Seroprevalence of cytomegalovirus in blood donors in the northwest of Iran

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Original Article

Abstract

BACKGROUND: Cytomegalovirus (CMV) is the causal agent of infection in immunocompromised patients and transplant recipients, or those patients who receive blood transfusion frequently. Seroprevalence of CMV has been reported to be highest in South America, Africa, and Asia, and lowest in Western Europe and United States. Data referring to the prevalence of anti-CMV antibody among healthy people in Iran is scanty, but its incidence may reach 100% among blood donors and recipients, likely due to condensed population and socio-economic status.

METHODS: The blood specimens of 200 volunteer donors were tested through ELISA for anti-CMV immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies in our hospital.

RESULTS: According to these analyses, 98.5% and 85% of the specimens were found to be positive for anti-CMV IgG and IgM antibodies, respectively. This study shows that like other regions, anti-CMV seropositivity is high in Iran and blood transfusion is an important route of CMV spread.

CONCLUSIONS: Since up to 95% of blood donors in Iran are seropositive for CMV, it would seem superfluous to screen blood donors for CMV, as few seronegative blood units would be available for transfusion. Leukoreduction could be a more appropriate and cost-effective prevention of transmission of CMV through infected blood in Iran.

KEYWORDS: Blood, Cytomegalovirus, Iran

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Introduction

Cytomegalovirus (CMV), a herpes virus, is endemic throughout the world. Its infections occur asymptomatically in healthy children or adults.[1] With worldwide distribution, CMV is seen as lifelong latent infection among 40 to 90% of adults.[2] Due to the increasing mortality rate of elderly people, and sensorineural hearing loss in the congenital infection and transmission via breast milk in low birth weight neonates, it is a community health problem throughout the world.[3-5]

CMV causes infection in immunocompromised, transplant recipients and those patients who are in need of frequent blood transfusion. Risk factors for primary CMV infection include blood transfusion (treatment for clotting factors, and etcetera), infected transplants, hemodialysis, and the

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frequency of dialysis in a week.[6]

CMV seroprevalence has been shown to be highest in South America, Africa, and Asia, while it is lowest in Western European countries and the United States.[7] Different results published in respect with anti-CMV immunoglobulin G (IgG) and immunoglobulin M (IgM) seropositivity around the world varies from 93–97%.[8-13]

The overall seroprevalence of CMV in hematologic disorders in Brazil was 89.4%, directly proportional to age and the amount of blood units transfused.[14]

Numerous studies in some regions of Iran have had different results regarding the prevalence and seropositivity of CMV. Sepehrvand et al. reported 77.4 and 7.1% of anti-CMV IgG and IgM positive, respectively, while only 15.5% seronegative among individuals in end-stage renal disease undergoing hemodialysis and screened for CMV infection.[15] Amin Zadeh et al. reported 91% seropositivity and 18.5% acute CMV infection in their analysis in Tehran.[16] A research conducted in Iran confirmed that 89.7% of children, under 14 years of age, and 98.7% of adults were infected with human cytomegalovirus (HCMV).[17]

Data regarding the prevalence of CMV antibody among healthy people in Iran is scanty. However, it is expected to reach up to 100% among blood or organ donors and recipients, likely due to the condensed population and socio-economic status.[18] The aim of this study was to determine the seropositivity of donors' blood bags in our hospita.

Methods

Laboratory procedures, including serological assays, culture methods, antigenemia tests, and molecular methods, are employed in diagnosis of CMV infection.[19] Often, in literature, infections caused by CMV are determined by seropositivity through ELISA; however, PCR confirmation can validate the active viral treatment.[15]

This is a cross-sectional study on 200 blood bags in our hospital in 2010. Inclusion criteria consisted of blood bags which were collected during the previous 24 hours and had the Iranian Society of Transfusion criteria for blood donation. The blood specimens of 200 volunteer donors were assayed by ELISA method for anti-CMV IgG and IgM antibodies in our hospital. The blood specimens of 2-3 cords of the blood bags were tested. The specimens were centrifuged for 10 minutes (3000-3500 cycles/minutes) and plasma were collected in wells and stored in -70°C. Then, the 200 collected plasma specimens were thawed and homogenized for Elisa assay (Genesis Diagnostics Ltd., UK). Diluted plasma specimens (1:100) were incubated for 20 minutes to allow specific antibodies to CMV to bind to the antigen-coated wells. After washing away unbound antibodies and other serum constituents, CMV specific IgG was detected using rabbit antihuman IgG conjugated to horseradish peroxidase. After 20 minutes of incubation, unbound conjugate was removed by washing, and TMB enzyme substrate was added for 10 minutes. A blue color developed if antibodies to CMV were present. The addition of stop solution gives a yellow color. The optical densities of controls, the standard(s), and samples were measured using a microplate reader.[20] After detecting seropositive cases, we determined percentages of IgG and IgM positive and negative cases. Because of ethical issues, we had no access to demographic findings of donors.

Results

Blood samples were obtained from 200 blood transfusion bags, 98.5% of which were found to be positive for anti-CMV IgG antibody. The lowest values for IgG and IgM were 0.4 and 0.1, and the highest values were 28.7 and 9.4, respectively. Out of 200 samples, 170 donors (85%) were shown to be IgM positive (> 1.9; which was the minimum level for positivity according to the kit manufacturer) and the other 30 (15%) samples were

seronegative. Three donors (1.5%) were assayed for IgG antibodies with value of lower than 3 and were identified as negative according to kit manufacturer criteria, while 98.5% were identified as positive anti-CMV IgG. We had only one donor who was negative for both IgG and IgM antibodies. All donors were negative for HB s Ag, HB s, and HB c Ab, and also HIV Ab.

Discussion

Cytomegalovirus (CMV) infection is a matter of concern for blood bank professionals and blood transfusion recipients, especially in cases of transfusions to immunocompromised patients.[9] The present study aimed to determine the seroprevalence of anti-CMV IgG and IgM antibodies among blood donors in the city of Tabriz in the northwest region of Iran.

Cytomegalovirus (CMV) infections are commonly seen in humans and are usually characterized with mild or asymptomatic status where a self-limited latent infection is associated with mononucleosis syndrome.[21,22]

Like other herpesviruses, the initial infection of CMV is followed by lifelong latent status along with the possibility of reactivation where infection may develop into symptomatic disease, especially in patients suffering from immunosuppression.[23]

CMV infections have significant medical risks in immunocompromised patients and have caused significant fatality in patients undergoing bone marrow transplant.[21,24]

Individuals acquire CMV through infected blood products or direct contact with infected people. Transfusion of seronegative blood products for immunosuppressed patients has vital importance in medical management.[21]

Significant amounts of data imply that initial infection of CMV and its reactivation or reinfection frequently occur after transfusion with infected blood products. The incidence of these infections appears to be related with both the number of donors and the volume of blood received by a certain patient.[7]

Similar to other hematology wards, our patients are treated more frequently for acute leukemia or other hematological malignancies and aplastic anemia where they need several transfusions in the admission period and outpatient clinic. Therefore, these patients are at great risk of CMV infection due to receiving a significant volume of donated blood. Due to their illnesses and undergoing treatments by cytotoxic drugs, these patients are regarded as immunocompromised and adversely influenced by cellular and humoral dysfunctions.

Reactivation of latent virus, either in donor white blood cells or host tissues, is most likely a primary event to CMV infection prior to blood transfusion. CMV seroprevalence within the United States has also provided substantial geographic variation, differing by as much as 30 percentage points between states, though differences may be explained by variation in the types of populations sampled.[7] Worldwide, seroprevalence among non-whites has shown to be 20-30% higher than that of whites. Studies on socioeconomic characteristics have had different results regarding anti-CMV seroprevalence. While Cannon et al.[7] reported high seropositivity among lower socioeconomic states, Souza et al.[9], and Shen et al.[25] provided no significant association.

Results concerning sex status of the cases had also shown to be varied in different studies. In the studies of Cannon et al.[7] in the U.S. and Gargouri et al. in Tunisia[11] females had higher seroprevalence than males; however, there was no difference between the reports by de Matos et al.[14] and Urwijitaroon et al.[10]

Age is another criterion in different studies. Kothari et al.[13] and Urwijitaroon et al.[10] reported no relation between age and seropositivity. Thai researchers suggested that CMV seronegative blood supply was very limited.[10]

Our donors' seropositivity for CMV IgG and IgM was very high and we had a very

limited number of seronegative donors. This study shows that anti-CMV seropositivity is high in IRAN, like the other regions.

Blood donors with antibodies to CMV (seropositive) are the source of CMV infection for patients lacking antibodies to CMV (seronegative).[22,26] These primary CMV infections can be prevented by using only blood products from seronegative donors.

Current data implies that using blood products from seronegative donors or seronegative patients not only is appropriate but also is a critical step in preventing CMV infection via blood transfusion.[22]

Providing seronegative blood in countries where the prevalence of CMV is high (> 90%) is difficult since this requires screening of a great number of blood donations.[21]

Screening all donated blood against certain viruses is mandatory in many countries,[27] but determination of CMV antibodies is not a part of the routine laboratory tests in blood transfusion centers and would just add up to screening cost.[21]

Because of the high frequency of seropositivity in normal people and also patients in Iran, the number of seronegative patients and donors are very low and we are unable to find them readily.[18] Therefore, we cannot use seronegative blood for our patients and we need another approach for preventing CMV reactivation.

The risk of CMV infection could be reduced by using frozen deglycerolized red blood cells. Removal of leukocytes (host cells for CMV) through filtration or differential centrifugation may also reduce the risk.[24] Leukocyte filtration should be performed at the blood bank with established quality standards. No controlled study has reported if there is an extra advantage in using either seronegative or filtered blood products.[28]

Due to the limited number of seronegative donors, high cost, and unavailability of frozen deglycerolized red blood cells, we expect that leukocyte removal by filtration or centrifugation may be an alternate method for Iranian patients and the leukocyte removal is the only alternate for prevention of post-transfusion CMV infection.

The present study had some limitations. We did not have access to demographic findings of the donors due to ethical issues and this is the critical shortcoming of this study. Therefore, we could not elaborate on the relations among seropositivity and age, sex, region of residence, and socioeconomic conditions of the donors. Moreover, these findings may not determine the CMV seroprevalence in the general population regarding the socioeconomic differences between donors and other people.

Conclusion

Since about 95% of blood donors in Iran 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.[17] Other preventive strategies, such as leukoreduction, and etc., could be more appropriate and cost-effective for the prevention of CMV transmission through infected blood to Iranian immunosuppressed individuals.

Conflict of Interests

Authors have no conflict of interest.

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