CMV infection among HIV / AIDS patients in Iraq

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Summary:

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Background: *The aim of the study was to determine the prevalence of CMV infection among HIV / AIDS patients in relation to disease progression, and to study the mortality during the period of the study.*

Patients and Methods: *The study included 155 HIV/AIDS patients (148 HIV- infected and seven AIDS patients) and 122 apparently "healthy" controls. CMV (IgG and 1gM) antibodies were determined by ELISA. The patients were followed up for a period of nine months, and retested frequently for development of active CMV infection.*

Results: *The prevalence of CMV (IgG) antibodies in the HIV/AIDS patients was 100%. A significant higher prevalence of CMV (IgM) among AIDS patients (42.9%) than among HIV infected patients (0.0%) and "healthy" controls (0.8%). No deaths were reported among asymptomatic HIV infected patients while the mortality among AIDS patients was (42.9%). Only one patient (7.7%) out of 13 asymptomatic HIV infected developed active CMV infection 10 years later by testing for CMV (IgM) in 1991 and 2001.*

Conclusion: *Demonstration of active CMV is of prognostic value in detection of development of AIDS and survival of patients.*

Introduction:

In human immunodeficiency virus (HIV) - infected subjects, cytomegalovirus (CMV) was a major cause of opportunistic infection and associated with accelerated progression to Acquired Immunodeficiency Syndrome (AIDS) and death before the introduction of highly active antiretroviral therapy (HAART) [4]. Clinical syndromes

associated with CMV infection in AIDS patients have included diseases in almost every organ including eyes, central nervous system, liver, gut, adrenals, mouth, oesophagus and lungs .

In Iraq, the health authorities did not admit the existence of AIDS in the country till 1991. However, Iraq is still among the low prevalence countries for HIV / AIDS [6].

This work was carried out to study the prevalence of CMV among HIV / AIDS patients in relation to disease progression through development of active CMV infection, in addition to study mortality during the period of the study.

Materials and methods

A total of 277 subjects were tested for the presence of CMV antibodies (IgG and IgM) in their sera for a period of nine months from Jan. to Sept. 2001, inclusive. They included 155 HIV /AIDS patients (148 HIV- infected patients and seven AIDS patients) and 122 apparently "healthy control" (all without any clinical evidence of CMV infection or AIDS). HIV /AIDS patients were followed up for the period of the study and retested frequently for the development of active infection by detection of CMV (IgM) antibodies or demonstration of fourfold rise in IgG antibody titer'.

Serological data regarding CMV infection were available for 13 patients out of the HIV / AIDS patients were included in the study as they were tested for the presence of CMV (IgG and IgM) in 1991 for the first time.

The death rate was calculated for all HIV / AIDS patients during the period of the study.

Serum testing was carried out at the Central Public Health Laboratory, Baghdad, by enzyme linked immuno-sorbent assay (ELISA) using the commercially available kits (Biokit, Spain). The methods used were as described in the instruction sheets.

Statistical analysis was done using z test and Fisher's exact probability test. P value < 0.05 was considered as statistically significant.

Results:

The prevalence of CMV (IgG) antibodies in the HIV / AIDS patients was 100% which is significantly ($p < 0.01$) higher than in the "healthy" controls (92.6%). A significantly higher ($p < 0.01$) prevalence of CMV (IgM) antibodies among

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AIDS patients (42.9%) than among HIV - infected patients (0.0%) and "healthy" controls (0.8%) was, also, demonstrated. These findings are shown in Table 1.

Table 1. Prevalence of CMV antibodies (IgG and IgM) among HIV / AIDS patients and "healthy" controls.

Group	No. tested	CMV antibodies	
		IgG	IgM
		No. (%)	No. (%)
HIV patients	148	148 (100)	0 (0.0)
AIDS patients	7	7 (100)	3 (42.9)
"Healthy" controls	122	110 (92.6)	1 (0.8)

Only one of HIV - infected asymptomatic patients and one, also, of "healthy" controls (0.68% and 0.8%, respectively) developed active CMV infection (as detected by demonstration of four fold rise in IgG antibody titer in HIV patients and by detection of IgM antibodies in the "healthy" control while four (57.1%) AIDS patients developed active CMV infection demonstrated by detection of CMV (IgM) antibodies in three of them and by fourfold rise in CMV (IgG) antibody titer in the other. No deaths were reported among asymptomatic HIV - infected patients, while the mortality among AIDS patients was 42.9% (three out of seven). All dead AIDS patients had developed active CMV infection indicating that 75% (three out of four) of AIDS patients with active CMV infection died during study period. Statistical analysis showed a statistical difference ($p < 0.05$) in mortality among asymptomatic HIV - infected and AIDS patients. These results are shown in Table 2.

Table 2. Prevalence of active CMV infection and mortality among HIV – infected, AIDS patients and "healthy" controls.

Group	No. tested	Active CMV infection	Mortality
		No. (%)	No. (%)
HIV patients	148	1 (0.68) [1]	0 (0.0)
AIDS patients	7	4 (57.1) [2]	3 (42.9)
"Healthy" controls	122	1 (0.8) [3]	0 (0.0)

[1] detected by fourfold rise in IgG antibody titer.

[2] demonstrated by detection of IgM antibodies in three patients and by detection of fourfold rise in IgG antibody titer in the other.

[3] demonstrated by detection of IgM antibodies.

Table 3 shows that only one patient out of the 13 asymptomatic HIV - infected patients (7.7%) developed active CMV infection 10 years later by testing for CMV (1gM) antibodies in 1991 and 2001. The difference in the prevalence of CMV (IgM) antibodies is statistically significant ($p < 0.01$).

Table 3. Prevalence of CMV antibodies (IgG and IgM) among HIV – infected patients tested in 1991 and 2001.

Year	No. tested	CMV antibodies	
		IgG	IgM
		No. (%)	No. (%)
1991	13	13 (100)	0 (0.0)
2001	13	13 (100)	1 (7.7)

Discussion:

The finding that 92.6% of "healthy" controls had CMV infection is in agreement with the finding of other workers in Iraq , who reported a prevalence of 95.4% [7] and 96.4% [8]. Similar findings have been reported in other Arabian and developing countries, where standard of high hygiene are low and overcrowding is common [9-12]. In developed countries which enjoy a high standards of hygiene, the prevalence of CMV infection is lower than that in developing countries 9- 3

The health system in Iraq suffered from continued neglect particularly over the last two decades and budgetary allocations did not reflect population needs [6]. For this reason means for detection of CMV antigens or nucleic acids in tissue specimen, CMV culture of blood and urine or even biopsy which may reflect active infection rather than end- organ disease, and even sensitive polymerase chain reaction (PCR) [5,14] were not available. Therefore, development of active CMV infection was detected by testing for CMV (IgM) antibodies or demonstration of fourfold rise in IgG antibody titer [5].

Fourfold rise in CMV (IgG) antibody or detection of IgM antibody was demonstrated in 57.1% of AIDS patients in comparison with 0.68% and 0.8% of HIV- infected subjects and "healthy" control, respectively. A significant difference in the prevalence of active CMV infection was demonstrated between AIDS patients and HIV-infected subjects. This finding was expected due to reactivation of latent CMV infection in severely immunosuppressed patients [1,5].

This study revealed that 42.9% of AIDS patients and that 75% of those who developed active CMV infection have died during the nine months period of the study indicating that CMV is a life threatening viral infection in advanced AIDS patients leading to death of those patients within few months. On the other hand no death was reported among HIV asymptomatic subjects. Other workers have reported that disseminated CMV infection was the most frequent life threatening opportunistic viral infection in patients with AIDS [15-17]. The finding of high mortality of AIDS patients within nine months in those who developed active CMV infection is in agreement with that of other workers [15.16] who found that CMV co-infection increase the risk of HIV disease progression.

Our finding that only 7.7% of the 13 HIV - infected patients developed active CMV infection (as demonstrated by detection of IgM antibodies) after 10 years period of first testing for presence of CMV (IgG and IgM) indicate that these patients had developed AIDS due to progressive immunosuppression . This result is comparable with that of Gallant et al [17]. Other workers stated that CMV virernia was the strongest predictor of death in AIDS patients 17-19.

It can be concluded from this study that detection of active CMV is of prognostic value in detection of development of AIDS and survival of patients.

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