

## Seroprevalence of Cytomegalovirus in Advanced HIV disease

Dr S Yamini, Dr C Tirumala, Dr S V Prasad, Dr D Jayasri, Dr KK Sharma,  
Dr K vineela

---

### Abstract

**Introduction:** Human cytomegalovirus (HCMV, CMV) is a ubiquitous agent that can cause infection at any time during the course of life. Infections by CMV are an important health problem in certain patient populations, such as newborns, organ recipients and HIV seropositive patients. The prevalence of CMV ranges from 40 - 100% in many parts of the world. (1) CMV remains latent in the host throughout life and rarely reactivates to cause clinical illness in immunocompromised patients. (2-4) This study reports on the high prevalence of immunoglobulin (Ig) G and Ig M antibodies to CMV and the risk factors for CMV infection among HIV/AIDS patients.

**Materials and methods:** A total of 50 known HIV seropositive patients were included in the study who were admitted at Govt General & Chest Hospital, Hyderabad during the period of March to July 2006. Socio-demographic data and 5 ml blood samples were collected from each patient. 10 HIV seronegative patients with pulmonary infection were taken as controls. Each sample was assayed for anti-CMV IgG/IgM using a CMV IgG and IgM Enzyme Linked ImmunoSorbent Assay (ELISA) kit.

**Results:** All control group were negative for antibodies to CMV infection. In study group, CMV seropositivity is more prevalent in male patients (90%). 2(6%) patients were positive for IgM antibody. 49 (98%) patients were positive for Ig G antibody to CMV. There is 4 fold rise of Ig G antibody in 2 patients with Ig M seropositivity.

**Conclusion:** This study has shown that greater percentages of HIV seropositive patients had active CMV infection. Therefore, routine screening for CMV infection is needed to decrease mortality and morbidity.

---

Date of Submission: 11-12-2019

Date of Acceptance: 26-12-2019

---

### I. Introduction

Human Cytomegalovirus (HCMV, CMV) is an ubiquitous agent found throughout the world in all geographic and socioeconomic groups. And also it is more widespread in developing countries and in areas of low socioeconomic conditions.

CMV is a member of the herpesviridae family, which includes the herpes simplex viruses and the viruses that cause chicken pox (varicella-zoster virus) and infectious mononucleosis (Epstein-Barr virus).

CMV Infection is important cause of morbidity and mortality in HIV seropositive patients with low CD4 count. Incidence of infection rise with age, and by adulthood, nearly half the population in developed countries infected with this virus. However, CMV infection is important in to certain high risk groups. Major areas of concern are (1) risk of infection to unborn baby during pregnancy, (2) the risk of infection to people who work with children, and (3) the risk of infection to immunocompromised person, such as organ transplant recipients and persons infected with human immunodeficiency virus (HIV).

In Pre (Highly Active Anti Retro Viral Therapy) HAART era, Nearly half of HIV infected patients developed CMV end organ disease (chorioretinitis, colitis, esophagitis, pneumonia and central nervous system disease). 90% of people with HIV had evidence of CMV at autopsy while about 10% CMV was considered to be the primary cause of death.

In patients with Acquired Immuno Deficiency Syndrome (AIDS), progressive impairment of immune function leads to CMV reactivation and replication. Asymptomatic excretion of CMV in urine can be detected in approximately 50% of HIV-infected individuals with a CD4 lymphocyte count <100 cells/ $\mu$ L. (5) Cell-to-cell transmission of CMV results in tissue necrosis in association with nonspecific inflammation. Transient episodes of CMV viremia can also occur. (6) Although the clinical significance of viremia is uncertain, such episodes probably result in dissemination of CMV to other organs (eg, the retina), thereby setting the stage for subsequent end-organ disease. Prior to the availability of effective antiretroviral therapy (ART), >90% of patients with AIDS in the United States had evidence of disseminated CMV infection at autopsy. (7) ART leads to at least a partial return of CMV immune responses in most patients and to substantial decreases in CMV titers in blood. (8) Thus, in settings where ART is in widespread use, CMV retinitis is usually seen in those who have not started or cannot tolerate ART. Surprisingly, CMV retinitis is relatively rare in patients with HIV viral loads

that increase despite ART. There appears to be a prolonged lag time between failure of ART and impairment of CMV immune responses to an extent that allows CMV retinitis to develop. Apparently, poor immune response leads to CMV replication which results in complications due to CMV.(8)

## II. Materials And Methods

A prospective study was conducted to evaluate the prevalence of Cytomegalovirus infection in patients with Retroviral disease admitted in Govt General & Chest Hospital, Hyderabad during the period of March to July 2006.

A total of 50 patients with retroviral disease admitted to Govt. General & Chest hospital, Hyderabad during March to July 2006 were taken into study as cases.10 HIV seronegative patients with pulmonary infection were taken as controls. Most of the patients belong to low socioeconomic group according to kuppuswamy classification. Institutional review board clearance (ethics committee) was obtained and Informed consent was taken before including these patients in the study. Epidemiological factors like Age, Sex, Marital status and socioeconomic status were included in the clinical data obtained from the patients. Study protocol followed the cases includes detailed clinical examination followed by investigations like HIV screening, CD4 count, Chest X ray PA view, Sputum for Gram stain\AFB and induced sputum for PCP staining apart from routine investigations for identification of bacteria in case of pneumonia. Ophthalmic funduscopy was performed in all cases for detection of CMV retinitis.

### INCLUSION CRITERIA

Advanced HIV disease with CD4count<200 cells/ul having pulmonary infections with or without other Opportunistic infections

### EXCLUSION CRITERIA

Exclusion criteria was HIV patients CD4 count >200cells/ul, Patients with other herpes viral infections like Varicella-Zoster and Epstein Barr virus. Patients on steroids and immunosuppressive treatment, pregnancy, malignancies and collagen vascular diseases.

Paired serum samples from the study population were collected and stored at 2-8\*c and tested for CMV serology (IgM and IgG antibodies) using Equipar ELISA kits by ELISA method

### DIAGNOSTIC CRITERIA

- Activity index of IgM >1.1.
- Activity index of IgG >1.1
- Four fold rise in IgG –AI Value.

A.I	Interpretation
<1.0	Negative
1.0-1.10	Equivocal
>1.1	positive

Estimation of antibody titres by ELISA method is qualitative and semi quantitative analysis where Activity Index (A.I) is unit of measurement. Values of A.I indirectly reflect antibody concentration of serum samples.

## III. Results:

Age group of 25-40 years constituted 85% of study population. There was a high in male preponderance (90%). Prevalence rate of IgG antibody is(49) 98% , IgM antibody is (2) 4% in study group and no IgM antibody positivity was observed in control group. 3 patients with IgM seropositivity had also shown four fold rise of IgG titres to CMV. Significant rise of IgG titres to CMV were observed in 13 (26%) of samples. Mean IgG titres in study group was 35 & 44 and mean IgG titres in control group was 2.43 & 2.51. Antibody titres of IgG in study group were much higher when compared to control group which is statistically significant (P =0.0217 for IgG1, p=0.002 in IgG2 titres) (ANNOVA). High Mean IgG titres was observed in 30-40 years than other groups.

## IV. Discussion

Cytomegalovirus (CMV) is a frequent infection in AIDS patients. The most common route of infection in adults is sexual transmission , though CMV can also be spread through oropharyngeal secretions, urine, breast milk, and blood.(9,10) CMV-specific antibody of the IgM class is a marker of active or recent primary infection with the virus. Post-transfusion CMV infection correlates positively with the receipt of blood from CMV IgM-positive donors.(11). Most patients with AIDS who develop clinical signs and symptoms of CMV infection probably have reactivation of previous infection rather than primary infection.(9,10)The prevalence of

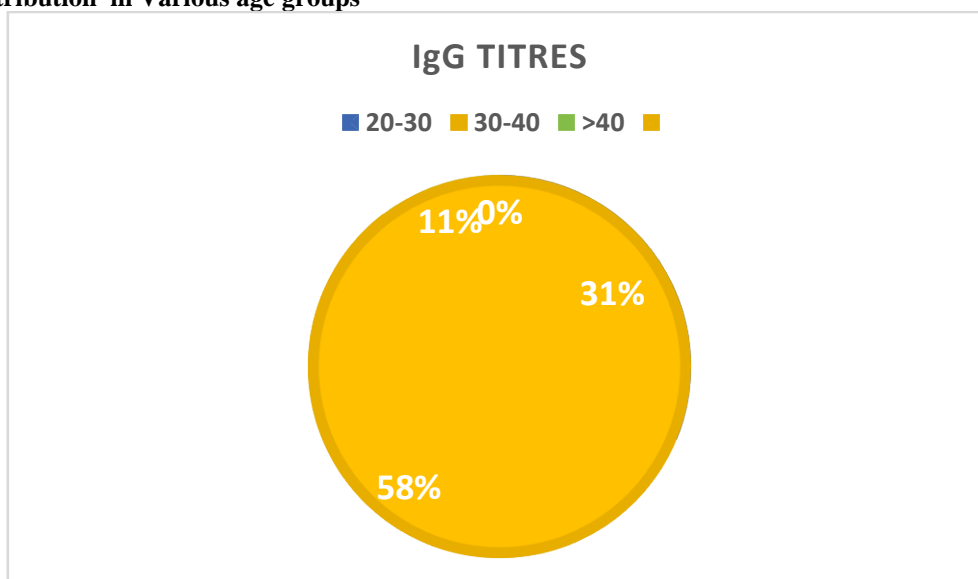
HIV/ AIDS in Sub Saharan Africa is high but the description of CMV infection as opportunistic infection amongst patients is scanty.(10) Nearly Total study population reported IgG seropositivity may indicate high prevalence rate of CMV infection in the community. In our study we found CMV IgG prevalence of 98% and IgM prevalence of 4% in study cases. In CMV infection there is only a transient rise of IgM and is found only during the first 2 weeks of infection which explains the low IgM seropositivity of 4%. Two cases with IgM seropositivity has also shown four fold rise of IgG titres is a more specific marker can well correlate with active CMV disease . In Adeola Fowotade et al conducted a study on CMV antibodies in HIV patients in Nigeria , showed that Ig M positivity was 11.1% and Ig G positivity was 93.3 %.(12) The seroprevalence of CMV IgG of 96.0% was reported by Akinbami et al.(13) Both studies were correlated with our study. Four fold rise of IgG titres observed in 13 cases ,with Interstitial pneumonia (7) Tuberculous pneumonia(5) and one case of Gastroenteritis may indicate active CMV disease. 58% of Interstitial pneumonia ,Gastroenteritis (33%) and tuberculous pneumonia(18%) with significant rise of IgG titres may suggest CMV as likely etiological agent. 25% of female cases in the reproductive agegroup showed significant rise of IgG-AI values which cause significant mortality and morbidity in Newborn. The study showed that the seropositivity of anti-CMV IgG and anti-CMV IgM antibodies were age dependent. The positivity for anti-CMV IgG and anti-CMV IgM antibodies was not found to be the same in all age groups. Antibodies to CMV were found to be more in age group of 25 – 40 years among HIV seropositive patients. This is also in keeping with the findings of previous studies. Our study showed that the prevalence of anti-CMV IgG and IgM antibodies was more in males. CMV infection constitute a real risk of pathogenicity in immunocompromised patient, it is likely that HIV infected patients who develop CMV infection may have a previous history of blood transfusion. (10) In our study ,One case of CMV retinitis with low CD4 count of 4 cells/ul has shown poor rise of IgG-AI values. This can be explained by poor immune response in advanced immuno-suppression.

Here AI values as given by kit manufacturers can be regarded as equivalent to antibody titres as in quantitative estimation methods like immunofluorescence and agglutination and thus is a qualitative and semiquantitative analysis. There is no linear relationship for CD4 count and antibody titres. No linear relationship was observed between CD4 count and IgG titres. Mean IgG titres in CD4 >100 cell/ul are high when compared to CD4 <1 cell/ul.

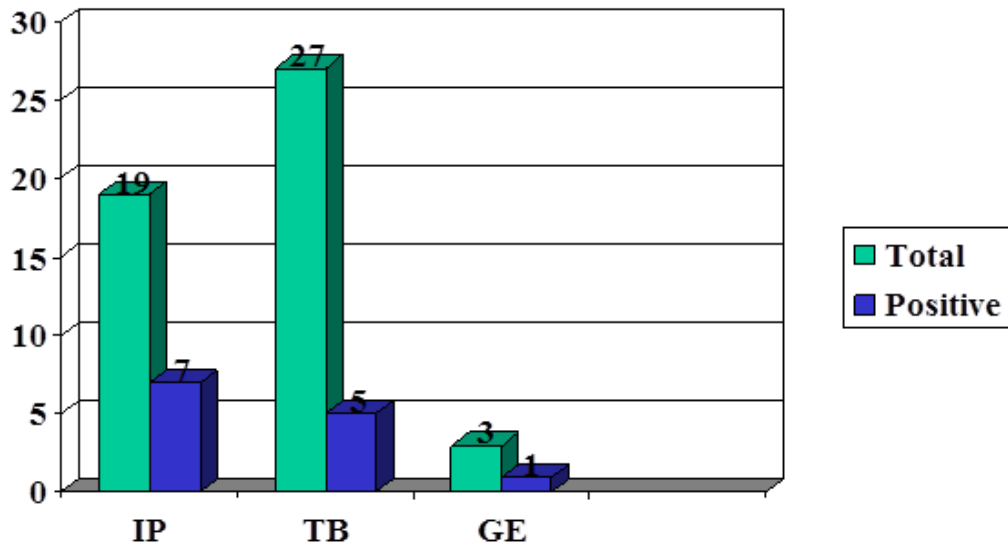
### V. Conclusion

This study shown that greater percentages of HIV seropositive patients had active CMV infection. Preventive measures must be taken to decrease the mortality and morbidity related to CMV infections.(14) Routine screening is mandatory for HIV infected patients who have CD4 count less than 200 cells /ul. Unfortunately, vaccines for CMV have not yet been developed. CMV chemotherapy and prophylaxis (Ganciclovir) may benefit in these cases.

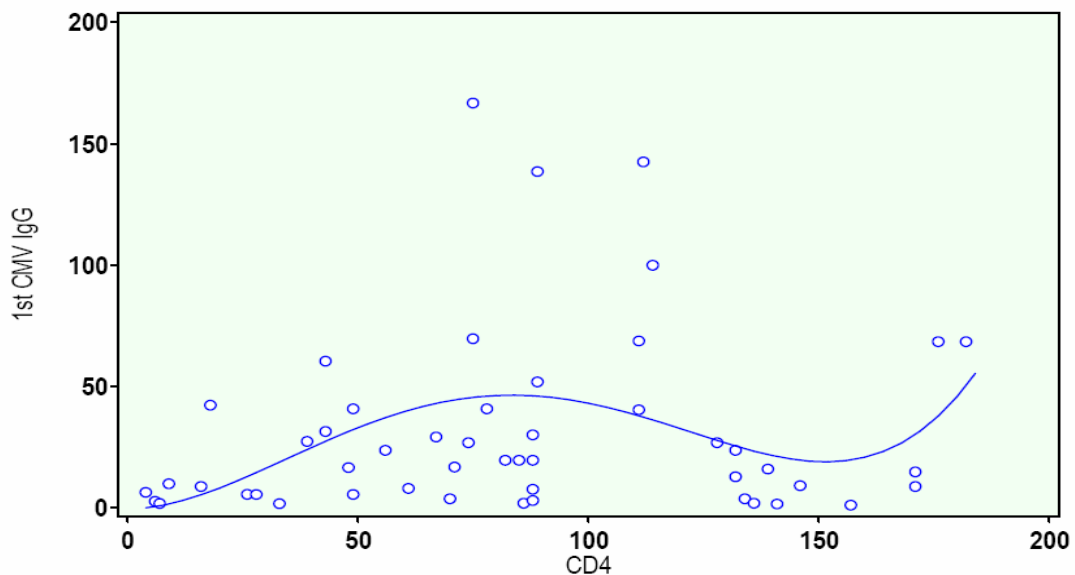
#### Ig G distribution in Various age groups



Proportion of cases showing fourfold rise of IgG titres respective disease conditions



DISPERSION OF IgG TITRES IN REALTION TO CD4 COUNT



References:

- [1]. Spector SA, Wong R, Hsia K, et al. Plasma cytomegalovirus (CMV) DNA load predicts CMV disease and survival in AIDS patients. *J Clin Invest.* 1998; 101: 497-502.
- [2]. Wohl DA, Zeng D, Stewart P, et al. Cytomegalovirus viremia, mortality, and end-organ disease among patients with AIDS receiving potent antiretroviral therapies. *Journal of Acquired Immunodeficiency Syndrome*, 2005; 38:538-544.
- [3]. Krech U. Complement-fixing antibodies against cytomegalovirus in different parts of the world. *Bulletin of World Health Organization* 1973; 49(1):103-106.
- [4]. Greffe A, van der Giessen M, van Son W, The TH. Circulating cytomegalovirus (CMV)-infected endothelial cells in patients with an active CMV infection. *Journal of Infectious Diseases*, 1993; 167 (2):270-277.
- [5]. Rodriguez-Barradas MC, Stool E, Musher DM et al. Diagnosing and treating Cytomegalovirus pneumonia in patients with AIDS. *Clin Infect dis* 1996;23:76-81.
- [6]. Minty L, Drew WL, Minr RC, Bralt EH, Cytomegalovirus infections in homosexual men. *An epidemiological study ann, Indian Mel.* 1983 sep. 99 (3) : 326-9.
- [7]. Marx J. L (1985) Cytomegalovirus: A major cause of birth defects.
- [8]. O'Sullivan CE, Drew WL, McMullen DJ, Miner R, Lee JY, Kaslow RA et al . Decrease of cytomegalovirus replication in human immunodeficiency virus infected-patients after treatment with highly active antiretroviral therapy. *J Infect Dis* 1999; 180:847-9.

- [9]. Klatt EC, Shibata D. Cytomegalovirus infection in the acquired immunodeficiency syndrome: clinical and autopsy findings. *Arch Pathol Lab Med.* 1988; 112:540-544.
- [10]. Akinbami AA, Akanmu AS, Adeyemo TA, Wright KO, Dada MO, Dosunmu AO. Cytomegalovirus Antibodies Amongst Immunocompromised (HIV) Patients At Lagos University Teaching Hospital (LUTH) Idi -Araba, Lagos. *Journal of Medicine,* 2010; 11 : 151-154.
- [11]. Lentz EB, Dock NL, McMahon CA, Fiesthumel SR, Arnold CB, Lamberson HV. Detection of anti-body of cytomegalovirus-induced early antigens and comparison with four serologic assays and presence of viruria in blood donors. *Journal of Clinical Microbiology,* 1988; 26: 133-135.
- [12]. Adeola Fowotade<sup>1</sup>, IheanyiOmezuruike Okonko<sup>2</sup>, Olajide Olubunmi Agbede<sup>3</sup> , S T Suleiman<sup>3</sup> . High seropositivity of IgG and IgM antibodies against cytomegalovirus (CMV) among HIV-1 seropositive patients in Ilorin, Nigeria. *African Health Sciences Vol 15 Issue 1, March 2015*
- [13]. Okwori AEJ, Olabode AO, Emumwen EG, Echeonwu GO, Lugos MO, Okpe ES et al. Sero-Epidemiological Survey of Human Cytomegalovirus Infection among Expectant Mothers in Bida, Nigeria. *The Internet Journal of Infectious Diseases,* 2009; Volume 7 Number 1.
- [14]. Uyar Y, Balci A, Akcali A, Cabar C. Prevalence of rubella and cytomegalovirus antibodies among pregnant women in northern Turkey. *New Microbiologia,* 2008; 31(4):451-455.

Dr S Yamini. "Seroprevalence of Cytomegalovirus in Advanced HIV disease." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 12, 2019, pp 45-49.