# Incidence of Cytomegalovirus Infection among Blood donors at Tripoli City, Libya

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**Abstract: Background**: Cytomegalovirus (CMV) can cause congenital infection and opportunistic infection in AIDS patients, and severe clinical problems in immunocompromised patients, *eg* during the first three months after renal transplantation. Transmission of the virus can occur via sexual contact, congenital infection, organ transplantation and blood transfusion. **The aim of this study:** was to assess the incidence and risk of infection among blood donors in 220 blood donors who underwent anti-CMV IgG and IgM antibody screening using ELISA technique. Also all specimens were tested by immunostaining to compare the relation between the seropositivity for both CMV-IgM and CMV IgG antibodies and immunofluorescence CMV antigenemia assay**. Results & discussion**: One hundred and eighty-six blood and serum samples were collected during January to August 2012 from the blood donors at the blood bank of EspeiaTeaching Hospital, Tripoli, Libya. Their ages were varied between <25->45 years. All specimens were tested by immunostaining and ELISA methods. The results proved that the percentage of blood donors with CMV antibodies was quite high, as indicated by , twenty cases were seropositive for CMV-IgM and one hundred and fourty six cases were seropositive for CMV-IgG. The results of the present study showed that there were no significant differences concerning seropositivity for CMV(IgG) and CMV(IgM) between different personal status. Nearly there was no apparent effect of surgical operation on seropositivity for CMV(IgG) and CMV(IgM). The lowest percentage of seropositive cases for CMV(IgG) in blood donors was in non educated women and the highest percentage of seropositive cases for CMV(IgG) in blood donors was among high school blood donors. The percentages of seropositive cases for CMV (IgG) in blood donors were approximately more or less the same among the different groups of occupation. An opposite results were observed with CMV(IgM), where the highest percentage of seropositive cases was observed in blood donors with administrative jobs and the lowest percentages of seropositive cases was among hospital worker blood donors. Higher percentage of seropositive cases for CMV(IgM), were found with those blood donors received blood transfusion one or more than one time, compared with blood donors that did not received blood transfusion. The results indicated that the percentage of seropositive cases for CMV(IgG) is more or less equal for blood donors living in urban areas and those living in rural areas. However, an opposite results were observed with CMV(IgM), where the percentage of seropositive cases for CMV(IgM) is lower in blood donors living in urban areas than those living in rural areas. The results of comparing the relation between seropositivity for CMV-antibodies illustrated that eighteen specimens (9.7%) gave positive results by immunostaining, twenty cases were seropositive for CMV-IgM and one hundred and fourty six cases were seropositive for CMV-IgG. **Conclusion and recommendation:** immunostaining along with ELISA detection of antibodies was useful to avoid CMV transmission through blood transfusion.

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## 1. Introduction

Cytomegalovirus (CMV), a member of the herpes virus group, is the most common cause of congenital viral infection, and the most common infectious cause of developmental delay and sensorineural hearing loss in the United States. Worldwide, 1% of all live-born infants are infected with CMV. CMV is ubiquitous, highly species specific, and, like other members of its family, infects almost all human beings at some point during their lives. The age at acquisition varies according to geographic and socioeconomic factors resulting in large differences in prevalence among groups[(1)].

The natural history of CMV infection is complex and characterized by lifelong latency punctuated by episodes of recurrent infection following a primary infection. After a primary infection, viral excretion from several different sites may persist for weeks to years before the virus becomes latent. Episodes of recurrent infection with renewed shedding often represent reactivation of latent virus but also can be caused by reinfection by an antigenically different

strain of CMV. Regardless of stage of infection, most episodes of CMV infection are asymptomatic and do not pose significant health threat to immunocompetent hosts [(2)].

Cytomegalovirus (CMV) is a virus that many people acquire during childhood or adolescence. In rural areas, about half the adults have been exposed to the virus; in urban areas often > 80% have previous exposure. In healthy people, the virus gives a flu-like illness or no symptoms at all. However, the virus stays alive in the body after infection, and can re-activate when the immune system is decreased [(3)].

Transmission of the virus can occur via sexual contact, congenital infection, organ transplantation and blood transfusion [(4)].

Transplant patients are at high risk of reactivation of the virus. In such patients, CMV can cause very serious complications, with inflammation of lungs, bowel, kidneys, liver, and eyes. Blood from a healthy donor without symptoms can also transfer the virus to a transplant patient. The virus may be present in the white cells of the donor blood. Leukocyte-removal already decreases the risk of this transfer. Therefore additional precautions for patients who are at the highest risk of serious CMV infection must be considered. Those high-risk patients will receive blood products that have been tested for CMV, and only products from CMV seronegative donors will be used. In order to minimize the rate of infection, it is necessary to avoid spreading of the virus, especially in the blood donors. Since spreading of the virus in the blood stream to various organs will occur by blood leukocytes, early and accurate identification of CMV in blood is important for treatment and for reducing the rate of infection [(5 & 6)].

In this study, immunostaining, which can be used to detect early CMV antigen, was introduced to assess the rate of CMV infection in Tripoli blood donors. The relationship for the presence of CMV antigen and the IgG and IgM antibodies was also performed, with a view to application to prevention of CMV infection in Tripoli, Libya.

**2.Material:**

Clinical samples: Peripheral blood samples were collected from 186 blood donors at the blood bank, of Espeia Teaching Hospital, Libya, Tripoli City. Blood samples, were collected from each person and divided into two parts; one for detection of CMV antigen and the other part for detection of CMV IgG and IgM antibodies.

CMV Brite immunofluorescence antigenemia kit (Biotest Diagnostics, Denville, N.J., and Immuno Quality Products, Groningen, The Netherlands).

Immunostaining monoclonal antibodies kit (Iq Products, Netherlands).

Kit for detection of anti-CMV antibodies (CMV IgG & IgM Enzyme Immunoassay test kit; Biochec Inc. CA, USA).

ELISA BioTek Instrument (Model ELx800):(Washer + Microplate Reader +Incubator )NY., USA.

**Methods:**

Detection of CMV antigen: The test was carried out in accordance with method mentioned by van der Bij [(7)]. Enzyme Immunoassay for the detection of CMV IgG & IgM antibodies: The tests were performed according to manufactures instructions.

**3.Results**:

A total number of 186 apparently healthy blood donors were entitled in this study. Only ten donors (10.75%) tested positive for anti-IgM CMV. On the other hand, 78.49% of blood donors were positive for IgG antibodies, indicating past exposure to the infection (Tables 1 & 2). Table (1) showed number and percentage of seropositive cases for CMV(IgG) among blood donors according to their ages. For age ranges <25, 26-29, 30-34 and 35-39, the percentage of seropositive cases were 92.85, 68, 85.7 and 70.6% respectively. Meanwhile 80% seropositive cases, their age range 40-44 and 75% seropositive cases, their age more than 45 years old. However detection of CMV(IgM) antibodies among blood donors according to their ages; for age ranges <25, 26-29, 30-34 and 35-39, the percentage of seropositive cases were 7.14, 8, 14.3 and 17.64% respectively. Meanwhile 0% seropositive cases, their ages more than 40 years old.

The results of the present study proved that there were no significant differences concerning seropositivity for CMV(IgG) and CMV(IgM) between different personal status(Tables 3 & 4).

N.B. In all of the following tables *% were correlated to the total number of blood donors in each group.

**Table(1) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to age.**

| Age (years) | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| < 25 Y | 26 | 92.85 | 2 | 7.14 | 28 |
| 26-29 | 34 | 68 | 16 | 32 | 50 |
| 30-34 | 48 | 85.7 | 8 | 14.3 | 56 |
| 35-39 | 24 | 70.6 | 10 | 29.4 | 34 |
| 40-44 | 8 | 80 | 2 | 20 | 10 |
| 45& more | 6 | 75 | 2 | 25 | 8 |

**Table(2) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to age.**

| Age (years) | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| 25 Y< | 2 | 7.14 | 26 | 92.85 | 28 |
| 25-29 | 4 | 8 | 46 | 92 | 50 |
| 30-34 | 8 | 14.3 | 48 | 85.7 | 56 |
| 35-39 | 6 | 17.64 | 28 | 82.35 | 34 |
| 40-44 | 0 | 0 | 10 | 100 | 10 |
| 45& more | 0 | 0 | 8 | 100 | 8 |

The effect of education state on seropositivity for CMV among the blood donors were obtained in tables (5&6). The results showed that, the lowest percentage of seropositive cases for CMV(IgG) in blood donors was **66.66**% in non educated women and the highest percentage of seropositive cases for CMV(IgG) in blood donors was **85**% among high school blood donors. Different results were also observed with CMV(IgM), where the percentage of seropositive cases was 0% in non educated women and the highest percentage of cases 20% among blood donors with only elementary school education.

Concerning the effect of occupation on seropositivity for CMV among the studied cases were obtained in tables (7& 8). The percentages of seropositive cases for CMV (IgG) in blood donors were approximately more or less the same among the different groups of occupation. An opposite results were observed with CMV(IgM), where the highest percentage of seropositive cases was **12.9**% in blood donors with administrative jobs and the lowest percentages of seropositive cases 0% among hospital worker blood donors.

**Table(3) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to personal status.**

| Personal status | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Single | 66 | 75 | 22 | 25 | 88 |
| Married | 80 | 81.6 | 18 | 18.4 | 98 |

**Table(4) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to personal status.**

| Personal status | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Single | 10 | 11.36 | 78 | 88.63 | 88 |
| Married | 10 | 10.2 | 88 | 89.8 | 98 |

**Table(5) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to the school level**.

| School level | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | **%** | |
| Non educated | 4 | **66.66** | **2** | **33.33** | **6** |
| Elementary | **8** | **80** | **2** | **20** | **10** |
| College education | **66** | **73.33** | **24** | **26.66** | **90** |
| High school | **68** | **85** | **12** | **15** | **80** |

**Table(6) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to the school level**.

| School level | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | **%** | |
| Non educated | 0 | 0 | **6** | 100 | **6** |
| Elementary | **2** | 20 | **8** | 80 | **10** |
| College education | **10** | 11.1 | **80** | 88.9 | **90** |
| High school | **8** | 10 | **72** | 90 | **80** |

**Table(7) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to the occupation**.

| Occupation | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Business man | 42 | 80.8 | 10 | 19.2 | 52 |
| Administrative | 96 | 77.42 | 28 | 22.58 | 124 |
| Hospital worker | 8 | 80 | 2 | 20 | 10 |

**Table(8) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to the occupation**.

| Occupation | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Business man | 4 | 7.7 | 48 | 92.3 | 52 |
| Administrative | 16 | 12.9 | 108 | 87.1 | 124 |
| Hospital worker | 0 | 0 | 10 | 100 | 10 |

Tables (9 & 10) showed number and percentage of seropositive cases for CMV(IgG) among blood donors according to residence. The results indicated that the percentage of seropositive cases for CMV(IgG) is more or less equal for blood donors living in urban areas (**80**%) and those living in rural areas (**77.6**%). However, an opposite results were observed with CMV(IgM), where the percentage of seropositive cases for CMV(IgM) is lower in blood donors living in urban areas (**2.86**%) than those living in rural areas (**15.5**%).

The effect of receiving blood transfusion on seropositivity for CMV among the studied cases was obtained in tables (11&12). Higher percentage (100%) of seropositive cases for CMV(IgM), were found with those blood donors received blood transfusion one or more than one time, compared with blood donors that did not received blood transfusion (**76.5**%). This was not the case for CMV(IgG) were lower percentage (0%) of seropositive cases were found with those blood donors received blood transfusion for one or more than one time, compared with pregnant women that did not received blood transfusion (**11.76**%).

Studying the effect of surgical operation on seropositivity for CMV among the studied cases were obtained in tables (13&14). Nearly there was no apparent effect of surgical operation on seropositivity for CMV(IgG) and CMV(IgM).

**Table(9) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to residence.**

| Residence | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | **%** | No | **%** | |
| Urban | 56 | **80** | 14 | **20** | 70 |
| Rural | 90 | **77.6** | 26 | **22.4** | 116 |

**Table(10) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to residence.**

| Residence | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | **%** | No | **%** | |
| Urban | 2 | **2.86** | 68 | **97.14** | 70 |
| Rural | 18 | **15.5** | 98 | **84.5** | 116 |

**Table(11) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to blood transfusion.**

| Blood transfusion | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Donors did not receive blood | 130 | 76.5 | 40 | 23.5 | 170 |
| Received blood for one time | 10 | 100 | **0** | 0 | 10 |
| Received blood for more than one time | 6 | 100 | **0** | 0 | 6 |

**Table(12) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to blood transfusion.**

| Blood transfusion | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Donors did not receive blood | 20 | 11.76 | 150 | 88.23 | 170 |
| Received blood for one time | **0** | 0 | 10 | 100 | 10 |
| Received blood for more than one time | **0** | 0 | 6 | 100 | 6 |

**Table(13) Number and percentage of seropositive cases for CMV(IgG) among blood donors according to the surgical operations**.

| Surgical operations | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| No operations | 116 | **79.45** | 30 | **20.55** | 146 |
| One operation | 28 | **77.77** | 8 | **22.22** | 36 |
| More than one operation | 2 | **50** | 2 | **50** | 4 |

**Table(14) Number and percentage of seropositive cases for CMV(IgM) among blood donors according to the surgical operations**.

| Surgical operations | Seropositive | | Seronegative | | Total |
|---|---|---|---|---|---|
| | No | % | No | % | |
| No operations | 18 | **12.33** | 128 | 87.67 | 146 |
| One operation | 2 | **5.55** | 34 | **94.44** | 36 |
| More than one operation | **0** | **0** | 4 | **100** | 4 |

In the current study Sera were screened for the presence of antibodies to CMV in parallel with immunofluorescence CMV antigenemia assay.

CMV antigen was detected in peripheral blood leukocytes collected from blood donors by the immunostaining method. 18/186(9.7%) were positive for CMV antigen. However; the number of blood samples showing seropositivity for CMV-IgM antibodies were 20/186(10.75%) and those with seropositivity for CMV-IgG antibodies were 146/186 (78.5%). The remaining blood samples gave seronegative results (166/186 for CMV-IgM; 40/186 for CMV-IgG and 168/186 negative immunofluorescence CMV antigenemia.

Twenty tested samples were positive for CMV-IgM antibodies, of which CMV antigen in blood were detected in 18 samples, using immunofluorescence technique. This means positive relationship of CMV infection demonstrated by immunostaining and the presence of anti-CMV-IgM antibodies.

**Table(15) Comparison of the results between immunostaining and ELISA techniques**.

| Immunostaining | | | | ELISA. | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | IgM | | | | IgG | | | |
| Positive | | Negative | | Positive | | Negative | | Positive | | Negative | |
| No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 18 | 9.7 | 168 | 90.3 | 20 | 10.75 | 166 | 99.25 | 146 | 78.5 | 40 | 21.5 |

**4.Discussion:**

The present study was undertaken to define further the epidemiology of CMV infection among a volunteer blood donor population, since volunteer donors may be expected to provide the major source of most blood transfusion requirements. In this study all blood donation, either inpatient or outpatient, comes from volunteer donors, and all were subjected to determine the prevalence of CMV antibodies among the different sexes and age groups in healthy blood donors.

Nevertheless, complications can occur, and each patient should be aware of these possible complications. Transfusion acquired CMV can be prevented by donor screening; donor titers of less than 1:4 do not result in transfer of infection [(8)].

In this study, the percentage of blood donors with CMV (IgG) antibodies was quite high (78.49%). On the other hand, only (10.75%) of blood donors were positive for CMV-IgM antibodies, indicating past exposure to the infection. The prevalence of antibody in the donors compared closely with another volunteer donor population in Seattle [(9)].

Kothari *et al.* carried out a similar study at New Delhi, but none of the 200 donors' blood units tested positive for anti-IgM CMV [(10)].

Other Indian studies gave similar prevalence rates for IgG antibody, but remain inconclusive for anti-IgM CMV [(11)].

A study conducted in similar settings at Military Hospital in Ghana, a developing country, found none of the 264 donor blood units to be positive for anti-IgM CMV, but anti-IgG CMV seroprevalence was 93.2% [(12)].

This high seroprevalence in Libya and other developing countries is in contrast to Western literature, which describes seroprevalence in voluntary blood donors ranging from 38%-75%[(13)].

A study representative of developed nations in the USA, by Staras *et al.,* found a seroprevalence of CMV infection in population aged 6 years or more to be 58.9% [(14)].

The decrease in the percentage seropositivity of CMV-IgM antibody with increasing age, suggests ongoing antigenic experience with CMV in adults. Since the majority of volunteer blood donors have serological evidence of prior exposure to CMV, which is clear by high CMV-IgG antibody seropositivity. Another explanation for blood donors above 40 years age groups may be most likely due to the fact that data in this age band are based on smaller numbers. This differs with western studies which showed a significantly increased seropositivity with increasing age of blood donors. This may possibly be due to earlier acquisition of CMV infection in Libya in childhood compared to the western populations, leading to higher seroprevalence even in younger adults [(13)].

There was no statistical difference between different ages, marital status, in the prevalence of CMV-IgG antibodies.

High seropositivity for anti-CMV IgM was noted among blood donors living in urban areas than those living in rural areas. This may be attributed to their socioeconomic profile reported.

Traveling away to another countries has no effect on seropositivity for CMV. However higher percentage of CMV(IgG) was detected in those blood donors which did not travel away of Libya; this means that infection in most cases acquired locally.

There was no relationship between the antibody titer and number of times of receiving blood transfusion and or surgical operation , concerning CMV-IgG antibodies detection among the blood donors participated in this study. This means that past infection with CMV, through other means other than blood transfusion or surgical operations.

The current study does not demonstrate any significant influence of educational state or even the job type on the prevalence of anti-CMV antibodies among the investigated blood donors.

Finally the results of the present study; it can be concluded that immunostaining method is quite useful for screening CMV in blood donors before giving blood to patients in addition to screening for the presence of CMV-IgM antibodies. Therefore immunostaining for detection of CMV in blood along with detection of CMV-IgM antibodies should be introduced to every blood bank in order to reduce CMV transmission rate and to reduce hazard of development of congenital diseases and other bad effects on immunsupressed persons .

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