Seroprevalence of Cytomegalovirus among Voluntary Blood Donors

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Abstract

Background: Primary cytomegalovirus (CMV) infection in immunocompetent host is self limiting infection, leading to latency of virus. However congenital CMV and CMV infections in immunocompromised patients are associated with high morbidity and mortality. Transfusion transmitted-cytomegalovirus (TT-CMV) infection in low birth weight neonate and immunocompromised transfusion recipients is being increasingly reported. Studies recommended transfusion of CMV free or CMV safe blood in prevention of TT-CMV. In this background, the study was undertaken to assess the CMV seroprevalence in blood donor.

Methods: A prospective study was conducted in which 431 voluntary blood donors were screened for CMV IgG and IgM by EIA (Enzyme Immuno Assay).

Result: A total of 379 (87.9 %) voluntary blood donors were seropositive for CMV IgG. There was no statistical difference of CMV seropositivity and age. Further, seven (1.6 %) subjects were both CMV IgM and IgG seropositive.

Conclusion: High seroprevalence of CMV in our donor population is a threat to the blood safety. Strategies in reducing the risk of TT- CMV are discussed. Use of prestorage leucodepleted 'CMV safe' blood components along with judicious use of blood is recommended in prevention of TT-CMV in high risk recipients.

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Key Words : Cytomegalovirus; Transfusion transmitted infections; Blood donors; Leucodepletion

Introduction

Cytomegalovirus (CMV) is the member of the Betaherpesvirinae subfamily of Herpesviridae. The herpes viruses share a characteristic ability to remain latent within the body over long periods [1]. Human CMV is a ubiquitous agent [1]. Acute primary infection in the immunocompetent children and adult is self limiting, followed by virus latency in CD34⁺ haemopoietic progenitor cell in bone marrow and CD13⁺, CD14⁺ peripheral blood monocytes [2]. Congenital CMV and CMV infection in low birth weight (LBW) neonates, immunocompromised patients, solid organ or haemopoietic stem cell recipients is associated with high morbidity and mortality [1,2]. CMV can be transmitted through transfusion of blood or blood components. Transfusion transmitted CMV (TT-CMV) can lead to primary infection in CMV-seronegative recipient or reinfection (superinfection) by a new strain in CMV seropositive recipient who receives blood products from CMV seropositive donor [3,4]. TT-CMV is an important cause of morbidity and mortality in immunocompromised transfusion recipients including LBW neonates [2,3].

A few studies from India have reported high seroprevalence of CMV in blood donors [5]. CMV has

also been reported in various high risk group patients [6-11]. This study was undertaken to assess the seroprevalence of CMV in blood donors.

Material and Methods

A total of 431 voluntary blood donors were enrolled for this prospective study. The standard blood bank questionnaire, medical examination and laboratory screening for transfusion safety were undertaken as per current National Blood Policy on all subjects. All enrolled subjects were medically fit and negative for routinely screened infection markers in transfusion safety. Their serum specimen was collected and stored below -20°C until assays.

All subjects were tested by commercially available anti CMV IgG (Radim S.p.A, Italia) EIA and anti CMV IgM (M antibody capture format) EIA (S.p.A Italiana Laboratori Bioti, Italia). The cut off calibrator of 10 RU/ml (calibrated against the WHO proposed International Standard (pIS) preparation, 1995 having 1 RU anti-CMV IgG = 0.141 IU) was used in CMV IgG EIA. Manufactures claimed sensitivity and specificity of 98.7% and 97.5% respectively of CMV IgG EIA. However relative sensitivity and specificity of CMV IgM EIA was 100% and 97% respectively. Tests were carried out as per manufacturer's instructions. The statistical comparison was done using Chi square test and a p value of <0.05 was considered significant.

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Results

All 431 subjects were healthy male voluntary donors. Their age ranged from 18 to 59 years with mean age of 28.2 ± 7.22 years. Out of 431 subjects, 379 (87.9 %) were seropositive for CMV IgG indicative of exposure to CMV. The mean age of seropositive and seronegative subjects was 28.4 ± 7.4 years and 26.6 ± 5.4 years respectively. The age wise distribution of CMV IgG seropositive donors is given in Table 1. There was no statistically significant difference in the CMV IgG seroprevalence in different age groups.

Of the 431 subjects, seven (1.6%) were CMV IgM positive and all of them were also CMV IgG positive. The mean age of CMV IgM positive subjects was 24 ± 5.5 years against 28.2 ± 7.2 years of IgM negative subjects. Age distribution analysis revealed that 2.4% (4/165), 1.6% (2/125) and 1.4% (1/73) blood donors of age group below 24, 25-29 and 30-34 year respectively were CMV IgM positive.

Discussion

CMV antibody positive (IgG and IgM) blood donors harbour CMV in their peripheral blood which can be potentially infectious. We reported seroprevalence of 87.9% in voluntary blood donors of which 1.6% were CMV IgM positive. Similarly Kothari et al [5], reported 95% seroprevalence in voluntary blood donors of Delhi, using EIA in screening CMV IgG. However, they did not find any IgM positive case amongst 200 donors [5]. It was suggested that anti-CMV IgM positive (CMV IgG +/-) donations are more infectious than IgG positive and IgM negative ones but this remains unproved [12]. Other studies from India reported CMV IgM in blood donors with positivity of 5.1%, 1.5% and 0.07% from Lucknow [13], Delhi [10], Pune [14] respectively. Factors such as assay methods, sample size, geographic distribution and socioeconomic status can explain difference in IgM incidence. High CMV seroprevalence ranging from 90-100% in blood donors was also reported from Malaysia [15], Mauritius [16], Ghana [17].

Studies from India also reported CMV infections in neonates after exchange transfusion [8,9] and from other high risk groups such as bone marrow transplant patients [10], renal transplant patients [11] and HIV/AIDS

patients [12]. CMV infection in these groups of patients is associated with life threatening CMV disease and CMV induced immunosuppression leading to superinfection by various other pathogens with high mortality [1-4]. Recipient factors such as CMV status, degree of immunosuppression, increase cytokine production (eg. patients of sepsis or burns) are associated with TT-CMV [2]. Further, it has been well documented that blood transfusion itself leads to immunomodulation with profound negative effects on the immune system which persists for many months [18]. All these indicate high risk and need for strategies in prevention of TT-CMV.

Traditionally, preventive strategies of TT-CMV in high risk transfusion recipients are transfusion of CMV 'free' (i.e. neither positive for CMV IgG nor CMV IgM) or CMV 'safe' prestorage leucodepleted blood components [2, 19]. Due to high seroprevalence of CMV in our donors, it is not feasible to transfuse CMV free blood to all high risk patients. Naturally, we have to consider option of prestorage leucodepletion of blood components. Leucodepleted blood product reduces risk of CMV by reducing the number of latently infected cells of blood components. In addition it reduces possibility of CMV reactivation in recipients by reducing cytokines release and other immunological trigger from donor leucocytes [2]. Current data suggests that 'acceptable' CMV safety can be achieved by pre-storage leucodepletion [2, 19]. It is reported risk reduction of TT-CMV to 93.1% and 92.3% in CMV-seronegative blood components and leucodepleted blood component respectively as against unscreened and non-leucodepleted blood components [19]. Presence of plasma viraemia prior to seroconversion and failure to achieve adequate removal of leucocytes have been implicated for residual risk of CMV in these blood components which is rarely encountered [2].

To conclude, high CMV seropositivity in blood donors is a threat to safety of blood transfusion. Transfusion of CMV seropositive blood can lead to severe TT-CMV with high mortality and morbidity in transfusion recipients. Transfusion of CMV safe prestorage leucodepleted blood components is recommended for prevention of transfusion transmitted cytomegalovirus infection in high risk recipients.

Conflicts of Interest

None identified

Intellectual Contribution of Authors

Study Concept : Surg Cdr CN Chaudhari, Col MS Bindra

Drafting & Manuscript Revision : Surg Cdr CN Chaudhari

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Table 1

CMV serostatus and age distribution of blood donors

Age group-year	CMV IgG positive (%)	CMV IgG negative (%)	Total
<24	143 (86.7)	22 (13.3)	165
25-29	107 (85.6)	18 (14.4)	125
30-34	66 (90.4)	7 (9.6)	73
35-39	28 (93.3)	2 (6.7)	30
>40	35 (92.1)	3 (7.9)	38
Total	379 (87.9%)	52 (12.1%)	431 (100%)

$\chi^2 = 2.74$, df = 3, p > 0.10 Not Significant

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