

## Prevalence of Cytomegalovirus infection among HIV sero-positive patients – Case Study from North India

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**ABSTRACT:** Cytomegalovirus is one of the opportunistic infections associated with significantly high morbidity and mortality among patients living with immunodeficiency syndrome. Cytomegaloviruses (CMV) are deoxyribonucleic acid (DNA) viruses and are members of the Herpesviridae family. CMV are recognized pathogens that cause community-acquired pneumonia (CAP) in compromised hosts. We investigated the prevalence of CMV among seropositive cases of human immunodeficiency virus (HIV) from Northern India. In this study we observed the relationship between CMV infections among the immunocompromised patients. This study was carried out in Department of Microbiology, King George's Medical University (KGMU), Lucknow and Dolphin (PG) Institute of Biomedical and Natural Sciences, Dehradun, Uttarakhand, India. Total 250 HIV sero-positive cases were considered in study of CMV infection. HIV status was confirmed by Enzyme linked immunosorbent assay (ELISA) done at antiretroviral (ART) center, KGMU, Lucknow. CMV positivity was evaluated by CMV-IgG and IgM antibodies using ELISA kit. Among 250 HIV positive cases 10.4% were found positive for CMV- IgG whereas 8.4% were positive for CMV- IgM however 1.2% were found to be positive for both CMV- IgG and CMV- IgM. Sero-prevalence of CMV IgG and IgM among HIV infected cases were 10.4% and 8.0% respectively. No significant difference was observed among gender and age group in CMV infection among HIV-positive cases.

**KEYWORDS:** HIV, cytomegalovirus, CMV – IgG and IgM antibodies, ELISA.

### 1 INTRODUCTION

Cytomegalovirus (CMV) is a large encapsulated double stranded DNA virus. It belongs to the beta – herpes virus group. Most likely it is one of the most common latent infections known to humans [1].

CMV infection is defined as isolation of the CMV virus or detection of viral proteins or nucleic acid in any body fluid or tissue specimen (e.g., plasma, serum, whole blood, peripheral blood leucocytes, CSF, urine, or tissue) [2].

It is probably one of the most common latent infections known to humans [1]. Normally it is controlled by the cellular immune response and hence characterized as a self-limiting infection in healthy individuals. In contrast, the CMV in immunosuppressed individuals as in case of HIV infection carries high morbidity and mortality [3]. Clinical disease due to CMV has been observed in up to 40% of the patients with advanced HIV disease [4].

HIV is undoubtedly an immune system disorder but ophthalmic disease can occur in up to 50% of HIV patients during the natural history of their infection [5]. However, it is more common in the developing nations and among people with lower socioeconomic background [6].

The ELISA is the most common test available for measuring CMV IgG (past exposure to CMV) and CMV IgM (recent or reactivation of CMV infection) [7]. Although CMV infection among HIV/AIDS patients has been reported in India [1], [8], [9]. But still the surveillance of CMV infection in immunocompromised cases needs to be investigated to meet the future health challenges. The present study has been designed with aim to investigate the prevalence of CMV infection among HIV sero-positive patients from North India.

## 2 MATERIALS AND METHODS

This study was conducted between January 2011, to January 2014, at the Department of Microbiology, King George's Medical University, Lucknow, Uttar Pradesh and Dolphin (PG) Institute of Biomedical and Natural Sciences, Dehradun, Uttarakhand, India.

### 2.1 STUDY POPULATION

The study population constituted of 250 HIV sero-positive patients both males and females. The age group was between < 10 to > 50 years at the time of interview and were about to be registered for treatment. Their HIV status was confirmed by using ELISA test in ART Center, KGMU, Lucknow UP India.

### 2.2 DATA COLLECTION

The data was collected through personal interview using structured questionnaire to provide information regarding age, sex, marital status, occupation and patient's history and clinical examination by physicians at the hospital.

### 2.3 BLOOD COLLECTION AND ANALYSIS

A 5 ml of whole blood was collected from each HIV infected patient by vein puncture into vacutainer. Serum was separated after centrifugation of blood at 3000 rpm for 10-15 minutes and then stored at -20 °C. The serum was later analyzed for CMV specific IgG and CMV specific IgM. ELISA method. It was supplied by NOVA TEC kit manufactured by Waldstrasse, 23A6 Dietzenbach, 63128, Germany. The assay was performed as per the manufacturer's instructions.

### 2.4 STATISTICAL ANALYSIS

The data collected was entered into Microsoft Excel and checked for any inconsistency. The descriptive statistics such as percentage calculated. The descriptive statistics such as percentage and mean( $\pm$ SD), Odds ratio, confidence interval were calculated.

## 3 RESULT

Out of 250 cases, IgG antibodies against CMV were detected in 26(10.4%) and IgM antibodies against CMV were 21(8.4%). Among these 60.8% were males and 39.2% were females. The most prominent age group in the present study was 31-40 years (39.2%). The mean( $\pm$ SD) age of the study population was 36.06( $\pm$ 11.34) years with range 7-58 years. The median age of the patients was found to be 38 years (Table-1).

Table 1: Age and sex distribution of study subjects

Age in years	No. (n=250)	Percent (%)
<20	28	11.2
20-30	38	15.2
31-40	98	39.2
41-50	74	29.6
>50	12	4.8
Mean±SD, median, range	36.06 ±11.34, 38, 7-58	
<b>Gender</b>		
Male	152	60.8
Female	98	39.2

Table 2: Percentage of IgG /IgM antibodies in HIV sero-positive patients

N=250	Positive	Negative
IgG	26 (10.4%)	224 (89.6%)
IgM	21 (8.4%)	229 (91.6%)
Both	3 (1.2%)	247 (98.8%)

Table -3: Prevalence of CMV according to Gender and Age

Gender and age	No. of patients	IgG +ve		IgM+ve No. (%)		Both+ve No. (%)	
		No. (%)	OR (95%CI), p-value <sup>1</sup>	No. (%)	OR (95%CI), p-value <sup>1</sup>	No. (%)	OR (95%CI), p-value <sup>1</sup>
<b>Gender</b>							
Male	152	15 (9.9)	0.86 (0.38-1.97), 0.73	13 (8.6)	1.05 (0.41-2.64), 0.91	2 (1.3)	1.29 (0.11-14.45), 0.83
Female	98	11 (11.2)	1.00 (Ref.)	8 (8.2)	1.00 (Ref.)	1 (1.0)	1.00 (Ref.)
<b>Age in years</b>							
<20	28	2 (7.1)	1.00 (Ref.)	5 (17.9)	1.00 (Ref.)	0 (0.0)	1.00 (Ref.)
20-30	38	2 (5.3)	0.72 (0.09-5.46), 0.75	2 (5.3)	0.25 (0.04-1.42), 0.12	1 (2.6)	NA
31-40	98	14 (14.3)	2.16 (0.46-10.16), 0.32	6 (6.1)	0.30 (0.08-1.07), 0.06	0 (0.0)	NA
41-50	74	7 (9.5)	1.35 (0.26-6.97), 0.71	7 (9.5)	0.48 (0.13-1.66), 0.24	1 (1.4)	NA
>50	12	1 (8.3)	1.18 (0.09-14.42), 0.89	1 (8.3)	0.41 (0.04-4.02), 0.45	1 (8.3)	NA

<sup>1</sup>Derived from binary logistic regression, OR-Odds ratio, CI-Confidence interval, Ref.: Reference category

The prevalence of IgG positivity was 14% lower among males compared with females (OR=0.86, 95%, CI= 0.38-1.97, p=0.73), although this was statistically not significant. However, the prevalence of IgM positivity was almost similar (p>0.05) among male and females. There was no significant association between age and prevalence of IgG and IgM. The positivity of both IgG and IgM was 1.29 times insignificantly higher among males than females (OR=1.29, 95%CI=0.11-14.45, p=0.83).

#### 4 DISCUSSION

Although tuberculosis was considered as single most common opportunistic infection in Indian patients with AIDS but CMV has also been reported as one of the frequent opportunistic infection in immune compromised individuals as in case of HIV infection.[10],[11],[1].

The infection with CMV is more common in the developing countries like India. The CMV positivity may be considered as marker of extremely severe immunosuppression which may ultimately lead to fatal outcomes in patients [6].

Only a few studies are available on the CMV infection in Indian patients with HIV/ AIDS. In one such report 45% among 125 HIV positive cases were found positive for CMV infection [12].

In present study, prevalence of CMV- IgG (10.4%) and CMV -IgM (8.4%) antibody in HIV positive patients has been observed. This is contrary to earlier report stating 89.4% IgG antibodies and 10.6% IgM antibodies in HIV positive patients [6].

One of the earlier study in North India reported that 32.4% of patients with HIV positive had CMV co-infection and part of the symptoms may be attributed to CMV in India [10]. In another study, 93% were CMV IgG positive CMV infection in HIV patients [13]. Patients had ophthalmic manifestations retinal detachment was reported in 70% in HIV positive patients in India. No significant association of CMV infection with gender and age observed [14].

CMV infection in 16% patients with minor lesions has been revealed which was contributory cause of death in these patients [15]. 59% HIV positive patients indicated histological evidence for CMV infection [16]. Our study shows the increase in CMV IgG sero-positivity with age which agrees with the findings made in a similar study in Iran [17].

Results of one study reports CMV IgM antibody sero-prevalence to be 8.4% and 9% among HIV infected Thai children [18]. Whereas higher than 2.3% recorded in USA [19]. The variation in sero-prevalence of CMV IgM observed may probably be due to epidemiological and methodological differences. Cytomegalovirus is a ubiquitous and infection caused by it has become endemic throughout the world. With its prevalence ranging 40 -100% [19].

One study from USA reports 100% of the sex workers and sexually active homosexual men positive for CMV infection. From England and France maximum prevalence has been reported in homosexual men [20]. The present study indicates the magnitude of the problem associated with active CMV infection among population of HIV infected patients from north India.

In our study presence of IgG antibodies (10.4%) indicates past infection and IgM antibodies (8.4%) indicates reactivation or reinfection of CMV , thus it is suspected that CMV infections are associated with an increased risk among AIDS patients.

The prevalence of IgG positivity was 14% lower among males compared with females (OR=0.86, 95%CI= 0.38-1.97, p=0.73), although this was statistically not significant. However, the prevalence of IgM positivity was almost similar (p>0.05) among male and females. There was no significant association between age and prevalence of IgG and IgM. The positivity of both IgG and IgM was 1.29 times insignificantly higher among males than females (OR=1.29, 95%CI=0.11-14.45, p=0.83).

There is need to further investigate the prevalence of CMV infection among immuno-compromised cases in other part of the country to have a better picture of the extent of this problem in Indian scenario.

## 5 CONCLUSION

The present study indicates that CMV infection among HIV positive cases although is statistically not significant, but the case study reveals the need of further investigation from different parts of the country to highlight the severity of the problem. It will help in better management of the HIV cases with early diagnosis of CMV antibodies in the patients.

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## REFERENCES

- [1] A Chakravarti, B Kashyap, M Matlani "Cytomegalovirus infection: An Indian perspective." *Journal of Clinical and Diagnostic Research*. vol. 27, no. 1, pp. 3-11, 2009.
- [2] Ljungman P, Griffiths P, Paya C, *et al.*, Definitions of cytomegalovirus infection and disease in transplant recipients. *Journal of Clinical Infectious Disease*, vol. 34, no.8, pp. 1094-7, 2002.
- [3] Kathryn L. Springer<sup>1</sup> and Adriana Weinberg "Cytomegalovirus infection in the era of HAART: a fewer reactivations and more immunity". *Journal of Antimicrobial Chemotherapy*. Vol 54, no.3, pp. 582-586, 2004.
- [4] Sundar Isaac Kirubakaran, "cytomegalovirus infection in HIV-infected patients – a review," *Clinical Microbiology Newsletter*, Vol. 26, no.18, pp 137–144, 2004.

- [5] Cunha BA. Cytomegalovirus pneumonia: community-acquired pneumonia in immunocompetent hosts. *"Infectious Disease Clinical North America"* vol. 24, no.1, pp.147-58, 2010.
- [6] Basawaraju Anuradha "Reactivation of CMV in HIV infected patients," *Journal of Clinical and Diagnostic Research*, Vol-5 no.4 pp.749-751, 2011.
- [7] Bhatia P, Narang A, Minz RW. "Neonatal cytomegalovirus infection: diagnostic modalities available for early disease detection." *Indian Journal Paediatrics*. vol.77 no.1, pp.77-9, 2010.
- [8] Sheevani, N Jindal, A Aggarwal "A Pilot Sero-epidemiological Study Of Cytomegalovirus Infection in Women of Child Bearing Age" *Indian Journal of Medical Microbiology*, vol.23, no.1, pp. 34-36, 2005
- [9] S. Mujtaba, S. Varma & S. Sehgal "Cytomegalovirus co-infection in patients with HIV/AIDS in north India" *Indian J Med Res*, vol. 117, pp 99-103, 2003.
- [10] Machler , *Ophthalmology*, 2014 [online] available [http://dx.doi.org/10.1016/S0161-6420\(83\)80071-2](http://dx.doi.org/10.1016/S0161-6420(83)80071-2) ( Feb 19, 2014)
- [11] Leach CT, Cherry JD, English PA, Hennessey K, Giorgi JV, "The relationship between T-cell levels and CMV infection in asymptomatic HIV-1 antibody-positive homosexual men." *J Acquire Immune Deficiency Syndrome*, vol. 6, no. 4, pp. 407-13, 1993.
- [12] Nilanjan Chakraborty ICMR Virus Unit "Current Trends of Opportunistic Infections among HIV- Sero-positive patients from Eastern India" *Japan. Journal of Infectious .Disease*. vol. 61, pp. 49-53, 2008.
- [13] Tsertsvadze T, Gochitashvili N, Sharvadze L, Dvali N; International Conference on AIDS. *International Conference AIDS*, vol. 14, pp. 7-12, 2002.
- [14] Sujit Gharai, Pradeep Venkatesh, Satpal Garg, S. K. Sharma and Rajpal Vohra "Ophthalmic Manifestations of HIV Infections in India in the Era of HAART: Analysis of 100 Consecutive Patients Evaluated at a Tertiary Eye Care Centre in India", *Ophthalmic Epidemiology*, , vol. 15, no. 4, 2008.
- [15] Dhaneshwar Namdeorao Lanjewar, The Spectrum of Clinical and Pathological Manifestations of AIDS in a Consecutive Series of 236 Autopsied Cases in Mumbai, India, *Pathology Research International*, 2011,[online], <http://dx.doi.org/10.4061/2011/547618> (2011)
- [16] Mehrkhani F, Jam S, Sabzvari D, Fattahi F, Kourorian Z, SeyedAlinaghi S. "Cytomegalovirus Co-Infection in Patients with Human Immunodeficiency Virus in Iran," *Acta Medica Iranica*, Vol. 49, no. 8, pp. 551-55, 2011.
- [17] Likitnukul S, Bhattarakosl P and Poovorawan Y. "Seroprevalence of Cytomegalovirus Infection in Children Born to HIV-1 Infected Women" *Asian Pac J Allergy Immunol*, vol. 21, no.2, pp. 127-130, 2003
- [18] Schoenfisch AL, Dollard SC, Amin M, Gardner LI, *et al*. "Cytomegalovirus shedding is highly correlated with markers of immunosuppression in CMV-seropositive women." *Journal of Medical Microbiology*. vol. 60, pp. 768–774, 2011.
- [19] Sinclair John and Patrick Sissons "Latency and reactivation of human cytomegalovirus" *Genral of Virology*, vol. 87, no. 7, pp. 1763-1779, 2006.
- [20] Vincent C. Emery Alethea V. Cope , E. Frances Bowen , Dehila Gor *et al* "The Dynamics of Human Cytomegalovirus Replication in Vivo." *journal of experimental medicin*, vol.190, no. 2, pp 177, 2001