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Seroprevalence of Cytomegalovirus IgG and IgM antibodies among voluntary blood donors in South India

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ABSTRACT

Purpose

Human Cytomegalovirus (CMV) infection is mild or asymptomatic in healthy individuals but causes serious disease in immunocompromised hosts and neonates with significant morbidity and mortality[1].Hence it is mandatory to screen blood and apheresis donations intended for transfusion to this high-risk population and pregnant mothers to avoid transfusion transmitted CMV (TT CMV)infection.[2] The present study was done with the aim of determining the seroprevalence of CMV IgG and IgM antibodies among healthy blood donors attending the Transfusion Department of Stanley Medical College and to look for possible associations between the age and blood group of donors with CMV serological status.

Materials and Methods

A cross-sectional study was conducted on 90 voluntary blood donorsover a 3 month duration from April to July 2021. Serological screeningof their blood samples was done for both Cytomegalovirus IgG and IgM antibodies by Enzyme Linked Immunosorbant assay (Calbiotech) in accordance with the manufacturer's instructions.

Results

The overall anti-CMV IgG seroprevalence in the study was 74.4% and that of anti-CMV IgM was 13.3% IgM seropositive donors indicating recent infection accounted for 2.2% of the study population. But combined IgG and IgM seropositive donors indicating sub-acute phase of infection accounted for 11.1% .

Conclusions

This study done among healthy blood donors in South India shows a lower anti CMV IgG seroprevalence but the combined IgM and IgG seroprevalence indicating subacute infection was moderately high emphasizing the need for regular screening of blood components for CMV to prevent and reduce primary CMV infections in the general population.

Keywords

Cytomegalovirus antibodies, Seroprevalence, Subacute infection, Blood donors Other preventive strategies, such as leukoreduction filtration, saline-washed RBCs, frozen deglycerolized RBCs, etc., are being increasingly recommended tominimize the transmission of CMV through transfusion

I. INTRODUCTION

Primary Cytomegalovirus infection is known to be a significant cause of morbidity and mortality following blood transfusion in children and immunocompromised CMV seronegative patients.[3] Transmission of infectious diseases is a major challenge in transfusion services worldwide.[4]Transfusion transmissible infections for which universal screening is recommended in all countries are HIV,HBV,HCV and syphilis and for which universal screening is recommended in some countries only or selective screening is recommended are Malaria, HTLV I/ II, Chagas and HCMV[2]It is not mandatory to screen donated blood for CMV in blood banks in many parts of the world.

The global seroprevalence HCMV infections ranges from60-90%.[5] In India, seroprevalence ranges from 90% to 100% [6,7]

Human cytomegalovirus (HCMV) is a betaherpesvirus. It is a large enveloped virus with double stranded DNA ,slow growing and causes massive enlargement of infected cells (cytomegalic).It has been isolated from lung, colon, kidneys, monocytes, T and B lymphocytes. The host immune response maintains HCMV in a latent state in seropositive individuals. Reactivations can cause disease more often in immunocompromised patients including organ transplant recipients, those

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on chemotherapy for malignancies and those with AIDS.

One-third of primary maternal infections can get transmitted in utero to fetus and cause generalised cytomeglic inclusion disease, with intrauterine growth retardation, jaundice, hepatosplenomegaly, thrombocytopenia, microcephaly and retinitis. Perinatal transmissions via genital tract or breast milk may only cause subclinical infection [8]

HCMV is spread through close personal contact with people who excrete the virus in body fluids (e.g., saliva, urine, breast milk, semen), by vertical transmission, through organ transplant, or via blood transfusion[9].

HCMV infection is typically asymptomatic or mild in the immunocompetent population presenting as mononucleosis-like syndrome with fever, malaise, myalgia,liver dysfunction and lymphocytosis several weeks after exposure[10].

In contrast, CMV infection in transplant patients may lead to severe illness including hepatitis, thrombocytopenia, haemolytic anaemia and pneumonia with potentially lethal outcome[11]. Latent CMV viruses associated with leucocytes are responsible for CMV transmission by transfusion (TT-CMV) of cellular blood components. There are strategies to prevent the spread of CMV via blood products, such as the transfusion of leukocyte-depleted blood products and screening to select CMV-seronegative blood donors[9,12].

Because of the high seroprevalence of CMV,about 95% among blood donors in India, it would seem superfluous to screen blood donors for CMV, as very few seronegative blood units would be available for transfusion. But documentation of the seroprevalence of anti CMV antibodies in the blood donor population is essential for better understanding of the likelihood of transmission through donor blood and for determining the best transfusion practices to prevent TT-CMV infection.

II. MATERIALS AND METHODS

2.1. Study design and Setting

A cross-sectional study was done to determine the Seroprevalence of Cytomegalovirus IgG and IgMantibodies among voluntary blood donors in the Departments of Microbiology and Transfusion Medicine,Government Stanley Medical College, Chennai.About 90participants suitable for blood donation were selected for the study which was done over a period of 3 months fromApril 2021 to July2021.The research protocol was approved by the Institutional Ethics Committee of Government Stanley Medical College

2.2 Participant Inclusion criteria

Healthy adults who had no recent illness, aged between 18 to 50 years, hemoglobin> 12.5 g/dL, screened for transmissible disease like HBV, HCV. malaria, syphilis, HIV and willing to participate in the study.

2.3 Participant Exclusion criteria

Individuals younger than 18 years, weight < 50 Kg, history of jaundice, high-risk sexual behavior and blood-borne infections ,and healthy donors not willing for the study

2.4 Sample collection and testing

The voluntary blood donors who were willing to participate were briefed about the study.Five ml of blood sample was collected from each of the 90 donors in red vacutainers. Serum was separated from the collected blood samples by centrifugation and stored at -20^{0}C.The sera were screened for CMV-specific IgM and IgG by ELISA techniquein accordance with the manufacturer's instructions (Calbiotech) and interpreted as per kit protocol.

2.5 Data Analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp). To find the significance in categorical data Chi-Square test was used. In the statistical tool the probability value .05 is considered as significant level.

III. RESULTS

Among the 90 blood donors who participated in the study, all 90 were males, no one was female.

The age group of the donors ranged from 18 to 50 years (mean 30.4 years). In this study, blood donors were more in the 21 – 30 years age group (44%) and least in the 18 -20 years age group (10%). Figure 1

Out of the total 90, 37 donors had blood group type B (41%), 31 donors type O (34%), 17 type A (19 %) and 5 type AB (6%).Most of the donors,86 were Rh + (95.6%) and 4 were Rh - (4.4%).χ^2 = 9.039 df=3 p=0.029 Statistically significant .Figure 1

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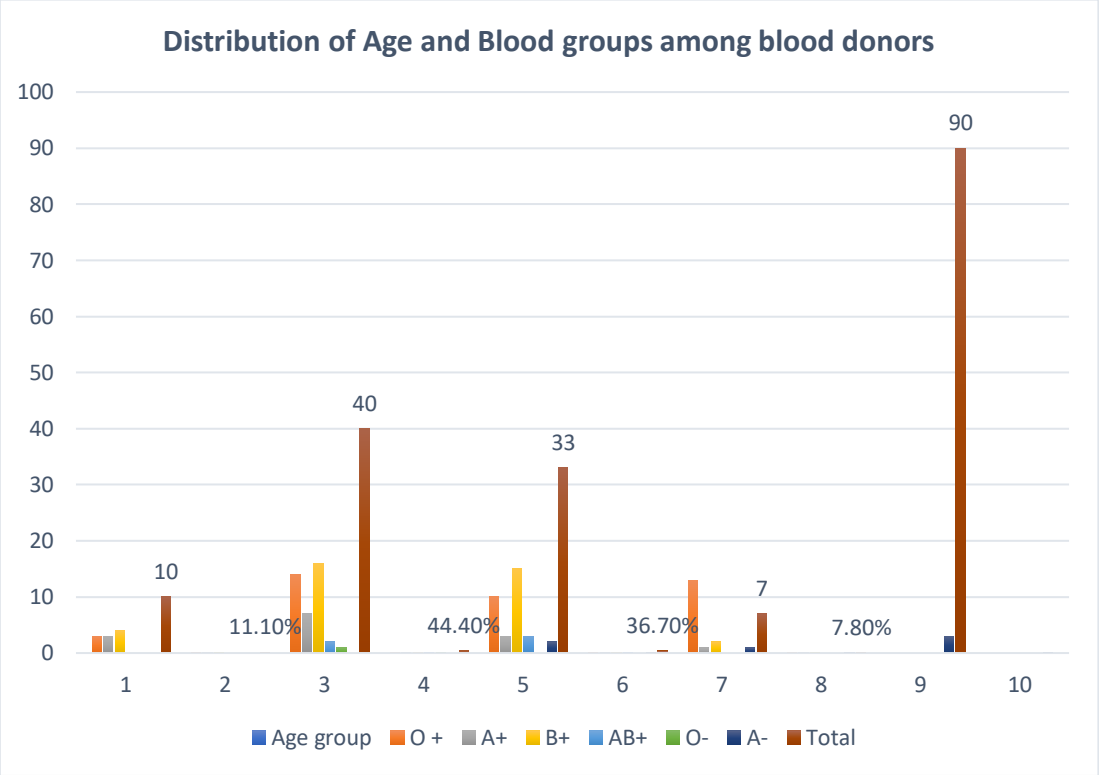

Figure 1 Distribution of Age and Blood groups among blood donors

χ^2 = 10.996 df=15 p=0.753 No statistical significance

Type B and Type O group blood donors were more in the 21-30 age group : Type B-16 donors (17.8%) and Type O -14 donors (15.6%) followed by 31-40 age group: Type B -15 donors (16.7%) and Type O -10 donors (11.1%) Figure 1

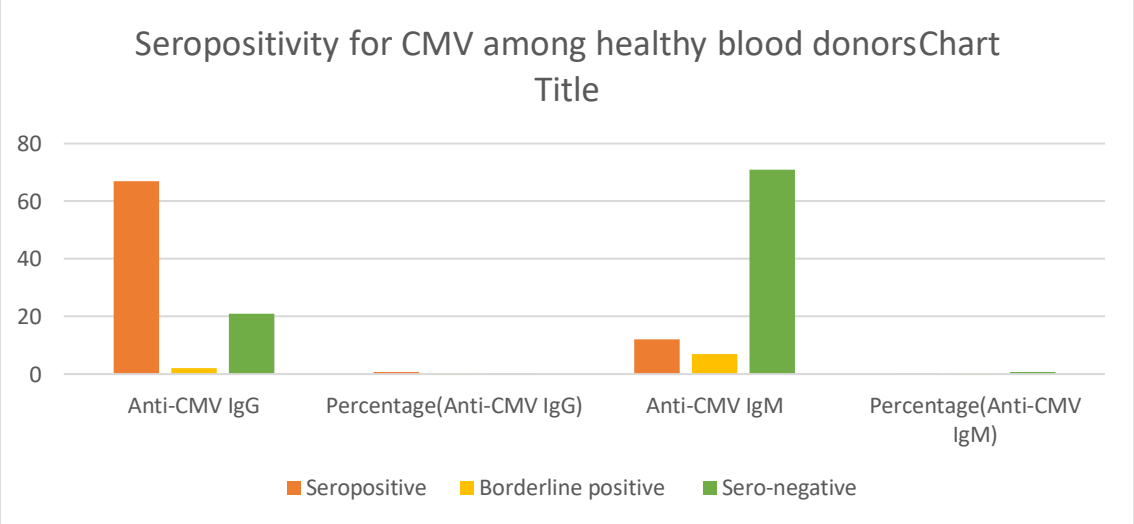

Figure 2 Seropositivity for CMV among healthy blood donors

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χ^2 = 68.243 df=2 p=0.0005 High statistical significance

Among the 90 blood donors , 67 were positive for anti-CMV IgG antibodies (74.4%)
and 12 (13.3%) were positive for anti-CMV IgM antibodies .

2 were borderline positive for anti-CMV IgG antibodies (2.3%)and 7 were borderline positive for anti-CMV IgM antibodies(7.8%) .21 donors were non-reactive for IgG antibodies (23.3%)and 71 were non-reactive for IgM antibodies(78.9%). Figure 2

Table 1 Distribution of Anti-CMV IgG and IgM levels in different age groups

	IgG level					IgM level				
Age	**18-20**	**21-30**	**31-40**	**41-50**	**Total**	**18-20**	**21-30**	**31-40**	**41-50**	**Total**
<9IU/ml (Negative)	3 (3.3%)	10 (11.1%)	7 (7.8%)	1 (1.1%)	21 (23.3%)	9 (10%)	34 (37.8%)	23 (25.5%)	5 (5.5%)	71 (78.9%)
9-11 IU/ml (Borderlin e positive)	1 (1.1%)	-	1 (1.1%)	-	2 (2.2%)	-	2 (2.2%)	4 (4.4%)	1(1.1%)	7 (7.8%)
>11 IU/ml Positive	6 (6.7%)	30 (33.33%)	25 (27.8%)	6 (6.7%)	67 (74.4%)	1 (1.1%)	4 (4.4%)	6 (6.7%))	1 (1.1%)	12 (13.3%)
Total donors	10 (11.1%)	40 (44.4%)	33 (36.7%)	7 (7.8%)	90	10 (11.1%)	40 (44.4%)	33 (36.7%)	7 (7.8%)	90

*Antibody Index Interpretation
<9 Negative
9-11 Borderline positive
>11 Positive

Among the 67 blood donors were seropositive for IgG(74.4%), seropositivity was observed more in the 21-30 year age group (33.3%) followed by 31-40 year age group (27.8%).They were seronegative more in the 21-30 age group(11.1%) Table 1

AntiCMV.IgG χ^2 = 4.82 df=6 p=0.567 No statistical significance

Out of the 12 blood donors seropositive for Anti CMV IgM (13.3%) ,seropositivity was seen more in the 31-40 year age group (6.7%) followed by 21-30 year age group (4.4%).They were seronegative more in the 21-30 age group(37.8%) Table 1
AntiCMV.IgM χ^2 = 4.108 df=6 p=0.662 No statistical significance

Table 2 Distribution of Anti-CMV IgG and IgM (Antibody Index) according to age group.

	18-20 years	**21-30 Years**	**31-40 years**	**41-50 years**	**Total**
IgG positive	5 (5.6%)	25 (27.8%)	17 (18.9%)	4 (4.4%)	51 56.7%)
IgM positive	-	1 (1.1%)	1 (1.1%)	-	2 (2.2%)
IgG +IgM positive	1 (1.1%)	3 (3.3%)	5 (5.6%)	1 (1.1%)	10 (11.1%)
IgG+ BorderlineIgM positive	-	2 (2.2%)	3 (3.3%)	1 (1.1%)	6 6.7%)
Borderline IgG + Borderline IgM positive	-	-	1 (1.1%)	-	1 (1.1%)
Borderline IgG positive	1 (1.1%)	-	-	-	1 (1.1%)
Negative	3	9	6	1	19

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	(3.3%)	(10%)	(6.7%)	(1.1%)	(21.1%)
Total	10	40	33	7	90

χ^2 = 14.151 df=18 p=0.719 No statistical significance

Anti CMV IgG seropositivity was maximum in 21-30 years age group (25, 27.8%) .IgM seropositivity alone was seen 1 each in 21-30 and 31-40 years age group.(1.1%)
Combined IgG and IgM seropositivity was seen more in 31-40 years age group (5, 5.6%).
Combined IgG and borderline IgM seropositivity was seen more in 31-40 years age group. Borderline IgG seropositivity was seen 1 each in 18-20 and 31-40 years age group. Highest number of seronegativity was seen in donors of 21-30 years age group (9, 10%) and least in 41-50 (1, 1.1%).Table 2

Table 3 Seropositivity of donors in different blood groups

Antibody Index*	O+	A+	B+	AB+	O-	A-	Total
IgG positive	16 (17.7%)	9 (10%)	19 (21.1%)	4 (4%)	1 (1.1%)	2 (2.2%)	51 (56.6%)
IgM positive	1 (1.1%)		1 (1.1%)	-	-	-	2 (2.2%)
IgG +IgM positive	5 (5.6%)	3 (3.3%)	2 (2.2%)	-	-	-	10 (11.1%)
IgG+ BorderlineIgM positive	1 (1.1%)	1 (1.1%)	3 (3.3%)	-	-	1 (1.1%)	6 (6.7%)
Borderline IgG + Borderline IgM positive	-	-	1(1.1%)	-	-	-	1 (1.1%)
Borderline IgG positive	1 (1.1%)	-	-	-	-	-	1 (1.1%)
Negative	6 (6.7%)	1 (1.1%)	11 (12.2%)	1 (1.1%)	-	-	19 (21.1%)
Total	30 (33.3%)	14 (15.5%)	37 (41.1%)	5 (5.65)	1(1.1%)	3 (3.3%)	90

χ^2 = 17.34 df=30 p=0.968 No statistical significance

IgG seropositivity was observed more in B+(19, 21.1 %)and O+(16, 17.7%)blood group donors . Only IgM seropositivity was seen in O+ and B+ donors ,1 each (1.1%). Seropositivity for both Anti-CMV IgG and IgM antibodies was seen more in O+ blood donors(5, 5.6 %) followed by A + blood donors (3 3.3 %) .
Borderline IgM seropositivity with IgG seropositivity was seen more in B+ blood donors , 3 (3.3%) . Seronegativity was seen mostly in B+ blood group donors (11 , 12.2%).Table 3.

IV. DISCUSSION

All the participants in this study were males (100%) similar to a sudy conducted by Rashid et al in Pakistan[12].

In this study ,voluntary blood donors were more in the 21 – 30 years age group (44%) and least in the 18 -20 years age group (10%). In a study by Matos et al , donors in 18-28 year age group were maximum , about 47.8 % [13]

41% of the blood donors had blood group B and 34% had blood group O in our study .This is similar to a study by Rashid et al where both O and B group blood donors were 36% each of the total study population [12]
Group B (17.8%)and Group O (15.6%) blood donors were more in the 21-30 age group.

The seroprevalence of anti-CMV IgG antibodiesin this study is 74.4% indicating past exposure to infection and of anti-CMV IgM antibodies is 13.3% indicating primary infection.

Our study was similar to the study by Barba et al wherein the anti CMV IgG seroprevalence was 71.9% but anti CMV IgM

seroprevalence was 0.9 %[14]. In the study by Marli et al the anti CMV IgM seroprevalence was 2.3%[15]. In a Libyan study by Bleiblo et al the anti-CMV IgM seroprevalence was 39% ,much higher than our study [16].

The overall seroprevalence of anti CMV IgG antibodies among healthy donors was 98.6% in the study conducted in North India by Das et al. In the study by Rashid et al, the seroprevalence of anti-CMV IgG antibodies was 96.5% and of anti-CMV IgM antibodies was 3.4 %[12].

Anti CMV IgG seroprevalence indication past infection was seen more in the 21-30 age group(33.3%) followed by 31-40 age group (27.8%). Study done by Islam Shaheen et al showed 89.5% in 28-37 age group and 92.5% in 38-47 age group [17].

Anti CMV IgM seroprevalence was seen highest in the 31-40 age group(6.7%) and borderline IgM positivity too was highest in that age group (4.4%)

In the Libyan study by Bleiblo et al IgM seropositivity was seen highest in 45-59 age group[16] and in the Bangladesh study by Islam Shaheen et al highest IgM seroprevalence was seen in 28-37 age group[17].

AntiCMV IgM was positive in 12 of the 90 participants ,among whom 2 were only IgM positive indicating recent infection and 10 donors were both IgG and IgM seropositive indicating a subacute phase of infection . Combined seropositivity was seen highest in the 31-40 age group.

In a study conducted by Adane et al the global seroprevalence of CMV IgG, CMV IgM, and both CMV IgM and IgG was 83.16% ,13.77% and 23.78% respectively [5] .In our study it is 56.6%,2.2%and 11.1% respectively

Donors of blood group B (21.1%) showed highest IgG seroprevalence followed by donors of blood group O (17.7%). Combined IgG and IgM seropositivity was seen in O group donors (5.5%) . Rashid et al study shows highest IgG (34.8%) and IgM (2.2%) seroprevalence in blood group B [12].

V. CONCLUSION

Human CMV is endemic in many parts of the world, although in some regions its incidence and prevalence have declined in recent years as living standards have improved. Transfusion transmitted Cytomegalovirus infection poses a great risk in immunosuppressed individuals. This study done among blood donors in South India shows a lower anti CMV IgG seroprevalence compared to many studies Though IgM seroprevalence was low, combined IgM and IgG seroprevalence indicating subacute infection was moderately high necessitating the need for routine screening of all blood components for CMV, or in the absence of screening, selective leucodepletion may be considered [2,18]Also,it is essential to maintain records of CMV seronegative blood in blood banks for availability to immunosuppressed recipients.

REFERENCES

[1] Nogalski MT, Collins-McMillen D, Yurochko AD. **Overview of human cytomegalovirus pathogenesis.** Methods Mol Biol. 2014;1119:15–28

[2] World Health Organization. Guidance on increasing supplies of plasma-derived medicinal products in low- and middle-income countries through fractionation of domestic plasma [Internet]. Geneva: World Health Organization; 2021 [cited 2021 Dec 29]. Available from: https://apps.who.int/iris/handle/10665/340171

[3] Lachmann R, Loenenbach A, Waterboer T, Brenner N, Pawlita M, Michel A, et al. **Cytomegalovirus (CMV) seroprevalence in the adult population of Germany**. Nevels M, editor. PLoS ONE. 2018 Jul 25;13(7):e0200267.

[4] Taylor GH. Cytomegalovirus. AFP. 2003 Feb 1;67(3):519–24.

[5] **Seroprevalence of cytomegalovirus among voluntary blood donors in Delhi, India**. - Abstract - Europe PMC [Internet]. [cited 2021 Dec 29]. Available from: https://europepmc.org/article/MED/12659416

[6] Henry N, Baiju NM, Bhaskaran R, Sudha SP, Thomas T. **Cytomegalovirus Seroprevalence among Blood Donors in Kerala.** 2016;3(10):3.

[7] Das B, Kaur G, Basu S. **Seroprevalence of cytomegalovirus antibodies among blood donors and Multitransfused recipients--a study from north India**. TransfusApher Sci.2014 Jun;50(3):438–42.

[8] Jawetz, Melnick &Adelberg's Medical Microbiology [Internet]. [cited 2021 Dec 29]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3074881

[9] Qu L, Tran MH. Cytomegalovirus (CMV) and transfusion medicine.Blood Bulletin. 2007;9(1).

[10] **Risk of cytomegalovirus transmission by blood products to immunocompromised patients and means for reduction** - Ljungman - 2004 - British Journal of Haematology - Wiley Online Library [Internet]. [cited 2021 Dec 29]. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2141.2004.04845

[11] Fulkerson HL, Nogalski MT, Collins-McMillen D, Yurochko AD. Overview of Human Cytomegalovirus Pathogenesis. Methods Mol Biol. 2021 Jan 1;2244:1–18.

[12] Chaudhry A, Mahmood R, Malik F, Hussain S, Ashfaq K, Akhtar T, et al. **Seroprevalence of cytomegalovirus among blood donors in local population.** International Journal of Pharmaceutical Chemistry. 2014 Jan 1;ISSN:2249–734.

[13] Matos SB, Meyer R, Lima FWM. **Seroprevalence of cytomegalovirus infection amonghealthy blood donors in Bahia State, Brazil**. Rev Bras Hematol Hemoter. 2010 Feb;32:45–9.

[14] Roberto BEJ. Prevalencia de citomegalovirusendonantes de sangre. :6.Rev Mex Patol Clin Med Lab. 2019;66(4):187-192.

[15] Souza MA, Passos AM, Treitinger A, Spada C. **Seroprevalence of cytomegalovirus antibodies in blood donors in southern, Brazil.** Rev Soc Bras Med Trop. 2010 Aug;43(4):359–61.

[16] Bleiblo F, Eljaki A, Bumadian M, Elwaheishi K, Almismary E, Aljlale M, et al. **Screening Donated Blood for Transfusion-Transmissible Cytomegalovirus Infection among Libyans.** JBM. 2020;08(01):5–12.

[17] Islam Shaheen, D. S. S., Hoque, D. M. A., & Ferdous, D. J. (2020). **Seroprevalence of Cytomegalovirus among Blood Donor in Transfusion Medicine: Study from Bangladesh.** IJIRMS, 5(01), 01 to 04. https://doi.org/10.23958/ijirms/vol05-i01/833

[18] Dean CL, Wade J, Roback JD. Transfusion-Transmitted Infections: an Update on Product Screening, Diagnostic Techniques, and the Path Ahead. J Clin Microbiol [Internet]. 2018 Jul 1 [cited 2021 Dec 29];56(7). Available from: https://europepmc.org/articles/PMC6018323

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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