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A Study of Sero-Prevalence of Cytomegalo Virus

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ABSTRACT

Background: CMV seroprevalence varies considerably in different population groups throughout the world. Sero-conversion results from close contact with virus positive individuals. It need to stop its transmission & save the population from CMV infection by adapting safety measures like safe sex, safe blood transfusion, screening ante-natal mothers for CMV & health education. **Methodology**: The study cohort consisted of 105 patients which included 60 males and 45 females. Seroprevalence of CMV IgG antibodies in HIV and non-HIV patients are done by ELISA. **Results**: The high seroprevalence CMV was reported in HIV positive patients sexually active age group of 16 to 49 yrs females than in males. Employee, lower educated, Heterosexual with single sex partners CMV was highly prevalent. In the HIV negative group the high seroprevalance of CMV was reported in patients with age group of 16 to59 years, males, laborers and low uneducated patients.It was more common in heterosexuals and in patients exposed to multiple partners.**Conclusion**: This study showed varying influences of demographic and social factors on the prevalence of CMV. The sexual factors and STD conditions showed common influence on seroprevalence of CMV.

Keywords: Cytomegalo virus, Seroprevalence, HIV.

Introduction

In the developed countries 40 to 80 % of young adults are infected by CMV. The Prevalence of CMV infection varies from one geographic area to other, but also with social, economic, environmental & professional activity. High rate of sero- positivity in poor socio-economic status people. Adolescence have an increased annual CMV sero-conversion rate from 2-10%[1,2]. In HIV infected persons CMV disease is due to re-activation of latent virus in the previously infected host. Although more than 90% of persons with HIV infection has antibodies to CMV indicating prior exposure & infection. The clinical manifestations of CMV infection do not generally manifest until the CD4 count falls below 100 cells/cumm. CMV infection is ubiquitous and by the age of 35 most of the population is infected.

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In pregnancy 1-2% of sero positives shed CMV from the cervix & it increases to 10-15% during the last trimester, increasing peri-natal infection to 0.4-2.6%[3]. CMV transmitted to the child causing intra-uterine death, congenital malformations & infection in the child with or without symptoms.

CMV belongs to Herpes group of viruses. CMV was first observed in kidney epithelial cells of a stillborn infant in 1881. Weller named the virus in 1960 based on its cytopathic effect[4]. The term cytomegalic inclusion disease was coined even before the virus was discovered, based on the large cells with intra nuclear inclusions. The family of herpesviridae is divided into 3 sub families based on biological differences alpha, beta, gamma[5].

CMV is a double stranded DNA virus a beta herpes virus replicate slowly and the cell it infects gets enlarged. CMV can't be grown readily in any experimental animal. Many sub types exist and are species specific. CMV exists in a latent state after the primary infection of life[6]. Once a person gets infected, the virus remains dormant and maintains latency for life. Rarely it causes disease if the immune

system is suppressed, therefore CMV infected is not a serious problem[7].

CMV infection causes asymptomatic infection & when immune system is deranged it causes infectious-Mononucleosis, Esophagitis, Colitis, Hepatitis, Pneumonitis, Nephritis & Retinitis[8]. CMV is a co-factor in causing progression from HIV to AIDS, Carcinoma cervix &Kaposi's sarcoma, CMV is also transmitted from mother to child causing malformations & abortions. There is every need to stop its transmission & save the population from CMV infection by adapting safety measures like safe sex, safe blood transfusion, screening ante-natal mothers for CMV & health education, So we take up the study[9].

Ig G and Ig M are present in sero positive cases but Ig M is present for short period of time in the body and unless steps are taken to exclude RF it may give false positive results were as Ig G antibodies against CMV appear 1-2 weeks of infection & persists throughout life so here we have assayed Ig G for conformation to be positive.

Methodology

The study was carried out on patients who consulted at outpatient department of dermatology venereology and leprosy (DVL) during a period of one year from June 2012 to May 2013. The study cohort consisted of 105 patients.

Our study includes clinical examination, covering medical questionnaire, covering personal family history, occupational tasks, social and professional conditions. A blood sample of 5 mL was collected into a sterile, non anticoagulated bottle from 105 consenting participants. The sample was centrifuged and the serum separated into a sterile bottle and stored at –20°C.

Sera were tested for IgG CMV using the ELISA test. The CMV-specific IgG antibodies were studied by the commercially available kit according to the manufacturer's instructions. All specimens were analyzed using the enzyme immunoassay test. The cutoff of IgG was set at 0.5 World Health Organization (WHO) IU/mL by the kit's manufacturer. Samples with a concentration ≥0.5 WHO IU/mL were considered positive for CMV IgG, while samples with a concentration below the cut off were considered as negative results. The controls and the calibrators passed the validation check recommended by the manufacturer of the kit.

Results

Statistical analysis of results was done using the SPSS software. When relating variables to each other, multivariate analysis was done. Chi-square test and student's t -test were employed to detect any significant correlation between different variables. A p value of <0.05 was considered to yield a statistically significant result.

A total of 105 participates were enrolled into the study. About 60% of them were between the ages of 20-29 year.

Table -1: Seroprevalence of CMV in relation to age group among HIV & non-HIV patients

Age (in years)	Total	HIV Positives		HIV Negatives	
		No.of cases	CMV +ve	No.of cases	CMV +ve
0-15	1	1	0	0	0
16-19	7	6	4	1	1
20-29	60	44	29	16	8
30-39	25	17	12	8	3
40-49	8	4	4	4	3
50-59	5	4	1	1	1

Table- 2: Seroprevalence of CMV in relation to sex among HIV & non-HIV patients

Sex	Total	HIV Positives		%	HIV Negatives		%
		No of cases	CMV +		No of cases	CMV+	
Male	60	40	25	62.5%	20	11	55%
Female	45	35	25	71.4%	10	5	50%

60 were males & 45 were females. Among males, HIV was + in 40 patients in whom CMV + in 25(62.5%). Male HIV –ve patients are 20 in whom CMV was + ve in 11 patients (55%). Among females. HIV was + ve in 35 patients with CMV +ve in 25 patients (71.4%) &HIV-ve patients were 10 in whom CMV was +ve in 5 patients (5%).

Table -3: Seroprevalence of CMV in relation to occupation among HIV and non-HIV patients

Occupation	Total	HIV Positive		%	HIV Negative		%
		No of cases	CMV+		No.of cases	CMV+	
Labourers	71	59	38	64.4%	12	7	58.3%
Students	6	Nil	Nil	Nil	6	3	50%
Employees	28	16	12	75%	12	6	50%

Laborers were 71 among whom HIV was + ve in 59 in whom, CMV was +ve in 38 patients (64.4%)& HIV was –ve in 12 patients in whom CMV was +ve in 7 patients (58.3%).total no. of students were 6 none were HIV +ve but 3 patients were CMV +ve (50%) in the HIV –ve patients. Out of 105 patients employees were enrolled were 28 in whom HIV was +ve on 16 patients & CMV was +ve in patients (75%). 12 employees were reported to be HIV –ve in whom 6 were CMV –ve (50%)

Table-4: Seroprevalence of CMV in relation to education among HIV & non-HIV patients

Education Status	Total	HIV Positive		%	HIV Negative		%
		No. of cases	CMV+		No. of cases	CMV+	
Higher	18	5	2	40%	13	6	46%
Lower	52	42	29	69%	10	6	60%
Uneducated	35	28	19	67.8%	7	4	57%

Out of 105 patients 18 were having higher education who were +ve for HIV in 5 ,among whom CMV was+ ve for 2(40%) and –ve for HIV in 13 who were +ve for CMV in 6 patients (46%). 52 patients were low educated among whom HIV was +ve in 42 patients with CMV +ve in 29 (69%) and 10 HIV patients were – ve im whom CMV was present in 6 patients (60%). The uneducated patients were 35 among whom HIV was + ve in 28 patients , in whom CMV was + ve in 19 patients (67.8%) & HIV was –ve in 7 patients among whom CMV was + ve in 4 patients (57%).

Table-5: Seroprevalence of CMV in relation to sexual orientation among HIV & non-HIV patients

Sexual orientation	Total	HIV Positive		%	HIV Negative		%
		No.of cases	CMV+		No.of cases	CMV+	
Hetero	101	71	48	67.6%	30	16	53.3%
Homo	2	2	1	50%	Nil	-	-
Bisexual	2	2	1	50%	Nil	-	-

101 reported heterosexuals with 71 HIV and 48 CMV +ve (67.6%) and among 30 HIV negative heterosexual patients CMV was positive in 16 cases (53.3%). Homosexuals were 2 both were positive for HIV & one of them positive for CMV (50%). In the same homosexual group no case was reported. Bisexual patients were 2 both were positive for HIV but 1 was positive for CMV (50%). In the same bisexual group no patient was reported.

Table-6: Seroprevalence of CMV in relation to number of sexual partners among HIV & non-HIV patients

No.of Partners	Total	HIV Positive		%	HIV Negative		%
		No.of cases	CMV+		No.of cases	CMV+	
Single	60	42	30	71.4%	18	9	50%
2-5	25	17	9	53%	8	7	87.5%
More than 5	20	16	11	68.7%	4	0	0

Table-7: Seroprevalence of CMV in relation to STDs among HIV & non-HIV patients

Diseases	Total	HIV Positive		%	HIV Negative		%
		No.of cases	CMV+		No.of cases	CMV+	
Asymptomatic HIV	30	30	17	56.6%	0	0	-
CA	7	7	2	28.5%	0	0	-
MC	5	4	3	75%	1	1	100%
SY2	2	1	1	100%	1	0	-
GC	1	1	1	100%	0	0	-

NSU	1	-	-	-	1	0	-
HSV	3	2	1	50%	1	0	-
AIDS	27	27	22	81.5%	0	0	-
OTHERS	29	3	1	33.3%	26	15	57.6%

Discussion

CMV infections are current public and occupational health concerns as is the case with other viral infections like HIV, Hep B &C etc. CMV infections are highly dependent on sexual, socioeconomic, hygienic conditions & follow a similar epidemiological pattern. It has been observed the CMV seroprevalence was increasing in homosexuals, heterosexuals with multiple partners in sexually active age groups[9,10].

This study showed 0% of CMV in HIV +ve age group of 0-15 years. According to Stagno et al , 5 to 10% of children being infected by the end of 1st year of life. Contact with infected maternal genital secretions during delivery or during breast feeding are the two main routes of infection[3]. Our study was not in agreement with that of Stagno et al. this might be due to one patient reported, in that age group of study.(Table-1). CMV seroprevalence had increased step wise from second decade to fourth decade and showed 100% at the end of 4th decade. According to Griffith and Baboonian the prevalence of CMV infection increases at the rate of 1% per annum, so that by the end of 4th decade nearly three fourth of individuals in developed countries and 100% in developing countries have become infected with CMV. The present study is not in close agreement with that of Griffith and Baboonian[10]. The step wise increase might be due to increase in sexual promisity with lack of knowledge about protective measures. Other risk factors might be sexual behavior, health care behavior which are directly related to the probability of exposure to STDS and infections following exposure. The variable seroprevalance of CMV [37.5-100%] among HIV negative patients of different age groups might be due to inadequate no of cases reported in our study.(Table-1)

The present study was an agreement with the study of Luby JP et al which inferred by the higher prevalence of antibodies of CMV were observed in females. Most of the CMV isolates [88%] were from the age 15-24 years. In the present study the females with HIV shown 71 % CMV and HIV negatives had 50% CMV depicting lower incidence in non-HIV. Factors contributing to the high prevalence of CMV in females are due to cervical carrier state, immune suppressive state, trauma in multiple pregnancy and multiple partners. Low prevalence of CMV might be due to immunocompetency in both the sexes. Our study is in agreement with the above mention study[11].

The present study showed seroprevalance of CMV [78%] in the HIV positive employee groups and 50% in the HIV negative group. Day care centre employees appear to be at greater risk than hospital and other health care provider, this may be due to increase emphasis on personal hygiene in the health care setting[12] day care centre employees are at increased risk for acquiring CMV, because children transmit CMV to their care takers[13] this an agreement with above mentioned study. The high influence of CMV in employees group has been noticed due to their staying away from family on occupational grounds leading to extra marital sex. (Table-3)

Laborers who migrate from rural to urban areas have more economic independence , during wage free days prostitution may emerge as adoptive response and play a social factor for the spread of STD due to lack of awareness and failure to use condom. Students are in the more sexually active age group. They have exposure to social networks, pornography, and peer group. They lack supervision, due to staying away from family may indulge in drug abuse, sexual adventurism without knowing the consequences. Non sexual transmission also plays role in the student community as they share usable items and live intimately especially in hostels. A less seroprevalance of CMV, about 50% was observed in all the groups who were HIV negatives. This might be due to immune competency.(Table-3)

Table 4 showed the seroprevalance of CMV in relation to the educational status. The high prevalence of CMV 69% has been observed among the lower educational status patients;67.8% among uneducated. 40% have been observed among higher educational patients with HIV Positive patients. The similar type of picture have been observed among HIV negative patients with 60% in the lower, 56% in the uneducated and 46% in the higher educated group. It has been mentioned by L.G. Jhonson that the CMV antibody prevalence is highest in the developing countries and in the areas where the people are living in the crowded places[14]. More than 90% of the population is seropositive for CMV in the under developed countries because of lower education, poverty ,which ultimately result in body contact with infected secretions[15]. Higher educated people know the usage of barrier methods to prevent STDS they have better personal hygiene and knowledge of STDS.

The uneducated people live in low socio economic condition with lack of knowledge about the usage of condom and less access to the medical facility. Prevalence of CMV in under developed countries where more than 90% of the population are seropositive for CMV by the age of two years due to overcrowding, breast feeding for longer periods and repeated contacts with body fluids.

In our study hetero-sexual mode of transmission was reported to be a major type of sexual activity. The mode of transmission is bidirectional hetero-sexual spread in our society. The risk factors associated with CMV among hetero-sexuals include multiple partners, sex with prostitutes. King K Homes states that CMV prevalence among hetero-sexuals 38 out of 70 were noticed (54.3%). [16,17] our present study is close agreement[67.6%] with the study mentioned above. Knox G E *et al* in their study of subclinical CMV and HSV infections say that the homosexual men have antibody prevalence of 94% compared to 54% in the heterosexual men attending our op. [17]. This study is not in agreement with our present study. King K Holmes states that the antibody to CMV was detected in 130 of 139 [93.5%] homosexuals[16]. The present study does not coincide with the above literature and this may be due to low incidence of homosexuality, which is probably more in the western world. In the present study the prevalence of CMV is more in the heterosexuals than in the homosexuals which is not in agreement with the world wild studies because only 2 patients in 105 gave the history of homosexuality which is inadequate figure to account for study.53.3% of CMV prevalence in HIV negative heterosexuals might be due to immunocompetency. 0% prevalence among homo and bisexuals might be due to low number of patients in this study [4 out of 105].(Table-5)

The highest prevalence of CMV [71.4%] in patients with single partner [spouse] might be due to their denial of extra marital sex due to social stigma attached with polygamy. The high prevalence of CMV [68.7%] was observed in patients having more than 5 sex partners and 23% in patients having between 2-5. Hansfield HH *et al* observed shedding of CMV and raised antibody titers correlated with number of sex partners, STDs which is in aggrement with my present study[18]. The high prevalence of CMV in HIV negative patients might be due to low socio economic factors, poor hygiene, overcrowding and non sexual modes of transmission. The 0% prevalence of CMV in the poor patients with more than 5 sex partners might be due to their immunocompetency and numbers of patients in this group were low. The present study showed high prevalence of CMV among high risk and non high risk group which is not in total agreement with the above studies. Their HIV positive patients status explains its high prevalence in the non risk group of patients with single partner. The risk of exposure to STDs is directly associated with no of sexual partners. The non-linear increase in STDs risk with increase in number of partners is well documented. The marginal increase in STD risk suddenly multiplies as the number of sex partners reaches certain threshold levels (Table-6)

The present study shown increased prevalence of CMV antibodies among the patients with STDs like secondary syphilis, gonococcal urethritis, HSV and AIDS. Studies examining the association of CMV and STDs have demonstrated high prevalence of CMV in women evaluated for STDs [83%] when compared to the controlled population [50%].

Drew *et al* and Conrod *et al* noticed that CMV infection is more common in patients attending DVL clinics than in the general population. The rate of isolation of CMV from the cervical secretions was higher [13.3%] in the suspected STDs vs controls[0%][19-21]. Clamydia was isolated from the cervices of CMV positives 14% vs 3%CMV negatives[13].The present study is in agreement with that of Jordan *et al* and Drew et al . The present study showed 81.5% of CMV seroprevalance among the AIDS patients which was in close agreement with previous studies[20].This high prevalence might be due to immune deficiency and non-HIV group. Factors like socio economic conditions might play a role.(Table-7)

Conclusion

The high seroprevalance of CMV was reported in HIV positive patients in the sexually active age group of 16 to 49 years seroprevalance of CMV In HIV positive patients was higher in females than in males. Employees outmarked CMV sero positivity in HIV positive group of patients. The lower educated and uneducated HIV patients showed higher prevalence of CMV than the higher educated. Heterosexual HIV positive patients, showed most CMV prevalence than homo and bisexuals. CMV seroprevalance was higher in the HIV positive patients with single sex partners than multiple sex partners.CMV was highly prevalent in secondary syphilis, gonorrhea and HIV-AIDS patients.

In the HIV negative group the high seroprevalance of CMV was reported in patients with age group of 16 to59 years, married, males, laborers and low uneducated patients.It was more common in heterosexuals, spouses and in patients exposed to

multiple partners. No seroprevalance of CMV is seen in Patients with STD.

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