Original   Article

Study of cardiac manifestations in patients with Human Immunodeficiency Virus Infection in West Bengal

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This case control study was done on 40 human immunodeficiency virus infected patients of North Bengal Medical College and Hospital compared with a healthy matched control group. The study was conducted to assess the cardiac chamber anomalies along with changes in pericardium. It was also aimed to check for lipid abnormalities and compare them with echocardiographic abnormalities and to document the relationship between CD_4 counts and echocardiographic abnormalities. Age and sex distribution and opportunistic infections were also studied. The mean age was found to be 34.15 years while maximum number of patients was in the age group 31- 40 years. Males outnumbered the females. Tuberculosis was the commonest opportunistic infections followed by Candidiasis. 85% of patients were asymptomatic from the cardiac point of view. It was obvious that total cholesterol, HDL cholesterol and LDL cholesterol of the study group were significantly lower than the control group though this was not the case with triglyceride levels. The study showed a positive correlation between CD_4 count and total cholesterol, HDL cholesterol and LDL cholesterol while inverse relation was seen with triglyceride and VLDL cholesterol. Pericardial effusion was the commonest echocardiographic finding. Low HDL cholesterol and LDL cholesterol were more significantly associated with pericardial effusion while low total cholesterol and high triglyceride were more significantly associated with diastolic dysfunction. Thus lipid levels could serve as markers for cardiac dysfunction where echocardiography is not available.

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In 1981, when the world was alerted to the first case of Acquired Immunodeficiency Syndrome (AIDS), no one could have imagined that it would claim more than 20 million lives in a matter of 20 years. The first report described 5 young homosexual men in whom a rare disease, *Pneumocystis carinii* pneumonia had developed. Each patient had abnormal ratios of lymphocyte sub-groups and was actively shedding cytomegalovirus[1]. In 1983, Human Immunodeficiency Virus was isolated from a patient with lymphadeno-pathy, and by 1984, it was demonstrated clearly to be the causative agent of AIDS.

Cardiac involvement is more frequent in the more advanced stages of infection and in patients with lower CD_4 counts. During the 1990s, the disease was transformed for many patients specially in industrialized nations from a predictably fatal infection to a chronic condition requiring daily medication and occasional visits to the doctor's chamber[2].

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Editor's Comment :
- Low LDL levels and low HDL levels were more significantly associated with pericardial effusion while low total cholesterol and high triglycerides were more significantly associated with diastolic dysfunction. Thus lipid levels could be used as markers for cardiac dysfunction where echo-cardigraphy is not available.

AIMS AND OBJECTIVES

1. To study cardiac chamber anomalies including left or right ventricular hypertrophy, and left ventricular systolic and diastolic dysfunction.

2. To note changes in the pericardium, myocardium and endocardium.

3. To check for lipid abnormalities and compare them with echocardiographic abnormalities.

4. To decipher any relationship between CD_4 counts and echocardiographic abnormalities.

MATERIALS AND METHODS

Study Area :

North Bengal Medical College and Hospital, Sushrutanagar, Darjeeling.

Study Population :

Human Immunodeficiency Virus positive patients residing in North Bengal.

Selection Criteria :

1. Age > 20 years.

2. Sex - Male and Female

3. Western Blot confirmed cases after preliminary ELISA was positive.

4. Cardiac manifestations not attributable to any other cause.

Exclusion Criteria :

1. Addiction to alcohol or cocaine.

2. Family history of cardiomyopathy, pericarditis or storage disorder.

3. History of drug intake such as procainamide, hydralazine, phenytoin, methysergide, doxorubicin, etc.

4. History of zidovudine and protease inhibitor group of antiretroviral drugs intake.

5. History of radiation exposure.

6. History of relevant trauma.

7. Patients suffering from acute myocardial infarction, uraemia, neoplasia or other confounding illnesses.

8. Pregnant and peripartum women.

9. Electrolyte abnormalities.

Sampling :

Random.

Study Group :

40 human immunodeficiency virus infected patients with or without symptoms.

Control Group :

Healthy matched control of 20 individuals not infected with human immunodeficiency virus.

Duration of Study :

1 year (2017-2018).

Identification data was collected and detailed history taken. This was followed by general examination and systemic physical examination. Routine investigations and special tests were done. Screening was done for opportunistic infections . Principle of flow cytometry was used for CD_4 counts.

Statistical Analysis :

Mean and standard deviations were calculated. Tests of significance used were a) Standard error of difference between two means b) Standard error of difference between two proportions c) Paired t-test d) Chi-square test e) Coefficient of correlation.

OBSERVATIONS

In our study group, 8 patients were symptom free. Mean age was 34.15 years. Maximum number of patients was in the age group 31- 40years. In each decade, males outnumbered the females (Table 1).

It was more common in goldsmiths(n=8) and drivers(n=5). In our study group, 80% of the patients were suffering from opportunistic infections. The commonest opportunistic infection was Tuberculosis (27.5%) followed by Candidiasis (20%) (Table 2).

There was a significant difference between the total cholesterol level of the study and the control group (t<0.01).

The correlation co-efficient (r) between CD_4 count and total cholesterol was 0.31 ie, there was a positive correlation. As CD_4 count diminished, Tc (Total cholesterol) also diminished and vice-versa. However, there was no statistically significant difference in CD_4 counts between patients with low cholesterol and those without low cholesterol, though there was a positive correlation between cholesterol levels and CD_4 count. This slight apparent paradox may be explained by the fact that most of our cases were newly detected or within the first few years of detection. It is well known that hypocholesterolaemia is an early manifestation of Human immunodeficiency virus infection and CD4 count might not have decreased proportionately to that extent.

By Chi-square test, diastolic dysfunction was significantly more in HIV infected patients with low Total Cholesterol (P<0.001). Similarly, low total cholesterol was significantly associated with pericardial effusion. However, there was no significant difference between the two groups with respect to systolic dysfunction (P>0.05).

Paired t-test showed that there was no significant difference in the triglyceride levels of the study and control groups. This was perhaps because increases in triglyceride levels occur at a later stage of HIV infection while most of our cases were newly detected or were within the first few years of detection.

The correlation coefficient (r) between CD_4 count and TG was -0.3 ie, there was a negative correlation between the two. However, there was a statistical

Table 1 — *Distribution of patients according to age*

Class interval	Frequency
21-30	16
31-40	18
41-50	3
51-60	2
61-70	1

Table 2 — *Opportunistic Infection*

Opportunistic Infection	No. of patients	% of patients
Candidiasis	8	20
Tuberculosis	11	27.5
Pneumonia Inc. PCP	3	7.5
Bacillary Dysentery	2	5.0
Genital Herpes	1	2.5
Syphilis	1	2.5
Toxoplasmosis	1	2.5
Cryptococcal Meningitis	1	2.5
Sinusitis	1	2.5
Hepatitis	1	2.5
Taenia Corporis	1	2.5

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difference in the CD_4 cell counts between patients with high TG levels and those with normal TG levels. Patients with high triglyceride had significantly more evidence of diastolic dysfunction (P<0.02). Pericardial effusion was significantly more common in the high triglyceride group. However, systolic dysfunction was not affected by the triglyceride levels.

HDL-cholesterol levels in the study group were significantly different from the control group (t<0.01). The correlation coefficient (r) between CD_4 count and HDL was +0.42, indicating a positive correlation between the two. There was a statistically significant difference in the CD_4 levels of the low HDL and the normal HDL level groups. Patients with low HDL levels were significantly more likely to have diastolic dysfunction as compared to those with normal HDL levels (P<0.01). Pericardial effusion was significantly associated with the low HDL group and the association was stronger than that with diastolic dysfunction (P<0.001). Again there was no significant difference between the low and the normal HDL groups with regard to systolic dysfunction.

The LDL- cholesterol levels in our study group were significantly different from those of the matched controls (t<0.01). The correlation coefficient (r) between CD_4 count and LDL was +0.38 indicating a positive correlation between the two. Diastolic dysfunction was significantly more common in those with low LDL than in those without so (P<0.01). Low LDL was significantly associated with pericardial effusion and the association was stronger as compared to diastolic dysfunction (P<0.001). However, there was no significant difference between the low and the normal LDL levels as far as systolic dysfunction was concerned.

Distribution of patients with echocardiographic manifestations in particular CD_4 range :

81.48% patients with CD_4 counts less than 200/µl had echocardiographic manifestations while only 7.69% of patients with CD_4 counts greater than 200/µl had echocardiographic manifestations. Since observed difference is more than 2 times the standard error of difference, the difference is statistically significant and not merely due to chance.

Discussion

Mean Age :

George J et al[3] conducted a study on 60 HIV infected patients and found a mean age of 30.3 years. K.Kothari et al's[4] study of 30 patients found a mean age of 32.76± 8.11 years. 34.9 ± 12 years was the mean age in the study by Sircar et al[5]. Our study group had a mean age of 34.15 +/- 9.39 years.

Gender :

In almost all the studies including ours, there is a male preponderance. The exact reason is not known but perhaps females being home bound have less scope of high risk behavior.Also there may be a bias of doing HIV test more in male patients. Bogaert's J et al[6] from Rwanda, Africa reported one such study on 2824 adults of whom 1578 were men and 1246 women. (Ratio 1.26:1). A study in Edinburgh, U.K by Brettle et al[7] enrolled 680 patients of whom 476 were men and 204 were women, giving a ratio of 2.3:1.

Clinical Manifestations :

In a study by Fink et al[8], none of the 15 patients had clinical evidence of myocardial disease. However,on echocardiogram, almost all patients had cardiac dysfunction. Similarly, Levy et al[9], discovered cardiac abnormalities in 53% of his patients, though clinicians suspected none as having cardiac disease. Blanchard et al[10] found echocardiographic abnormalities in both symptomatic (52%) and asymptomatic (40%) patients. In our study, patients were asymptomatic from cardiologic point of view in 85% cases.

Lipids :

We compared our study group to a matched control group without HIV infection. It was obvious that total cholesterol, HDL cholesterol and LDL cholesterol of our study group were significantly lower than the control group. Hypocholesterolemia has been documented in various studies the world over[11, 12]. Authors opine that hypocholesterolemia occurs early in the course of HIV infection. This is well endorsed by our study comprising of mostly newly detected cases or cases within 1-2 years of detection.

Triglyceride levels in our study group were not significantly different from the control group (t>0.05). This was perhaps because hypertriglyceridemia occurs in the advanced stages of the disease as seen in studies by SA Mullamithai and A R Pazare[12]. Our study group comprised mostly of newly detected cases.

Low HDL levels as reported in our study were also reported from France[11] and Brazil[13]. However, a study from TNM College, Mumbai[12] did not find statistically different HDL levels compared to controls.

Our finding of low HDL is corroborated by C Fernandez- Miranda et al[14] and J. Constans et al[15]. Our study showed a positive correlation between CD_4 cell count and total cholesterol, HDL cholesterol and LDL cholesterol while inverse relation was seen with triglyceride and VLDL cholesterol. Similar conclusions were drawn by A Treitinger and C. Spada et al[13]. J

Ducobu and MC Payen also opined that lipid changes are proportional to the lowering of CD_4, which reflects the severity of infections [11].

Echocardiographic Abnormalities :

In our study group, 24 patients (60%) showed echocardiographic manifestations though only 6 (15%) had cardiac symptoms. Among them systolic dysfunction was present in 8 (20%), while diastolic dysfunction in 15 (37.5%). Systolic dysfunction was mild while diastolic dysfunction moderate in 3 (7.5%) and severe in 1 (2.5%). 2 patients (5%) had both systolic and diastolic dysfunction. Mitral regurgitation was present in 4 cases (10%) while tricuspid regurgitation in 7 cases (17.5%). 2 patients suffered from hypokinesia of which 1 was global in distribution. There were 2 cases of atrial septal defect which were perhaps incidental findings. Pericardial effusion was the commonest finding accounting for 40% of the patients.

A study by G. Minardi *et al* from Italy[16] on HIV positive subjects showed a cardiac involvement in 75% of HIV infected patients; 35% had myocardial dysfunction, 37% pericardial disease, 31% infective pericarditis. H.M.Steffan *et al*[17] studied 128 patients (28%): small to moderate pericardial effusions (n=34) and left ventricular dilatation (n=5).

CD_4 Count and Echocardiography :

81.48% of our patients with CD_4 counts less than 200/µl had echocardiographic manifestations compared with only 7.69% of patients with CD_4 count more than 200/ µl. There was a statistically significant difference between the two. GL Werneck and E. T. Mesquita et al from Brazil reported that patients with a more advanced infection (those with a CD_4 count less than 500/mm^{3}) had a significantly abnormal LV systolic function and a higher incidence of pericardial effusion and mitral regurgitation[18].

Lipids *versus* Echocardiographic Findings :

Hypocholesterolemia ($\leq$130mg/dl) was significantly associated with diastolic dysfunction (P<0.001) and pericardial effusion (P<0.02). Significant association of high triglyceride (>150mg/dl) with diastolic dysfunction (P<0.02) and pericardial effusion (P< 0.05) was evident. Low HDL cholesterol level (<35mg/dl) had a significant association with diastolic dysfunction (P<0.01) and pericardial effusion (P<0.001). Low LDL cholesterol level (<100mg/dl) was significantly associated with diastolic dysfunction (P<0.01) and pericardial effusion (P<0.001).Thus low HDL cholesterol and LDL cholesterol are more significantly associated with pericardial effusion than diastolic dysfunction, while in low total cholesterol and high triglyceride it is just the opposite.

Thus total cholesterol and triglyceride could serve as markers for diastolic dysfunction while HDL cholesterol and LDL cholesterol could serve as markers for pericardial effusion where echocardiographic facilities are not available. However, more studies specially large scale ones with high statistical power are required.

Limitations :

Small study group of 40 patients limited to newly detected patients or patients within the first 1 or 2 years of detection. Also we had to depend mostly on our indoor patients for our study.

Conclusion :

Cardiac complications are frequently encountered in the HIV infected population. Cardiac care providers should implement appropriate preventive, screening and therapeutic strategies to maximize survival and quality of life in this increasingly treatable chronic disease. All HIV infected patients should undergo echo to identify sub-clinical cardiac dysfunction and implement proper primary and secondary prevention strategies. Lipid profiles should also be done.

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