Original Research Article

Cardiovascular dysfunction in patients of cirrhosis of liver

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ABSTRACT

Background: Cirrhosis of liver refers to a progressive condition that disrupts the normal architecture of the liver. It is increasingly recognized that cirrhosis per se can cause cardiac dysfunction. The aim was to assess cardiovascular dysfunction electrocardiographically and echocardiographically in patients with cirrhosis of liver and to find the correlation between cardiovascular dysfunction and severity of liver cirrhosis as per child-PUGH score.

Methods: Total 90 patients of cirrhosis of liver of both sexes were included in this cross-sectional study conducted from January 2018 to August 2019 in SGRDIMSR, Sri Amritsar. The severity of liver cirrhosis was assessed as per Child Pugh Score. QTc interval was calculated by Bazett's formula. Systolic and Diastolic dysfunction was seen on 2D-echocardiography.

Results: QTc interval increased linearly with the severity of liver cirrhosis. Mean values of QTc in Child Pugh Class A=425.00(±20.97), Class B=437.35(±42.60), Class C=479.71(±29.48) with p value of 0.04 which is significant. Diastolic dysfunction was also related with the severity of liver cirrhosis. In Child Pugh Class A= 2(33%) patients had grade 1 diastolic dysfunction, Class B=23(59%) patients had grade 1 diastolic dysfunction while in Child Pugh Class C=3(7%) had grade 1 diastolic dysfunction, 33(73%) patients had grade 2 diastolic dysfunction and 1(2%) patients had grade 3 diastolic dysfunction with p value of 0.04 which is significant. Systolic function was found normal in all the patients.

Conclusions: Diastolic dysfunction and QTc interval prolongation are both related with the severity of liver cirrhosis and are major criteria of cirrhotic cardiomyopathy.

Keywords: Cardiomyopathy, Child pugh score, Cirrhosis, Diastolic dysfunction, QTc interval

INTRODUCTION

Cirrhosis of liver 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.[1] 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.[2] The severity of liver cirrhosis can be assessed by child-Pugh score and MELD score. Child-Pugh score has higher sensitivity than MELD score. Child-Pugh score depends on jaundice, ascites, encephalopathy, serum albumin levels and prothrombin time (Table 1).[3] Cardiac dysfunction in cirrhosis, a problem on the 'blind side of the heart', often remains ignored. However, cirrhosis is associated with a host of cardiovascular abnormalities including hyperdynamic circulation, portal hypertension, hepato-pulmonary syndrome and changes in several different vascular territories such as the renal and cerebral vasculature.[4]

There is hyperdynamic circulatory state, decreased arterial blood pressure, decreased peripheral resistance,

and increased cardiac output. Because of reduced systemic vascular resistance and increased arterial compliance, left ventricular failure may be latent in cirrhosis.[5]

Cardiac abnormalities in cirrhosis are usually attributed to the toxic effect of alcohol on the heart. However, it is increasingly recognised that cirrhosis per se can cause cardiac dysfunction.

The definition of cirrhotic cardiomyopathy is the presence of one or more of the following:

- Baseline increased cardiac output but blunted ventricular response to stimuli;
- Systolic and/or diastolic dysfunction;
- Absence of overt left ventricular failure at rest;
- Electrophysiological abnormalities including prolonged Q-T interval on electrocardiography and chronotropic incompetence.[6]

Diastolic function is a predictor of mortality in cirrhotic patients.[7]

The objective of the study was to assess cardiovascular dysfunction electrocardiographically and echocardiographically in patients with cirrhosis of liver and to find the correlation between cardiovascular dysfunction and severity of liver cirrhosis as per CHILD-PUGH SCORE.

Table 1: Child PUGH Score.

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 (sec)	<4.0	4.0-6.0	>6.0
Ascites	None	Mild	Moderate-severe (or refractory)
Hepatic encephalopathy	None	Grade 1-2	Grade 3-4

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

METHODS

A cross-sectional study was conducted in 90 diagnosed patients of liver cirrhosis visiting OPD/Indoor of SGRDIMSR, Sri Amritsar from January 2018 to August 2019.

Cirrhosis was labeled on the basis of:

- Clinical (reduced liver span <8 cm on clinical exam with ascites/or splenomegaly).
- Biochemical (prolonged prothrombin time>12 seconds and reduced level of serum albumin <3.5g/dl).
- Radiological (increased liver echo pattern, shrunken liver <8cm in mid-clavicle line, portal vein diameter >1.3 cm and spleen size >13 cm longitudinally).

The severity of liver cirrhosis was assessed and according to the child Pugh score, patients were grouped into:

- Group 1: - patients of Liver cirrhosis with child Pugh class-A (Score 5-6).
- Group 2: - patients of Liver cirrhosis with child Pugh class-B (Score 7-9).
- Group 3: - patients of Liver cirrhosis with child-Pugh class-C (Score 10-15).

ECG was done in all the patients. ECG abnormalities:

QTc: QTc values was calculated in all patients by following formula,

$$QTc = QT (sec)/\sqrt{RR} (sec)$$

The value of QTc of >0.44 sec (440msec) was considered as prolonged.[8]

2D Echocardiography

2D M mode Colour Doppler Echocardiography was done by commercially available Echocardiography machine, and used to assess cardiac status with special reference to left atrial diameters, left ventricle end diastolic volume, I.V. septal thickness, left ventricular posterior wall thickness and to assess E/A ratio where E stands for early maximum left ventricular filling velocity, and A for late diastolic left ventricle filling velocity.

Left ventricular systolic function was assessed by ejection fraction. Left ventricular diastolic function was assessed by E/A ratio. Grades of diastolic dysfunction:

- Grade 1: impaired relaxation pattern with normal filling pressures.
- Grade 2: pseudo-normalised pattern.
- Grade 3: reversible restrictive pattern.
- Grade 4: irreversible restrictive pattern.

Inclusion criteria

- Age group > 18 years of either sex.
- Alcoholic and non-alcoholic patients with clinical features and laboratory tests suggestive of cirrhosis of liver (including ultrasonography).
- Patients with compensated and decompensated cirrhosis.

Exclusion criteria

- Patients suspected of or having malignancy of liver.
- Patients of CAD/Valvular heart disease, conduction defects, cardiac arrhythmias and congenital heart defects.
- Known cases of diabetes and hypertension.
- Hepatic encephalopathy.
- Renal Failure.
- Thyroid Dysfunction.

Patients were verified with inclusion and exclusion criteria. All patients and their relatives were informed about the study in their vernacular language, written consent was taken. A detailed history of each patient along with complete clinical examination was done and routine investigations like complete blood count, urine complete examination, renal function tests, serum electrolytes- sodium, potassium, calcium, liver function tests, PTI, HBA1C, T3, T4, TSH, ECG, USG ABDOMEN, 2D echocardiography were done.

This study was carried out after approval from hospital ethical committee and obtaining informed consent from patients or their relatives. The data from the present study was systematically collected, compiled and statistically analysed to draw relevant conclusions using SPSS Statistics-20 version.

The observations were tabulated in the form of mean±standard deviation (SD). Continuous variables were analysed using analysis of variance (ANOVA). In parametric data, student-t test was used. Quantitative variables were correlated using chi-square test. The data was analysed and level of significance was determined as its 'p' value with $p<0.05$ as significant, $p<0.001$ as highly significant and $p>0.05$ as non-significant.

RESULTS

A total of 90 patients of cirrhosis of liver were selected for cross-sectional study by simple random sampling method. All patients were evaluated for QTc interval prolongation and systolic as well as diastolic dysfunction.

In the present study, the maximum number of patients were in the age group of 41-60 years constituting 56.7% of the patients followed by age group of 18-40 years constituting 22.2% of the patients. Cirrhosis was more common in males (91.1%) as compared to females (8.89%). The maximum number of patients were alcoholics (75.6%) followed by HCV (37.8%), NASH (3.3%), HBV (2.2%). Most of the patients presented with more than one presenting complaint. Most common clinical symptom with which patients presented was abdominal distention 39(43.33%)patients, hematemesis was present in 34 patients (37.78%), yellowish discoloration of eyes/urine in 30 patients (33.33%), malena in 19 patients (21.11%), abdominal pain in 12 patients (13.33%), fever in 7 patients (7.78%). Ascites

was present in 80.0% patients, pallor in 66.67% patients, splenomegaly in 54.44% patients, icterus and pedal edema in 44.44 % patients, hepatomegaly in 17.78% patients.

Anemia was present in 84(93.34%) patients out of 90. Most of the patients i.e. 67(74.45%) patients had Hemoglobin level between 7.1-12gm/dl. Only 5(5.56%) patients had Hemoglobin <5gm/dl and 6(6.67%) patients had Hemoglobin >12gm/dl.

53(58.89%) patients out of 90 had hypoalbuminemia, 20% patients had serum albumin <2.8g/dl with mean of 1.96±0.53, 38.89% patients had serum albumin in the range of 2.8-3.5g/dl with mean of 3.17±0.21, 41.11% patients had serum albumin >3.5g/dl with mean of 4.2±0.57.

52(57.77%) patients out of 90 had clinical jaundice, 40(44.44%) patients had total bilirubin >3mg/dl with mean of 11.59±7.4, 12(13.33%) patients had total bilirubin between 2 to 3mg/dl with mean of 2.29±0.22, 38(42.22%) patients had total bilirubin <2mg/dl with mean of 1.11±0.47.

PT prolongation of >6secs was present in 49(54.44%) patients with mean of 15.47±7.92, 13(14.44%) patients had PT prolongation in the range of 4 to 6secs with the mean of 5.62±0.51, whereas 28(31.11%) patients had PT prolongation of <4secs with the mean of 1.86±1.33.

The mean QTc value was higher in patients with ascites as compared to the patient without ascites, with p-value of 0.75 which is non-significant (Table 2).

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 0.425 (Table 3).

The mean QTc was higher in patients with serum bilirubin levels of more than 3mg/dl (mean= 477.75±32.32) as compared to the patients with serum bilirubin levels of less than 2mg/dl(mean= 431.87±39.1), with the p-value of 0.000 which is highly significant (Table 4).

The mean QTc value was higher in patients with serum albumin levels of less than 2.8g/dl (mean= 461.87±41.94) as compared to the patients with serum albumin levels of more than 3.5g/dl (mean= 438.5±17.68), with the p-value of 0.001 which is significant (Table 5).

The mean QTc value was higher in patients with PT prolongation of more than 6secs (mean= 469.33±34.36) as compared to the patients with PT prolongation of less than 4secs (mean 434.07±42.52), with the p-value of 0.712 which is non-significant (Table 6). QTc prolongation increased linearly with the severity of liver cirrhosis. In child-Pugh class C the mean QTc was

479.71±29.48 which was higher as compared to CHILD-PUGH CLASS B and A (mean QTc of class A-425.00±20.97 and mean of QTc of class B was 437.35±42.60) with the p value of 0.04 which is significant (Table 7). Grade of diastolic dysfunction was related with the severity of liver cirrhosis. In child-Pugh class A 2(33%) patients had grade 1 diastolic dysfunction, in child Pugh class B 23(59%) patients had grade 1 diastolic dysfunction, whereas in child Pugh class C 3(7%) patients had grade 1 diastolic dysfunction , 33(73%) patients had grade 2 diastolic dysfunction and 1(2%) patients had grade 3 diastolic dysfunction with p-value of 0.040 which is significant (Table 8).

Table 2: Relation of QTc interval with the severity of ascites.

QTc Interval (m sec)							
Ascites (ML)	n	Normal*		Prolonged**		Mean±SD	p value
		n	%	n	%		
None	18	7	38.89	11	61.11	451±35.27	
Mild (≤200ML)	35	10	28.57	25	71.43	459.77±41.03	0.75
Moderate-Severe (>200ML)	37	11	29.73	26	70.27	459.03±45.45	

*normal ≤440msec; **prolonged >440msec

Table 3: Relation of QTc interval with age of patients.

QTc Interval (m sec)							
Age (Years)	n	Normal*		Prolonged**		Mean±SD	p value
		n	%	n	%		
18-40	20	6	30.00	14	70.00	467.1±35.73	
41-60	51	17	33.33	34	66.67	453.29±44.44	
61-80	16	4	25.00	12	75.00	464.19±38.85	0.425
>80	3	1	33.33	2	66.67	435.67±40.41	

*normal ≤440msec; **prolonged >440msec

Table 4: Relation of QTc interval with serum bilirubin levels.

QTc Interval (m sec)							
Total bilirubin (mg/dl)	n	Normal*		Prolonged**		Mean±SD	p value
		n	%	n	%		
<2	38	24	63.16	14	36.84	431.87±39.1	
2 to 3	12	1	8.33	11	91.67	472.75±33.47	0.000
>3	40	3	7.50	37	92.50	477.75±32.32	

*normal ≤440msec; **prolonged >440msec

Table 5: Relation of QTc interval with serum albumin levels.

Serum albumin (g/dl)	n	Normal*		Prolonged**		Mean±SD	p value
		n	%	n	%		
<2.8	69	19	27.54	50	72.46	461.87±41.94	
2.8-3.5	19	8	42.11	11	57.89	444.63±39.92	0.001
>3.5	2	1	50.00	1	50.00	438.5±17.68	

*normal ≤440msec; **prolonged >440msec

Table 6: Relation of QTc interval with prothrombin time.

QTc Interval (m sec)							
PT prolongation (sec)	n	Normal*		Prolonged**		Mean±SD	p value
		n	%	n	%		
<4	28	17	60.71	11	39.29	434.07±42.52	
4 to 6	13	4	30.77	9	69.23	464.85±45.96	0.712
>6	49	7	14.29	42	85.71	469.33±34.36	

*normal ≤440msec; **prolonged >440msec

Table 7: Relation of QTc interval with child PUGH score.

QTc Interval (m sec)							
Child PUGH score	n	Normal*		Prolonged*		Mean±SD	p value
		n	%	n	%		
GROUP 1: A (5-6)	6	5	83.3	1	16.7	425.00±20.97	0.04
GROUP 2: B (7-9)	39	21	53.8	18	46.2	437.35±42.60	
GROUP 3: C (10-15)	45	2	4.4	43	95.6	479.71±29.48	

*normal ≤440msec; **prolonged >440msec

Table 8: Relation of diastolic dysfunction (dd) with child Pugh score.

Child Pugh score	n	Normal DD		Grade 1 DD (impaired relaxation)		Grade 2 DD (pseudonormal)		Grade 3 DD (reversible restrictive)		p value
		n	%	n	%	n	%	n	%	
Group 1 (class A: 5-6)	6	4	67.00	2	33.00	0	0	0	0	
Group 2 (class B: 7-9)	39	16	41.00	23	59.00	0	0	0	0	0.040
Group 3 (class C: 10-15)	45	8	18.00	3	7.00	33	73	1	2.00	

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 appears 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 QTc interval prolongation has been found in patients with alcoholic liver disease. QTc abnormality is closely related to the severity of cirrhosis. QTc prolongation is independent of the etiology of cirrhosis.

Echocardiographically, left ventricular diastolic dysfunction is the main cardiac change observed in patients with cirrhosis, and it is also one of the main diagnostic criteria of cirrhotic cardiomyopathy.

Disruptions in systolic function are harder to detect, as they are subtle in the resting state and may only be detectable upon aggravation under physiological stress or in response to drugs.

In the present study, the maximum number of patients were in the age group of 41-60 years constituting 56.7% of the patients followed by age group of 18-40 years constituting 22.2% of the patients while a study conducted by Patil et al, included 60 patients of cirrhosis of liver, in which 70% were in age group of 40-60 years, 26.66% above 60 years and 3.33% were below 40 years of age.[8]

Cirrhosis was more common in males (91.1%) as compared to females (8.89%) while a study conducted by Bhatti A B et al, included 166 patients of confirmed liver cirrhosis in which it was seen that cirrhosis was more common in males(58%) as compared to the females(42%).[9]

In the present study, the maximum number of patients were alcoholics (75.6%) followed by HCV (37.8%). In a study conducted by Naik et al included 50 patients of cirrhosis of liver, in which history of alcohol consumption was present in 72% of the patients.[10]

Most of the patients presented with more than one presenting complaint. In the present study, most common clinical symptom with which patients presented was abdominal distention (43.33%), hematemesis was present in 34 patients (37.78%), yellowish discoloration of eyes/urine in 30 patients (33.33%), malena in 19 patients (21.11%), abdominal pain in 12 patients (13.33%), fever in 7 patients (7.78%). In a study conducted by Sukhwani N et al, included 35 patients of cirrhosis of liver. The most common presentation was decrease appetite (88.5%), abdominal distension (88.5%), hematemesis and malena in 54.2%.[11]

Ascites was seen in 80.0% patients, pallor in 66.67% patients, splenomegaly in 54.44% patients, icterus and pedal edema in 44.44 % patients, hepatomegaly in 17.78% patients. In a study conducted by Sukhwani N et al, included 35 patients of cirrhosis of liver. Among the 35 patients' common clinical signs were ascites (94.2%), splenomegaly (80%) edema (68.5%), icterus (48.5%) and pallor (42.8%).

Anemia was present in 84(93.34%) patients out of 90. In a study conducted by Singhal A et al, included 102 patients of chronic liver disease, in which anemia was seen in 91.1% patients.[12]

In the present study, 53(58.89%) patients out of 90 had hypoalbuminemia. Similar study conducted by Dhoat P S et al, revealed 50(55.5%) patients out of 90 with hypoalbuminemia.[13]

In the present study, 52(57.77%) patients out of 90 had clinical jaundice, while a study conducted by Sukhwani N et al included 35 patients of cirrhosis of liver, out of which clinical jaundice was seen in 48.5% patients.

PT prolongation of >6secs was present in 49(54.44%) patients with mean of 15.47±7.92, 13(14.44%) patients had PT prolongation in the range of 4 to 6secs with the mean of 5.62±0.51, whereas 28(31.11%) patients had PT prolongation of <4secs with the mean of 1.86±1.33 whereas a study conducted by Siddiqui S.A in 171 patients of chronic liver disease, prothrombin time was prolonged in 150(88%) patients.[14]

The mean QTc value was higher in patients with ascites as compared to the patient without ascites, with p-value of 0.75 which is non-significant while a study conducted by Dhoat P S et al, 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.

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 0.425 which is similar to a study conducted by Dhoat P S et al, in which 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.

The mean QTc was higher in patients with serum bilirubin levels of more than 3mg/dl (mean= 477.75±32.32) as compared to the patients with serum bilirubin levels of less than 2mg/dl(mean= 431.87±39.1), with the p-value of 0.000 which is highly significant. Results were similar to a study conducted by Dhoat P S et al, 90 patients of cirrhosis were being taken and it was seen that 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 of less than 2mg/dl (mean=0.46), with the p value of <0.001 which is highly significant.

In the present study, the mean QTc value was higher in patients with serum albumin levels of less than 2.8g/dl (mean= 461.87±41.94) as compared to the patients with serum albumin levels of more than 3.5g/dl (mean= 438.5±17.68), with the p-value of 0.001 which is significant. In a study conducted by Dhoat P S et al, 90 patients of cirrhosis were being taken and it was seen that 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. Similar findings were observed in both studies.

In the present study, the mean QTc value was higher in patients with PT prolongation of more than 6secs (mean= 469.33±34.36) as compared to the patients with PT prolongation of less than 4secs (mean 434.07±42.52), with the p-value of 0.712 which is non-significant whereas a study conducted by Dhoat P S et al, the mean QTc value was higher in patients with PTI prologation 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.

QTc prolongation increases linearly with the severity of liver cirrhosis. In CHILD-PUGH CLASS C the mean QTc was 479.71±29.48 which was higher as compared to CHILD-PUGH CLASS B and A (mean QTc of class A-425.00±20.97 and mean of QTc of class B was 437.35±42.60) with the p value of 0.04 which is significant similar to a study conducted by Dhoat P S et al, in 90 patients of 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-490).

Grade of diastolic dysfunction was related with the severity of liver cirrhosis. In child-pugh class A 2(33%) patients had grade 1 diastolic dysfunction, in child pugh class B 23(59%) patients had grade 1 diastolic dysfunction, whereas in child Pugh class C 3(7%) patients had grade 1 diastolic dysfunction , 33(73%) patients had grade 2 diastolic dysfunction and 1(2%) patients had grade 3 diastolic dysfunction with p-value of 0.040 which is significant, as shown in a study conducted by Prashant S. Sidmal et al, severity of cirrhosis and diastolic dysfunction had a significant correlation (p=0.048). By increasing severity of cirrhosis from Child A to Child C, diastolic dysfunction was seemed to worsen.[15]

CONCLUSION

The QTc interval prolongation increased with the severity of liver cirrhosis. Mean QTc interval was more in Child Pugh Class C as compared to Child Pugh Class A and B. The prolonged QTc interval predicts severe arrhythmias and sudden death, and they are ideal candidates for liver transplantation. Diastolic dysfunction, which is a major criterion of cirrhotic cardiomyopathy as measured by E/A ratio was proportional to the severity of liver cirrhosis. Specifically, all patients showed normal LV systolic function.

REFERENCES

1. Heidelbaugh JJ, Bruderly M. Cirrhosis and Chronic Liver Failure: Part I. Diagnosis and Evaluation. American family physician 2006;74(5):756-62.
2. Silvestre OM. QT interval prolongation. Annals of Hepatology 2013;12(1):85-91.
3. McCormick PA, Jalan R. Hepatic Cirrhosis. In: Dooley JS, Lok ASF, Tsao GG and Pinzani M, eds. Sherlock's Diseases of the Liver and Biliary System. 13th ed. Hoboken, NJ: Wiley; 2018:107-126.
4. Bernardi M, Rubboli A, Trevisani F, Cancellieri C, Ligabue A, Baraldini M, et al. Reduced cardiovascular responsiveness to exercise-induced sympathoadrenergic stimulation in patients with cirrhosis. J Hepatol. 1991;12(2):207-16.
5. Genovesi S, Pizzala DM, Pozzi M, Ratti L, Milanese M, Pieruzzi F, et al. QT interval prolongation and decreased heart rate variability in cirrhotic patients: relevance of hepatic venous pressure gradient and serum calcium. Clini Sci. 2009 Jun 1;116(12):851-9.
6. Alqahtani SA, Fouad TR, Lee SS. Cirrhotic cardiomyopathy. Semi Liver Dis. 2008;28(1):59-69.
7. Ruíz-del-Árbol L, Achécar L, Serradilla R, Rodríguez-Gandía MÁ, Rivero M, Garrido E, et al. Diastolic dysfunction is a predictor of poor outcomes in patients with cirrhosis, portal hypertension, and a normal creatinine. Hepatol. 2013;58(5):1732-41.
8. Patil S, Lal B, Pandey M, Haldia SS, Rishi JP. A clinical study of cardiovascular dysfunction in patients of cirrhosis of liver. Ann Int Med Den Res. 2016;2:212-5.
9. Bhatti AB, Ali F, Satti SA. Prolonged QTc interval is an electrophysiological hallmark of cirrhotic cardiomyopathy. Open J Int Med. 2014 Mar 7;4(01):33-9.
10. Naik K, Gagiya A, Parmar A, Kothari P, Kheni P. Evaluation of cardiac function in patients with liver cirrhosis: A hospital based cross-sectional study. Natl J Med Res 2014;4(3):208-11.
11. Sukhwani N, Nayak OP, Kumbhkar T. Cardiac changes in patients with chronic liver disease: A prospective descriptive study. Int J Med Res Rev. 2016;4(4):569-74.
12. Singhal A, Jain HK, Jatav O. Alcoholic liver disease-Clinical profile and correlation of severity with the help of electrocardiography. Inter J Multidisciplinary Res Develop. 2015; 2(2):541-9.
13. Dhoat PS, Arshdeep, Chandey M, Nivenjit. To Study the Prevalence of QTc Interval Prolongation in Cirrhosis of Liver And Its Relationship with the Severity of Disease. Int J Med Res Prof. 2019;5(3):92-101.
14. Siddiqui SA, Ahmed M, Ghani MH, Memon MA, Mustafa G, Ghori MA. Coagulation abnormalities in patients with chronic liver disease in Pakistan. J Pak Med Assoc. 2011;61(4):363-7.
15. Sidmal PS, Prashanthkumar BG, Shekarappa KC. Pattern of diastolic dysfunction in alcoholic and non-alcoholic cirrhotic portal hypertensive patients with or without ascites in rural population in South India. Int J Res Med Sci. 2015;3(9):2316-22.