ORIGINAL ARTICLE

Cytomegalovirus (CMV) Sero-Positivity in Children with Multiple Blood Transfusions

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ABSTRACT

Background: Blood transfusion is very important in children with diseases require blood, especially children with hematological or oncological diseases. The hazard of CMV sero-positive is thought high in children receiving multiple blood transfusions.
Aim: To assess the frequency of CMV sero-positivity in individuals of pediatric age group receiving more than one blood transfusions
Methods: This cross-sectional study was piloted in children age 6 months to 12 years old in the OPD for 6 months. Children receiving blood transfusions i.e., >1 within 6 months were included by applying the non-probability purposive sampling technique. Blood sample was taken for PCR and IgG and IgM sero-positive were assessed. CMV was labeled positive if IgM or IgG were higher.
Results: The mean age of children was 6.5±3.6 years. There were 94 (62.7%) males and 56 (37.3%) females. About 69(46%) children had acute lymphoblastic leukemia followed by thalassemia [40 (26.7%)] and aplastic anemia 7(4.7%). CMV sero-postivity was detected in 35(23.3%) cases.
Conclusion: Thus the frequency of CMV sero-positivity is high in children receiving multiple blood transfusions and cannot be ignored.
Keywords: *Cytomegalovirus (CMV) Sero-positivity, Multiple Blood Transfusions, IgG, IgM*

INTRODUCTION

Blood transfusions are basic way to treat hematological diseases but these can have substantial increasing risks. Blood transfusions are important part for the management of patient with hematological or oncological diseases.[1] But, the blood transfusion can be risky because of transmission of contagious agents including viruses of malaria, hepatitis C or B, human immunodeficiency virus, as well as Cytomegalovirus (CMV). Though, several precautionary strategies are already proposed which can help to reduce the hazard of transmission of such infections but the risk cannot be completely eradicated[2]. Infection of CMV is mostly asymptomatic, in initial stages or in primary infection, re-infection or re-activation, because all these infections are controlled by normal immune system of the body. Though, CMV has been grown as a very important pathogen in cases with weak or compromised immune system[3]. To prevent the transmission of CMV and development of CMV infection, anti-viral prophylaxis and pre-emptive remedy are two most common methods[4].

Frequent blood transfusions result in Primary infection and reoccurrence of CMV infection. In immunocompetent host CMV infection has a benign and self-limited course. On the other hand, in medical literature there are a number of reports depicting severe clinical manifestations due to CMV infection in Immunocompromised patients[5]. Children receiving blood transfusions show various type of responses to cytomegalovirus (CMV) infection. These responses can be subclinical or symptomatic including polyneuritis, encephalitis, pneumonitis, hepatitis, uveitis, retinitis, colitis and pericarditis[6,7].

In South African & Asian countries, the CMV sero-positivity is the highest. However, in Western European countries & in United States, the prevalence is least[8,9]. it has been reported that children with multiple blood transfusions develop CMV sero-positivity in around 4 out of 7 cases (57.1% cases)[10]. The estimated overall CMV sero-positivity hazard is around 6.5%.[11] Child's age and the number of blood transfusions was in direct proportion to the CMV seroprevalence[12.]

CMV IgM antibody seroprevalence was found higher (24%) in children with multiple blood transfusions as compare to control group (2%) reflecting primary CMV infection, or re-infection. The rate of CMV sero-positivity was found to be negligible in controls in comparison to multi-transfused children.[13] A research was conducted on neonates receiving sero-positive (CMV) blood, and results showed that the risk increases from 12.5% in single transfusion to 25% in multiple blood transfusion. P value was significant i.e.; 0.0118, while, the frequency of CMV seropositivity in single transfused children was not negligible[14].

The prevalence of CMV sero—positivity is higher in developing countries like Pakistan. The risk of CMV sero—positivity is higher as compared to developed countries,

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because of major proportion of population belongs to low socioeconomic class. Moreover, the screening methods for CMV sero—positivity are not readily available in Pakistan and the data regarding CMV sero—positivity is scarce for the Pakistani population. So we designed this study to determine the prevalence of CMV sero—positivity in Pakistani children receiving multiple blood transfusions.

MATERIALS AND METHODS

This cross-sectional study was done to determine the frequency of CMV sero-positivity among children receiving multiple blood transfusions at the Department of Pediatrics, Mayo Hospital, Lahore for 6 months. Children fulfilled the selection criteria by applying non-probability, purposive sampling technique. The estimated sample size was 150 by keeping the confidence level at 95%, margin of error at 7% and anticipated percentage of CMV sero-positivity i.e. 25% in children receiving multiple blood transfusions. Children receiving one or more blood or bloo products transfusions during the last 6 months, were recruited and labeled as multi-transfused children. All the children of age 6 months to 12 years of both genders, receiving multiple blood transfusions were enrolled. They were receiving transfusions for diseases inducing leukemia, hemophilia, anemia, thalassemia, lymphoma, idiopathic thrombocytopenia. But, children underwent splenectomy were not included in the study. Informed consent was obtained from parents or relatives attending clinic with the child. Demographics like age, sex and number of transfusions were noted. About three milliliter of venous blood was taken, for CMV serology (IgM and IgG) by ELISA. The samples were labeled and case numbers were allocated. A commercially available kit was used for this serology. The test was carried out in the pathology laboratory of the same hospital. Reports were examined for detection of antibodies against CMV. If the antibody titer was > 1.1 AU/ml for IgG or >0.600 for IgM, CMV sero-positivity was labeled. A proforma was used to collect the data.

SPSS 17 was used to enter and analyze the data. Numerical data was presented by using mean and standard deviation. Frequency and percentage was used to present categorical data like gender and CMV seropositivity.

RESULTS

For this research purpose total 150 children were enrolled. The mean age of children was 6.5 ± 3.6 years. There were 94 (62.7%) male children and 56 (37.3%) female children. The male to female ratio was found 1.6:1. The underlying medical conditions were 69 (46%) acute lymphoblastic leukemia, 40 (26.7%) thalassemia, 7 (4.6%) aplastic anemia, 6(4%) acute myeloid leukemia and 28 (18.7%) miscellaneous cases. The mean IgM level was 0.7±0.6 and mean IgG was 5.5±4.8. Table 1

Based on IgM levels, CMV sero-positivity was observed in 35 (23.3%) cases, while 149 (99.3%) cases showed sero-positivity based in IgG level. There were 35 (23.3%) cases of CMV sero-positivity who were positive on both; IgM & IgG while both were negative in only 1 (0.7%) case. Mean blood transfusions were 14.5 ± 8.7 in CMV seropositive cases, while 6.0 ± 3.5 in CMV sero-negative cases (p – value = 0.000). Table 2

In children aged < 6 years, 10 were IgM sero-positive while 75 were IgG positive. In children aged ≥ 6 years, 25 were IgM sero-positive while 74 were IgG positive. The difference between age groups was significant for IgM ($p<0.05$) but insignificant for IgG ($P>0.05$). In male children, 23 were IgM sero-positive while 93 were IgG positive. In female children, 12 were IgM sero-positive while 56 were IgG positive. The difference between both genders was insignificant for both IgM and IgG ($P>0.05$). Table 3

Table 1: Demographics of children

N	150
Age (years)	6.5 ± 3.6
Gender	
Male	94 (62.7%)
Female	56 (37.3%)
Diagnosis	
ALL	69 (46%)
Thalassemia	40 (26.7%)
Aplastic anemia	7 (4.7%)
AML	6 (4.0%)
Misc.	28 (18.7%)
IgM	0.7 ± 0.6
IgG	5.5±4.8

Table 2: Distribution of positive CMV

	Positive	Negative
IgM	35 (23.3%)	115 (76.7%)
IgG	149 (99.3%)	1 (0.7%)
Mean transfusions	14.5 ± 8.7	6.0 ± 3.5

Table 3: Comparison of CMV in stratified groups

Age (years)	IgM		IgG		p-value for IgM	p-value for IgG
	Positive	Negative	Positive	Negative		
<6	10	66	75	1	0.003	0.322
≥6	25	49	74	0		
Gender						
Male	23	71	93	1	0.670	0.439
Female	12	44	56	0		

DISCUSSION

Cytomegalovirus (CMV) belongs to beta-herpesvirus family and its transmission occurs by direct person-to-person contact. Healthy children may remain asymptomatic or show mild flu like illness after CMV infection.[15] About 40 - 60% of blood donors showed CMV seropositivity in different studies[16,17].

CMV seroprevalence is found to be highest in all the South American, African as well as in Asian countries, while the prevalence if least in the Unites States as well as in many Western European countries.[18] Several findings have been published regarding the seropositivity of the antibodies against CMV that is; IgG & IgM, all over the world and it ranges from 93 to 97 percent[19,20,21].

Results of our research revealed that prevalence of CMV (IgM positive) was 35(23.3%); while 115(76.7%) cases were negative for CMV.

To get rid of CMV infection many studies were conducted by Kim, et al[22] in endemic areas of Korea, those reflected that transfusion of irradiated blood products like packed red blood cells and platelets were not helpful in minimizing the transfusion-related CMV infection in very low birth weight infants. And if infections develop in these cases, the effect of infection or illness is not as severe as in CMV sero-negative candidates. Further large cohorts are required to verify these findings. It has been observed among neonates, in those who receive the CMV sero-positive blood, the hazard of obtaining CMV sero-positivity significantly doubled from 12.5% to 25% in single to multiple blood transfusions (p - value = 0.0118). However, the frequency of CMV sero-positivity in children received only one blood transfusion is also not ignorable[14].

Another observational study, conducted in Iran, showed that there were 91% cases of CMV sero-positivity while 18.5% cases had acute CMV infection[23]. One more observational study, conducted in Iran, determined that there were 89.7% pediatrics, while 98.7% adults had CMV sero-positivity after multiple blood transfusions[24].

In our study, male to female ratio was found 1.6:1. There was no relation established between CMV and gender of the children. A clinical research conducted in 186 hospital on cases of CMV from 2003 to 2007 exhibited that the age of onset of cytomegalovirus infection is normally within the first year of life, predominantly in male children and male to female ratio (1.9:1)[25].

Gender based seroprevalence of CMV was found varied in different studies. Various studies conducted [18] in the U.S. showed higher seroprevalence of CMV in females as compare to males. However on contrary, some researches established that either gender has showed equal risk for CMV seropositivity.

Another criterion is age in different studies. Kothari et al., [20] found that no relation exist between the ag of child and the CMV sero-positivity. But we observed that there was a significant impact of age on IgM sero-positivity in children.

In our study the mean number of blood transfusions was 14.5±8.7 in seropositive cases while it was 5.97±3.47 in seronegative cases. The difference between these two groups came out to be statistically significant with p-value< 0.0001. This demonstrated that increased transfusion numbers causes a higher risk of CMV seropositivity in children with multi - transfusions. In immunocompromised children, the repeated blood transfusions may result in reactivation of the virus. Hence, it is recommended to screen the blood for CMV before transfusion in special circumstances.

CONCLUSION

Among children who have received multiple transfusions, the frequency of CMV seropositivity is found to be high. Now we have generated our local estimate of CMV seropositivity among pediatric children undergoing multiple transfusions. Moreover, it is recommended that along with Hepatitis B, C and HIV screening, CMV screening and detection should be carried out strictly before transfusion in special circumstances.

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