patients, of whom 21 (88%) were hemophiliacs, followed by heterosexual transmission in 9 (22%) of patients. HBsAg was detected in 11 (3%) patients. Heterosexual transmission was the most common risk factor for HBV and HIV infection in 8 (73%) patients, followed by blood/blood product transfusion in 2 (18%) patients. The results of this study concluded that HCV and HBV are ten and twenty times more prevalent among those infected with HIV than in the general population, respectively [100].

Survey data from Saudi Arabia released in 2007 revealed prevalence of HBV of 0.22% among adults. The average reported prevalence was 0.15% and the variation in prevalence was wide (ranging from 0 to 0.72%) [101,102]. The prevalence of HCV infection in Saudi blood donors clearly shows between 0.4% to 1.7% among adults and 0.1% among children. [103,104]. In a large study in Riyadh province among 557 813 Saudis of all ages, the prevalence of HCV in adults was 1.1%, while the prevalence in children was 0.1%. [105].
In 24173 (23952 males and 221 females), 20423 Saudi and 3750 non-Saudi blood donors, the serological markers of HBV, HCV and HIV were studied using commonly produced kits three years in Riyadh, from January 2000 to December 2002. The investigators examined different sexes, ages, and nationalities for the prevalence of confirmed-positive test results for these viruses. This research found prevalence rates of 1.5 percent for HBV and 0.4 percent for HCV, and 0 cases of retroviral infections. For males, the incidence was not substantially higher than for female donors. With an increase in age, HBsAg and anti-HCV positivity appear to increase. Compared to Saudi donors, the prevalence of HBsAg and anti-HCV positivity was much more prevalent among non-Saudi donors. The prevalence was the lowest among Saudi and young donors. Extensive recruiting of Saudi and young donors should also help ensure that blood supply is increased in the long term without jeopardizing protection [99].

The risk of Targeted temperature management (TTM) is complicated because, for a long, relatively-asymptomatic time, infectious organisms may remain viable in the blood. In Saudi Arabia, *Falciparum malaria* is normal and can persist in the bloodstream for years while displaying no infection signs [58]. Therefore, most facilities for blood transfusions have a policy of excluding donors that may be at risk. Many countries mandate a waiting period ranging from 6 months to 3 years, depending on the possible health risk [59]. While a deferral policy can work, the increase in people who are ineligible to donate blood can cause a shortage of stock in non endemic countries [106].

The incidence of transfusion malaria in Saudi Arabia is unknown. However, it was noted that a report documented two cases of postoperative transfusion malaria after heart surgery [107] and another two neonates transfused from the same blood donor were described in Riyadh [108]. Furthermore, over six years out of the 137,402 blood donors checked in Riyadh, a total of 18/100,000 were reported [109]. These studies do not fully capture the burden of transfusion malaria that can only be measured through a comprehensive national surveillance program.

Saeed and his colleagues [110] evaluated ELISA screening's potential usefulness for malaria antibody and *falciparum* antigen among Saudi blood donors. One thousand seven hundred fifty-six donors were analyzed, 1,028 in the Southern Region where malaria was endemic and 656 donors from the malaria-free Riyadh area. The antibody prevalence for the antibody was 7.6%, compared with just 0.17% for the antigen. In the non-endemic region, the antibody positivity rate was seven percentage points lower than that of the endemic region, 4.8%. They determined that excluding antibody-positive blood donors in malaria-endemic countries like Saudi Arabia would result in too much wastage of blood donations. Although antigen-based malaria testing is useful, only a few donations were rejected.

In 2005, the Prince Sultan Military Medical City, Saudi Arabia, started to screen their blood donors for malaria. Of all blood donors, 120,000 were screened for malaria from June 2006 to June 2015. The researchers found over 180,000 donations of blood screened for malaria. Seventy-nine thousand percent of the donors were Saudi, and only 13 % were non-Saudi. As of this data, the prevalence rate was zero percent among the blood donors with negative thick blood films, which are the only screening test for blood donors. They believed that blood donors' current screening methods could not be deemed fit for low-level identification of parasitaemic malaria cases. A new collection and upgrade of reference tests are suggested [58]. The prevalence rate of malaria among blood donors from Prince Sultan Military Medical City was different from similar studies conducted in Saudi Arabia [109-111].

The prevalence of *T. gondii* infection varies in blood donors between countries. A recent Saudi Arabian study found that blood donors' infection ranges between 37.5 and 52.1% [112,113].

A cross-sectional analysis involving all blood donors in the target population at Al-Noor Hospital, located in Makkah, Saudi Arabia, from June to August 2017. In this research, the total population was 220 male donors (100%). About 43 of the 220 samples showed positive IgG antibodies for chronic toxoplasmosis, with a prevalence rate of 19.5%. The laboratory detected no IgM in the study target group. A significant difference between getting chronic toxoplasmosis and age group 30-39 years was recorded. Asian race was more suspected to be infected by chronic toxoplasmosis. High significant was detected between working in the home garden and infection acquired with chronic toxoplasmosis. The results obtained from this survey suggests that long-term exposure to
Toxoplasma gondii exists in blood donors. Latent toxoplasmosis may become acute in the body in certain conditions. [114].

A cross-sectional analysis examining platelet bags was performed at a tertiary care hospital in Saudi Arabia from January to June 2012. Samples were taken from blood bags for bacterial identification and biochemical examination of platelet bags on day 6 of the donation. The investigators recorded that on day 6 of collection, 1(0.28%) of 352 platelet bags showed bacterial growth. Staphylococcus epidermidis was the bacterium. The platelet bag's glucose and pH levels were 144.14 mg/dl and 5 mg/dl, respectively [115].

There is very little data on sexually transmitted diseases in Saudi Arabia and other Islamic countries. Detailed information on HIV epidemiology has recently been released in Saudi Arabia [116]. A five-year surveillance study was conducted to evaluate and ascertain the prevalence of sexually transmitted diseases in Saudi Arabia [117].

In the ten-year data from 2006-2015, the Elyamany et al. analysis was performed at the Prince Sultan Military Medical City in Riyadh, Saudi Arabia. They evaluated the seroprevalence of infection and compared sex and other variables. In the study period, approximately 240,000 blood donors were screened and examined. Most blood donors (98.3%) were male, and 89 percent were citizens of Saudi Arabia. However, according to their results, they reported that about 0.044 % of all blood donors had syphilis positive cases in the last ten years. No cases of syphilis among stem cell donors have been confirmed as positive. Just 60 blood donors tested syphilis positive. In addition, during the same time, we examined 202 stem cell transplant donors, of which % were male, and none were positive for syphilis [58].

Until now, no case report on MERS transmitted by blood transfusion has been published. An interesting article from Saudi Arabia is here. Aburizaiza et al. analyzed donated blood samples through immunofluorescence assay during the emerging illness in Saudi Arabia and registered no positive findings [118]. This could mean that MERS transmission through blood transfusion is low or not at risk. There are, however, many factors. First, it may be possible to use the immunological approach to evaluate the MERS virus, but it is not the gold standard. The standard PCR test is inferior to the immunological process. Fortunately, the risk of finding the virus in blood samples is also very low in confirmed MERS cases [119].

An earlier cross-sectional study at the King Abdullah Hospital was conducted between 2019-2020. Data from donor attendance records, mobile blood drives and blood inventory records were obtained retrospectively. Donor participation and blood supply at blood bank-based collections showed a decrease of 39.5% after imported cases of COVID-19 were registered in Saudi Arabia. Blood demand, on the other hand, was decreased by 21.7% [120].

Mahallawi and Al-zalabani investigated antibody prevalence in blood donors in Al-Madinah, Saudi Arabia, between mid-May and mid-July 2020, against SARS-CoV-2 among blood donors [121]. A total of 1,212 individuals were studied here. The donors were males and met the blood donation requirements. The researchers reported that the SARS-CoV-2 prevalence in blood donors was nearly 19%. They found significant differences according to blood groups. In their study, researchers found a high rate among blood donors, demonstrating a high level of SARS-CoV2 exposure in the population [121].

Between 2015 and 2016, a cross-sectional study and a total of 910 healthy and eligible Saudi male blood donors were selected from the blood banks of Hira General Hospital and Holy Makkah Regional Laboratory. The researchers studied the prevalence of dengue virus and its serotypes. The overall prevalence was 3.2 % and 2.3 % for primary and secondary infections [122].

3. CONCLUSION

In Middle Eastern countries, transfusion-transmitted infection remains a formidable problem. A similarly wide constellation of economic and operational challenges in the area parallels the diverse array of pathogens; this calls for a systemic solution that, as proposed by the WHO, involves regulatory, structural, and training initiatives. The contribution of creative, tailored methods, such as donor recruiting, and innovations, such as rapid testing, which aim to make substantial gains in the future, should not be ignored. In order to be both suitable and effective, initiatives will need to be adapted to that of the region. This depends on awareness within the continent of the enormous heterogeneity.
4. LIMITATION

Regarding this research's limitations, a poorly organized paper file and a computerized database are the main difficulties we encountered during our study. This literature review did not involve projects for university study and theses from students. Also, not all TTIs, such as Leishmaniasis, Human T-cell lymphotropic virus 1 and 2, Herpes Viruses, and Cytomegalovirus, have not been covered. Besides, in order to reduce the effect of studies with small sample sizes on the estimated prevalence, we excluded studies with fewer than 1,000 participants.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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