ORIGINAL ARTICLE

Oman Medical Journal [2020], Vol. 35, No. 6: e189

The Prevalence of Transfusion-transmitted Infections among Blood Donors in Hospital Universiti Sains Malaysia

Marini Ramli[1,2], Zefarina Zulkafli[1,2]*, Geoffrey Keith Chambers[3], Raja Sabrina Amani Raja Zilan[2,4], and Hisham Atan Edinur[2,4]

[1]School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, Malaysia
[2]Transfusion Medicine Unit, Hospital Universiti Sains Malaysia, Universiti Sains Malaysia, Kelantan, Malaysia
[3]School of Biological Sciences, Victoria University of Wellington, Wellington, New Zealand
[4]School of Health Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, Malaysia

ARTICLE INFO

Article history:
Received: 22 July 2019
Accepted: 17 May 2020

Online:
DOI 10.5001/omj.2020.86

Keywords:
Hepatitis B virus; Blood Donors; Blood Banks; Malaysia; HIV Infections; Transfusion Reaction; Blood Transfusion; Hepatitis C.

ABSTRACT

Objectives: Blood bank centers routinely screen for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) to ensure the safety of blood supply and thus prevent the dissemination of these viruses via blood transfusion. We sought to evaluate the detection of transfusion-transmitted infection (TTI) markers using standard serological methods and nucleic acid testing (NAT) among blood donors in Hospital Universiti Sains Malaysia. ***Methods***: Donated blood units were assessed for the presence or absence of HBV, HCV, and HIV using two screening method: serology and NAT. Reactive blood samples were then subjected to serological confirmatory and NAT discriminatory assays. ***Results:*** A total of 9669 donors were recruited from September 2017 to June 2018. Among these, 36 donors were reactive either for HBV, HCV, or HIV by serological testing and eight by NAT screening. However, only 10 (three for HBV and seven for HCV) donors tested positive using serological testing and five (two for HBV and three for HCV) by NAT discriminatory assays. Note that all five NAT positive donors detected in the NAT discriminatory assays were confirmed to be serologically reactive. Therefore, the prevalence of HBV, HCV, and HIV was 0.03%, 0.1%, and 0.0%, respectively, in our donor pool. ***Conclusions:*** Both serological and NAT screening and confirmatory assays should be used routinely to reduce the risk of infection transmission via the transfusion of blood and blood components.

Blood transfusion is an important part of patient management in hospitals. However, blood transfusion is not without risks, including hemolytic transfusion reaction and transfusion-transmitted infection (TTI).[1,2] Therefore, all donated blood units are routinely screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) to ensure the safety of the blood supply and prevent dissemination of these viruses via transfusion. Enzyme-linked immunosorbent assay and line immunoassay (LIA) for detections of viral antibodies and antigens are the commonly used serological screening and confirmatory techniques.[3] However, these infectious agents can be challenging to recognize or entirely undetectable serologically due to the limited or absence of viral antigens and human antibodies during the early phase (window period) and occult infections.[4] These limitations of phenotyping assays have been recently resolved by testing viral DNA in donated blood using the molecular technique nucleic acid testing (NAT). Several blood donation centers have reported that the incidence of transfusion-transmitted HBV, HCV, and HIV infections and the number of discarded blood donation units have been reduced by combined serological and NAT screenings,[3–5] and the rate has further decreased with the inclusion of serological confirmatory and NAT discriminatory assays.[3,6–9]

In September 2017, the Transfusion Medicine Unit, Hospital Universiti Sains Malaysia (HUSM) implemented two screening methods for donated blood: serology and NAT. These methods detected the presence or absence of HBV, HCV, and HIV. Reactive blood samples are then subjected to serological confirmatory and NAT discriminatory assays. To date, there is no documented data on the prevalence of transfusion-transmissible HBV, HCV, and HIV among blood donors in Malaysia.

*Corresponding author: ✉zefarinazulkafli@gmail.com

Therefore, this study was conducted to provide statistics for these infections among blood donors registered at HUSM from September 2017 to June 2018. We also aimed to evaluate the relative efficiency of serological and NAT techniques to detect TTIs in our donor population.

METHODS

Blood samples were collected from 9669 voluntary donors registered at the Transfusion Medicine Unit, HUSM, from September 2017 to June 2018. They all fulfilled the criteria for blood donation as described by Saleh et al.[5] A total of 6 mL of peripheral venous blood were collected into three blood collection tubes for laboratory analyses. Tube one contained EDTA and was used for ABO and Rhesus blood regrouping. Tube two contained coagulant separating gel and was used for serological screening and confirmatory testing of HBV surface antigen (HBsAg), antibody to HCV (anti-HCV), and HIV antigen/antibody (HIV Ag/Ab), and tube three contained inert gel and spray-dried K_2EDTA anticoagulant and was used for NAT screening and discriminatory testing. Informed consent was obtained from each participant, and the study was reviewed and approved by the Human Research Ethics Committee, Universiti Sains Malaysia (certificate number: USM/JEPEM/18070311).

The serological screening of donated blood samples was conducted in the hospital microbiology laboratory using chemiluminescent microparticle immunoassay technology (Abbott Architect Immunoassay Analyzer, USA). The cut-off point for seropositivity was set at > 1 OD.

The HBsAg, anti-HCV, and combo HIV Ag/Ab reactive blood samples were then subjected to the serological confirmatory test. The serological confirmatory test for reactive HBV blood samples was performed in the hospital microbiology laboratory using a neutralization test, while reactive HCV and HIV blood samples underwent confirmatory testing using the LIA (Fujirebio, Japan).

These NAT tests for HBV, HCV, and HIV were performed by a referral laboratory (Synapse Sdn. Bhd., Petaling Jaya). This organization implemented individual donation NAT screening and discriminatory testing using Procleix® systems (PROCLEIX® ULTRIO® assay and PROCLEIX® HIV-1, HCV, and HBV discriminatory assays, respectively) for target amplification of HBV DNA, HCV RNA, and HIV RNA. The NAT discriminatory assay was only used on blood samples found to be reactive by NAT screening. This was done to identify the exact type of viral infection present in that particular blood donor. Results of NAT discriminatory testing were normally obtained within two weeks, and results were sent to HUSM staff via email.

The prevalence of HBV, HIV, and HCV in our donor pool was calculated by direct counting. This was done by dividing the number of positive cases by the total number of donated blood samples.

Table 1: Demographic statistics of the 9669 blood donors.

Gender	n (%)
Gender	
Male	5370 (55.5)
Female	4299 (44.5)
Age group, years	
17–18	1133 (11.7)
19–24	3732 (38.6)
25–29	1058 (10.9)
30–34	977 (10.1)
35–39	796 (8.2)
40–44	629 (6.5)
45–49	529 (5.5)
50–54	428 (4.4)
> 54	387 (4.0)

RESULTS

Table 1 shows the demographic data of 9669 blood donors. The majority of our donors were male (55.5%) and aged < 34 years old. Among the total collection of blood samples, 36 were reactive by serological screening [Table 2]. Anti-HCV showed the highest number (n = 7) of positives by serological confirmatory screening, followed by HBsAg with three positives. No positives were recorded with combo HIV Ag/Ab assays. Thus, out of 36 cases

Table 2: The number of reactive blood samples by serological and NAT screening.

Screening Methods	Number of positive samples
Serological screening	36
NAT screening	8

NAT: nucleic acid testing.

Table 3: Number of reactive and non-reactive samples detected using serological confirmatory and NAT discriminatory assays.

	Indeterminate NAT-	Serology+ NAT+	Serology+ NAT-	Serology- NAT+	Serology- NAT-
HBV	0	2	1	0	9666
HCV	5	3	4	0	9654
HIV	0	0	0	0	9669

NAT: nucleic acid testing; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus.

identified as reactive by serological screening, only 10 cases were confirmed positive by serological testing [Table 3]. Initial NAT screening only showed eight reactive cases, and of these, five were confirmed by NAT discriminatory assays [Tables 2 and 3]. All these five blood samples were also positive by confirmatory serological testing [Table 3]. It is important to note that five samples were assigned as indeterminate for HCV by serological confirmatory assays and actual infectious status can only be assured after follow-up testing of their blood samples.

DISCUSSION

The prevalence of confirmed HBV and HCV in our donor pool was 0.03% and 0.1%, respectively, and none of the donors was found positive for HIV using either serological confirmatory or NAT discriminatory assays. The low prevalence of TTIs in our donor pool could be attributed to effective blood transfusion practices, including donor screening, an effective deferral system, and a policy of unpaid voluntary donation.[5] As recommended by the World Health Organization,[10] we have also targeted low-risk donor groups, especially university students and government workers. In this context, the frequencies of TTI among blood donors at HUSM reported in this study may not reflect the overall prevalence of HBV, HCV, and HIV in the country. Therefore, further studies are urgently needed to get accurate figures for HBV, HCV, and HIV occurrence in the general population; such statistics can be used for formulating a better blood recruitment strategy.

In this study, three out of the eight initially NAT positive samples [Table 2] were negative by serological confirmatory and NAT discriminatory assays [Table 3]. It is claimed that NAT screening is highly sensitive for detecting low viral load during the window period or in occult infections[3,8,9] that may go undetected by the less sensitive serological confirmatory and NAT discriminatory assays. This may sometimes give discrepant results and may mistakenly give a false positive in initial NAT screening. Thus, transfusion services should block all NAT-initial reactive blood units from being used regardless of the outcome of serological confirmatory and NAT discriminatory assays.[8,9] In this case, the three unconfirmed NAT-initial reactive samples merit further investigation, and blood for these donors should be checked carefully when collected in their next visits for repeat blood donation.

Furthermore, we found that NAT assays failed to detect five cases that were positive by serological screening and confirmatory assays [Table 3]. This might be because the infected person's viral concentration was below the detection threshold level at that time.[8] Another possible explanation is the presence of new viral strains formed by point mutation or genetic recombination between different sub-types of viruses. These new strains may not be detectable (even with very slight nucleotide changes) by the oligonucleotide probes used for the NAT assays.[11] In this context, the donors of these samples should be tagged and contacted for another round of blood screening for accurate determination of their TTI status and viral type. Our findings showed that serological techniques should continue to be used alongside NAT for the detection of TTIs. This is because samples with a low viral load but containing adequate levels of antibodies may sometimes not appear reactive by NAT, but can still be detected serologically.[8] Therefore, the implementation of both serological and NAT screening and confirmatory assays should continue to be used to improve TTI marker detection and reduce the risk of infection transmission via transfusion of blood and blood components.

CONCLUSION

Blood transfusion is a medical intervention for severe bleeding and anemia. However, this

medical procedure requires transfusion of not only compatible blood units but ones that are also free from bloodborne pathogens. Our results showed a very low prevalence of HBV, HCV, and HIV infections among blood donors in HUSM as detected using serological and NAT assays. The present study also indicates that NAT could not replace the well-established serological testing, but both techniques can be used together with NAT to ensure the safety of blood supplies in Malaysia. In summary, findings from our study provide important information for designing an effective donor recruitment strategy and achieving zero-risk blood transfusion in HUSM.

Disclosure
The authors declared no conflicts of interest. No funding was received for this study.

Acknowledgements
This work was supported by the Research University Grant (Universiti Sains Malaysia RUI grant; 1001/PPSP/812187). We would like to thank all the staff at the Transfusion Medicine Unit and Management staffs of Hospital Universiti Sains Malaysia, Kelantan. Geoffrey Chambers thanks Victoria University of Wellington for Alumnus Scholar support.

REFERENCES

1. World Health Organization. The clinical use of blood handbook. Geneva: WHO; 2002.
2. Al-Riyami AZ, Al-Marshoodi I, Zia F, Al-Huneini M, Al-Rawas AH, Jose S, et al. Transfusion consent in Oman: physicians' perception at a tertiary care university hospital. Oman Med J 2016 Jul;31(4):253-257.
3. Yaseen SG, Ahmed SA, Johan MF, Kiron R, Daher AM. Evaluation of serological transfusion-transmitted viral diseases and mutliplex nucleic acid testing in malaysian blood donors. Transfus Apher Sci 2013 Dec;49(3):647-651.
4. Chigurupati P, Murthy KS. Automated nucleic acid amplification testing in blood banks: an additional layer of blood safety. Asian J Transfus Sci 2015 Jan-Jun;9(1):9-11.
5. Saleh RM, Zefarina Z, Che Mat NF, Chambers GK, Edinur HA. Transfusion medicine and molecular genetic methods. Int J Prev Med 2018 May;9:45.
6. Fang CT, Field SP, Busch MP, Heyns AduP. Human immunodeficiency virus-1 and hepatitis C virus RNA among South African blood donors: estimation of residual transfusion risk and yield of nucleic acid testing. Vox Sang 2003 Jul;85(1):9-19.
7. Alaidarous M, Choudhary RK, Waly MI, Mir S, Bin Dukhyil A, Banawas SS, et al. The prevalence of transfusion-transmitted infections and nucleic acid testing among blood donors in Majmaah, Saudi Arabia. J Infect Public Health 2018 Sep - Oct;11(5):702-706.
8. Shrivastava M, Mishra S. Nucleic acid amplification testing for enhancing blood safety. National Journal of Laboratory Medicine 2017 Apr;6(2):IR01-IR06.
9. Kumar R, Gupta S, Kaur A, Gupta M. Individual donor-nucleic acid testing for human immunodeficiency virus-1, hepatitis C virus and hepatitis B virus and its role in blood safety. Asian J Transfus Sci 2015 Jul-Dec;9(2):199-202.
10. Gregory H, Tarik J. More voluntary blood donation essentials. World Health Organization. 2012 [cited 2019 June 20]. Available from: http://www.who.int/mediacentre/news/releases/2012/blood_donation_20120614/en/.
11. Shyamala V. Factors in enhancing blood safety by nucleic acid technology testing for human immunodeficiency virus, hepatitis C virus and hepatitis B virus. Asian J Transfus Sci 2014 Jan;8(1):13-18.