

# Seroprevalence of Cytomegalovirus among Voluntary Blood Donors in Delhi, India

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## ABSTRACT

Cytomegalovirus (CMV) is known to be a significant cause of morbidity and mortality following blood transfusion in children and immunocompromised adults. In India, it is not mandatory to screen donated blood for CMV in blood banks. Very few studies have been conducted in India to estimate the seroprevalence of this infection in voluntary blood donors. This study was conducted to estimate the seroprevalence of CMV among voluntary blood donors in Delhi, India. In this study, none of 200 donors tested positive for CMV IgM antibody, but 95% were positive for CMV IgG antibody. There was no statistically significant difference in seropositivity of CMV based on distribution of age. Of the 200 donors, 3% tested positive for HBsAg, 1% for HIV, 2% for hepatitis C virus, and 4.5% for syphilis. Since about 95% of blood donors in India are seropositive for CMV, it would seem superfluous to screen blood donors for CMV, as very few seronegative blood units would be available for transfusion. Other preventive strategies, such as leukoreduction, etc., could be more appropriate and cost-effective for the prevention of transmission of CMV through infected blood to immunosuppressed individuals.

**Key words:** Cytomegalovirus; Blood transfusion; Blood screening; India

## INTRODUCTION

Cytomegalovirus (CMV) has emerged as a significant cause of morbidity and mortality in children and immunocompromised adults. Traditionally, congenital CMV disease is known to be the most serious, but perinatal and postnatal acquired infections are also an important cause of morbidity in infants. Humans are believed to be the only reservoir for human CMV (HCMV), and natural transmission occurs by direct or indirect, close or intimate person-to-person contact. Sources of virus include oropharyngeal secretions, urine, cervical and vaginal excretions, semen, breastmilk, tears, faeces, and blood (1). Besides contact with seropositive

mothers (passage through genital tract, breastmilk, etc.), blood transfusion is the most important mode of perinatal/postnatal spread of CMV to neonates (2,3).

There is significant morbidity and mortality following HCMV seropositive blood transfusion to immunocompromised seronegative recipients, including preterm infants. Perinatal/postnatal infections may be associated with protracted interstitial pneumonitis (4) or can sometimes lead to growth and developmental anomalies (5).

HCMV infection has been associated with decreased graft survival and a wide variety of clinical disease in the post-transplant period (6,7). Besides being one of the most important opportunistic infections encountered in patients with AIDS, it also may influence the natural history of HIV infection independently (8).

An estimate of the seroprevalence of CMV among voluntary blood donors may be of help to decide whether screening for CMV would eliminate transmission of

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infection to high-risk groups. Such feasibility studies have been very few in India. The current study was undertaken in an attempt to address this aspect.

### MATERIALS AND METHODS

The study population consisted of 200 consecutive voluntary blood donors taken over a 4-day period at the Regional Transfusion Centre, Guru Teg Bahadur (GTB) Hospital, Delhi, India.

The inclusion criteria for recruiting voluntary blood donors, as laid down by the Regional Transfusion Centre, GTB Hospital, were: age between 18 and 60 years; weight >45 kg; haemoglobin >12.5 g/dL; normal blood pressure (BP), pulse, and temperature; not belonging to any high-risk group, i.e. homosexually/heterosexually promiscuous; intravenous drug addicts; patients of sexually transmitted diseases; and no history of any severe current or chronic illnesses.

Blood samples of all 200 blood donors were collected, and sera were separated and stored at -40 °C until testing.

CMV-specific IgM was detected in each sample using CMV HUMAN ELISA IgM Antibody test kits (HUMAN). This was a sandwich enzyme immunoassay for the detection of IgM class antibodies to CMV in serum. CMV IgM-positive control was calibrated against Paul-Ehrlich-Institute reference material. The tests were performed, and the results were calculated according to the instructions of the manufacturer.

HBsAg, anti-hepatitis C virus (HCV) antibodies, and anti-HIV antibodies were detected in the 200 voluntarily-donated blood units using enzyme immunoassay kits in the Regional Blood Transfusion Centre, GTB Hospital, as part of normal testing of donated blood units. HBsAg was detected using HEPALISA, a microwell ELISA test for the detection of hepatitis B surface antigen (J. Mitra & Co. Ltd.). Anti-HCV antibodies were detected using the LG HCD 3.0 enzyme immunoassay (LG Chemical Ltd.) for detection of antibody to hepatitis C virus. Anti-HIV antibodies were detected using the Biotest Anti-HIV Tetra ELISA (Biotest) for in-vitro detection of antibodies against HIV-1/-2. Venereal Disease Research Laboratory (VDRL) test for syphilis was also done at the same centre as part of routine testing. VDRL antigen was obtained from the Laboratory of Serologist, Government of India, and the standard technique of

VDRL slide flocculation test was used (as specified in Manual of Laboratory of Serologist, Government of India, VDRL antigen).

Statistical analysis of results was done using the SPSS software. When relating variables to each other, multivariate analysis was done. Chi-square test and student's *t*-test were employed to detect any significant correlation between different variables. A *p* value of <0.05 was considered to yield a statistically significant result.

### RESULTS

Of the 200 blood donors, 189 (94.5%) were male and 11 (5.5%) were female. The mean age of the sample was 29.8±8.3 years (median 22 years, range 18-56 years). 29.5% had blood group O, 22.5% blood group A, and 38% blood group B, while 10% had AB blood group. Ninety-five percent of the blood donors were Rh+ve, while only 5% were Rh-ve.

None of the 200 voluntary blood donors gave a positive test for CMV IgM antibody. However, 95% were seropositive for CMV IgG antibodies, with mean titres of 90.7±38.8 HUMAN Units (HU)/mL (≥25 HU/mL was taken as positive). The median was 93 HU/mL with a range of 2.5-176.9 HU/mL.

Age distribution (years)	CMV-seropositive	
	No.	%
≤20	21	95.2
21-30	101	95
31-40	52	94.2
41-50	21	100
≥51	5	80

95.2% of the blood donors aged ≤20 years (n=21) were seropositive for CMV against 95% in 21-30-year (n=101), 94.2% in 31-40-year (n=52), 100% in 41-50-year (n=21), and 80% in ≥51-year (n=5) age groups. There was no statistically significant difference in the CMV IgG status in different age groups (Table). Also, no significant correlation between CMV IgG status and sex or blood group was detected.

Of the 200 blood donors, 3% tested positive for HBsAg, 1% for HIV, 2% for HCV, and 4.5% for syphilis. There was no significant correlation of CMV IgG status with either HBsAg, HIV, HCV, or VDRL status of the study subjects. All those who were positive for HIV, HBsAg, HCV, or syphilis were also IgG-positive for CMV.

## DISCUSSION

As is evident from the results shown in our study, none of the donor blood units tested positive for CMV IgM, indicating *prima facie* an absence of primary CMV infection in them. On the other hand, 95% of the blood donors were positive for CMV IgG antibodies, indicating past exposure to infection.

Previous Indian studies have also shown similar results. A study by Pal *et al.* in Chandigarh showed 100% seropositivity for CMV in the population aged above 20 years (9), while Madhavan *et al.* in Pondicherry showed that 84-96% of adults had the antibody (10). A study in Vellore showed a seroprevalence of 92% in normal individuals (11). This high seroprevalence in India is in contrast to Western literature which describes seroprevalence in voluntary blood donors ranging from 38% to 75% in different parts of the world (12).

Although several studies on the prevalence of CMV antibody in different parts of the world have been done, the results are not comparable in detail because methodologies used are different. The study by Krech (13) is an important one in this respect since complement-fixing antibody assay (using the same control serum) was used on sera from donors of comparable ages. His results showed that seropositivity of CMV varies between 40% in industrialized countries and 100% in developing countries. Interestingly, the prevalence of antibody in Japan and Hongkong is over 90%, although they cannot be considered 'developing' nations.

The high seroprevalence in adults in our country indicates the endemicity of infection. This could be related to socioeconomic, environmental and climatic factors (10).

In our study, 3% of the donors also tested positive for HBsAg, 4.5% for syphilis, 1% for HIV, and 2% for HCV. This reflects the disease burden of hepatitis B, hepatitis C, syphilis, and HIV in our sample population, i.e. blood donors in Delhi. However, there was no association of seropositivity of CMV either with HIV, syphilis, hepatitis B, or hepatitis C. This is an expected finding since CMV can spread by various modes, including close person-to-person contact, sexual intercourse, blood transfusion, saliva, urine, faeces, etc. However, although serology of syphilis was positive in 4.5% of the donors and the sexual transmission of CMV is known, the lack of correlation between these two in this study may require a more detailed evaluation.

No correlation was observed between seropositivity of CMV and either sex or blood group. This is similar to the findings of other investigators (14).

In our study, the seroprevalence of CMV among the blood donors varied with age ranging from 80% in the  $\geq 51$ -year age group to 100% in the 41-50-year age group. The decrease in the percentage seropositivity in the  $\geq 51$ -year age group is most likely due to the fact that data in this age band are based on smaller numbers. There is no statistically significant difference in seropositivity of CMV based on distribution of age. This differs with western studies (14) which showed a significantly increased seropositivity with increasing age of blood donors. This may possibly be due to earlier acquisition of CMV infection in India in childhood compared to the western populations, leading to higher seroprevalence even in younger adults (10).

Estimation of IgG avidity index offers some help in discriminating re-activation and re-infection. A low avidity index for IgG antibodies would indicate early primary infection, whereas a high avidity index would indicate re-activation or re-infection (15). This would have further helped in giving a clearer picture of seroprevalence of CMV among blood donors in India and also in evaluating the risk of transmission of infection to recipients.

The American Association of Blood Banks has recommended transfusion from donors who are seronegative for CMV or the use of deglycerolized frozen RBCs whenever transfusion is contemplated in a seronegative preterm (<1,200 g) child born to a mother with negative or unknown immune status with regard to CMV infection (16). These guidelines have helped in eliminating transfusion-induced CMV infection syndrome in preterm infants in the West. However, since about 95% of all blood donors in India are seropositive for CMV, it would be superfluous to screen blood donors for CMV as very few seronegative blood units would be available for transfusion.

Other preventive strategies, such as leukoreduction filtration, saline-washed RBCs, frozen deglycerolized RBCs, etc., are being increasingly recommended to minimize the transmission of CMV through transfusion (2). These may be more appropriate and cost-effective in the Indian scenario for the prevention of transmission of CMV through infected blood to immunosuppressed individuals. More studies in the Indian context need to be done to elucidate the transmission of transfusion-

associated CMV before proper guidelines on routine screening for CMV in voluntary blood donors can be formulated.

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