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Co-Infection of Cytomegalovirus infection among newly diagnosed HIV infected patients at R.I.M.S. Imphal, Hospital, Manipur

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I. Introduction

Human cytomegalovirus (CMV) is a vernacular name of the human herpesvirus 5, a highly host specific virus of the Herpesviridae family. In 1956, Margaret G. Smith recovered the first isolate from the submaxillary gland tissue of a dead infant. It is a enveloped virus with a double stranded DNA genome.

Initial infection with Cytomegalovirus occurs during childhood.Transmission is via body fluids such as tears, urine, saliva, milk, semen, vaginal secretion also by organ transplants, transplacentally or by blood transfusions. CMV poses an important public health problem as it may cause morbidity & mortality in congenitally infected newborn and immunocompromised patients, most notably transplant recipients and HIV infected persons. The magnitude of the problem in India has not been adequately investigated and still remains a major health problem.[1] Like other herpes viruses this virus has a natural ability to enter latency after asymptomatic or mild symptomatic primary infection in immunocompetent host. [2] In immunocompromised setting such as HIV/AIDS the virus undergoes periodic episodes of reactivation [3,4].

Clinical manifestations such as *chrioretinitis, esophagitis, colitis, pneumonitis, adrenalitis* and neurological disorders have been observed in upto 40% of HIV-infected patients that are not on highly active antiretroviral therapy (HAART).[6] Their counterparts who are on HAART tend to have lower incidence of CMV disease[7]. 70% of the Hospital deaths were HIV related deaths and many of them was diagnosed to be having infections with CMV[9].

CMV is a member of the herpesvirus group. The human herpesvirus group member comprises of Alpha herpesviruses, ,Betaherpes viruses and gammaherpes viruses [9]. CD4+T cells and CD3+ T cells, natural killer cells & antibodies that reorganise surface antigens play a crucial role in the immune response to CMV,preventing the development of CMV disease in the immunocompetent host.[10] A synergistic effect may worsen the immunologic profile and could potentially translate into a more rapid disease progression as transactivation of HIV-1 gene expression and release of a rays of different cytokines by CMV infected-cells could activate the latent HIV proviral DNA . The risk of CMV is highest when CD4 counts are below 50 cells/µl and is rare with more than 100 cells/ µl.[.....] Upto 30% of people develop retinitis and in additional 5-10% develop disease in other organs[11].Usually decrease in CD4+T cell counts leads to reactivation of these infections. Post mortem studies have shown that CMV viral load is higher than HIV load and is suspected to be the cause of death in most of patients already diagnosed as AIDS[13]. The CMV infection is endemic throughout the world. The infection with CMV is more common in the developing nations and among the people who belong to the low socioeconomic section of the society. The CMV IgG antibodies are present in long standing CMV seropositive people but the clinical manifestation of the CMV disease donot generally present until the CD4 count drops below 100 cells/cumm[16] The CMV active infection might be a marker of extremely severe immunosuppression which may ultimately lead to a fatal outcome in the patients. The reactivation is indicated by the presence of IgM antibodies which also indicates the acute infection in such persons. There is reactivation of the CMV in healthy and immunosuppressed HIV positive patients. Therefore, the early diagnosis of the reactivation of the virus is useful before the development of the clinical manisfestations[16]. Human Cytomegalovirus co-infection of patients with HIV infection occurs frequently probably because of their similar modes of transmission. Blindness is a common feature in 20% of AIDS patients when CD4+ count is less than 50 cells/cumn. There may be occurrence of dementia, encephalitis, oesophagitis, enterocolitis. The drug regimen for both primary prophylaxis, prevention of recurrence of HCMV infections in AIDS include ganciclovir, cidofovir, foscarnet. Oral valganciclovir is also licensed for the treatment of HCMV chorioretinites[17]. The magnitude of this problem in India and particularly in Manipur has not been adequately investigated and it is still a major health problem warranting strong preventive measures as Manipur is having the epidemic of HIV

and AIDS, this study will throw light in the occurrence of HIV and CMV and also the importance to start prophylactic and curative measures against CMV in this state .

Aims And Objects

1.To study the co infection between Cytomegalovirus and HIV infection
2.To study the correlation between coinfected patients with the CD 4+ T lymphocytes

II. Materials And Methods

STUDY DESIGN:Cross-sectional study
CTC
SETTING:The study will be conducted in the Department of Microbiology,RIMS,Imphal

DURATION:Study will be conducted for one and ahalf calendar years from November 2013 to April 2015.

STUDY POPULATION:HIV infected patients attending the FACS Count centre and ICTC,RIMS,Imphal

INCLUSION CRITERIA: 1.Seropositive cases of HIV infection

EXCLUSION CRITERIA: 1.Patients who refused to participate in the study

2.Paediatric age group

Source of controls:

1. Normal healthy healthcare workers
2. Medical students

Diagnosis of HIV infection:

The clients/patients attending the ICTC were given pre test counselling.Necessary consent was also taken. Blood sample(5 ml.) was taken and sera was separated from the blood samples. Strategy III of testing by 3 rapid test was done as recommended by National AIDS Control Organization, Government of India.[36]

The three rapid kits used are:

1. Comb AIDS
2. Parikhit
3. AIDScan

Necessary post test counselling was given at the time of giving the reports.

CD4 Testing:

The blood samples will be collected from the seropositive cases for CD4 testing.

The estimation of the CD4 will be done by using Fluorescent Activated Cell Sorter (FACS) count system (Becton Dickinson Immunocytometry systems, San Jose, CA 95131-1807). The procedure for the testing was as per manufacturers guidelines.[37]

Cytomegalovirus IgG antibody & IgM antibody:

The blood sample(5 ml) was collected from the patients and sera was separated. Cytomegalo IgG antibody and IgM antibody was detected using the MAGLUMI CMV IgM (CLIA) and MAGLUMI CMV IgG (CLIA) kits.The procedure of the test was as per manufacturers guideline

Analysis:

Descriptive statistical analysis will be carried out as per needed depending on the type of study at the time of completion of study.

Consent:

Informed consent will be taken from all the participants.In case of minor informed consent will be taken from the guardians or parents.Privacy and confidentiality will be maintained in all cases .

Ethical Issues:

Ethical approval wll be taken from the institutional ethics committee,RIMS,Imphal before the beginning of the study.

III. Results

- Commonest age group was 30 to 40 years which is 42.3% among the males and 43.7% among the females.
- The maximum cases i.e 62(48.4%) was among the risk groups belonging to the spouse of the seropositive cases followed by IDUs(38.2%)

96.8% of the study groups was positive for CMV IgG which is slightly higher than their study.
prevalence of CMV Ig M among the IDUs is 42.1%

- In the present study CMV IgM positivity was found in the CD4 count :CD4< 50 :2(10.5%),CD4 count 51-100:1(5.2%), CD4 count 101-200:8(42.1%),CD4 count 201-300:6(31.5%),CD4 count 301-350:1(5.2%),CD4 count >350: 1(5.2%)

RESULTS

Table: 1

Age and Sex distribution of the study groups (n=128)

Age groups	Male	percentage	Female	percentage
2 – 20	3	4.6%	2	3.1%
> 20 – 30	13	20.3%	19	29.68%
> 30 - 40	27	42.3%	28	43.75%
> 40 – 50	18	28.1%	12	18.75%
> 50 – 60	2	3.1%	3	4.68%
> 60 & above	1	1.5%	0	

Table: 2

Risk group among the study groups(n=128)

Risk group	Number	percentage
Spouse of seropositivity cases	62	48.4%
IDUs	49	38.28%
Heterosexual	13	10.1%
Parent to child transmission	4	3.1%

Table: 3

Gender distribution of CMV seropositive cases among the study groups

Gender	CMV IgG seropositive	CMV IgM seropositive
Male	62(50%)	12(63.1%)
Female	62(50%)	7(36.8%)

Table: 5

CMV seropositivity among the cases & control

	Study groups n = 128	Controls n = 54
IgM	19 (14.8 %)	-
IgG	124 (96.8 %)	34 (62.9 %)

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CMV seropositivity among the cases & control

	Study groups n = 128	Controls n = 54
IgM	19 (14.8 %)	-
IgG	124 (96.8 %)	34 (62.9 %)

Table: 6

- Correlation between CD4 status & CMV seropositivity amoung the study groups

CMV seropositivity	CD4 count < 50	CD4 count 50 - 100	CD4 count 101 - 200	CD4 count 201-300	CD4 count 301 -350	CD4 count >350
IgM +ve	**2**	**1**	**8**	**6**	**1**	**1**
IgG + ve	**6**	**5**	**13**	**25**	**16**	**59**

IV. Discussion

- Commonest age group was 30 to 40 years which is 42.3% among the males and 43.7% among the females.
- The maximum cases i.e 62(48.4%) was among the risk groups belonging to the spouse of the seropositive cases followed by IDUs(38.2%)
- A study at Ghana by Compston LI et al[18] found that more than 90% of the heterosexually acquired HIV infected persons are positive for CMV IgG.In the present study 96.8% of the study groups was positive for CMV IgG which is slightly higher than their study.
- A study by Shepp DH et [19] found that the prevalence of CMV IgM among the IDUs was 67% while the present study found the prevalence of CMV Ig M among the IDUs is 42.1% which is lower in the present study.

- In the present study CMV IgM positivity was found in the CD4 count :CD4< 50 :2(10.5%),CD4 count 51-100:1(5.2%), CD4 count 101-200:8(42.1%),CD4 count 201-300:6(31.5%),CD4 count 301-350:1(5.2%),CD4 count >350: 1(5.2%)

V. Conclusion

- Primary prophylaxis by antiviral drugs i.e ganciclovir,cidofovir,valganciclovir etc can be given based on CD4 count which should be started at a higher level of CD4 cell count which is shown by our study.
- Early diagnosis is also needed to control the rapid progression of HIV as con infection with CMV also brings about the rapid progression of HIV.
- Early diagnosis of CMV Ig M antibodies and CD4 estimation will help in early detection of infection or reactivation of virus before the development of clinical manifestations.It will guide the clinicians for chemoprophylaxis and further management of the of the the opportunistic infection by CMV in PLWHA (People living with HIV and AIDS)

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