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Original Research Article.

To Study the Prevalence of QTc Interval Prolongation in Cirrhosis of Liver And Its Relationship with the Severity of Disease

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ABSTRACT

Background: Cirrhosis of liver is considered as chronic disease of liver characterised by the triad of parenchymal inflammation, necrosis and regeneration with diffuse increase in fibrosis and formation of nodules around regenerating liver parenchyma. A retrospective study of 90 patients of liver cirrhosis visiting OPD/Indoor of SGRDIMSR, Vallah, Sri Amritsar were included in the study conducted from Jan 2017 to Aug 2018 to assess QTc interval in patients with cirrhosis of liver due to any etiology and to find the correlation between QTc interval and severity of liver cirrhosis as per Child-Pugh Score.

Methods: The severity of liver cirrhosis was assessed and according to the Child Pugh Score, divided into Class A, Class B and Class C of 30 patients each. QT interval was noted in all the patients. QTc was calculated by Bazett's formula. From above parameters we try to find out whether there is any correlation between QTc and severity of disease.

Results: The mean value of calculated QTc interval in: Class A=0.474; Class B=0.490 and Class C=0.583. The QTc interval increased linearly with the severity of the disease and the p value was less than 0.001 which is highly significant.

Conclusion: In our study we concluded that the prolongation of QTc interval is co-related with liver function and its prevalence increases with the severity of liver dysfunction. Prolongation of the QTc interval was statistically confirmed in Child-Pugh C and B. The prolonged Q-T interval predicts severe arrhythmias and sudden death, and they are the ideal candidates for liver transplantation.

Keywords: Cirrhosis, QTc Interval, Child Pugh Score.

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INTRODUCTION

The term cirrhosis[1] was first introduced by Laennec in 1826. It is derived from the Greek term Scirrhus and refers to the orange or tawny surface of the liver at autopsy. Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injury characterised by necrosis, inflammation and fibrosis of liver parenchyma.[2]

Cirrhosis of liver is considered as chronic disease of liver characterised by the triad of parenchymal inflammation, necrosis and regeneration with diffuse increase in fibrosis and formation of nodules around regenerating liver parenchyma.[3] Liver cirrhosis refers to a progressive condition that disrupts the normal architecture of the liver. Upto 90% of liver parenchyma undergo destruction before liver failure becomes clinically visible.[4] In developing countries, Hepatitis B and C have been described as the leading causes of cirrhosis, whereas in developed countries, Alcoholic Liver Disease (ALD) and Non-Alcoholic Steatohepatitis (NASH), in addition to Hepatitis C are the leading causes of cirrhosis.[5]

PROGNOSTIC SCORES IN CIRRHOSIS[6]

With regard to cirrhosis, two empirical scores are in common use: Child Pugh Score (CPS) and model for end-stage liver disease (MELD) score. Child-Pugh Score has higher sensitivity than MELD Score. MELD Score was mainly created to predict the survival of patients with end-stage liver disease undergoing TIPS whereas Child-Pugh Score has been widely used to assess the severity of liver dysfunction in clinical work.

The QT-interval represents the length of ventricular electrical systole and its prolongation may provide the substrate for ventricular arrhythmias and sudden death.[8-10] Acquired prolongation of QT interval has been documented in alcoholic liver disease, cirrhosis and liver failure.[11,12] The QT prolongation was found to be independent of the etiology of the hepatic disease. Liver transplantation in patients with liver cirrhosis has been shown to reverse this anomaly. This may imply that the QTc prolongation in cirrhosis is a phenomenon, which derives from the pathophysiology of cirrhosis itself independent of the etiology of the disease.[13,14]

Table 1: Child-Pugh Score[7]

Measure	1 Point	2 Points	3 Points
Total bilirubin, (mg/dL)	<2	2-3	>3
Serum albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time, prolongation (s)	<4.0	4.0-6.0	> 6.0
Ascites	NONE	Mild	Moderate to Severe
Hepatic encephalopathy	NONE	Grade I-II	Grade III-IV

Child-Pugh Score 5-6: Class A; 7-9: Class B; 10-15: Class C

QT interval is the measure of the time between the beginning of Q wave and end of the T wave. The QT interval is dependent on the heart rate. Faster the heart rate, shorter the QT interval. QT interval is adjusted according to the heart rate by Bazett's Formula:[15,16]

$$QTc = \frac{QT\ (sec)}{\sqrt{RR\ interval(sec)}}.$$

Prolonged QT interval on ECG is indicative of an imbalance between right and left sympathetic innervations and is thought to increase the risk of arrhythmias. The mechanisms of producing the cardiovascular changes during cirrhosis are poorly clarified.

ELECTROCARDIOGRAPHY

QT interval is the measure of the time between the start of Q wave and end of the T wave in the heart electrical cycle. In general the QT interval represents the electrical deplorization and repolarization of left and right ventricles.

The QT interval is dependent on the heart rate in an obvious way (faster the heart rate, the shorter the QT interval) and may be adjusted to improve the detection of patients at increased risk of ventricular arrhythmia.

QT interval and QT dispersion were measured as follows:

Bazett's formula Named after Physiologist Henry Cuthbert Bazett was used for calculating the heart rate-Corrected QT Interval (QTC)

$$\mathbf{QTc} = \frac{\mathbf{QT}}{\sqrt{\mathbf{RR}}}$$

QTc= QT interval corrected for heart rate and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex, measured in seconds, often derived from the heart rate (HR) as 60/HR (Here QT is measured in milliseconds).

The measurement of QT interval is subjective. This is because the end of T wave is not always clearly defined and usually merges gradually with the baseline. QT interval in an ECG complex can be measured manually by different methods such as threshold method in which the end of T wave is determined by the point at which the component of T wave merges with the isoelectric baseline or the tangent method in which the end of T wave is determined by the intersection of a line extrapolated from isoelectric baseline and the tangent line, which touches the terminal part of T wave at the point of maximum downslope.

Three lead ECG is recorded in Lead I, avL and V6 because in these leads beginning of QRS complex is best determined. Mean QT interval is calculated by adding QT interval of six beats i.e. 2 each in all the three leads as stated above. Similarly mean RR interval will be calculated. From these values QTc will be calculated as described above.

QT dispersion is simply defined as the difference between the longest (QT Max) and shortest (QT Min) QT Interval within 12 lead ECG. Each of the 12 QT intervals was individually measured to determine the values of these extreme indices.

As said above, QT interval on its own vary according to the heart rate, the QTC i.e. QT interval corrected for heart rate using Bazett's formula and therefore QT Dispersion=Difference between QTc max and QTc min i.e., corrected QT max –corrected QT min.

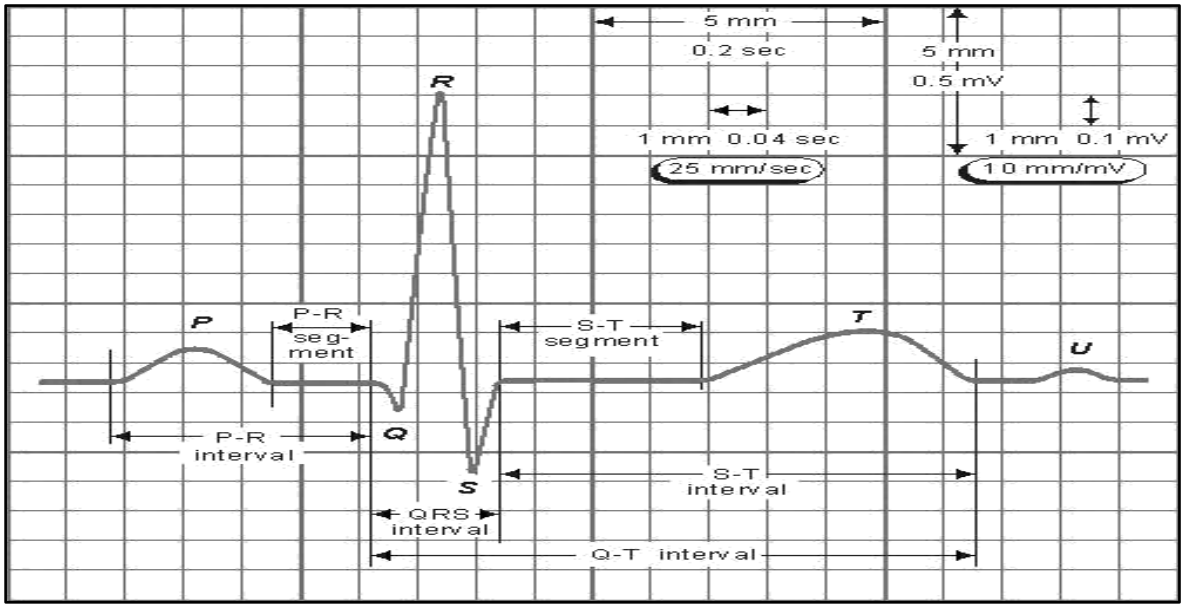

Figure 1: ECG showing QT Interval.

MATERIALS AND METHODS

90 patients of liver cirrhosis visiting OPD/Indoor of SGRDIMSR, Vallah, Sri Amritsar were included in the study.

The severity of liver cirrhosis was assessed and according to the Child Pugh Score, patients were grouped equally into:

Group 1: 30 patients of Liver cirrhosis with Child Pugh class-A (Score 5-6)

Group 2: 30 patients of Liver cirrhosis with Child Pugh class-B (Score 7-9)

Group 3: 30 patients of Liver cirrhosis with Child Pugh class-C (Score 10-15)

- QT interval was noted in all the patients.
- QTc was calculated by Bazett's formula in the study.
- From above parameters we tried to find out whether there was any correlation between QTc and severity of disease (according to CHILD PUGH SCORE).

Inclusion Criteria

All patients of cirrhosis of liver (diagnosed on the basis of clinical, biochemical and USG abdomen examination) were included in the study, irrespective of the etiology of cirrhosis.

Exclusion Criteria

The following patients will be excluded from the study:

1) Patient's suffering from cardiac problems like ischaemic heart disease, Conduction defects, atrial fibrillation, cardiomyopathy.
2) Patient's drugs that prolong QT INTERVAL eg: CCB, antipyschotics, amiodarone, antihistamines, macrolides, quinolones.

3) Patient's suffering from any other condition causing prolongation of QT interval (electrolyte abnormalities) and patients with renal failure.

Laboratory Parameters

- Complete Blood Count.
- Urine complete examination.
- Renal Function Tests
- Serum Electrolytes- Na^{+}, K^{+}, Mg^{+2}, Ca^{2+}
- Liver Function Tests
- TSP/DSP
- PTI
- ECG
- USG Abdomen(spleen size and liver status)
- Upper GI Endoscopy.
- Viral markers.
- Serum ANA levels(Autoimmune profile as per required).

Procedure

90 patients of liver cirrhosis attending OPD/Indoor of SGRDIMSR, Vallah, Sri Amritsar after applying the inclusion and exclusion criteria were assessed for above mentioned parameters. A detailed history and examination was done on the patients and patients were investigated for presence of liver cirrhosis. Patients were then divided into three groups as per Child Pugh Score.

Then all the patients were evaluated for QTc on ECG. A correlation between QTc and severity of liver cirrhosis as per Child-Pugh Score was seen. The observations and interpretations were recorded and results obtained were statistically analysed.

Statistical Analysis

All analysis was done using SPSS version 17.0. Chi- Square test, One-Way ANOVA test and Pearson Correlation coefficient tests were used for comparing the mean values.

RESULTS

In this study 90 patients were included and divided into three groups of 30 each as per Child-Pugh score. QTc interval was calculated in all the patients. The prevalence of QTc interval prolongation was seen in these patients with cirrhosis of liver. QTc prolongation was compared with the following parameters:

1. Sex of the patient.
2. Etiological parameters (HBV, HCV, Autoimmune, Alcohol).
3. HIV status.
4. Severity of ascites.
5. Severity of encephalopathy.
6. Serum Bilirubin levels.
7. Serum albumin levels.
8. PTI prolongation.
9. Severity of anaemia.
10. Age of the patients.
11. Child-Pugh Score.

In the present study, the maximum number of patients was in the age group of of 41-50 years constituting 30% of the patients followed by age group of 51-60 years constituting 28.3% of the patients. (Table 2)

As shown in the data given in the table 3, in the present study the cirrhosis was more common in males (78.88%) as compared to the females (14.44%)

In the present study the major cause of cirrhosis was alcohol (67 patients were alcoholic) and in non-alcoholics the major cause of cirrhosis was hepatitis C. (Table 4)

Many patients presented with more than one presenting complaint. In the present study, most of the patients presented with yellowish discolouration of eyes and urine (65.55%), abdominal distension was present in 41 patients.(53.33%), lower limb swelling in 35 (38.3%) of patients and altered sensorium in 24 (26.66%) of patients. Abdominal pain and bleeding was present in 14(15.55%) and 9(10%) patients respectively. (Table 5)

In our present study pallor was seen in 83.33% patients, icterus was seen in 46.66% patients, ascites in 45.5%, edema in 44.44%, splenomegaly in 42.22%, signs of chronic renal failure in 40% and hepatomegaly in 26.6%.(Table 6)

In our present study anaemia was present in 75 (83.33%) out of 90 patients. Most of the patients i.e., 50 patients (55.55%) had haemoglobin level between 5-9 gm/dl. Only 8 patients had haemoglobin level <5gm/dl and 15 patients had haemoglobin>11gm/dl. (Table 7)

42 patients (46.6%) out of 90, in this study group had clinical jaundice while 25 patients had raised bilirubin (1.0-2.0 mg%) without clinically evident jaundice. Rest of the patients (25.5%) had normal bilirubin. (Table 8)

50 (55.5%) out of 90 patients had hypoalbuminemia, 22 patients (23.91%) had serum albumin in the range of 2.0-2.5 gm%, 7 patients (7.6%) between 2.5-3.0 gm% and 15 patients (16.66%) had between 3.0-3.5 gm%. 19 patients (29.11%) serum albumin between 3.5-4.0 gm% and 5 patients (5.55%) had serum albumin between 4.0-4.5 gm %. 21 patients had very low serum albumin of less than 2 gm%. (Table 9)

In our present study the mean value of serum bilirubin (total) is 3.58±5.40, serum bilirubin (direct): 2.26±0.45; SGOT-150.52±3.321; SGPT-96.5±4.41; ALP-65.06±2.99;Total serum protein-6.82±3.65; serum albumin-2.7±2.65. (Table 10)

Table 2: Distribution According To Age

Age Group in years	No. of patients	Percentage
<=30	2	3.3%
31-40	19	15%
41-50	28	30%
51-60	27	28.3%
61-70	17	11.67%
>70	7	11.67%
Total	90	100%

Table 3: Distribution According To Sex

Sex	CP Class						Total
	Class I		Class II		Class III		
	N	%	N	%	N	%	
Male	25	83.30	20	66.70	26	86.70	71
Female	5	16.70	10	33.30	4	13.30	19
Total	30	100.00	30	100.00	30	100.00	90

Table 4: Etiology of Cirrhosis

Etiology	CPS-A		CPS-B		CPS-C		Total
	(N)	(%)	(N)	(%)	(N)	(%)	
HCV	6	20	13	43.3	6	20	25
HBV	4	13.3	6	20	5	16.7	15
Alcoholic	21	70	20	66.7	26	86.7	67
Autoimmune	2	6.7	1	3.3	0	0	3

Table 5: Distribution According To Symptomatology

Symptoms	No. of patients	Percentage
Yellowish discoloration	42	65.55%
Abdominal Distension	41	53.33%
Lower Limb Swelling	35	38.88%
Altered sensorium	34	37.77%
Abdominal Pain	14	15.55%
Bleeding	9	10%
Fever	2	2.22%

Table 6: Distribution According To Signs Seen In Patients

Signs	Frequency	Percent (%)
Pallor	75	83.33%
Icterus	42	46.66%
Ascites	41	45.55%
Pedal edema	40	44.44%
Splenomegaly	38	42.22%
Signs of chronic liver failure	36	40%
Hepatomegaly	24	26.66%

Table 7: Distribution According To The Haemoglobin Level Of Patients In Study Group

Haemoglobin (gm)	No of patients	Percentage
<5	8	8.88%
5-6.9	27	30%
7-8.9	23	25.55%
9-11	17	18.88%
>11	15	16.66%

Table 8: Distribution According To The Serum Bilirubin Levels Of Patients In Study Group

Serum Bilirubin (mg%)	No of patients	Percentage
<1	23	25.76%
1.0-1.9	25	27.77%
2.0-2.9	15	16.66%
3.0-5.0	11	12.22%
>5	16	17.77%

Table 9: Distribution According to the Serum Albumin Level of Patients in the Study Group

Serum Albumin (gm%)	No of patients	Percentage
<2.0	21	23.33%
2.0-2.4	22	24.44%
2.5-2.9	7	7.77%
3.0-3.4	15	16.66%
3.5-3.9	19	21.11%
4.0-4.5	5	5.55%
>4.5	1	1.11%

Table 10: Showing Mean Value of Biochemical and Haematological Parameters in Study Group

Parameters	Mean Value
Serum Bilirubin (Total)	3.58 ± 5.40
Serum Bilirubin (Direct)	2.26 ± 0.45
SGOT	150.52 ± 3.21
SGPT	96.5 ± 4.41
ALP	65.06 ± 2.99
Total Serum Protein	6.82 ± 3.65
Serum Albumin	2.7 ± 2.65

Table 11: Prevalence of QTc in Patients with Cirrhosis of Liver

Child Pugh Score	n	No. of Patients With Prolonged QTc Interval	%
A	30	23	76.66%
B	30	28	93.33%
C	30	30	100%

Table 12: Correlation of Sex with the QTc Prolongation

Sex	N	Mean QTc	Std. Deviation	P value
Male	71	0.51	0.05	0.666
Female	19	0.52	0.06	

P value- Not significant

Table 13: Correlation of Alcoholism with the QTc Prolongation

Alcoholic	N	Mean QTc	Std. Deviation	P value
No	23	0.51	0.05	0.666
Yes	67	0.52	0.06	

P value- not significant

Table 14: Correlation of HIV Status with the QTc Prolongation

HIV	N	Mean QTc	Std. Deviation	P value
Non-reactive	88	0.52	0.060	0.916
Reactive	2	0.52	0.057	

P value- not significant

Table 15: Correlation of HCV Status with the QTc Prolongation

HCV	N	Mean QTc	Std. Deviation	P value
Non-reactive	65	0.52	0.06	0.671
Reactive	25	0.51	0.05	

P value- not significant

Table 16: Correlation of HBV Status with the QTc Prolongation

HBV	N	Mean QTc	Std. Deviation	P value
Non-reactive	75	0.51	0.06	0.58
Reactive	15	0.52	0.05	

P value- not sigificant

Table 17: Correlation of Autoimmune Status with the QTc Prolongation

Autoimmune	N	Mean QTc	Std. Deviation	P value
No	87	0.52	0.060	0.516
Yes	3	0.49	0.061	

P value- Not significant

Table 18: Correlation of the QTc Prolongation with the Severity of Ascites

Ascites	N	Mean QTc	Std. Deviation	P value
None	49	0.48	0.036	<0.001**
Mild	24	0.54	0.057	
Moderate	7	0.57	0.036	
Severe	10	0.60	0.017	

P value- Significant

Table 19: Correlation of the QTc Prolongation with the Severity of Hepatic Encephalopathy

Hepatic encephalopathy	N	Mean QTc	Std. Deviation	P value
None	56	0.48	0.042	<0.001**
Grade 1	7	0.53	0.048	
Grade 2	7	0.57	0.069	
Grade 3	13	0.58	0.035	
Grade 4	7	0.58	0.041	

P value- Significant

Table 20: Correlation of the QTc Prolongation with the Serum Bilirubin Levels

T. Bilirubin	N	Mean QTc	Std. Deviation	P value
<2	49	0.46	0.051	<0.001**
2-3	13	0.48	0.035	
>3	28	0.56	0.058	

P value- Significant

Table 21: Correlation of the QTc Prolongation with the Serum Albumin Levels

Albumin	N	Mean QTc	Std. Deviation	P value
>3.5	18	0.47	0.039	<0.001**
2.8-3.5	24	0.50	0.053	
<2.8	48	0.54	0.058	

P value- Significant

Table 22: Correlation of the QTc Prolongation with the Prothrombin Time Prolongation

PTI Prolongation	N	Mean QTc	Std. Deviation	P value
<4.0	69	0.50	0.055	<0.001**
4.0-6.0	5	0.53	0.067	
>6.0	16	0.57	0.054	

P value- Significant

Table 23: Correlation of the QTc Prolongation with the Severity of Anaemia

Anaemia	N	Mean QTc	Std. Deviation	P value
Mild (9-11)	49	0.51	0.051	
Moderate (7-9)	13	0.49	0.035	0.516
Severe (<7)	28	0.50	0.058	

P value- not significant

Table 24: Correlation of Prolonged Qtc Interval with Age of Patients

Age Group	Mean QTc	P Value
<50	0.511	
51-69	0.499	0.561
>70	0.521	

P value- not significant

Table 25: Correlation of QTc Interval with the Severity of Cirrhosis as Per Child-Pugh Score

CP Class	N	QTC Mean	SD	ANOVA	P Value
Class A	30	0.474	0.039		0.209
Class B	30	0.490	0.035	F=83.038	<0.001
Class C	30	0.583	0.032	P<0.001	<0.001

P value<0.01, highly significant.

In present study, 71 (78.88%) out of 90 patients of liver cirrhosis have QTc prolongation. (Table 11)

In the present study, QTc was prolonged both in males (mean=0.51) and in females (0.52) with the p-value of 0.666 which is not significant; thereby predicting that QTc prolongation was independent of the sex of the patient. (Table 12)

In the present study, QTc was prolonged both in alcoholic (mean=0.52) and in non-alcoholics (0.51) with the p-value of 0.666 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease. (Table 13)

In the present study, QTc was prolonged both in HIV negative (mean=0.52) and HIV positive patients (mean=0.52) with the p-value of 0.916 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease. (Table 14)

In the present study, QTc was prolonged both in HCV negative (mean=0.52) and HCV positive patients (mean=0.51) with the p-value of 0.671 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease. (Table 15)

In the present study, QTc was prolonged both in HBV negative (mean=0.51) and HBV positive patients (mean=0.52) with the p-value of 0.58 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease. (Table 16)

In the present study, QTc was prolonged both in autoimmune cirrhosis (mean=0.49) and in non-autoimmune cirrhosis (mean=0.52) with the p-value of 0.516 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease. (Table 17)

In the present study the mean QTc value was higher in patients with severe ascites (mean=0.60) as compared to the patient without ascites, with p-value of 0.001 which is highly significant. (Table 18)

In the present study the mean QTc value was higher in patients with grade 4 encephalopathy (mean=0.6) as compared to the patient without encephalopathy, with p-value of 0.001 which is highly significant. (Table 19)

In the present study the mean QTc value was higher in patients with Serum bilirubin levels of more than 3mg/dl (mean = 0.56) as compared to the patients with serum bilirubin levels of less than 2mg/dl (mean=0.46), with the p-value of <0.001 which is highly significant. (Table 20)

In the present study the mean QTc value was higher in patients with serum albumin levels of less than 2.8mg/dl (mean=0.54) as compared to the patients with serum albumin levels of more than 3.5mg/dl (mean=0.47), with the p-value of <0.001 which is highly significant. (Table 21)

In the present study the mean QTc value was higher in patients with PTI prolongation more than 6 sec (mean=0.57) as compared to the patients with PTI prolongation of less than 4 sec (mean=0.50), with the p-value of <0.001 which is highly significant. (Table 22)

In the present study, QTc was prolonged both in severe anaemia (mean=0.50) and in patients with mild anaemia (mean-0.51) with the p-value of 0.516 which is not significant; thereby predicting that QTc prolongation was independent of severity of anaemia. (Table 23)

In the present study, QTc was prolonged in liver cirrhosis irrespective of the age of the patients. Correlation between prolongation of QTc interval and age of the patients is not significant with p value of 0.561. (Table 24)

In our present study, QTc prolongation increases linearly with the severity of liver cirrhosis. In Child-Pugh Class C the mean QTc was 583 which were higher as compared to Child-Pugh Class B and C. (mean QTc of class A-474 and mean QTc of class B was 490). (Table 25)

DISCUSSION

In cirrhosis, scar tissue replaces normal, healthy liver tissue blocking the flow of blood through the organ. On ultrasonography, liver of long standing cirrhosis appear shrunken. The normal echo pattern is lost and it appears as coarse echo pattern often associated with splenomegaly, ascites and portal hypertension.

A frequent occurrence of Q-Tc interval prolongation has been found in patients with alcoholic liver disease. Q-Tc abnormality is closely related to the severity of cirrhosis. Q-Tc prolongation is independent of the etiology of cirrhosis.

Q-Tc length also correlated with a number of variables reflecting either the impairment of liver function or the presence of circulatory and renal function abnormalities of advanced cirrhosis, but multivariate analysis showed that the Child-Pugh score was the only independent predictor of Q-Tc length variability.

When patients with cirrhosis are selected, the impact of alcohol toxicity are overwhelmed by factors related to liver failure, patients with cirrhosis show a prolonged Q-T interval, which parallels the severity of the disease, regardless of the etiology of cirrhosis.

Electrophysiologic cardiac abnormalities are well documented in patients with ESLD. Although the exact mechanism for QT prolongation in ESLD remains to be established, previous studies have suggested QT prolongation in ESLD may be multifactorial and related to abnormalities in potassium channels involved in repolarization, high plasma concentrations of bile salts, and autonomic dysfunction .Even though the mechanism of the prolongation of QT intervals is not fully elucidated, it is attributed to autonomic changes caused by cirrhosis.

In our present study 90 patients of cirrhosis of liver (diagnosed on the basis of clinical, biochemical and USG abdomen examination) were included in the study, irrespective of the etiology of cirrhosis. They were divided equally into 3 groups: Child-Pugh Score A,B and C. ECG was recorded in all the patients. QT interval was noted and QTc was calculated.

Age Distribution

In the present study, the maximum number of patients was in the age group of of 41-50 years constituting 30% of the patients followed by age group of 51-60 years constituting 28.3% of the patients.

In a similar study conducted by DAY CP et al., 69 patients were taken with cirrhosis of liver. Among these patients maximum patients were in the age group of 50-59 patients constituting 29% of the patients followed by the age group of 41-50 years.[17]

Sex Distribution

In our present study the cirrhosis was more common in males (78.88%) as compared to the females (14.44%).

A similar study conducted by BERNADI et al, Include 94 patients of liver cirrhosis. Among these patients maximum were males constituting 84% of the total patients included in the study.[18]

Etiology of Cirrhosis

In the present study the major cause of cirrhosis was alcohol (67patients were alcoholic)and in non-alcoholics the major cause of cirrhosis was hepatitis C.

In a study conducted by K. Mimidis in 2003, 53 patients were taken having end-staged liver disease.in this study it was seen that alcohol was the most common cause of cirrhosis(74.89%).[19]

Presenting Complaints

Many patients presented with more than one presenting complaint. In the present study, most of the patients presented with abdominal distension 59 (98.3%), jaundice was present in 48 (80%) of patients followed by lower limb swelling in 35 (58.3%) of patients and altered sensorium in 24 (40%) of patients. Abdominal pain and bleeding was present in 14 (23.3%) and 9 (15%) patients respectively.

Haemoglobin Level of Patients in the Study Group

In our present study anaemia was present in 75 (83.33%) out of 90 patients. Most of the patients i.e., 50 patients (55.55%) had haemoglobin level between 5-9 gm/dl. Only 8 patients had haemoglobin level <5gm/dl and 15 patients had haemoglobin>11gm/dl.

Distribution of Serum Bilirubin of the Patients

42 patients (46.6%) out of 90, in this study group had clinical jaundice while 25 patients had raised bilirubin (1.0-2.0 mg%) without clinically evident jaundice. Rest of the patients (25.5%) had normal bilirubin.

Distribution of Serum Albumin of Patients in Study Group

50 (55.5%) out of 90 patients had hypoalbuminemia, 22 patients (23.91%) had serum albumin in the range of 2.0-2.5 gm%, 7 patients (7.6%) between 2.5-3.0 gm% and 15 patients (16.66%) had between 3.0-3.5 gm%. 19 patients (29.11%) serum albumin between 3.5-4.0 gm% and 5 patients (5.55%) had serum albumin between 4.0-4.5 gm %. 21 patients had very low serum albumin of less than 2 gm%.

Correlation of Alcoholism with the QTc Prolongation

In the present study, QTc was prolonged both in alcoholic (mean=0.52) and in non-alcoholics (0.51) with the p-value of 0.666 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease.

Correlation of Sex with the QTc Prolongation

In the present study, QTc was prolonged both in males (mean=0.51) and in females (0.52) with the p-value of 0.666 which is not significant; thereby predicting that QTc prolongation was independent of the sex of the patient.

Correlation of HIV Status with the QTc Prolongation

In the present study, QTc was prolonged both in HIV negative (mean=0.52) and HIV positive patients (mean=0.52) with the p-value of 0.916 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease.

Correlation of HCV Status with the QTc Prolongation

In the present study, QTc was prolonged both in HCV negative (mean=0.52) and HCV positive patients (mean=0.51) with the p-value of 0.671 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease.

Correlation of HBV Status with the QTc Prolongation

In the present study, QTc was prolonged both in HBV negative (mean=0.51) and HBV positive patients (mean=0.52) with the p-value of 0.58 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease.

Correlation of Autoimmune Status with the QTc Prolongation

In the present study, QTc was prolonged both in autoimmune cirrhosis (mean=0.49) and in non-autoimmune cirrhosis (mean=0.52) with the p-value of 0.516 which is not significant; thereby predicting that QTc prolongation was independent of the etiology of the disease.

Correlation of the QTc Prolongation with the Severity of Ascites

In the present study the mean QTc value was higher in patients with severe ascites (mean=0.60) as compared to the patient without ascites (mean=0.48), with the p-value of <0.001 which is highly significant.

Correlation of the QTc Prolongation with the Severity of Hepatic Encephalopathy

In the present study the mean QTc value was higher in patients with GRADE 4 encephalopathy (mean=0.58) as compared to the patient without encephalopathy (mean=0.48), with the p-value of <0.001 which is highly significant.

Correlation of the QTc Prolongation with the Severity of Serum Bilirubin Levels

In the present study the mean QTc value was higher in patients with Serum bilirubin levels of more than 3mg/dl (mean=0.56) as compared to the patients with serum bilirubin levels of less than 2mg/dl (mean=0.46), with the p-value of <0.001 which is highly significant.

Correlation of the QTc Prolongation with the Severity of Serum Albumin Levels

In the present study the mean QTc value was higher in patients with serum albumin levels of less than 2.8mg/dl (mean=0.54) as

compared to the patients with serum albumin levels of more than 3.5mg/dl (mean=0.47), with the p-value of <0.001 which is highly significant.

Correlation of the QTc Prolongation with the Severity of Prothrombin Time

In the present study the mean QTc value was higher in patients with PTI prolongation more than 6 sec (mean=0.57) as compared to the patients with PTI prolongation of less than 4 sec (mean=0.50), with the p-value of <0.001 which is highly significant.

Correlation of the QTc Prolongation with the Severity of Anaemia

In the present study, QTc was prolonged both in severe anaemia (mean=0.50) and in patients with mild anaemia (mean-0.51) with the p-value of 0.516 which is not significant; thereby predicting that QTc prolongation was independent of severity of anaemia.

Correlation of the QTc Prolongation with the Severity of Liver Cirrhosis as Per Child-Pugh Score

In our present study study it was seen that QTc interval is prolonged in patients with cirrhosis of liver. Also QTc prolongation increases linearly with the severity of liver cirrhosis. In Child-Pugh Class C the mean QTc was 583 which were higher as compared to Child-Pugh Class B and C. (Mean QTc of class A-474 and mean QTc of class B was 490).

Kosar F[20] demonstrated a similar increasing frequency with results of 25%, 51% and 60% respectively. (Child-Pugh A: 452 ± 25 ms, Child-Pugh B: 483 ± 62 ms and Child-Pugh C: 510 ± 45 ms, p < 0.001).

The frequency of QTc prolongation in our study population was found to be 24.7% in a study presented by Zuberi et al.[21] However, other international studies have shown a wide range of values.

In a study with 38 cirrhotic patients (50% male), Genovesi et al.[22] showed that corrected QT values were higher in Child-Pugh C cirrhotic patients (Child-Pugh A: 462 ± 25 ms, Child-Pugh B: 493 ± 62 ms and Child-Pugh C: 520 ± 45 ms, p < 0.001).

In a study of 409 cirrhotic patients, Bal JS et al[23] reported higher corrected QT in the Child-Pugh C group than the Child-Pugh B group (451±43 vs434 ± 31 ms, p < 0.001).

In our present study 90 patients of cirrhosis of liver (diagnosed on the basis of clinical, biochemical and USG abdomen examination) were included in the study, irrespective of the etiology of cirrhosis. They were divided equally into 3 groups: Child-Pugh Score A, B and C. ECG was recorded in all the patients. QT interval was noted and QTc was calculated.

It was observed that patients with Child-Pugh Score C had prolonged QTc interval. This prolonged QTc has great prognostic significance as it can cause arrthymias leading to sudden death.

It was observed that there was no electrolyte balance in these patients. The average serum Na^{+},K^{+},Ca^{+2} and Mg^{+2} of these patients are within the normal limits, therefore they have no etiological role.

The incidence of prolonged QT interval in the present study is almost like previous studies and like others there is no electrolyte imbalance in patients showing QT interval prolongation. Prolongation of QT interval is probably due to certain undefined changes as a result of alcoholic cirrhosis.

Table 26: Various studies showing correlation between mean QTc prolongation with Child-Pugh score.

Study	No. of patients	QTc in Child-Pugh A	QTc in Child-Pugh B	QTc in Child-Pugh C	Electrolyte Imbalance
Kosar F[20](2007)	166	462±25	493±62	520±45	NIL
Genovesi[22] (2009)	38	462+25 ms	493+62	520+45	NIL
Adnan Bashir Bhatti[24](2013)	52	445	480	489	NIL
Bal JS[23] et al (2013)	409	434+31	451+43	510+43	NIL
Pedro Gemal Lanzieri[25] (2017)	67	428+34	436+25	459+33	NIL
Present Study	90	474	490	583	NIL

Electrolyte imbalance cannot be claimed as a cause of QTc prolongation, because the serum level of the electrolytes were within the normal limit in these patients.

The pathogenesis of prolonged QTc in liver cirrhosis remains unexplained. QT interval can be prolonged either because activation of the ventricular myocardium is slowed or the complex process of repolarisation is prolonged. The dynamic process of repolarisation is prolonged because of electrolyte abnormalities/some cardiac diseases and these are being excluded in our study.

It is more likely that the complex cardiovascular and physiological changes that occur in liver disease in some may modulate the cardiac function which causes prolonged QTc interval.

In our present study, it is concluded that QTc interval is prolonged in patients of liver cirrhosis. QTc interval prolongation increases linearly with the severity of liver cirrhosis. The etiology of this prolongation is not a disturbance in serum electrolyte levels.

The recording of QTc in patients with cirrhosis of liver helps in predicting the prognosis of the patient as Life threatening arrthymias are triggered in these individuals during stressful conditions.

A prolonged QTc interval also heralds torsede de pointes. The prevalence and severity of QTc interval prolongation are proportional to severity of liver disease and ECG becomes mandatory in patients before prescribing any drug which may cause increase in the QTc interval.

CONCLUSION

In our study we concluded that the prolongation of QTc interval is co-related with liver function and its prevalence increases with the severity of liver dysfunction. Prolongation of the QTc interval was statistically confirmed in Child-Pugh C and B. The prolonged Q-T interval predicts severe arrhythmias and sudden death, and they are the ideal candidates for liver transplantation.

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