Status of CMV IgM Seropositivity Before and After Starting Chemotherapy in Patients with Haematological Malignancies

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ABSTRACT

Background: Even after significant improvement in management of haematological malignancy, post chemotherapy infection is still causing significant mortality and morbidity. Cytomegalovirus (CMV) is an important cause of morbidity and mortality in immunocompromised patients. This study was designed to assess the status of CMV IgM seropositivity in patients with haematological malignancies. Haematol J Bangladesh. 2022; 6(2):20-24.

Methodology: This was a prospective type of observational study and patients were selected by purposive sampling. Assessment of CMV IgG and IgM antibody test had been done at the time of 1st diagnosis and IgM antibody for CMV reassessed 6 weeks after initial chemotherapy. Antibodies were detected by Chemiluminescence method (LKCV1, LKCM1, Siemens, UK) from Virology department of BSMMU. Statistical analysis was done both manually and Windows based software device with Statistical Package for Social Science (SPSS). A p-value of <0.05 was taken as significant during data calculation.

Result: During a period of 12 months, we tested CMV IgM & IgG of 45 patients of haematological malignancy. Out of 45 patients, 28 were male (62%) and 17 were female (38%) and male female ratio was 1.65:1. The youngest of the participants was 15 and oldest was 70 years old. The mean age of the participants was 35.77 years with SD of 16.93. Among 45 patients of the study ALL, AML, NHL, HD patients were respectively 20 (44.4%), 17 (37.8%), 5 (11.1%) and 3 (6.7%). Before starting chemotherapy, all participants were CMV IgG positive (100%) and none was CMV IgM Positive (0%). Six weeks after chemotherapy we found that, 3 (6.7%) cases were positive for CMV IgM antibody, and 42 (93.3%) cases were negative for CMV IgM antibody.

Conclusion: This small study found that all participants were CMV IgG seropositive (100%). It indicates that higher percentages of haematological malignancy patients are previously infected with CMV so there is more risk of reactivation after chemotherapy or BMT. Post chemotherapy CMV IgM seropositivity (new infection or reactivation of CMV) was low 6.7% in this study. Percentage could be high if the tests were carried out with more sensitive and specific tests for CMV like PCR, pp65 antigenemia or CMV DNA.

Key words: Haematological malignancy, Post chemotherapy, CMV, IgG antibody, IgM antibody, seropositive.
**Introduction**

The outcome of patients with haematological malignancy (HM) has tremendously improved mainly because of new and more effective therapies, combination protocols and improvements in supportive care. But still mortality and morbidity in HM due to infection after chemotherapy, bone marrow transplant (BMT) or radiation is high, mainly during neutropenic period. Viral infections are a frequent cause of severe disease in HM, other cancers or patients undergoing haematopoietic stem cell transplantation. Cytomegalovirus (CMV) is an important cause of morbidity and mortality in immunocompromised patients.\(^1\)

Haematological malignancy is primary cancers originating from cells of the bone marrow and lymphatic system\(^2\) and they comprise two main categories – leukaemia and lymphoma. There are four common types of leukaemia are: acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myeloid leukaemia (CML), chronic lymphocytic leukaemia (CLL). The two types of lymphoma are: non-Hodgkin lymphoma (NHL) and Hodgkin’s disease (HD). Other haematological malignancy includes myelodysplastic syndrome (MDS), myeloproliferative disorders, multiple myeloma (MM).\(^3\)

The range of therapeutic options available to treat patients with haematological malignancy is chemotherapy, radiotherapy, immunotherapy, molecular therapies and bone marrow transplantation along with general supportive care. As a general rule, the greater the duration and severity of immunosuppression, the greater the risk of life-threatening infection with a bigger range of organisms. Causal pathogens of febrile neutropenia (FN), most frequently bacterial or fungal are identified and confirmed by culture in 25–35% of the cases.\(^4\) In other 15–25% of patients with FN, bacterial or fungal pathogens are suspected clinically. The remaining 50% of cases are classified as a fever of unknown origin (FUO) and may be caused by other pathogens, namely viruses that are more difficult to detect by conventional diagnostic methods.\(^5\)\(^6\)\(^7\)

Human cytomegalovirus (CMV), a β-herpes virus, causes a variety of infections, such as congenital infections in neonates, infectious mononucleosis in healthy individuals, and reactivation in immunocompromised patients. After its primary occurrence becomes latent and periodic reactivation with intermittent viral shedding may continue throughout life.

In immunocompromised patients with malignant tumours, especially leukaemias and lymphomas, CMV is of major concern in causing tissue injury and death.\(^1\)

At least 3 factors that may play role in active CMV infection among immunocompromised patients. First, receiving large amount of blood products; second, immunosuppressive therapy and the third, due to pathogenesis of disease.\(^8\)

The aim of the study was to assess the status of CMV IgM seropositivity in patients with haematological malignancy at diagnosis and after starting chemotherapy by serology test. By finding out the infection rate we will be able to provide supportive care more effectively to patients of chemotherapy due to haematological malignancy.

**Method**

This was a prospective type of observational study and conducted in Department of Haematology of Bangabandhu Sheikh Mujib Medical University (BSMMU). All the patients undergoing chemotherapy for acute leukaemia (ALL & AML) and lymphoma (NHL, HD) during the study period were primarily selected and those who gave consent were included in the study. After sampling, complete clinical history, clinical examination, specific & baseline investigations and CMV antibody study (IgG and IgM) was done according to study design. Detection of CMV IgG and IgM antibody was done by Chemiluminescence method (LKCV1, LKCM1, Siemens, UK) from Virology department in BSMMU. The participants were reassessed for CMV IgM antibody 6 weeks after...
chemotherapy. After collection of data, editing and compilation was done manually. Statistical analysis was done both manually and window-based software device with statistical package for social science (SPSS).

**Results**

During the 12 months study period, a total 45 patients of haematological malignancy were analysed for CMV IgG and IgM antibody test at diagnosis and CMV IgM antibody test 6 weeks after chemotherapy. Out of 45 HM patients, 28 were male (62%) and 17 were female (38%), male female ratio was 1.65:1 (Figure 1).

The youngest of the participants was 15 and oldest was 70 years old. The mean age of the participants was 35.77 years with SD of 16.93. They were divided in four groups, 15-29 yrs, 30-49 years, 50-64 years, and more than 65 yrs. Maximum 20 patients (44.4%) were in the 15-29 years age range group and minimum 2 patients (04.5%) were in the more than 65 years age group (Figure 2).

Among 45 haematological malignancy patients of the study, distribution of participants according to diagnosis is depicted in Figure 3.

Before chemotherapy all participants were CMV IgG positive (100%) no one was CMV IgM Positive. After chemotherapy, Distribution of participants according to IgM Positivity is shown in Figure 4.

At diagnosis CMV IgM antibody were negative in all cases 45 (100). Six weeks after chemotherapy 42 (93.3%) cases were CMV IgM antibody negative and only 3 (6.7%) cases were positive for CMV IgM antibody and it was not statistically significant (Table I).
In developing countries like Bangladesh, seropositivity of CMV IgG is very high. Among the healthy blood donor in our country, CMV IgG seropositivity is 97%, and in India, it is 95%. In this study, CMV IgG seropositivity was also high (100%). This may be attributed to the surrounding environment as high prevalence of CMV was previously observed in poor socioeconomic status, overcrowded and poor living conditions.

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### Discussion

The risk of Cytomegalovirus (CMV) infection in acute leukaemia patients was recognized almost 30 years ago. This study was focused on the serologic diagnosis of CMV in haematological malignancy and control group at diagnosis and also tried to know CMV infection or reactivation 6 weeks after starting chemotherapy by serological test.

In this study, a total number of 45 acute haematological malignancy patients were recruited. Among the participants, male (62%) were predominant over female (38%). The male and female ratio was 1.65:1. About similar result has been reported by Smith et al where male and female ratio was 1.35:1.

Regarding age, Unlike Western countries, the haematological malignancies in Bangladesh seem to afflict younger population as is indicated by the overall median age at diagnosis was 35.7 years in this study. This study is agreed with recent study in our country and in India but disagreed with Smith et al where median age at diagnosis was 70.6 years and the reason for this difference was explained by Hossain et al. Age distribution in among different HM in this study is nearly same as other study was done by in Bangladesh and India. Again, it is not compatible with western countries like UK.

Frequency of HM was also analysed, shows that ALL (44.4%) was slightly more than AML (37.8%) and NHL (11.1%) and HD (6.7%) were in low frequency. It may be due to sample was taken purposively and only admitted patients were included in this study within 12 months period.

### Table I: Comparison of Anti IgM at diagnosis with 6 weeks after chemotherapy

<table>
<thead>
<tr>
<th>Group</th>
<th>At diagnosis</th>
<th>6 weeks after chemotherapy</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Negative</td>
<td>45 (100.0)</td>
<td>42 (93.3)</td>
<td>0.250*</td>
</tr>
<tr>
<td>Positive</td>
<td>0 (0.0)</td>
<td>3 (6.7)</td>
<td></td>
</tr>
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*McNemar test was done to measure the level of significance.

### Conclusion

At diagnosis, IgM antibodies were not detected in 0/45 (0.0%) investigated HM patients. That means no CMV IgM seropositivity was found in any HM patients at diagnosis. This finding is compatible with Yang et al and Loutfy et al.

6 weeks after chemotherapy, CMV IgM antibody test was done in all 45 HM patients. CMV IgM seropositivity was found in 3 patients (6.7%), among them AML was 1/17 (5.9%), ALL was 1/20 (5%), NHL was 1/5 (20%) and no patient seropositive in HD 0/3 (0.0%). This finding may reflect a recent active infection or reactivation of CMV. This study shows low CMV reactivation or infection than previous other study. Capria et al shows CMV active infection or reactivation after chemotherapy in AML patients was 35% (21/59); 9/59 (15.2%) patients after induction and 12/59 (20%) post-consolidation. Lunghi et al shows in ALL, reactivation of CMV occurred in 2/13 (15.3%) but no reactivation in AML patients. Another study by Yang et al 2012 shows reactivation before transplant in NHL was 15.9%. This study is not compatible with previous study as previous study shows high rate CMV reactivation after chemotherapy, it may be due to post chemotherapy CMV infection was detected by PCR, DNA or pp65 antigenemia test in all previous study which are more sensitive test than IgM antibody test. Above diagnostic test is costly and not easily available in our country.
previously infected with CMV so there is more risk of reactivation after chemotherapy or BMT. Post chemotherapy CMV IgM seropositivity (new infection or reactivation of CMV) was 6.7% which was not statistically significant. This study recommends a larger multicentre study with more sensitive & specific tests for CMV (e.g., PCR, pp65 antigenemia or CMV DNA) to understand broader perspective of CMV seropositivity in post chemotherapy patients.

References