Cytomegalovirus Seroprevalence among Blood Donors in Kerala

Nittin Henry[1], Nithya M Baiju[2], Ramesh Bhaskaran[1], S.P. Sudha[3], Tom Thomas[4]

ABSTRACT

Introduction: Primary infection with cytomegalovirus (CMV) leads to lifetime persistence of CMV IgG and a transient IgM response that may occur during primary infection, reactivation of latent infection or re-infection with a different strain. Study was done to check the prevalence of CMV infection and the existing risk of TT-CMV for the susceptible transfusion recipients in the respective demographic area.

Material and Methods: The present study evaluated seroprevalence of CMV infections among 453 blood donors from Kerala, a state in South India using a commercial chemiluminescence assay.

Results: Results revealed CMV IgG reactivity in 94.9% of the blood donors (CI = 92.90-96.94) while 0.44% (CI =-0.17-1.05) had detectable CMV IgM. A total of 91.84% donors aged under 20 years showed CMV IgG reactivity.

Conclusion: We suggest that the leukoreduction of donor blood might be a feasible and cost effective strategy to limit blood borne transmission of CMV in resource limited settings in the future.

Keywords: CMV, seroprevalence, seroconversion, leukoreduction

INTRODUCTION

CMV or Human Herpes virus 5 is a double stranded enveloped DNA virus of the herpes viridiae family. Primary infection is mostly asymptomatic, seroconversion being the only indication. The virus tends to reside in the body as latent infection mostly restricted to WBCs. Primary infection and reactivation are asscociated with circulating viremia in the plasma. CMV infection can be detrimental in preterm neonates and immunocompromised patients.[1-3] Primary infection leads to lifetime seropositivity with CMV IgG while CMV IgM appears only for a brief time period (few months) during primary infection, reactivation of latent infection and/or during the reinfection with a different strain.CMV IgM positivity has a higher possibility for transfusion transmissibility due to higher prevalence and concentration of CMV DNA in both whole blood and plasma samples.[4]

The virus is mostly transmitted through the oropharyngeal route and the genital route. The other modes include breast feeding, organ transplantation and blood transfusion. Primary infection mostly occurs early in life during childhood or adolescence.[5] Primary infection (15-50%) has a higher chance of transmission compared to secondary infection (0.15-1%). Transfusion-transmitted CMV infections (TT-CMV) were first described by Kääriäinen and co-workers in 1966 and the molecular evidence was provided by Tolpin et al in 1985.[6,7] CMV seroprevalence varies depending on the demography. It has been shown that developing countries (80-95%) have a higher CMV seroprevalence compared to developed (40 -65%) countries.[1-3] In India CMV seroprevalence data is available from New Delhi, Chandigarh, Pune and Pondicherry showing a CMV IgG prevalence of 95-99% and CMV IgM prevalence of 0-0.07%. No such data is available from Kerala. From 1980s leukoreduced and CMV seronegative blood products were introduced to minimize this problem. Both these technologies are minimally used in the transfusion services in South India. This study was done to assess the prevalence of CMV infection and the existing risk of TT-CMV for the susceptible transfusion recipients in the respective demographic area. This study can provide an idea regarding the best suitable technique that is feasible to minimize the risk of TT-CMV.

MATERIAL AND METHODS

This was a cross sectional descriptive study on 500 randomly selected donors in a teaching institute, Kerala. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Average donations at the centre are 7000/per year. The significance level (alpha) of 0.05, precision at 5% and power of 80% was targeted. Based on previous prevalence, 500 samples were included in this study. Samples were selected by convenient sampling method. Prospective donors who came to the blood bank as voluntary or replacement donors were randomly selected over a period of 6 months and included in the study. Informed consent was obtained from the donors. All the samples which were unyielding with either of the two results or borderline were excluded from the study. Blood was collected in a plain vaccutainer (BD) during blood donation. The serum from the clotted sample was then collected and tested for CMV IgG and IgM antibodies using Enhanced Chemiluminescence Technology with Orthocare Vitrios 3600 Immunodiagnostic system.

CMV IgG kit used in the study had a specificity of 100.0% (95% CI, 98.6% to 100.0%) and a sensitivity of 99.9% (95% CI, 99.2% to 100.0%). The CMV IgG results of the analytes were expressed as units/ml. Sample tests which gave CMVIgG with results ≤4.99 U/mL were flagged as “negative”, samples with results ≥5.00 and ≤7.99 U/mL were flagged as “borderline” and samples with results ≥8.00 U/mL were flagged as “reactive”. The CMV IgM kit had a specificity of 99.5% (95% CI, 98.6% to 99.9%) and a sensitivity of 100% (95% CI, 97.1% to 100.0%). The CMV IgM results of the samples were expressed as a fraction (signal of the test/ cut off value). Samples with results

[1]Assistant Professor, [2]Junior Resident, [3]Professor, Department of Transfusion Medicine, [4]Biostatistician, Jubilee Mission Medical College and Research Institute, India

Corresponding author: Dr Nittin Henry, MD (IH and BT), Assistant Professor, Department of Transfusion Medicine, Jubilee Mission Medical College and Research Institute, India

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Age Group	18-20	21-30	31-40	41-50	51-60	Total Count
Count	49 (10.8%)	222 (49.0%)	103 (22.7%)	66 (14.6%)	13 (2.9%)	453 (100%)
IgM R	0	1 (0.45%)	1 (0.97%)	0 (0.0%)	0 (0.0%)	2 (0.45%)
IgM N	49 (100%)	221 (99.54%)	102 (99.3%)	66 (100%)	13 (100%)	451 (99.55%)
IgG R	45 (91.84%)	210 (94.59%)	98 (95.15%)	65 (98.5%)	12 (92.3%)	430 (94.92%)
IgG N	4 (08.16%)	12 (5.41%)	5 (4.9%)	1 (1.5%)	1 (7.7%)	23 (5.08%)

Table-1: CMV Seroprevalence with respect to Age of Donors

<0.90 were flagged as "negative", samples with results ≥0.90 and <1.20 were flagged as "borderline" and samples with results ≥1.20 were flagged as "reactive".

STATISTICAL ANALYSIS

The variables that were included were the basic demographic information and the responses to donor questionnaires. We used Microsoft Excel 2007 software (Microsoft Corporation) for data entry and SPSS ver. 20 software (SPSS Inc.) for data analysis. The seroprevalance status of the donors were then analysed with respect to the age of the donor using Chi-square test. The seroprevalence among the donors were correlated with the age of the donors. For all statistical test, probability less than 0.05% (alpha) was considered as significant. PCR test of the positive samples could have explained the infectivity better, but this was not done due to resource constraints.

RESULTS

After the application of exclusion criteria, results were obtained from 453 (90.6%) samples. Among the 453 donors 437 (96.5%) were males and 16 (3.5%) females. The mean age of the donors were 30.55±9.22 years (range 18 -60 years).

Out of the 453 donors, 430 (94.9%) (95% CI: 92.90- 96.94) were found to be IgG reactive and 23 (5.1%) (95%CI: 3.06-7.10) donors were IgG non-reactive. None of the samples were IgG non-reactive and IgM reactive. 2(0.44%) (95% CI: -0.17-1.05) donors out of 453 were found to be IgM reactive and 451 (99.6%) (95% CI: 98.95-100.17) donors were IgM non-reactive. 428 (94.48%) IgG reactive donors were IgM non-reactive, while 2 were IgM reactive.There was no variation among various age groups with respect to CMV IgG or IgM seoprevalence.

91.84% (95% CI: 84.57 - 99.50) (table 1) of the donors in the age group between 18-20 years showed to be reactive for CMV IgG which was not much different from the other age groups. Among the 16 female donors all were IgM non-reactive and IgG reactive.

DISCUSSION

CMV seroprevalence among the donor population was 94.9 % (which was similar to the data from Delhi (95%) and (98.6%).[2,9] Similar results were also obtained from Pondicherry, Chandigarh, Iran,Thailand and Lagos (Nigeria).[10-14] But significantly lower results were obtained in general population based studies conducted in Portugal (77%) and U.S.A (50.4%) respectively.[3,15] Since all of the other studies were done using other methodologies comparison amongst them was not ideal.

2 donors out of 453 donors were found to be IgM reactive. Other studies done in Delhi (0.00048%, 0%), Pune (0.071%) and Thailand (0.006%) gave similar results.[2,9,14,16] Akinbami et al in 2009 had observed 19.5% IgM reactivity among tested donors in Nigeria.[12] 2.6% was the IgM reactivity of donor population in a study done in Iran.[14] 5.52% of IgG reactive donors were IgM reactive showing potential to transmission.

The high CMV IgG seroprevalence among 18-20 year old donors (table-1), which was similar to the older age groups showed that most of the population is exposed to infection at a very early age. CMV spreads through breast feeding and has a tendency to become reactivated in lactating mothers who are already CMV IgG reactive. Infants less than one year are more prone for seroconversion in developing countries like India with high maternal seroprevalence and breastfeeding.[13-14] Preschool (2-4 yrs) and school going (5-15 yrs) children and adolescents are prone to infection through close contact from day care centers, schools, handlers and seropositive parents.[13] Studies in adolescents between 15-19 yrs from various countries showed a CMV IgG seroprevalence of 51.5% (USA) to 78% (Russia).[3,13] Sex related variations which has been described in other studies could not be analysed because of the low number of female donors among the study group. Other factors which can determine CMV seroprevalence are socioeconomic level, environmental and psychological factors including stress.[3,13,14,17] Newly seroconverted donors are most likely to have CMV DNA in plasma and has more possibility of transmitting the infection during transfusion. Window phase donation occurs very rarely among seroconversion cases and lower than 0.5% donors among the seroconverted still has detectable CMV DNA after an year. Further, probability of seronegative window period donors and reactivated longterm seropositive donors are similar.[8,18]

CONCLUSION

Minimal transmission risk from latent infection, extremely high seroprevalence of CMV IgG and drastically low CMV IgM makes serological testing among blood donors a rather impractical proposition. Leukoreduction is more feasible with respect to CMV prevalence among our donor population and cost effectiveness. Selective leukoreduction is a more rational approach than universal leukoreduction with respect to financial constraints in health sector. In the future, when serological CMV testing becomes more affordable, leukoreduced blood from long term seropositive and seronegative donors could be considered for patients at risk.

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