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PREVALENCE AND ASSOCIATED CHARACTERISTICS OF CYTOMEGALOVIRUS (CMV) IMMUNOGLOBULIN ANTIBODIES AMONG BLOOD DONORS AT A UNIVERSITY TEACHING HOSPITAL IN NIGERIA
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ABSTRACT

***Background*: The screening for cytomegalovirus (CMV) specific antibodies is not routine in our setting, thus the transfusion of blood portends high risk for susceptible individuals.**
***Objective*: To determine the prevalence of IgG and IgM specific antibodies and associated characteristics in blood donors seen at a referral teaching hospital in Nigeria.**
***Design*: Prospective, cross-sectional and descriptive study.**
***Setting*: Blood Bank and Serology Unit of the Department of Haematology and Blood Transfusion, Obafemi Awolowo University Teaching Hospitals' Complex, Ile-Ife, Nigeria.**
***Subjects*: One hundred and eighty four blood donors negative for human immunodeficiency virus, hepatitis B and C viruses and syphilis were assessed for their levels of CMV specific IgG and IgM antibodies (AccuDiagTM ELISA, DIAGNOSTIC AUTOMATION INC, USA) using the enzyme linked immunosorbent assay technique (ELISA).**
***Results*: Ninety six percent of the donors were males while those with secondary education and below (61.3%), unmarried (70%), artisans and unemployed including students (82.5%) were in the majority. The prevalence of CMV IgG and IgM antibodies were 97.4% and 52.6%, while CMV IgG antibody range from 94.7% to 100% in all types of donation. All female donors (3.8%) were positive for IgG and IgM antibodies. The level of education of the donors predicts IgM antibody positivity, those with secondary education or less are more likely than others to be positive ($p < 0.05$; $X2 = 15.98$). Linear logistic regression showed that male donors and those in the artisan group are more likely to be positive for IgM antibody ($p < 0.05$).**
***Conclusion*: The prevalence of CMV antibodies is very high (IgG = 97.4%; IgM = 52.6%) in our setting. Donors with low educational status and artisans are more likely to be IgM positive. Therefore, a more stringent donor selection, adoption of leukodepleted blood and blood products for uninfected patients especially the immuno-compromised and adoption of a national policy on CMV infected blood is advocated.**

INTRODUCTION

Human cytomegalovirus (CMV) is a transfusion transmissible infection which belongs to the herpes viruses; it is the largest member of the herpes family with its genome of about 230 kb encoding a total of 160 genes (1). It infects adults in the range of 50%-100% worldwide (2); in the US, close to 60% of the adult population were infected while 25-40% of the UK donors are CMV antibody positive and up to 50% of pregnant women show evidence of exposure to CMV infection (3, 4). The virus is distributed in all geographic and socioeconomic groups, and the sero-prevalence increases with advancing age and poor socioeconomic conditions in addition to environmental and climatic factors (5, 6). Cytomegalovirus could be transmitted through

direct contact with body fluids, and also sexually. It can be spread through transplanted organs and transfusion of blood and blood products. CMV may circulate in leucocytes or free in plasma following primary infection or re-activation. Interestingly, once acquired it remains latent in the white blood cells. Following infection and subsequent seroconversion, CMV specific immunoglobulin G (CMV IgG) remain persistent with cellular immune response. Such individual is both infected and potentially infectious for life (7). The presence of CMV specific IgM is not only indicative of primary infection but may suggest re-infection or reactivation of prior infection. Unlike in the developed and highly industrialized countries, previous reports from developing and less industrialized nations showed CMV prevalence of 92% to 100% (8-12). The seroprevalence varies between countries and between populations within a country, factors responsible for this among others include crowding, hygienic standard and practices, age of onset of sexual activity and the number of sexual partners (13).

The standard methods for the prevention of transmission transmissible CMV (TT-CMV) include the transfusion of CMV negative blood or the use of leucodepleted blood from unscreened donor (similar to using CMV infected blood) (14). Cytomegalovirus in blood donors has been shown to be carried by leukocytes and several studies have shown that leukocyte depletion by current methods is highly effective in preventing transfusion-transmitted CMV. In the UK, leucodepleted blood has been in routine use since 1999; antibody screening to detect total CMV antibody (IgG and IgM) is a standard practice by the Blood Services to provide CMV negative inventory of cellular components (7). In our setting, screening for CMV is not routine (15) and there appears to be no formal guidelines on the management of CMV sero-positive blood; thus patients receiving multiple transfusions and immuno-compromised individuals are exposed to infection and re-infection with multiple CMV strains from unscreened and CMV positive blood and blood products (16-18).

MATERIALS AND METHODS

The study population consisted of 184 consecutive eligible blood donors seen at the blood bank of the Obafemi Awolowo University Teaching Hospitals' Complex (OAUTHC), Ile-Ife, Nigeria from February to April 2013. This cross-sectional study assessed the levels of CMV IgG and IgM antibodies using ELISA method (AccuDiagTM ELISA, DIAGNOSTIC AUTOMATION INC, USA) in all the 184 blood donors; the donated blood had previously been screened and found negative for HIV infection (using ELISA method), hepatitis B and C viruses and syphilis.

In a designed proforma, the age, gender, marital status, level of education and occupation were documented. Also, the type of donation and history of prior donations were noted. One hundred and sixty (87%) of the study participants had complete data and were documented in this report. All the participants gave informed consent and the study protocol was approved by the Research and Ethics Committee of the hospital.

From each subject, 5 mls of venous blood was obtained in a plain specimen bottle, spun and serum was separated and stored at -30°C for batch analysis for CMV specific IgG and IgM using ELISA technique and following the manufacturer's instruction. Results were reported as negative or positive for CMV immunoglobulin antibodies. Equivocal results (two for IgG and seven for IgM) were reported as positive. The data was analyzed using descriptive statistics, Chi-square was used to show association between immunoglobulins and other variables and we performed bivariate and multivariate analysis to assess the likelihood of positive CMV antibodies among the donors. Tables were used for data presentation and all data entry was done using SPSS version 16 and a p-value less than 0.05 was considered significant.

RESULTS

The mean age (± SD) of the donors was 26.8 ± 6.5 years (range = 18-48 years). Of the 160 participants with complete data, majority of them were males (96.2%) and seventy percent were unmarried. A large proportion (n=156; 97.4%) of the donors were positive for CMV IgG antibody while 84 (52.6%) were positive for CMV IgM, and similarly positive for both IgG and IgM antibodies. Only four donors (2.5%) were negative for both antibodies. All the females (n=6; 3.8%) were positive for both antibodies. A significant number of the donors (n=132; 82.5%) were unemployed, student or artisan while 61.3% had secondary education or less. Tables 1 to 5 summarise antibody positivity among the gender, the different occupation of the participants, their marital status, educational level and the different types of donations respectively. No statistical significant difference was observed in the prevalence of CMV IgG antibody in the marital status, the level of education and the different type of donation. Using Pearson's correlation, the level of education of the donors predicts IgM antibody positivity while those with secondary education or less are more likely than others to be positive ($p < 0.05^{X2} = 15.98$). Linear logistic regression (Table 6) showed that male donors and those in the artisan group are more likely to be positive for IgM antibody ($p < 0.05$).

Table 1
Anti CMV antibodies and gender

Gender		Male (%)	Female (%)	Total (%)
IgG	Positive	150 (97.4%)	6 (100%)	156 (97.4%)
	Negative	4 (2.6%)	0 (0%)	4 (2.6%)
IgM	Positive	78 (50.7%)	6 (100%)	84 (52.6%)
	Negative	76 (49.3%)	0 (0%)	76 (47.4%)

Table 2
Anti CMV antibodies and occupation

Occupation		Unemployed (%)	Students (%)	Artisan (%)	Traders (%)	Clerics (%)	Professionals (%)
IgG	Positive	10 (100%)	20 (100%)	98 (96.1%)	10 (100%)	2 (100%	16 (100%)
	Negative	0 (0%)	0 (0%)	4 (3.9%)	0 (0%)	0 (0%)	0 (0%)
IgM	Positive	4 (40%)	4 (20%)	60 (58.9%)	8 (80%)	2 (100%)	6 (37.5%)
	Negative	6 (60%)	16 (80%)	42 (41.2%)	2 (20%)	0 (100%)	10 62.5%)

Table 3
CMV antibodies and marital status

Marital status		Single (%)	Married (%)
IgG	Positive	108 (96.4%)	48 (100%)
	Negative	4 (3.6%)	0 (0%)
IgM	Positive	58 (51.8%)	26 (54.2%)
	Negative	54 (48.2%)	22 (45.8%)

Table 4
Anti CMV antibodies and educational level

Educational level		Primary (%)	Secondary (%)	Post Secondary (%)
IgG	Positive	6 (100%)	88 (95.7%)	62 (100%)
	Negative	0 (0%)	4 (4.3%)	0 (0%)
IgM	Positive	2 (33.3%)	64 (69.6%)	18 (29%)
	Negative	4 (66.7%)	28 (30.4%)	44 (71%)

Table 5
Anti CMV antibodies and type of donation

Type of donation		Commercial (%)	Replacement (%)	Voluntary (%)
IgG	Positive	72 (94.7%)	82 (100%)	2 (100%)
	Negative	4 (5.3%)	0 (0%)	0 (0%)
IgM	Positive	42 (55.3%)	42 (51.2%)	0 (0%)
	Negative	34 (44.7%)	40 (48.8%)	2 (100%)

Table 6
Linear logistic regression of the likelihood of donors having IgG or IgM antibody positivity by socio-demography characteristics and type of donation

Variable	Likelihood of blood donors having IgG or IgM antibody positive					
	MODEL I (IgG)			MODEL II (IgM)		
	Odds-ratio (SE)	p-value	95% C I	Odds-ratio (SE)	P-value	95% C I
Age Group						
15-24 years	RC			RC		
25-34 years	0.05 (0.05)	0.29	-0.46–0.15	- 0.02 (0.14)	0.84	-0.30–0.23
35+ years	0.04 (0.09)	0.65	-0.13– 0.21	0.19(0.24)	0.45	-0.30– 0.67
Sex						
Male	RC			RC		
Female	-0.10 (0.10)	0.87	-0.22–0.19	0.63 (0.28)	0.03*	-0.07–1.20
Marital Status						
Single	RC			RC		
Maried	0.002 (0.06)	0.97	-0.12- 0.13	- 0.07 (0.31)	0.69	-0.41–0.27
Education						
Primary	RC			RC		
Secondary	- 0.07 (0.10)	0.47	-0.27–0.13	0.31 (0.27)	0.26	-0.24–0.86
Post secondary	- 0.07 (0.11)	0.54	-0.29- 0.15	-0.17 (0.31)	0.59	-0.79 - 0.45
Occupation						
Unemployed/students	RC			RC		
Artisans	0.10 (0.75)	0.89	-0.14–0.16	-0.45 (0.21)	0.03*	-0.86–0.04
Professionals	- 0.03 (0.06)	0.63	-0.16–0.10	-0.24 (0.18)	0.18	-0.61–0.12
Traders	- 0.02 (0.08)	0.85	-0.17–0.14	-0.02 (0.22)	0.93	-0.45–0.41
Type of Donation						
Commercial	RC			RC		
Replacement	0.04(0.04)	0.309	-0.04– 0.13	0.02(0.12)	0.89	-0.22–0.26
Voluntary	0.02 (0.18)	0.932	-0.32 -0.38	0.32 (0.51)	0.53	-1.33 - 0.69

Notes: RC-Reference Category, SE-Standard Error; CI-Confidence Interval and P-value significant at <0.05*

DISCUSSION

The results from this study are very similar to report of earlier studies conducted in various other parts of Nigeria, and other countries with similar socio-economic conditions (6,10-12). This contrasts the reports from developed countries (5, 7). In this series, the prevalence of CMV IgG antibody was 97.4%, while that for IgM antibody was 52.6%. In a more recent study, Ojide et al found a prevalence of 96.8 % for IgG antibody (19), almost equivalent with our result. In contrast however, the prevalence of IgM antibody from this study is rather high compared with the previously documented reports. Akinbami *et al* (11) found a prevalence of 19.5% while Ojide *et al* found a prevalence of 3.1% in various other parts of the country. Our findings and the earlier reports suggest that probably the prevalence of CMV IgM antibody varies more widely within our population when compared with the CMV IgG antibody (13). It also imply that rate of new infection, re-infection or reactivation of prior CMV exposure varies widely across our population. Incidentally 52.6% of the donors were also positive for both IgG and IgM antibodies which appears to suggest that this percentage of our donors could have had primary CMV infection (20).

The gender distribution of the donors showed that many more males donated (Table 1) reflecting our cultural attitude towards blood donation, it is

important to note that all the female donors were positive for both IgG and IgM specific antibodies, this was also reported by Ojide *et al* (19); this may be linked to sexual transmission. However, male donors were found to be more likely positive for CMV IgM antibody ($p < 0.05$) (Table 6). This finding may be related to the fewer number of female in the donor population. The sero-prevalence of CMV IgG antibody is similar across the occupational groups and marital status ranging from 96 to 100% (Table 2 and Table 3). Although, this may not be reflective of the general population because a significant number of the donors (n=132; 82.5%) were unemployed, student or artisan while 61.3% had secondary education or less (Table 4). As previously observed by Tookey et al (13), level of education and occupational status significantly predict CMV antibodies positivity; those with secondary education and artisans were more likely to be IgM positive ($p < 0.05$). This group of people was within the low socio-economic status. Majority of the donors are commercial or replacement donors, a small number (n=2; 1.25%) were voluntary donors contrary to the advocacy of voluntary non remunerated donation; all were however positive for IgG CMV antibody (Table 5). The type of donation did not preclude a high prevalence of CMV antibody. There was no significant difference (IgG, p=0.658; $p>0.05$ and IgM, p=0.329; $p>0.05$) in the prevalence of CMV antibodies in the different type of donation from this study. The high prevalence of CMV specific IgG and IgM indicate the need for more proactive measures to reduce cytomegalovirus transmission in our population. Although there were conflicting reports on the superiority of leukodepletion to CMV-sero-negative blood (21-23); Bowden et al in a comparative study affirm the usefulness of leukodepletion as an effective alternative to the use of sero-negative CMV blood (23). Considering the high sero- prevalence of CMV antibodies in this study and earlier studies among Nigerian donors; screening for CMV antibody negative blood may be superfluous in our population.

In conclusion, the prevalence of CMV antibodies is very high (IgG = 97.4%; IgM = 52.6%) in our setting. Donors with low educational status and artisans are more likely to be IgM positive. Therefore, a more stringent donor selection, adoption of leukodepleted blood and blood products for uninfected patients especially the immuno-compromised and adopting a national policy on CMV infected blood is advocated.

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