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Research Article

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ABSTRACT

Cytomegalovirus is a virus of paradoxes and can be a potential killer or a silent lifelong companion. The CMV infection in immunocompromised patients carries high morbidity and mortality. CMV infection is a common opportunistic viral infection among HIV/AIDS patients. This research therefore aimed at Studying Cytomegalovirus infection among HIV Positive Patients Attending Infectious Diseases Hospital, Kano, to ascertain the seroprevalence of specific CMV IgM antibodies among HIV positive patients and to correlate the infection rate with immune status (CD^+_4count) of the patients. A total of 207 clients who were reactive to HIV-1/HIV-2 antibodies were enrolled in the study. Sera samples were screened serologically for the presence of specific CMV IgM antibodies by using microwell ELISA kits manufactured by Immunodiagnostics Inc. Out of 207 HIV positive patients, 27 (13.0%) were seroreactive to the specific CMV IgM antibodies of which 9 (4.3%) were males and 18 (8.7%) were females. Patients with low CD^+_4 lymphocyte(< 100 cells/µl) were more infected by CMV.-High seroprevalence of specific CMV IgM antibodies was found among HIV patients and therefore monitoring of HIV patients with low CD^+_4 counts for the presence of specific CMV IgM antibodies may be of paramount importance to identify those at risk of CMV disease so as to carry prophylactic treatment before they develop clinical manifestation of CMV disease (end organ disease).

Keywords: CD^+_4 Cells, Cytomegallovirus, Human Immunodeficiency Virus, IgM Antibodies, Infection, Seroprevalence.

INTRODUCTION

Cytomegalovirus (CMV) is ubiquitous herpes virus that generally causes asymptomatic or mildly symptomatic infections in immunocompetent hosts. In contrast, the CMV infection in immunocompromised patients carries high morbidity and mortality (Springer and Weinberg, 2004). All herpes viruses share a characteristics ability to remain latent within the body over a long period (Ryan and Ray, 2004).

Human Immunodeficiency Virus (HIV) causes progressive impairment of the body's cellular immune system leading to increased susceptibility to infections and tumours, and a fatal condition known as Acquired Immunodeficiency Syndrome (AIDS) (Cheesbrough, 2005). HIV infects cells bearing the CD4 antigen receptor, the most important being T – helper lymphocyte (CD4 T = cells). These cells regulate cellular and humoral immunity by interacting with other T – lymphocytes, B – lymphocytes, macrophages and natural killer cells. When CD^+_4 positive T – cells are depleted, immune defences are weakened (Cheesbrough, 2005).

Cytomegalovirus (CMV) is a widely distributed opportunistic agent seen with AIDS (Akinbami *et al*., 2010).It is a beta – herpesvirus; the major cause of non – Epstein – Barr virus infectious mononucleosis in the general population and an important pathogen in immune-compromised hosts, including patients with AIDS, 'neonates and the transplant recipients (Krech, 1973). In most people with a fully functional immune system, the initial infection with CMV may cause a mild flu like illness and later the virus remains dormant. A damaged immune system permits the reactivation of CMV. A synergistic effect may worsen the progression in HIV infected persons (Chakravarti *et al.,* 2009). During advanced AIDS, CMV can produce debilitating end – organ disease (EOD) including retinitis, colitis, and pneumonitis. Previous to the HAART (highly active antiretroviral therapy) era, some studies observed that the rates of the CMV EOD among the patients with advanced HIV infection were approximately 40% or greater (Basawaraju *et al*., 2011). With the advent of HAART, the incidence of the CMV EOD has reduced (Basawaraju *et al*., 2011).

Sexual transmission appears to be the most common route of infection in adults, though CMV can also be spread through Oropharyngeal secretions, urine, breast milk and blood (Akinbami *et al*., 2010). Most patients with AIDS who develop clinical signs and symptoms of CMV infection probably have reactivation of previous infection rather than primary infection (Klatt and Shibata, 1988).

The prevalence of HIV/AIDS in sub – Saharan Africa is high but, the description of CMV infection as an opportunistic infection amongst patients is scanty (Akinbami *et al*., 2010). Akinsola *et al*. (1997) have reported a few cases of CMV retinitis in HIV infected Nigerians.

Antibody testing can be used to determine if someone has had recent or past exposure. IgM antibodies are the first to be produced by the antibody in response to a CMV infection. They are present in most individuals within a week or two after the initial exposure. On the other hand, IgG antibodies are produced by the body several weeks after the initial infection. Antibody testing and viral CMV detection may be used to help diagnose primary CMV infection in young adults, pregnant women, and some immunocompromised people. By comparing the presence or absence of IgG and/or IgM in the sample, active and latent CMV infection can be ascertained (Lab. Test online, 2012). Hence, the aim of this study was to determine the presence of specific CMV IgM antibodies in immunocompromised subjects.

MATERIALS AND METHODS

This cross sectional study was carried out at Infectious Diseases Hospital (IDH), Kano. A heterogenous two hundred and seven (207) HIV – positive volunteers that filled informed consent form were enrolled into the investigation from January, 2011 to December 2011 after obtaining ethical clearance from the State Hospital Management Board ethical committee irrespective of their sex, age, educational and socioeconomic background. There were no patients that received primary or secondary CMV prophylaxis as CMV prophylaxis are often not administered in Nigeria.

Five millilitres of blood was collected into sterile plain bottle, the samples were centrifuged at 3000 rpm for 5 minutes, sera separated into sterile bottles on each collection day, for storage at -20^0C prior to the time when the assay was carried out. Another 5ml was collected into EDTA bottle for CD_4 counts at the same day of collection. Screening for CMV IgM specific antibodies was done using commercial ELISA kit.

The cut-off optical density (O.D) was obtained in accordance with the manufacturer's instructions, the CMV index of the samples was calculated by dividing the O.D value of each of the samples with the obtained Cut-off O.D value (C.OD).

S/C.OD	**Interpretation**
CMV index<0.90	Negative
CMV index 1.0 and above	Positive

CD^+_4 Estimation

CD_4 was determined using an automated Cyflow CD_4^+ cell counter. Twenty microlitre (20ul) $_{CD}{}^+_4$perierythene antibody was added into partec test tube (Rohren tube) followed by twenty microlitre (20ul) of well mixed whole blood, mixed gently and incubated in the dark for 15 minutes at room temperature. Eight hundred microlitre (800ul) of CD^+_4buffer was added and also mixed gently. The tube was then plugged on the sensor for counting.

RESULTS

A total of 207 HIV positive patients were enrolled in the study of which 70 (33.8%) were males while 137 (66.2%) were females. Total number of positive cases was found to be 27(13%).The infective/reactive rate was significantly higher among females 18 (8.7%) than in males 9 (4.3%).

Table 1 summarizes percentage frequency distribution of the studied population. Out of the 207 patients screened for the study, 27(13.0%) were reactive to specific CMV IgM antibody whereas 180 (87%) were not.

Table 2 indicates the distribution of specific CMV IgM antibodies in relation to sex; among the male respondents, 9 (4.3%) were reactive while 61(29.5%) were non reactive. Among the females, 18(8.7%) were reactive and 119(57.5%) were non reactive. The infective/reactive rate was significantly higher among females 18 (8.7%) than in males 9 (4.3%) ($P > 0.01$) (Table 2).

The distribution of specific CMV IgM antibodies in relation to age was also ascertained (Table 3), the highest occurrence was found in the 21 – 30 age group 10 (4.8%) while the lowest being 11-20 and 61 – 70 age brackets 1(0.5%).

Distribution of specific CMV IgM among HIV – patients in relation to their CD^+_4 lymphocyte counts is presented in Table 4. Patients with CD^+_4 lymphocyte counts of less than 100 cells/µl shows the highest susceptibility to CMV with 19 (9.2%) followed by those that have CD^+_4 lymphocyte count of 100 - 350 cells/µl with 7 (3.4%) infected while the least susceptibility was shown by those that have CD^+_4 lymphocytes counts of greater than 350 cells/µl with only 1 (0.48%) patient infected with CMV.

Table 1: Distribution of Specific CMV IgM Antibodies among HIV Patients

	Frequency	Percentage (%)
Reactive	27	13
Nonreactive	180	87
Total	**207**	**100**

Table 2: Distribution of Specific CMV IgM Antibodies in Relation to Sex

Sex	Reactive (%)	Nonreactive (%)	Total (%)
Male	9 (4.3)	61 (29.5)	70 (33.8)
Female	18 (8.7)	119 (57.5)	137 (66.2)
Total	**27 (13.0)**	**180 (87.0)**	**207 (100.0)**

Table 3: Distribution of Specific CMV IgM Antibodies in Relation to age

Age group (years)	Reactive (%)	Nonreactive (%)
11 – 20	1 (0.5)	9 (4.3)
21 – 30	10 (4.8)	58 (28.1)
31 – 40	6 (2.9)	65 (31.4)
41 – 50	4 (1. 9)	35 (16.9)
51 – 60	5 (2.4)	11 (5.3)
61 – 70	1 (0.5)	1 (0.5)
71 – 80	0 (0.0)	0 (0.0)
81 – 90	0 (0.0)	1 (0.5)
Total (%)	**27 (13.0)**	**180 (87.0)**

Table 4: Distribution of Specific CMV IgM Antibodies in Relation to CD^+_4 Count of HIV Patients

CD^+_4 Count (cells/µl)	Reactive (%)	Non reactive (%)
< 100	19 (9.2)	36 17.4)
100 – 350	7 (3.4)	107 (51.7)
> 350	1 (0.48)	37 (17.9)
Total (%)	**27 (13.0%)**	**180 (87.0)**

DISCUSSIONS

The CMV active infection might be a marker of extremely severe immunosuppresion, which may ultimately lead to a fatal outcome in the patients. The presence of the IgM antibodies may be due to primary infection, reactivation or re-infection by CMV (Chakravarti *et al*., 2009).

In this study, the specific CMV IgM antibodies seropositivity was found to be 27(13%). This prevalence is on the high side when compared to developing countries (8.0-8.5%) (Ray and Mahajan, 1997; Hizal *et al*.,1972). It is equally higher than the world range (0 – 10%) (Turbadkar *et al.,* 2000). The prevalence rate is higher when compared to work done by Akinbami *et al.* (2010) (6.6%) in his study among immunocompromised (HIV) patients at Lagos University Teaching Hospital. It is high when compared to the work of Basawaraju *et al.* (2011) (9.52%) that carried out his study among AIDS patients in India. The prevalent rate does not correlate with those of Chakravarti *et al*. (2009); Chakravarti *et al*. (2010); Mujtaba *et al*. (2003); and Vajpayee et al. (2005) in India in which they have observed positivity rates of about 3 – 10%. It is slightly high when compared to the work done by Neusa *et al.* (1998) in Brazil among HIV infected prison inmates where prevalent rate of 11.36% was reported. It is however lower, when compared to the work done by Tsertsvadze *et al* (2002) where prevalent rate of 19 (14%) among HIV patients was reported. Racial differences between the populations, enormous cultural and economic differences between developed countries (where the study was previously carried out) and developing countries like Nigeria are valid factors that might be responsible for this variation in prevalent rate obtained as also reported by Neto *et al*. (2004); and Nishimura *et al*. (1999).

The study revealed that females living with HIV are more susceptible to specific CMV IgM antibodies than their male counterparts; female subjects showed high prevalent rate of 18 (8.7%) than males 9(4.3%). The infective/reactive rate was significantly higher among the females than in the males ($P > 0.01$).

Seropositivity of specific CMV IgM antibodies in relation to different age groups revealed that CMV antibodies are high between age groups 21 – 30 and 31 – 40 years. This finding is in concordance with the study conducted by Okwori *et al.* (2008). This trend could be attributed to the fact that the above mentioned age groups represent active and sexually matured youths with the tendency towards sexual promiscuity and its resultant likelihood of high infection rates (Zhong and Ma, 1999).

The result obtained in the study showed that, HIV patients with CD^+_4 count < 100 cell/µl showed high prevalence of specific CMV IgM antibodies which is in concordance with other studies that showed the risk of CMV disease is highest when the CD^+_4 count is < 100 cells/µl and it is rare when the count is greater than 100 cells/µl (Cunha *et al*. 2002). Likewise, it has been shown that CD^+_4 lymphocytes levels below 50 cells/µl are important markers in the prognosis of the clinical manifestation of CMV and that they also indicate a disease phase which is frequently defined as advanced AIDS (Chakravarti *et al.,* 2009). The correlation analysis between CD^+_4 lymphocytes count and specific CMV IgM antibodies distribution among HIV positive patients was found to be positive but non-significant.

CONCLUSION

The study reveals high prevalent rate (13%) of CMV IgM antibodies among HIV positive patients. Equally, it shows that the number of females living with HIV are higher (8.7%) than their male counterparts with prevalent rate of 4.3% and that CMV antibodies are highest among HIV patients with CD^+_4 count less than 100 cells/µl, hence, the distribution of the specific CMV IgM antibodies among studied population is high among HIV patients in the study population.

RECOMMENDATION

It is important that patients are tested for specific CMV IgM antibodies and also specific CMV IgG antibodies in order to identify those at risk of CMV disease that are HIV positive with low CD4+ counts**.**

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