

## FREQUENCY OF PROLONGED CORRECTED QT INTERVAL IN CHILD PUGH CLASS IN PATIENTS OF CIRRHOSIS OF LIVER

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### ABSTRACT

**Objective:** To determine the frequency of prolonged corrected QT interval (QTc) in Child Pugh Class in patients of liver cirrhosis presenting to Combined Military Hospital Peshawar.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** Department of Medicine, Combined Military Hospital Peshawar, from Dec 2013 to Jun 2014.

**Material and Methods:** One hundred and thirty three patients with liver cirrhosis fulfilling the inclusion criteria were included in the study using non-probability consecutive sampling after taking informed consent. All patients were assigned their Child's Class either A, B or C. Electrocardiogram (ECG) was done and QTc was calculated using Bazett's formula. QTc of more than 0.44 seconds was taken as prolonged.

**Results:** Out of 133 patients, QTc was prolonged in 78 patients yielding frequency of QTc prolongation in cirrhosis of 58.64%. Frequency of QTc prolongation was 61.18% in males and 54.17% in females. QTc prolongation was 15% in Child Pugh grade A, 54.76% in Child Pugh grade B and 73.24% in Child Pugh grade C. There was a statistically significant association between QTc prolongation and the severity of cirrhosis ( $p < 0.001$ ).

**Conclusion:** This study concludes that there was a statistically significant increase in frequency of QTc prolongation with worsening of Child Pugh Class thereby indicating an association between QTc prolongation and the severity of cirrhosis.

**Keywords:** Cardiomyopathy, Cirrhosis, QT Interval.

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### INTRODUCTION

Cirrhotic cardiomyopathy is characterized by increased cardiac output, decreased response to physiologic and pharmacologic stimuli, systolic and diastolic dysfunction, and electrophysiologic abnormalities in the absence of any known cardiac disease<sup>1</sup>. A prolonged QT interval on electrocardiography (ECG) is the hallmark of cirrhotic cardiomyopathy<sup>2</sup> with prevalence of 21.6%<sup>3</sup> in cirrhotic patients. Prolonged QT interval is an independent predictor of mortality and is a risk factor for fatal arrhythmias and sudden death<sup>4</sup>. Identification of QT prolongation is also important so as to be careful regarding use of QT prolonging drugs like quinolones and vasopressin analogues

which are routinely used in cirrhotic patients with infectious and bleeding complications respectively<sup>5</sup>.

Genovesi et al has shown that QTc was progressively prolonged from the Child A to the Child C group. QTc was greater than 440ms in 19% of Child A patients, 67% of Child B patients and in 86% of Child C patients<sup>6</sup>. Mozos et al showed similar results<sup>7</sup>. A local study conducted by Abbasi et al has shown that difference was observed between the Child A and B, while there was no difference of QT between Child B and C, this is contrary to internationally published data<sup>8</sup>.

Liver transplantation program has been launched in the Armed Forces and the hepatologists are bound to face the cardiovascular complications of cirrhosis after liver transplantation. This study will establish the presence of QT prolongation in cirrhotic patients in their set up to help provide local statistics thus

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Received: 07 Dec 2016; revised received: 17 Mar 2017; accepted: 17 Mar 2017

making the foundation for a sustained effort to create greater awareness regarding cirrhotic cardiomyopathy.

## MATERIAL AND METHODS

This cross sectional study was carried out at Combined Military Hospital (CMH) Peshawar from Dec 2013 to Jun 2014. Permission from hospital ethical review committee was taken. Sample size was calculated using WHO calculator for sample size determination in health studies keeping confidence level = 95%, absolute precision = 7%, anticipated population proportion = 21.6%<sup>3</sup>. A total number of 133

prolongation of QT interval were excluded from the study.

A brief history was taken from each patient including onset and duration of cirrhotic ailment, medication history and various complications like upper gastrointestinal (GI) bleed, ascites, hepatic encephalopathy and hepatocellular carcinoma. A brief clinical examination was carried out to find out above mentioned complications. Relevant laboratory investigations including complete blood counts, liver function test (LFTs), Prothrombin time (PT), serum albumin, renal function tests, electrolytes

**Table-I: Age and Gender wise distribution of patients in each child class.**

Age (Years)	Child Class A	Child Class B	Child Class C
Mean $\pm$ SD	48.17 $\pm$ 15.663	55.79 $\pm$ 18.842	55.80 $\pm$ 17.064
<b>Gender n(%)</b>			
Male	14 (70.0)	23 (54.76)	48 (67.61)
Female	6 (30.0)	19 (45.24)	23 (32.39)
Total	20 (15.04)	42 (31.58)	71 (53.38)

**Table-II: Gender, Age and Child Class of patients\* QT cross-tabulation.**

Variable	QT		Total	p-value
	Prolonged	Normal		
<b>Age of the patients n(%)</b>				
30-60	38 (47.50)	42 (52.50)	80	0.001
61-90	40 (75.47)	13 (24.53)	53	
<b>Gender of patients n(%)</b>				
Male	52 (61.18)	33 (38.82)	85	0.097
Female	26 (54.17)	22 (45.83)	48	
<b>Child Class (n)</b>				
Child A	3	17	20	<0.001
Child B	23	19	42	
Child C	52	19	71	

patients with cirrhosis were selected after taking informed written consent by non-probability consecutive sampling.

Patients of age more than 30 years with cirrhosis from any cause were included in the study. Patients who were suffering from any cardiac problem including ischemic heart disease, hypertension, conduction defects, and atrial fibrillation, patients taking drugs that may prolong the QT Interval like calcium channel blockers, antihistamines, antipsychotics, macrolides, quinolones and amiodarone, patients suffering from any other condition causing

and blood glucose were also sent. All the parameters were carried out in clinical laboratories affiliated with the hospital and reports were verified by a qualified pathologist. Ultrasound scan was done in all the patients to confirm cirrhosis. ECG was done in all patients to determine the presence or absence of QT interval prolongation. All findings were recorded on a specially designed proforma.

Data analysis were done by using SPSS 20 statistical software. Mean and standard deviation (SD) were calculated for quantitative variables i.e. age. Frequencies and percentages were calculated

for qualitative variables like gender, Child Class and QTc prolongation. QTc prolongation was stratified among age, gender, and Child Class using cross-tabulation test to see the effect modifiers. A *p*-value for age, gender and Child Class was calculated by using chi square test.

## RESULTS

A total of 133 patients fulfilling the inclusion/exclusion criteria were included in study. The mean age of child class A was  $48.17 \pm 15.66$  years, child class B was  $55.79 \pm 18.84$  years

respectively. Association of Child Pugh Scoring with QTc prolongation was determined and it was found to be statistically significant with  $p < 0.001$  (table-II, figure).

## DISCUSSION

The prevalence of cirrhosis is on the rise in Pakistan owing to the rapid spread of chronic viral hepatitis B and C<sup>3</sup>. The wide spread prevalence of cirrhosis has resulted in greatly improved knowledge among medical professionals regarding this disease and its complications. But cirrhotic cardiomyopathy is a

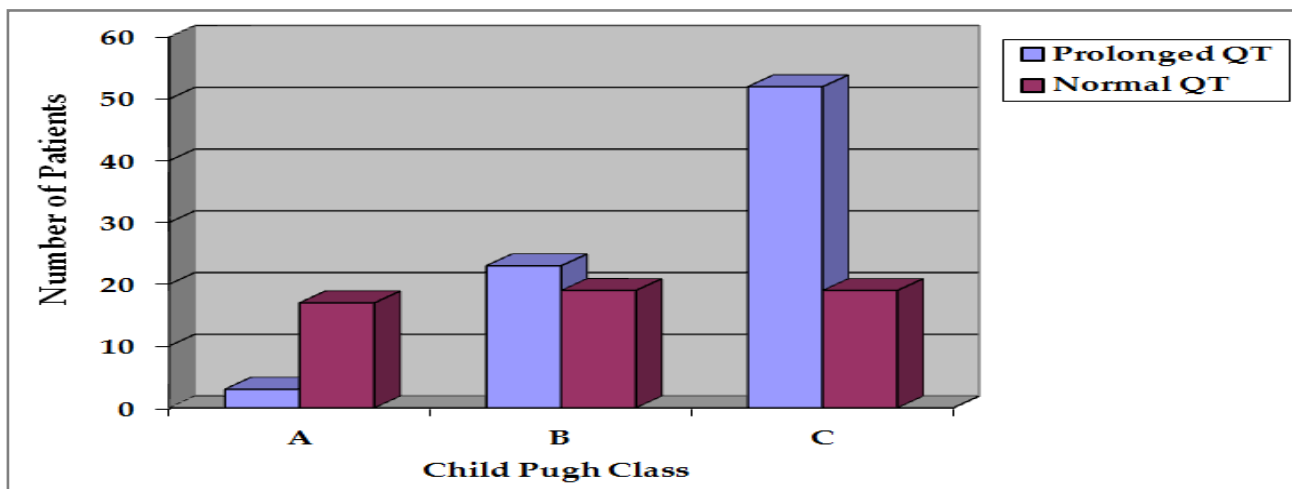


Figure: Patients with prolonged QTc interval according to child PUGH class.

and child class C was  $55.80 \pm 17.06$  years (table-I).

In our study, there were 63.91% (n=85) males and 36.09% (48) females. Out of 133 patients, 15.04% (n=20) were classified as Child Pugh A, 31.58% (n=42) as Child Pugh B, and 53.38% (n=71) as Child Pugh C (table-I).

Frequency of QTc prolongation was 47.5% in age group 30-60 years and 75.47% in age group 61-90 years, *p*-value=0.097. Frequency of QTc prolongation was 61.18% in males and 54.17% in females, *p*-value=0.001 (table-II). The *p*-values for both age and gender were not significant statistically.

Frequency of QTc prolongation were 15%, 54.67% and 73.24% in Child Pugh Class A, B and C respectively. QTc was normal in 85%, 45.24% and 26.76% in Child Pugh Class A, B and C

relatively less known yet very important complication of cirrhosis. It alters the way a patient responds to stressful stimuli and can lead to acute cardiac decompensation and heart failure before and during perioperative period of liver transplant<sup>9</sup>.

The findings of this study are in agreement with a study carried out by Genovesi et al. This study shows similar age distribution when QTc prolongation was measured in cirrhotic patients<sup>6</sup>.

Our patients were distributed unevenly among Child Pugh grade A, B and C with majority being in grade B and C since the sample was taken mostly from the inpatient department and Child Pugh grade A patients are admitted less often than patients with a worse score. Zuberi et al also had a similarly skewed

distribution of patients with more than half of them being in Child Pugh Grade C<sup>10</sup>.

Frequency of QTc prolongation in our study population was found to be 58.64%. This is close to the conclusion Bal et al<sup>11</sup> had drawn in their study in which they showed the frequency of QTc prolongation to be 56%. It was found out to be 46.2% in a study by Bernardi et al<sup>5</sup>, 46.93% in a study by Li et al<sup>12</sup>. This discrepancy may be explained by the presence of other compounding factors such as electrolyte disturbances, concomitant cardiac problems, use of QTc prolonging drugs which were excluded in my study and might have been included in other studies.

The results showed a progressive increase in the frequency of QTc prolongation with the worsening of the Child Pugh Score. Our study showed QTc prolongation in 15% patients with Child Class A, 54.76% in Child Class B and 73.24% in Child Class C. Li et al had results showing prolongation frequency of 21.05%, 56.89% and 59.60% among Child A, B and C showing a rising trend<sup>12</sup>. Bernardi et al demonstrated a similar increasing frequency with results of 25%, 51% and 60% respectively<sup>5</sup>.

Our study had limitations; firstly the sample size was small, secondly QTc is affected by a number of factors other than cirrhosis itself, such as electrolyte disturbances and certain drugs so the frequency of QTc prolongation may be even higher when cirrhotics with these compounding factors are included in the study, thirdly it did not assess prognosis in patients with QTc prolongation. This is the direction for future research, to identify factors and prognosis associated with prolonged QTc in liver cirrhosis and to create awareness among health care professionals regarding these factors, to help them identify and better manage the condition.

## CONCLUSION

This study concludes that there was a statistically significant increase in frequency of QTc prolongation with worsening of Child Pugh Class thereby indicating an association between QTc prolongation and the severity of cirrhosis.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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