ORIGINAL ARTICLE

Correlation of Cardiac Autonomic Dysfunction with CD4 Count in Human Immunodeficiency Virus Patients

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Abstract:

Background: Almost all organs and systems in the body are affected by Human Immunodeficiency Virus (HIV) infection. Autonomic nervous system involvement and cardiac autonomic dysfunction is known to affect severely the quality of life in HIV patients due to fatal consequences in later stages of the disease. *Aim and Objectives:* Assessment of cardiac autonomic dysfunction on HIV infection/Acquired Immunodeficiency Disease Syndrome (AIDS) patients and to correlate the degree of dysfunction with Cluster of Differentiation 4 (CD4) count. *Material and Methods:* Fifty one human HIV sero-positive patients with 20 HIV sero-positive patients without AIDS and 31 with AIDS and 51 controls were studied for cardiac autonomic dysfunction in a tertiary care medical college hospital. The assessment of cardiac autonomic function was done by series of autonomic function tests. The number of abnormal test results correlated with CD4 count. *Results:* In patients with HIV, abnormal cardiac autonomic functions were observed in 5.6% of patients without AIDS and 37.5% of patients with AIDS. Significant differences between HIV patients and controls was observed for systolic blood pressure response to standing ($p<0.001$), diastolic blood pressure response to persistent handgrip ($p<0.001$), heart rate variability to standing ($p<0.001$), Valsalva maneuver ($p<0.001$) and to deep breathing ($p=0.001$). Abnormalities in cardiac autonomic function occurred at all levels of CD4 counts. Our study showed an increase in incidence of cardiac autonomic dysfunction as the CD4 count decreased. *Conclusion:* The affection of various organs and systems is a consequence of autonomic dysfunction in HIV infection and often invasive procedures are required for diagnostic and therapeutic decisions. When HIV patients present with symptoms like dizziness and headache which can be present in many conditions, cardiac autonomic dysfunction should be first ruled out by performing simple autonomic dysfunction tests before resource consuming expensive and invasive tests were performed later only if needed.

Keywords: Autonomic dysfunction, Human immunodeficiency virus, Valsalva maneuver

Introduction:

According to Global Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Disease Syndrome (AIDS) statistics-2018 estimate, there are 36.9 million (31.1 million-43.9 million) people globally were living with HIV in 2017 [1]. The National Aids Control Organization (NACO) Annual Report 2017-2018, estimates adult HIV prevalence in India of 0.30% among males and 0.22% among females as of 2015 [2]. Almost all organs and systems in the body are affected by HIV infection along with involvement of central nervous system Autonomic Nervous System (ANS) is also affected. The quality of life in HIV patients is severely affected by autonomic nervous dysfunction [3, 4]. In later stage of the disease autonomic nervous dysfunction is known to cause fatal consequences which require invasive diagnostic or therapeutic procedures. Screening for cardiac autonomic dysfunction can help identify HIV patients at risk of syncope or cardiovascular collapse and as such extra precautions may be taken in these individuals

before any invasive procedures are done. It may also help avoid unnecessary expensive investigations for symptoms such as syncope which maybe be expected once the ANS is involved. Screening for cardiac autonomic dysfunction may also identify risks apart from immunological deterioration and contribute to risk stratification in HIV infected patients. Autonomic nervous system involvement in HIV patients is one of the less studied topics in India. Hence this study was taken up to assess ANS involvement in HIV patients.

Material and Methods:

The information for the study was collected from HIV positive patients admitted to a tertiary care medical college hospital. The controls were patients admitted for other diseases who were not HIV sero-positive but fit the exclusion criteria. They were matched for age, gender, educational status and occupation with the study group (Table 1). Information was collected through a prepared performa from each patient. All patients were interviewed as per the prepared performa and then complete clinical examination was done. Inclusion Criteria for the study included HIV sero-positive patients diagnosed as per NACO guidelines [5]. Patients with history of diabetes mellitus, cardiovascular diseases like acute coronary syndrome, congenital heart diseases and known alcoholics were excluded. Very ill patients who were unable to perform the autonomic function tests were also excluded.

The following tests were performed to assess the autonomic functions in the above patients:-

1. Heart rate variation to Valsalva maneuver, deep breathing and standing from supine position.
2. Blood pressure response to standing up and sustained handgrip.

Each autonomic function test was graded and the results were classified into normal, borderline, and abnormal depending on the score 0, 1 and 2 respectively (Table 2).

Table 1: Demographic Data

Demographic Parameters	Study Group	Control Group
Age	36.6 years	35.35 years
Sex		
Male **Female**	70.58% 29.42%	66.66% 33.44%
Education		
Graduate **Matriculate** **Primary schooling** **Uneducated**	3.8% 17.6% 19.6% 58.82%	7.84% 13.72% 39.21% 39.21%
Employment		
Employed **Unemployed**	74.51% 25.49%	60.78% 39.21%

Table 2: Cardiac Autonomic Function Tests Scoring

Parameters	Range	Score
Systolic BP Response to standing from supine position (mm of Hg)	Normal ⩽10 Borderline 11-29 Abnormal ⩾ 30	0 1 2
Diastolic BP response to sustained handgrip (mm of Hg)	Normal ⩾ 16 Borderline 11-15 Abnormal ⩽ 10	0 1 2
HR variation to deep breathing. (beats/min)	Normal ⩾ 15 Borderline 11-14 Abnormal ⩽ 10	0 1 2
HR Variation on standing from supine position (ratio)	Normal ⩾ 1.04 Borderline 1.01 - 1.03 Abnormal ⩽ 1.00	0 1 2
HR Variation to Valsalva (ratio)	Normal > 1.21 Abnormal ⩽ 1.21	0 2

Depending on an overall score it was considered as normal (score ⩽ 3), borderline (score >3 and <8) and abnormal (score ⩾ 8). Cluster of Differentiation 4 (CD4) count and number of abnormal test results were correlated. The data was entered in MS Excel Sheet and analyzed using SPSS 18 software. Appropriate statistical test like Chi square standard deviation mean and 'z' test were used.

Results:

Age group ranged from 17-60 years with mean age of 36.6 years. Majority of patients were in the age group of 26 to 35 years, which was the most sexually active and economically productive group. Male to female ratio was 12:5. Male sex was predominantly affected. The difference was not statistically significant. (p=0.6). The most common symptoms associated with autonomic dysfunction were dizziness and headache. The least presentation was blurred vision. The mean CD4 count was 231 cells/µl. and thirty patients had CD4 count below 200 cells/µl. There were significant differences between HIV sero-positive patients and controls for systolic blood pressure response to standing ($p<0.001$), diastolic blood pressure response to persistent handgrip ($p<.0.001$), Heart rate variability to standing ($p<0.001$) Valsalva maneuver ($p<0.001$) and to deep breathing heart rate variability to deep breathing, Valsalva ratio ($p=0.001$) (Fig.1).

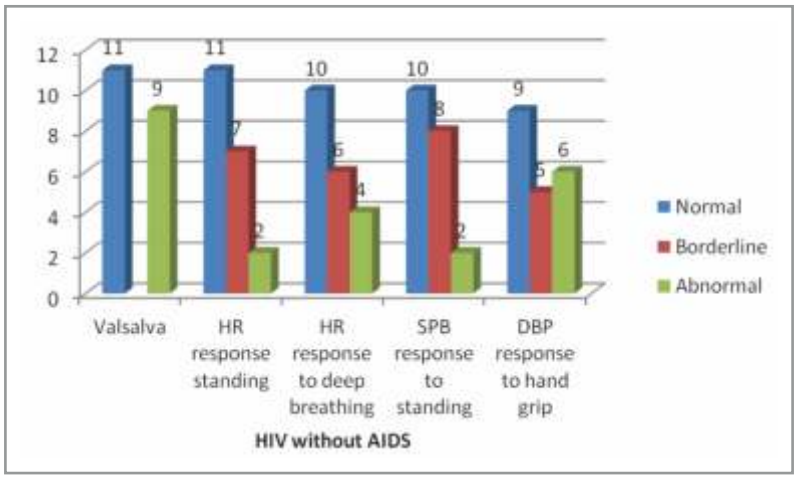

Fig. 1: Abnormal Autonomic Function in HIV without AIDS Group

Of the cardiac autonomic function tests, the results of systolic BP response to standing and heart rate response to deep breathing was not statistically significant in AIDS patients than the HIV positive without AIDS group. Rest of the tests, maneuver, diastolic blood pressure response to persistent handgrip and heart rate variability to standing showed AIDS patients having statistically significant results compared to HIV without AIDS patients. The results of autonomic function tests were analyzed and it was observed that the tests were abnormal in 32% AIDS patients (n-8), 12% HIV positive patients without AIDS (n-3) and none in HIV negative patients. Only 8% of 25 AIDS patients (n-2) had normal and than 55% of HIV infected patients had borderline autonomic function. The observational results were statistically significant ($p < 0.001$).

Also the results of autonomic function tests were analyzed in AIDS patients with and without opportunistic infections. The results were abnormal in 25.80% of AIDS with opportunistic infections and none in AIDS patients without opportunistic infections. The effect of opportunistic infection on autonomic function was statistically significant ($p < 0.001$) (Fig. 2).

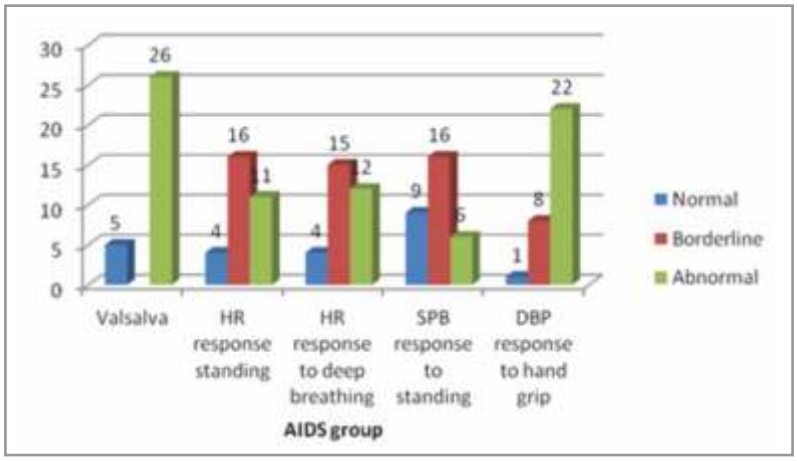

Fig. 2: Abnormal Autonomic Function in HIV with AIDS Group

Discussion:

It has been more than thirty years since HIV was first discovered in homosexuals in United States [6]. With the concentrated effort of government institutions, non-governmental organizations and world health organization for the first time new HIV infections are declining. AIDS related deaths have fallen by 30% since its peak in 2005. The UNAIDS in its Global Report 2013 publication on AIDS epidemic has noted a historic decline in AIDS-related deaths and new HIV infections [1]. In this study conducted in a tertiary medical college hospital, 51 HIV patients with or without AIDS were studied to know cardiac autonomic dysfunction and its correlation to CD4 count. This study observed that there is evidence that HIV infection affects autonomic nervous system and significant cardiac autonomic dysfunction occurs in HIV patients compared with controls [7].

When the HIV patient group was further divided into HIV positive without AIDS and those with AIDS it was found that the latter group was having greater incidence of cardiac autonomic dysfunction. Incidence of cardiac autonomic nervous dysfunction increased with HIV disease progression. Our findings corroborated with other similar studies, Nzuobontane *et al.* reported a >80% and Becker *et al.* who found a 61.3% incidence of autonomic dysfunction compared to our finding of 50.98% Rogstad *et al*. reported an incidence of 20% [8-10].

Cardiac autonomic function tests were abnormal at all levels of CD4 count but more with CD4 count of <200 cells/mm^3, which was also the case with Becker et al and Rogstad *et al.* [9, 10]. All studies showed an increase in incidence of cardiac autonomic dysfunction as the CD4 count decreased. All the studies had mean age of their participants ranging between 30 to 40 years. Most of those affected were in the age bracket of 26 to 35 years which is considered to the most economically productive group. In our study age group ranged from 17-60 years with mean age of 36.60 years. As in most of the studies there was a male preponderance with a male to female ratio of 12:5. Nzuobontane *et al*. had 7:4 ratios with Mittal *et al*. having 16:5 [11].

The higher incidence in male population can be attributed to increased travel and contact with multiple sexual partners compared to females of the region. Our study was based on the model of Nzuobontane *et al.* who studied autonomic dysfunction in HIV patients by using standard blood pressure and heart-rate tests to assess cardiovascular autonomic function and did not find statistically significant difference in cardiac dysfunction in heart response to deep breathing and standing whereas in our study systolic blood pressure response to standing and heart rate response to standing test results when comparing HIV group without AIDS to the one with AIDS [8]. Our study also found significant cardiac dysfunction in three of the five studies. 37.5 % of AIDS group showed abnormal autonomic function compared to 4.2% and 14.1% of Nzuobontane *et al.* and Rogstad *et al.* studies [9,10].

Maximum number of patients in the HIV without AIDS and AIDS patients had borderline dysfunction in several clinical studies. Unlike other clinical studies, the present study considered AIDS patients with opportunistic infections on ART to know that the presence of opportunistic infection had any effect on autonomic function. The antiretroviral drugs like Stavudine, Didanosine and Zalcitabine are capable of causing autonomic neuropathy. The presence of opportunistic like tuberculosis is known to cause

autonomic dysfunction due to adrenalitis and adrenal calcification. There was no significant effect on autonomic function due to presence of opportunistic infection and therapy with ART in this study. Simple bedside tests like blood pressure responses to standing or handgrip and other tests, can give a clue of cardiac autonomic dysfunction in HIV infected patients.

Conclusion:

This study found a significant cardiac autonomic dysfunction in HIV positive patients compared to general population. The severity of dysfunction increases with decrease in CD4 count. When HIV patients present with symptoms like dizziness and headache which can be present in many conditions, cardiac autonomic dysfunction should be first ruled out by performing simple cardiac autonomic dysfunction tests and resource consuming expensive tests must be performed later only if needed. In cases where invasive diagnostic or therapeutic tests are needed extra caution is needed. Anti retroviral therapy does not have any effect on autonomic dysfunction.

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