

Research Article

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Prevalence of residual risks of the transfusion-transmitted infections in Riyadh hospitals: A two-year retrospective study

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Abstract: This study aimed to evaluate the prevalence and trends of transfusion-transmitted infections (TTIs) in two hospitals in Riyadh, as well as to judge the best type of tests to ensure blood transfusion safety. By using serological and nucleic acid test (NAT) tests, these donors were screened for human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV), human T-lymphotropic virus type 1 (HTLV-1), human T-lymphotropic virus type 2 (HTLV-2), syphilis, and malaria infection as a first time of donation. Out of 58,898 blood units, 336 units were reacted for HBsAg, 5,318 units for HBcAbs, 506 units for HCV antibodies, 214 units for HIV Ab/Ag combinations, 206 units for HTLV antibodies, 355 units for syphilis antibodies, and 81 units for malaria. Moreover, the genotypic prevalence of these products showed that 349 units reacted for HBV DNA, HCV RNA, and HIV RNA in blood donation. This study

reflects the seriousness of the residual risk of TTI, which is still a threat factor for the transmission of blood-borne infectious diseases. It was discovered that utilising (NAT) could increase test sensitivities while also lowering residual TTI risks, improving blood safety, and being cost-effective.

Keywords: transfusion-transmitted infections, prevalence, Riyadh, NAT

1 Introduction

Blood transfusion (BT) is a life-saving procedure that saves millions of lives annually worldwide. Annually, more than 118 million units of blood are donated, according to the World Health Organisation [1,2]. However, it is accompanied by the risks of adverse consequences. Therefore, practitioners should be aware and able to identify these issues even though it is a common and safe medical procedure. One to two recipients out of every 1,000 receive contaminated blood containing viral, bacterial, or parasitic infections [1,2]. Potential infectious agents like parasites, viruses, and bacteria can be transferred to the recipient patient through BT are defined as transfusion-transmitted infections (TTIs) [3]. Several cases of serious morbidity and mortality have been reported due to microbial blood contamination [4]. The most prevalent known TTIs are hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), human T-cell lymphotropic viruses I/II (HTLV I/II), West Nile Virus, malaria, and syphilis [5]. Moreover, in some countries, cytomegalovirus is considered as TTI. As well as, malaria represents a big health issue in the public population, where in 2016, there were an estimated 216 million cases in about 91 countries [6]. Unsafe BT remains a major health alert for the global spread of TTIs [7]. These TTIs can be transmitted via direct exposure to infected blood and blood products, organ transplantation,

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hemodialysis, intravenous drug use, BT, and tattooing [8]. The BT transmission route is considered more common than other routes of transmission [9]. The rate of viral transmission by blood donation has been reduced due to some strict laws imposed on blood donors [10]. As well as, it should be taken into consideration that the viral transmission is mainly depending on the prevalence of viruses in the population and geographical location [11]. According to the Ministry of Saudi Health (MOH), the incidence of HIV infection cases among Saudi citizens and non-Saudis is low, with roughly 1.5 newly discovered HIV infections per 100,000 Saudis per year [12]. Furthermore, analysis of blood donor screening data for HCV infections refers to prevalence rates of 0.4–1.1% [13]. To guarantee the safety and quality of donated blood products, they should undergo to accurate, sensitive, and strict microbial blood tests. The most widely used techniques for screening transfusion-transmitted pathogens are serological and nucleic acid test (NAT). However, serologic tests have some limitations, such as the fact that all infectious agents cannot be detected in blood donations due to asymptomatic donors, occult infections, and other factors [14]. The serological detection of antibodies takes longer to appear than antigens after the onset of infection [15]. As an example, HIV antibodies take roughly three weeks to emerge, whereas HIV p24 antigen takes 3–10 days to appear in the blood; hence, early identification minimizes the serological window period [16]. In turn, it produces a safety margin during BT and reduces the transmission of contaminated blood. In other words, sometimes, the serology results are negative, while the viral nucleic acid can be lively [15]. The same theory is also applied to HBc antibodies, which are lasting for life, thus no way to differentiate whether the infection cures or moves forward to chronicity [5]. In addition, HCV antibodies function similarly in that they take 30–60 days to emerge, whereas antigens appear between 0 and 20 days. The introduction of some sensitive and accurate tests, such as NAT that can determine blood-borne infectious markers at an earlier stage prompted the rate of HIV, HCV, and HBV transmission by blood products to decrease over the previous two decades [17]. Also, NAT has the ability to differentiate between two different window periods of HBV, acute and chronic [18]. Moreover, it has been found that NAT can also detect HBV DNA in occult HBV infection, i.e., virus is present in plasma, and the antibodies are not showing up [19]. Therefore, the study was conducted to discover two main important purposes: first, to estimate the prevalence of circulating pathogens transmitted during BT; second, to specify the optimal laboratory testing that reduces BT

hazards, which in turn maintains a high safety standard, and to increase the safety margin during BT that reflects on the amount of discarded blood.

2 Patients and methodology

2.1 Design of the study

A 2-year retrospective analysis was done at two hospitals from 1 January 2017 to 31 December 2018 (King Saud Medical City Hospital and Al-Imam Abdulrahman Al Faisal Hospital in Riyadh) in Saudi Arabia. A total of 58,898 donated blood units were analysed anonymously for serological screening for HBV, HCV, and HIV infections, as well as malaria, HTLV, and syphilis. As well as transfusion reaction cases were tracked. Furthermore, the studied samples were subjected to genotypic analysis.

2.2 Inclusion and exclusion patient criteria

This study contained the data of all eligible blood donors who met the national blood bank selection criteria. These include age, body weight, haemoglobin level, pulse rate, and blood pressure. Alongside, the exclusion criteria were taken into consideration, such as history of jaundice cupping, surgical operation, hypertension or current fever, recent illness or transfusion, and not giving consent [20]. Table 1 summarises the inclusion and exclusion criteria.

2.3 Sample processing and laboratory tests

In order to perform serological and genotypic assays of the donor blood units, two blood samples were taken from each donated blood unit: one with EDTA and the other without EDTA. There were some precautions that should be considered before the start of sample processing to avoid a false result. Hemolysed (red) and hyperlipidaemic (milky) samples must be removed, as must samples containing fibrin, heavy particle remnants, or microbiological filaments and bodies. All donors were evaluated for TTIs markers using enzyme-linked immunosorbent assay (ELISA) and molecular NAT kits, according to instructions by the manufacturer (Table 2).

Table 1: Inclusion and exclusion criteria

Criteria	Inclusion	Exclusion
Donor age	18–50 years	<18 years or >50 years
Body weight	>50 kg	<50 kg
Haemoglobin level	14–18 g/dl for male and 12.5–16 g/dl for female	<12.5 g/dl for female and 14 g/dl for male
Pulse	60–100 per minute	>100 per minute
Blood pressure	(systolic of 100–140 mmHg and diastolic of 60–90 mmHg)	>140 of systolic and >90 of diastolic
History of diseases	No history of diseases	History of diseases

Table 2: Different principles and methods are used to test the blood donor

	Method	The instrument used for analysis	Target
Phenotypically	ELISA*	Dade Behring-Peb 111	HBc Abs/HCV Abs HIV Abs/Ag combination HTLV Abs HBV Ag
	Hemagglutination assay, ELISA (for confirmation)	ALINITY	Treponema pallidum Abs
Genotypically	ELISA	Evolis	Malaria
	PCR*	Cobas 6800	HIV RNA HCV RNA HBV DNA

*Enzyme-linked immunoassay (ELISA), Polymerase Chain Reaction (PCR).

2.3.1 Enzyme-linked immunosorbent assay (ELISA)

By automated Dade Behring-Peb 111 (Siemens), serum samples were screened for anti-HBc, HCV antibodies, HIV Ag/Ab combinations, and HTLV antibodies utilising several ELISA types.

2.3.1.1 Anti HCV antibodies detection

Highly pure antigens that comprise sequences from the NS3, NS4, and NS5 regions of the core HCV were coated on microwells to detect anti-HCV antibodies. The peroxidase-conjugated monoclonal anti-human IgG was used.

2.3.1.2 HBV detection

Reagents from Monolisa HBsAg Ultra (Biorad), Monolisa Anti-HBc Plus (Biorad), and Monolisa Anti-HBsAg Plus (Biorad) were used for HBV (HBsAg and Anti HBc) detection. In order to detect HBsAg, monoclonal antibodies are coated on the Monalisa HBsAg Ultra solid phase (a one-step enzyme immunoassay based on the concept of the (sandwich) type employing monoclonal and polyclonal antibodies). On the other hand, MONALISA anti-HBc PLUS solid phase produced with recombinant HBc antigen (indirect

ELISA type) is used to detect total antibodies to the HBV core in human serum or plasma. While the principle of Anti HBs PLUS is a direct sandwich enzyme immunoassay that uses polystyrene microwells coated with native HBsAg as the solid phase and a conjugate containing HBsAg that has been labelled with horseradish peroxidase.

2.3.1.3 HIV and HTLV-I/II detection

A reagent of Genscreen Ultra HIV Ag-Ab (Biorad) was used to identify HIV and HTLV-I/II. Since the Genscreen Ultra HIV Ag-Ab is an enzyme immunoassay based on the theory of sandwich technique for the detection of HIV P24 antigen (major core protein) and antibodies to HIV-1 and HIV-2 in human serum/plasma.

2.3.1.4 Syphilis and malaria detection

A rapid RPR kit from Crescent was used to test donor plasma for the presence of syphilis using the ALINITY analyser. ELISA was also enlisted to identify malaria using an Evolis machine and a Biorad kit. The main concept of the test was to coat the wells of a microplate with recombinant proteins that represented immunodominant epitopes of *Plasmodium* species from two hospitals.

2.3.2 NAT PCR

The cobas 6800 (Roche molecular diagnostics GmbH) automated system was used to detect probes for HIVI, HIVII, HCV, HBV, and internal control (IC) nucleic acid. The cobas 6800 system includes ready-to-use assay reagents for NAT testing (cobas® MPX, Roche Diagnostics GmbH, Penzberg, Germany).

2.4 Statistical analysis

SPSS statistical software (version 25, SPSS Inc, Chicago, Illinois, USA) was used to analyse the data. For the primary purpose of description, all data are presented as frequencies and percentages. The annual TTIs seroprevalence rates for the whole study population and various sociodemographic subgroups were presented. According to sociodemographic characteristics, the seroprevalence rates of TTIs were compared between blood donor groups using the Chi-square test, and the effect of categorical variables on TTIs seropositivity was assessed. In order to analyse the variations in TTIs trends over these two years, a Chi-square test was also used. *p* Values of less than 0.05 were considered significant in terms of statistics.

3 Results

3.1 Prevalence of blood-borne infections

Seroprevalence assays revealed that 5,318 (9%) of the units tested positive for HBc antibodies, 336 (0.6%) for HBsAg, 506 (0.9%) for HCV antibodies, and 214 (0.4%) for HIV Ab/Ag combinations (Figure 1). Furthermore, 206 (0.4%) units reacted to HTLV antibodies, 355 (0.6%) units reacted to *Treponema pallidum* (TP) antibodies, and 81 (0.1%) units reacted with malaria antigens. About 349 (0.6%) units showed positive NAT. As for the NAT, the mentioned results, including HBV, HCV, and HIV, were considered confidential.

According to the study, NAT (just for HCV, HBV, and HIV) has an advantage over the serological test, which is more sensitive and accurate (Figure 2). This, in turn, has a cost and time effect as well as reducing the discarded amount of blood to a minimum.

3.2 Correlation between unit status and donation years

The overall correlation between unit status and the donation year showed statistical significance where $p < 0.01$.

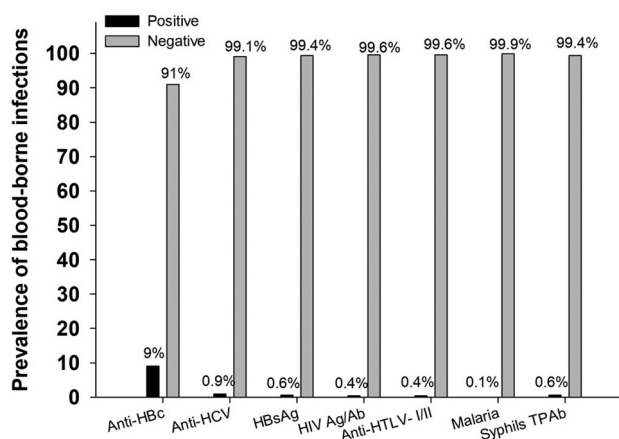


Figure 1: Prevalence of blood-borne infections. *Anti-HBc, Anti hepatitis B core; anti-HCV, anti-hepatitis C virus; HBsAg, Hepatitis B (surface) antigen; HIV Ag/Ab, human immunodeficiency antigen/antibody; anti-HTLV-I/II, anti-human T-cell lymphotropic viruses I/II; NAT, nucleic acid test; TPAb, *Treponema pallidum* antibody.

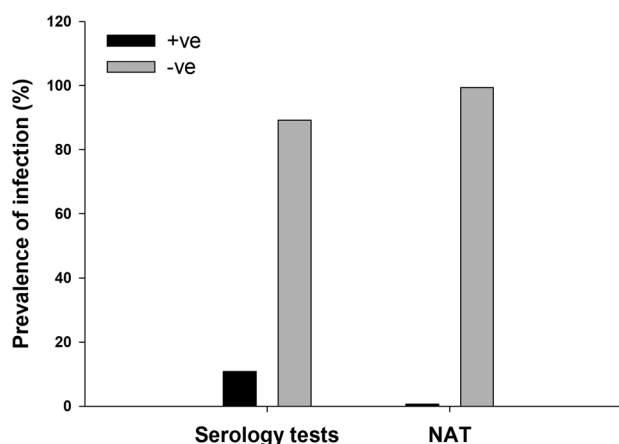


Figure 2: Comparison between the accuracy and sensitivity of serological technique and NAT. NAT, nucleic acid test.

The data showed that rejection rates increased in 2018 by 0.53% compared to those of 2017 (Figure 3).

3.3 Correlation between transfusion reaction cases and some sociodemographic parameters

Alongside the screening of the risk of TTIs, transfusion reaction cases were denoted. During the study period, there were 94 transfusion reaction cases. Of these cases, we found that the gender factor did not play a significant role, whereas 48 (51.1%) were males and 46 (48.9%) were females. While at the level of age groups, the study showed

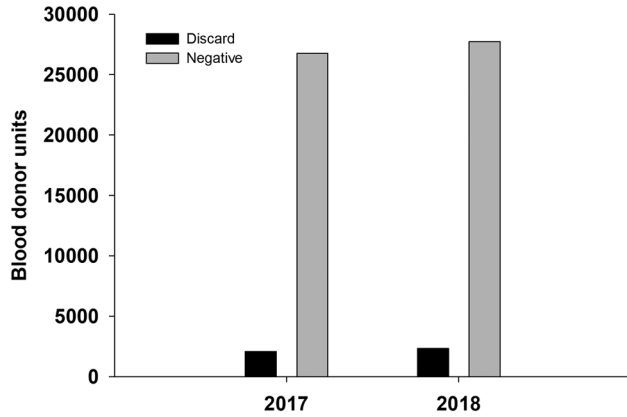


Figure 3: Correlation between unit status and donation years. In the figure above, there is a slight difference between 2017 and 2018, especially in the rejected units, and on the opposite side, the number of accepted units increased by 0.53%.

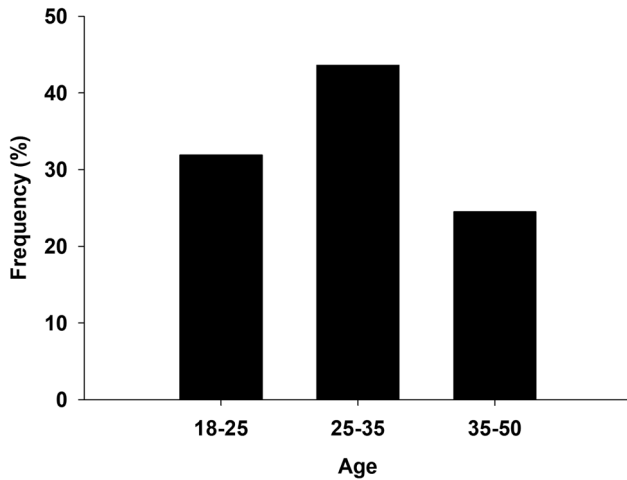


Figure 4: Age distribution chart for the transfusion reaction cases. Frequency of age distribution among transfusion reactions. The age composed of three categories: age between 18 and 25 consists of 31.9%, 25–35 = 43.6%, 35–50 = 24.5%.

that the age group between 25 and 35 years was greatly affected (43.6%), followed by the age group between 18 and 25 years (31.9%), finally the lowest affected group was between 35 and 50 years (24.5%) (Figure 4).

In addition to evaluating the instances based on nationality, the study discovered the following: (45) 57.4% were Saudi, while (40) 42.6% were non-Saudi.

3.3.1 Correlation between type of reaction and gender

Among the 94 reactive instances, allergic reactions were the most common (46.81%), followed by febrile non-hemolytic

Table 3: Correlation between type of reaction and gender

Type of reaction	Gender		Percent	P-value
	M	F		
Allergic	19	25	46.81	0.000
Fever	2	3	5.32	
FNHTR*	18	9	28.72	
NTD**	9	9	19.15	

*Febrile non-hemolytic Transfusion Reaction. **Not Test Done.

reactions (28.72%), and fever (5.32%); however, 19.15% of the cases were not evaluated. Moreover, the correlation between the type of reaction and gender showed a statistical significance at $p < 0.05$ (Table 3).

3.3.2 Descriptive analysis of patients' wards in relation to transfusion reactions

A descriptive analysis was generated to correlate the patients' wards and transfusion reactions. The majority of transfusion reactions (67.0%) were recorded in adult and paediatric emergency departments, followed by the delivery room, obstetrics and gynaecology, and maternity (13.8), the intensive care unit, neuro-intensive care unit, and cardiac care unit (9.6%), the female and male medical wards (5.3%), surgery, tower medical, and acute kidney unit (3.2%). The lowest recorded ward reactions were from the neonatal intensive care unit and paediatric intensive care unit (1.1%) (Table 4).

Table 4: Descriptive analysis of patients' wards in relation to transfusion reactions

Ward*	Frequency	Percent
PEDIA, PEDIA ER, ER	63	67.0
NICU, PICU	1	1.1
ICU, NEURO ICU, CCU	9	9.6
FMW, MMW	5	5.3
DR, OBG, MATERNITY	13	13.8
SURGERY, TWR MEDICAL, AKU	3	3.2
Total	94	100.0

*ER, emergency; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit; ICU, intensive care unit; CCU, cardiac care unit; FMW, female medical ward; MMW, male medical ward; DR, delivery room; OBG, obstetrics and gynaecology; TWR, tower medical; AKU, acute kidney unit.

4 Discussion

In contemporary medicine, BT is a life-saving and indispensable procedure. However, TTIs are a significant burden on the world's healthcare systems, including Saudi Arabia. To reduce patient mortality and morbidity, it is still crucial to comprehend TTIs in blood donors [9]. The main method for preventing TTIs and ensuring the safe supply of blood and blood components is laboratory testing of the blood. The study's objectives were to find out the prevalence and trends of TTIs in the two selected hospitals as well as to build a solid idea about the most sensitive and accurate screening methods for residual TTIs. According to our findings, HBcAb was the most common TTI marker among blood donors, followed by anti-HCV. However, an earlier study conducted in Saudi Arabia showed that HBV is the most common type of TTI [21]. Multiple studies were undertaken in various Saudi Arabian locations. Similarly, a retrospective study conducted by Sarah *et al.* [22] in the Hail region found that 8.6% of samples reacted to HBsAg, 8.2% reacted to HbcAbs (compared to our result, anti-Hbc = 9%), 2.2% reacted to HTLV antibodies, and 4.7% reacted to HIV antibodies. Furthermore, 1.7% of the samples tested positive for syphilis. In Taif, however, Bamaga *et al.* [23] discovered that 0.33% of samples reacted to HbsAg. A study in Jeddah found a considerably higher response to HBsAg (6.11%) [24]. Despite tremendous efforts in Saudi Arabia over the last 30 years to reduce HBV prevalence, the number of HBV-reported cases has remained constant over the last 10 years, and it remains a persistent concern [21]. As a result, other investigations in various parts of Saudi Arabia have been conducted to estimate HBcAb reactivity, such as a research conducted in Dammam by Morsi [25], which discovered HBcAb reactivity (9.15%) remarkably identical to our record (9%). Other research, on the other hand, found a greater HBcAb reactivity rate (11.5%) in Taif, whereas Mecca had the lowest anti-HBc frequency (6.7%) [23]. Outside Saudi Arabia, HBV recorded a transfusion problem in Shiraz, Iran, where the reactivity of anti-HBc was (6.55%) but it is still less than our reported result. [26]. Similarly, in Switzerland, 3.0% of donation units were reactive for anti-HBc [27]. However, in compliance with our results, the seroprevalence of anti-HBc was estimated at 8.1–10.3% in the Federal District and the Central-West region in Brazil, and the seroprevalence of HBsAg antigen was 0.19, 0.47, and 0.60% in the Northeast, Central-West, and Federal District, respectively [28]. Consistent with our results (anti-Hcv = 9%), a study in Dammam found that (0.83%) of the samples reacted to HCV antibodies [25]. On the other hand, HCV seroprevalence was reported at 0.4 and 0.41% in Riyadh

and Jazan, respectively [13,29,30]. Furthermore, our findings contradicted those of Pereira *et al.* [31], who discovered that anti-HCV reactivity was 1.38% in the state capitals of the five macroregions and the Federal District of Brazil, but 0.68% in the Northeast and 2.10% in the North.

Regarding the variation, it has been shown by seroprevalence tests particularly for hepatitis virus B, since HBc antibody 5,318 (9%) units were more reactive than HBsAg 336 (0.6%) units. The reasons might be returned to: first, the effect of mass anti-HBV vaccination, the rising of knowledge of HBV infection believed to have played a significant role in the decreasing prevalence of HBsAg as well [32]; secondly, the presence of latent infection; finally, it is well known that anti-HBc lasts for life (in addition to the strict laws imposed on blood donors) [10].

Concerning the lower seroprevalence rate of malaria in the current study, this was also confirmed by Bashwari *et al.* where it was found that most cases were imported and had a history of travel [33]. The genotypic analysis (NAT) of HBV DNA, HCV RNA, and HIV RNA in donated blood units revealed a 0.6% prevalence rate; however, the detailed NAT result was confidential. In Islamic nations, data on HIV incidence and prevention methods are scarce [34]. In addition, when comparing the seroprevalence and NAT results of HBV, HCV, and HIV, it was found that NAT results were more accurate and sensitive since NAT has the ability to reduce the serological window period and detect the viruses in occult cases [16,18]. This is reflected in the amount of blood wasted as well as the time and cost wasted. Generally, the prevalence rate of syphilis is low, especially in the Kingdom of Saudi Arabia and among Middle Eastern countries. Syphilis transmission through blood donation has become very rare in the past few decades. This is due to the accurate selection process of donors, development of serological screening everywhere in the world, and the recruitment of refrigerated blood instead of fresh blood [35].

The study revealed that (0.16%) of the samples developed transfusion reactions. In addition, the most recorded reactions were allergic, fever, and FNHTR, in contrast to Yeh *et al.* where it was found that the most common reactions were fever, chills, pruritus, or urticaria, which disappeared immediately without certain complications or treatment [36].

This study has a few limitations. First, this study did not find nationalities for donations. Second, this study did not find accessible data on donor genders. Third, this study did not find accessible data on volunteers or replacement donors. Finally, the results of the NATs for HBV, HCV, and HIV were considered confidential.

5 Conclusions

The current study shed light on the importance of TTIs, which represent hazard determinants in spreading blood-borne infection. In addition, it urges the revision of the national screening guide to be ready for any newly emerging infection. Nowadays, it is well known that NAT is more effective for reducing these risks than serology tests. Moreover, it has been found that NATs improve test sensitivity and decrease the residual risk of TTIs more than standard serology tests. Therefore, it enhances blood safety and reduces the amount of excluded blood. As a result, the NAT should be used as a standard in Saudi Arabia when donating blood.

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Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: This study was approved by the Ethical Research Committee of King Saud University, Riyadh, Saudi Arabia (approval number: CAMS-032-3940).

Data availability statement: The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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