

## ORIGINAL ARTICLE

# Clinical Study of Cardiac Autonomic Dysfunction and QT Dispersion in Newly Diagnosed HIV/AIDS Patients and its Correlation with CD4 Count

Utsav Kumar Sahu<sup>1</sup>, Maniram Kumhar<sup>2\*</sup>

## Abstract

**Objectives:** To evaluate the cardiac autonomic dysfunction and QT dispersion in newly diagnosed HIV/AIDS patients and to correlate the cardiac autonomic dysfunction with CD4 count.

**Methods:** It was a prospective study conducted on 50 patients (25 HIV positive without AIDS and 25 HIV with AIDS) and 50 healthy controls in the department of General Medicine, JLN Hospital, Ajmer. Autonomic function was assessed by Ewing battery of autonomic function tests and QT dispersion was calculated.

**Results:** In the present study 16% of HIV positive with AIDS had abnormal autonomic dysfunction and 4% of HIV positive without AIDS had abnormal autonomic dysfunction. 48% of patients in AIDS group and 16% of patients in HIV positive without AIDS group showed abnormal QT dispersion. There was no statistically significant correlation with CD4 count.

**Conclusion:** Apart from opportunistic infections, autonomic dysfunction itself can contribute to mortality and morbidity in HIV/AIDS patients. Our study showed that cardiac autonomic dysfunction is a common and relevant clinical problem. It is significantly affected in both HIV positive without AIDS and HIV positive with AIDS groups. QT dispersion is a sensitive predictor of cardiac dysautonomia. But there is no statistically significant correlation with CD4 count.

## Introduction

Cardiovascular autonomic dysfunction has been demonstrated to severely debilitate HIV infected patients, namely by postural hypotension and syncope. It has important implication in health care of HIV patients. Presence of autonomic neuropathy signals the need for added precautions when invasive procedures are performed on HIV patients.<sup>1-3</sup>

QT dispersion is an electrocardiographic abnormality that may cause severe arrhythmias including torsades de pointes and ventricular fibrillation. QT dispersion is well documented in many conditions like diabetes mellitus with dysautonomia but not well proved in HIV infected patients, and that may be one of the important causes of mortality in HIV infected patients along with the opportunistic infections. Since QT prolongation may determine the

ventricular arrhythmias, a study is required to validate the reliability of QT dispersion as an indicator of the presence of autonomic neuropathy.<sup>4,5</sup>

QT interval due to regional autonomic denervation leads to increased QT dispersion. Thus, QT dispersion is a sensitive, non-invasive, simple and cost effective predictor of cardiac dysautonomia. QT dispersion was determined by subtracting heart minimum QT interval (QT min) from maximum QT interval (QT max) from standard electrocardiogram. QT dispersion >40 ms was considered as abnormal. Severity of cardiac autonomic neuropathy strongly correlated with QT dispersion.<sup>6,7</sup>

Present study was carried out to evaluate the presence and extent of autonomic dysfunction and QT dispersion in HIV/AIDS patients and to correlate autonomic neuropathy with CD4 count. There is scanty literature

on autonomic effects of HIV infection in Indian patients hence this study is being taken up to address question of cardiac autonomic dysfunction in the Indian scenario.

## Material and Methods

The study was carried out in the department of General Medicine, JLN Hospital, Ajmer for a period of 1 year starting from 1<sup>st</sup> July, 2013. This was a prospective study conducted on 50 patients (25 HIV positive without AIDS and 25 HIV with AIDS) who fulfilled the inclusion and exclusion criteria and 50 healthy age and sex matched controls. All HIV positive/AIDS patients were evaluated according to a detailed pro forma with elicitation of history, symptoms, signs and routine and specialized investigations.

### Inclusion Criteria

- HIV infection diagnosed as per NACO guidelines.

### Exclusion Criteria

- H/o cardiovascular disease before testing.
- Very ill patients unable to perform the autonomic test maneuvers.
- Patients with diabetes mellitus.
- Patients on Antiretroviral Therapy.
- Known alcoholics.

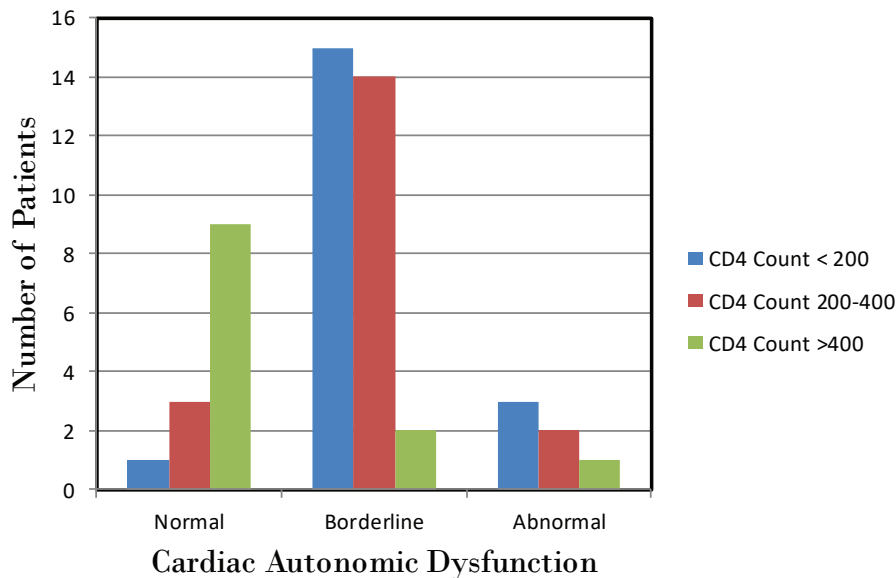
Autonomic function was assessed by Ewing battery<sup>8</sup> of autonomic function tests.

- Heart rate response to Valsalva maneuver
- Heart rate variation to deep breathing
- Heart rate response to standing

<sup>1</sup>Resident, <sup>2</sup>Professor, Jawahar Lal Nehru Medical College and Hospital, Ajmer, Rajasthan; \*Corresponding Author  
Received: 21.07.2015; Accepted: 08.02.2018

**Table 1: Analysis of ewing's test battery and QT dispersion between HIV positive with AIDS, HIV positive without AIDS and control group**

| Name of test (results) (p value)                     |            | HIV positive with AIDS | HIV positive without AIDS | Control |
|--|------------|------------------------|---------------------------|---------|
| Valsalva Ratio (p<0.001)                             | Normal     | 4(16%)                 | 5(20%)                    | 46(92%) |
|  | Borderline | 5(20%)                 | 8(32%)                    | 4(8%)   |
|  | Abnormal   | 16(64%)                | 12(48%)                   | 0       |
| HR response to deep breathing (p<0.001)              | Normal     | 5(20%)                 | 9(36%)                    | 46(92%) |
|  | Borderline | 6(24%)                 | 6(24%)                    | 2(4%)   |
|  | Abnormal   | 14(56%)                | 10(40%)                   | 2(4%)   |
| HR response to standing (p<0.001)                    | Normal     | 11(44%)                | 11(44%)                   | 48(96%) |
|  | Borderline | 10(40%)                | 6(24%)                    | 2(4%)   |
|  | Abnormal   | 4(16%)                 | 8(32%)                    | 0       |
| Systolic fall of BP on standing (p<0.05)             | Normal     | 17(68%)                | 22(88%)                   | 46(92%) |
|  | Borderline | 6(24%)                 | 3(12%)                    | 4(8%)   |
|  | Abnormal   | 2(8%)                  | 0                         | 0       |
| Diastolic rise of BP on sustained hand grip (p=0.05) | Normal     | 19(76%)                | 21(84%)                   | 44(88%) |
|  | Borderline | 4(16%)                 | 3(12%)                    | 6(12%)  |
|  | Abnormal   | 2(8%)                  | 1(4%)                     | 0       |
| QT Dispersion (p<0.001)                              | Normal     | 21(84%)                | 13(52%)                   | 49(98%) |
|  | Abnormal   | 4(16%)                 | 12(48%)                   | 1(2%)   |

**Fig. 1: Correlation of CD4 cell count with cardiac autonomic dysfunction score (calculated from ewing test battery) in HIV/AIDS group**

- SBP response to standing
- DBP response to persistent handgrip

Grading was given for each autonomic function test results were classified into normal, borderline and abnormal (scored 0, 1 and 2 respectively).

An overall score  $\leq 3$  was considered as normal,  $>3$  and  $<8$  was considered as borderline and score  $\geq 8$  was considered as abnormal. CD4 count was correlated with number of abnormal test results.

QT dispersion was calculated and was correlated with CD4 cell count.

## Results

A total of 50 patients and 50 controls were studied of which 70% were males in each group. The bias in the sex was in concordance with the admission statistics of the hospital. Majority of patients were in the age group of 26-35 years which is the economically productive age group.

The most common symptoms were dizziness and lower GI symptoms and least common were sexual disturbances. Majority of the AIDS patients (as defined by the revised WHO staging) had a CD4 range of 101-200 and majority of the HIV positive patients

had a CD4 count in the range of 301-400.

In the present study 16% of HIV positive with AIDS had abnormal autonomic dysfunction and 4% of HIV positive without AIDS had abnormal autonomic dysfunction.

Abnormal Valsalva response was present in 64% of HIV positive with AIDS group. Abnormal diastolic BP response to sustained hand grip was present in 8% of HIV positive with AIDS group. Abnormal heart rate response to deep breathing was present in 56% of HIV positive with AIDS. Abnormal heart rate response to standing was present in 32% of HIV positive with AIDS group. Abnormal systolic BP response to standing was present in 8% of HIV positive with AIDS group.

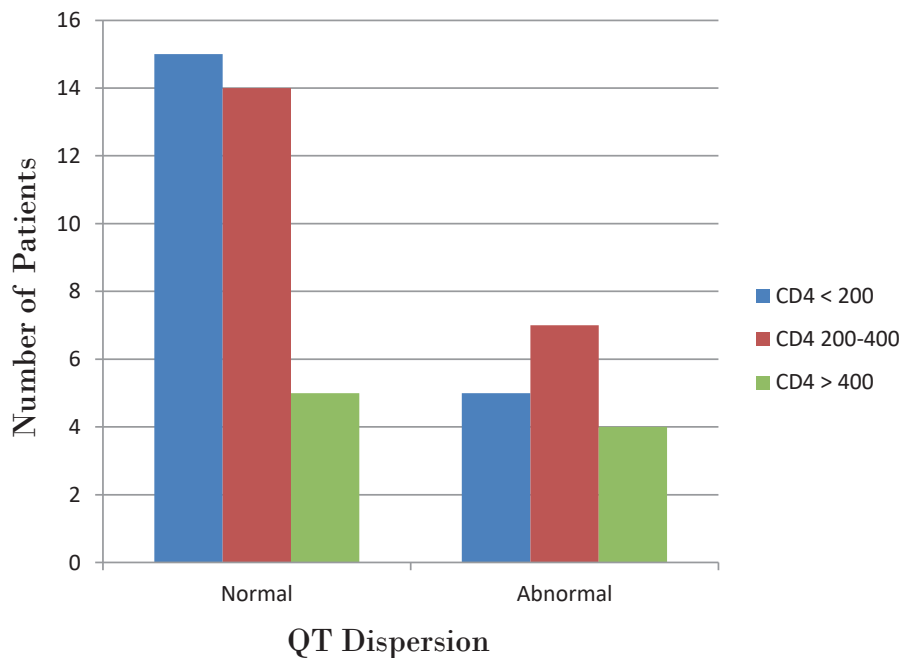
Abnormal Valsalva ratio was present in 48% of HIV positive without AIDS. Abnormal diastolic BP response to sustained handgrip was present in 4% of HIV positive without AIDS. Abnormal heart rate response to deep breathing was present in 40% of HIV positive without AIDS. Abnormal heart rate response to standing was present in 16% of HIV positive without AIDS. There were no abnormal results for systolic BP response to standing in HIV positive without AIDS (Table 1).

There were significant difference between AIDS/HIV positive patients and control group for HR response to standing (P<0.001), Valsalva ratio (P<0.001), HR response to deep breathing (P<0.001), SBP response to standing (P<0.001), however there was no significant difference to DBP response to sustained hand grip (p>0.05).

Abnormalities in autonomic function occurred at all levels of CD4 counts. More number of abnormal results were found below 200 CD4 range. But the difference was not statistically significant (Figure 1).

There were significant difference between AIDS/HIV positive patients and control group for QT dispersion (P<0.001). 48% of patients in AIDS group and 16% of patients in HIV positive without AIDS group showed abnormal QT dispersion.

Abnormalities in QT dispersion occurred at all levels of CD4 counts. More number of abnormal results were found below 200 CD4 range. But there was no statistically significant correlation with CD4 count (Figure 2).



**Fig. 2: Correlation of CD4 cell count with QT dispersion in HIV/AIDS group**

## Discussion

50 HIV/AIDS patients were studied to evaluate the presence and extent of autonomic dysfunction and to correlate autonomic neuropathy with levels of CD4. It was observed in this study that there was evidence of substantial autonomic dysfunction in HIV and AIDS patients compared with controls. Incidence of cardiac autonomic nervous dysfunction increases with HIV disease progression. Abnormal tests of heart rate variation occurred at all levels of CD4 count but more number of abnormal results were found at a CD4 count below 200 cells/mm<sup>3</sup>.

Two similar studies have been conducted on the African population, one in Kenya by Rogstad et al<sup>9</sup> and the other in Cameroon by Nzubontane D et al<sup>10</sup>. Our study is the first such study conducted on the Indian population.

In the present study 16% of patients with AIDS showed abnormal results which was comparable to the results of Rogstad et al (20% AIDS) while it was more in the study of Nzubontane D et al (27.6% AIDS). In the study 4% of

HIV positive group showed abnormal results which is comparable the study of Nzubontane D et al (4.2% of HIV positive) while it was more in the study of Rogstad et al (14.1% of HIV positive group).

The mean CD4 range of the present study is slightly higher than seen in the other two studies. In this study autonomic dysfunction occurred at wide range of CD4 cell count. However more number of abnormal results were found below 200 CD4 range and more number of normal results found in CD4 range over 400. Although results are statistically insignificant, more number of abnormal results were found below CD4 count of 100 in study by Nzubontane D et al and below CD4 count of 300 in study by Rogstad et al.

## Conclusion

Cardiac autonomic nervous dysfunction is a common and relevant clinical problem. It is significantly affected in both HIV positive without AIDS and HIV positive with AIDS groups. It may provide an alternative explanation for symptoms commonly

observed in HIV infected individuals such as bowel and bladder dysfunction, impotence, syncope and sweating abnormalities.

Reduced heart rate variability is the commonest manifestation of autonomic dysfunction noted in both HIV positive without AIDS and HIV positive with AIDS groups. Diastolic BP response to sustained handgrip has a limited role in discriminating autonomic function in HIV infected patients. There is no statistically significant correlation with the CD4 level and the presence of autonomic nervous system dysfunction in both the groups.

QT dispersion is a sensitive predictor of cardiac dysautonomia. Severity of cardiac autonomic neuropathy in HIV strongly correlated with QT dispersion. Autonomic dysfunction may contribute to morbidity and mortality in HIV patients apart from opportunistic infections and we recommend routine autonomic evaluation in every patient of HIV/AIDS.

## References

- Mathias CJ, Frankel HL 1983: In autonomic failure. A text book of clinical disorders of ANS, Oxford; page 453-468.
- Rewari BB, Joshi PL, Epidemiology of HIV/AIDS with special reference to India. Medicine update, Association of Physicians of India 2003; 77-86.
- Mittal CM, Wig N, Mishra S, Deepak KK. Heart rate variability in human immunodeficiency virus positive individuals. *International Journal of Cardiology* 2004; 94:1-6.
- Fiorentini A, Petrosillo N, Cicalini S, Borgognoni L, Chinello P. QTc interval prolongation in HIV-infected patients: a case-control study by 24-hour Holter ECG recording. *BMC Cardiovascular Disorders* 2012; 12:124.
- Elming H, Holm E, Jun L, et al. The prognostic value of the QT interval and QT interval dispersion in all-cause and cardiac mortality and morbidity in a population of Danish citizens. *Eur Heart J* 1998; 19:1391-1400.
- Surawicz B. Will QT dispersion play a role in clinical decision making?. *J Cardiovasc Electrophysiol* 1996; 7:777-784.
- Charbit B, Rosier A, Bollens D, Boccaro F, Boelle PY, Koubaa A. Relationship between HIV protease inhibitors and QTc interval duration in HIV-infected patients: a cross-sectional study. *Br J Clin Pharmacol* 2009; 67:76-82.
- Ewing DJ, et al. The value of cardiovascular autonomic function test 10 years experience in diabetes. *Diabetes Care* 1995; 8:491-498.
- Rogstad K, Shah R, Tesfaladet G, Abdullah M. Cardiovascular autonomic dysfunction in HIV infected patients. *Sex Transm Inf* 1999; 95:264-277.
- Nzubontane D, Ngu BK. Cardiovascular autonomic dysfunction in Africans infected with HIV. *JR Soc Med* 2002; 95:445-447.