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Research Article

Association of electrocardiogram abnormalities in human immunodeficiency virus infected patients with special reference to QTc interval

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ABSTRACT

Background: Cardiac manifestations of human immunodeficiency virus (HIV) and AIDS are gaining its importance as a reason for increasing morbidity and mortality. A higher prevalence of QT prolongation has been reported among HIV infected patients. However, specific data and clinical evidences are lacking in this regard from the Indian patient population. The objective of this study was to study the ECG abnormalities in HIV patients with special reference to QTc interval.
Methods: The study was conducted at the Anti-Retroviral Therapy (ART) Centre of the Department of Medicine, G R Medical College, Gwalior, MP India between March 2012 and November 2013. A total of 130 patients who were HIV positive and either taking antiretroviral therapy or not were included in the study. The patients with history of cardiovascular disease, drugs causing prolonged QTc except antiretroviral therapy were excluded from the study. Detailed history, examination and relevant investigations were done. ECG of all the patients was done and analysed for any abnormality. CD4 count estimation was done.
Results: Out of total 130 patients, there were 88 (67.6%) males and maximum (78.4%) no of patients were in age range of 25-44 years. Socioeconomic status of the patients was low, middle and high in 64.6 %, 23.07 and 12.3 % respectively. 77.7% patients were married, 60% were engaged in heavy physical work. ECG was normal in 79 (60.7%) patients, sinus tachycardia in 30 (19 on ART and 11 pre ART patients), LBBB in 4, features of IHD and RBBB in 3 patients each. Prolonged QTc interval was exclusively found in 11 patients (8.46%) who were on ART ($p<0.0001$). The QTc prolongation was more in patients with lower CD4 count, 6 patients had CD 4 count between 100-150 and 2 were with CD4 count between 150-200. Almost 50% of the patients had CD 4 count <300.
Conclusions: ECG was abnormal in 39.2 % HIV positive patients and was more in patients who were on ART. The most common abnormal ECG finding was sinus tachycardia. QTc prolongation was seen in 8.46 % patients and all of them were on ART therapy.

Keywords: HIV, QTc prolongation, Antiretroviral therapy

INTRODUCTION

Cardiac manifestations of human immunodeficiency virus (HIV) and AIDS have become increasingly important causes of morbidity and mortality. Patients with HIV infection can have a variety of cardiovascular manifestations including pericarditis, myocarditis, cardiomyopathy, pulmonary vascular disease, pulmonary hypertension, valvular disease and an increased incidence of vascular disease including coronary artery disease.[1-3] As the epidemiological transition transforms the cardiovascular disease as an emerging cause of mortality worldwide, the association of cardiovascular disease with HIV gain even more prime importance.[4]

Electrocardiogram (ECG) has shown abnormalities in AIDS patients whether or not they were suspected to have cardiac disease clinically. ECG abnormalities described includes sinus tachycardia, QTc prolongation, low-voltage QRS complexes, nonspecific ST-segment and T-wave changes, poor R-wave progression, different types of arrhythmia right bundle branch block and enlargement of various heart chambers.[5]

A higher prevalence of QT prolongation has been reported among HIV infected patients.[6]

Low frequency of ECG testing has been reported in HIV patients despite a high use of medications associated with QTc prolongation. It was found that the risk of abnormal QTc interval was highest among patients with chronic kidney disease, hypertension and hepatitis C virus co infection.[6,7] QT prolongation in HIV patients may be possibly related to the various drugs prescribed to these patients or to an acquired form of long QT syndrome (LQTC).[6,8]

HIV-infected patients receiving cART have been associated with prolonged QTc interval and increased QT dispersion, independent of autonomic dysfunction and antiretroviral drugs, which may have led to the potentially higher risk of ventricular arrhythmia and cardiac mortality. Drugs like some antibacterial, antifungal, psychotropic and antihistamines have been found to be associated with QT prolongation or torsades de pointes (TdP), a life threatening ventricular arrhythmia.[9]

Alterations in cardiac innervations have been described in HIV infection and AIDS due to autonomic neuropathy and these alterations may be responsible for QT interval prolongation. Moreover most of the protease inhibitors are potent inhibitors of CYP3A, which can be responsible for various drug drug interactions with potential to clinically alter the serum levels of various drugs. The precise electrophysiological mechanisms underlying drug-induced QTc prolongation in relation to protease inhibitors and its clinical implications have been well understood and have been well described and some studies have reported prolonged QTc interval and increased QT dispersion, independent of autonomic dysfunction and antiretroviral drugs.[6,9]

Studies have demonstrated that QT dispersion is a better predictor of serious ventricular tachyarrhythmia and cardiac mortality than corrected QT (QTc) interval.[6] However, specific data and clinical evidences are lacking in this regard from the Indian patient population. Since, ECG is an important tool for early detection of cardiovascular complication, the present study was planned to evaluate the ECG changes, particularly QTc prolongation in HIV patients irrespective of whether they are receiving ART or not.

METHODS

The present study was conducted at a tertiary care centre of a teaching hospital Gwalior, India, during March 2012 to November 2013, among the HIV infected patients presenting at the ART centre. The patients were subjected to detailed history, examination and investigations; information on age, sex and anthropometric measures were recorded from all case. As per ART centre norms biochemical parameters were studied in 130 patients. The exclusion criteria applied was age <15 years, BP >140/90 mmHg, pregnancy and puerperium (in females), history of MI, cerebral injury, diabetes mellitus, drugs causing prolonged QTc except HAART therapy. The patients has 12 lead ECG recording in which heart rate, cardiac axis, PR interval, QRS duration was calculated is of the standardised manner. CD4 count was done in all the patients.

RESULTS

The mean age of the study population was 38.8 years and 88 (67.69%) were males. Majority of patients were in the age group of 35-44 years (40%) and 25-34 years (38.46%). About three fourth (101/130) of the patients were married while others were either widow or unmarried. Occupational profile of the patients showed labourers (42), housewives (38), farmers (24) and truck drivers (12). The commonest mode of HIV transmission in both male and female was sexual mode through commercial sex worker and infected spouse.

Of the total of 130 patients, 72% of patients manifested with AIDS; 94 patients (72.3%) were on ART. The duration of ART treatment in patients were <1 year in 59.57%, 1-2 year in 33.07% and >2 years in 7.6 % of the patients.

Most of the patients reported more than one symptom; commonest symptom was fever and weight loss (63.8%), cough (17.6%), diarrhoea (3.07 %), skin lesion (7.6 %), oral candidiasis (2.9%), neurological symptoms (1.54%) and pain in abdomen (1.5%). Common opportunistic infections in the present study were candida infection (9.2%), herpes zoster (7.6%) and tuberculosis (6.9%). Pulmonary tuberculosis was the commonest systemic manifestation in 9 (6.9%) patients with the X-ray finding of cavity and infiltration.

ECG findings in all the patients are shown in Table 1. Using logistic regression model for prolonged QTc and adjusting for serum electrolyte, age, and gender, mean QTc in ART patients, differ significantly from non-ART patients (p=0.349). Prolonged QTc interval was exclusively seen in patients who were on ART which is statistically significant (p<0.0001). Only 3 patients had ECG changes suggestive of ischemic heart disease. mCD4 Count was <300 in 64 (49.23%). Patients and the lower CD4 count correlated with higher incidence of QTc prolongation.

Table 1: ECG findings in patients of HIV with or without ART.

ECG Finding	ART (n=94)		Pre ART (n=36)		p value
	No.	%	No.	%	
Normal (n=79)	58	61.7	21	58.3	0.001*
Sinus tachycardia (n=30)	19	20.2	11	30.55	0.144
Features of IHD (n=3)	2	2.17	1	2.77	0.563
RBBB (n=3)	2	2.17	1	2.77	0.563
LBBB (n=4)	3	3.19	1	2.77	0.317
Prolonged QTc (n=11)	11	8.46	0	0	<0.0001*

*Statistically significant, ART - Antiretroviral therapy

DISCUSSION

The prevalence of cardiovascular disease in HIV has been reported upto 28% and these patients can have a variety of cardiovascular manifestations. The present study was done to study the ECG abnormality in HIV patients. Majority of our patients were of age below 45 years showing the involvement of young adults as was reported by Chatterton-Kirchmeier et al.[10]

Most of the patients in our study were from the low socioeconomic status suggesting the higher prevalence in this group, similar to the study published by Bhandarkar et al.[11] The high number of HIV positive patients were suffering from full blown AIDS (72%) and it may be due the referral pattern as the hospital is a tertiary care centre.

ECG was abnormal in our 51 (39.2%) patients though they were asymptomatic clinically and the findings varied from alterations in heart rate, bundle branch blocks to ischemic changes and these findings were similar to the findings as noted in the landmark SMART study.[12]

A prolonged QTc is a predictor of cardiovascular mortality even in the absence of overt heart disease and is associated with risk of potentially lethal arrhythmias especially Torsades de pointes (TdP).[13,14]

Prolonged QTc was present in 11 (8.46%) of patient on ART, whereas there was no QTc prolongation in patients who were not on ART. Similarly, a study from Nigeria reported that HIV-positive asymptomatic subjects have higher prevalence of QTc prolongation compared to HIV-negative subjects and, as they moved to AIDS, the prevalence of QTc prolongation increased which was responsible for higher cardiovascular mortality.[13]

Kocheril et al. demonstrated higher prevalence of QTc prolongation in HIV patients, than a general hospital-based population and this may be due to an unrecognized acquired form of the long QT syndrome.[15] Reinsch et al. in the HIV HEART study demonstrated that nearly 20% prevalence of QTc prolongation in an HIV-infected population which is higher than our study and this could have been influenced by factors like gender, diabetes, and arterial hypertension.[16] The majority of our patients were accustomed to the daily physical activity like heavy labour work, truck drivers etc, which mitigated the inherent risk of arrhythmias and QTc prolongation, in contrast to the higher incidence of ECG repolarization heterogeneity noted with the sedentary habits [15]

The electrophysiological mechanisms underlying drug induced QTc prolongation in relation to protease inhibitors and its clinical implications has been well described by Singh et al.[9] All the patients with QTc prolongation in our study were on ART, a finding similar to the one by Patel et al. which has reported QTc prolongation in 27.5% patients who were taking ART in their study of 454 HIV patients.[8] Reinsch et al.[16] showed that the QTc was pronged in patients with lower CD4 count as compared to patients with higher CD 4 count and this is similar to our finding as most of our patients with QTc prolongation had lower CD 4 count (<200). The studies had shown that lower CD4 count were associated with ECG abnormalities and this may be related to the drugs, autonomic dysfunction like sympathetic and parasympathetic dysfunctions. Drug induced prolongation of QTc may be explained by block of human either go-go related gene (HERG) potassium channel, and protease inhibitors like nelifinavine, ritoravine, squinavine cause dose dependant block of HERG channel, which suggest that protease inhibitor predispose individual to QTc prolongation.[9] Efavirenz a novel NNRTI is also reported to cause QTc prolongation and TdP.[19]

To conclude, ECG changes are not uncommon in HIV patients who are not even having cardiovascular symptoms. The chances of ECG abnormalities particularly QTc prolongation are more in patients on ART. As various drugs including HAART are prescribed to the HIV patients depending on their clinical presentation, we should be cautious about the cardiovascular effects and regular ECG screening to be done which may help in early detection of future complication.

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