

DISSERTATION TITLED

**“CORRECTED QT DISPERSION AND ITS CORRELATION WITH
SEVERITY OF CHRONIC LIVER DISEASE”**

Submitted in partial fulfilment of

Requirements for

M.D.DEGREE EXAMINATION

BRANCH-I GENERAL MEDICINE

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI



INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI - 600003.

APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled “ **A STUDY ON CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE** ” is a bonafide work done by **DR. A.VIGNESH** , Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under our guidance and supervision, during the academic year 2010 - 2013.

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I solemnly declare that the dissertation entitled “**A STUDY ON CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE**” is done by me at Madras Medical College, Chennai-3 during May 2012 to November 2012 under the guidance and supervision of Prof . K.S. CHENTHIL, M.D., to be submitted to The Tamilnadu Dr M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D DEGREE IN GENERAL MEDICINE BRANCH-I.

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ABBREVIATIONS

CLD	Chronic liver disease.
QTc	Corrected QT interval.
QTcd	Corrected QT dispersion.
QTcmax	Corrected QT maximum.
QTcmin	Corrected QT minimum
MELD	Model for End Stage Liver Disease.
NASH	Nonalcoholic steatohepatitis
NAFLD	Nonalcoholic fatty liver disease
PT	Prothrombin time
INR	International normalized ratio
AST	Aspartate transaminase
ALT	Alanine transaminase
ALP	Alkaline phosphatase
ANTI-LKM	Anti liver kidney microsomal antibody

ANA	Anti-nuclear antibody
ANTI-SMA	Anti smooth muscle antibody
PBC	Primary biliary cirrhosis
PSC	Primary sclerosing cholangitis
LFT	Liver function tests
ECG	Electrocardiogram
USG	Ultrasonogram
ms	milliseconds

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INTRODUCTION

Chronic liver disease is increasing in frequency worldwide and is among the top ten causes of death at present. Moreover those who suffer from chronic liver disease needs repeated hospitalization and prolonged medical attention, which leaves them physically, and psychologically devastated. The mortality rate is also very high; the median survival in patients with decompensated chronic liver disease is about two years. Patients usually die of complications of liver disease such as hepatic encephalopathy, bleeding varices, hepatorenal syndrome, infections, but sudden death due to cardiac arrhythmias has also been frequently reported.

Several studies has demonstrated that QT interval in standard electrocardiogram is prolonged in patients with chronic liver disease which may lead to sudden death and poor survival of chronic liver disease patients. The QT interval reflects the total duration of myocardial depolarization and repolarization. The various factors implicated in QT prolongation are increased bilirubin levels, low testosterone levels, autonomic neuropathy leading to decreased sensitivity of baroreceptor and heart rate variability, high sympathetic activity, electrolyte imbalance, however patients with alcohol related chronic liver disease and those who

are in Child Pugh's class C clearly have prolonged QT interval in electrocardiogram.

Corrected QT dispersion (QTcd) has been defined as inter lead QT interval variability (difference between maximum and minimum QT interval).

Increased QTcd is a direct reflection of disparity in myocardial recovery, and determination of QTcd may help to predict arrhythmic events in chronic liver disease patients. Several studies in the past has documented prolongation of QT interval in chronic liver disease, unfortunately very few studies have been done regarding QT dispersion in chronic liver disease. In this study we aim to analyze corrected QT dispersion and its correlation with the severity of chronic liver disease.

AIMS AND OBJECTIVES

- To study the relationship between corrected QT dispersion and severity of chronic liver disease based on Child-Pugh's classification.
- To evaluate the usefulness of corrected QT dispersion in assessing severity of chronic liver disease.
- To study the relationship between corrected QT dispersion and various factors implicated in prolongation of QT interval.

REVIEW OF LITERATURE

CHRONIC LIVER DISEASE:

Chronic liver disease is a term used to define a disease process that leads to progressive destruction of liver parenchyma and regeneration that leads to fibrosis and cirrhosis. It is a progressive fibrosing and nodular condition that disrupts the architecture of entire liver.

Chronic liver disease and cirrhosis is the twelfth leading cause of death in US ⁽¹²⁾, and its burden is increasing worldwide. Up to forty percentages of patients with cirrhosis were asymptomatic until the occurrence of decompensation in the form of bleeding varices, hepatic encephalopathy, and spontaneous bacterial peritonitis. Previously fibrosis and cirrhosis was thought to irreversible but new evidence suggests that fibrosis may be reversible in some but not all patients with chronic hepatitis B, hemochromatosis⁽⁹⁾.

Cirrhosis represents an advanced stage of fibrosis and characterized by distortion of hepatic parenchymal anatomy and formation of regenerative nodules. The pathogenesis of fibro genesis is activation of stellate cell which is the cardinal feature of hepatic fibrosis. The stellate cells lies within the space of disse is in direct contact with the hepatocytes, inflammatory cells,

endothelial cells, they store vitamin A in normal liver, about 40- 70% of body retinoid is stored in stellate cell. Scar formation is mediated through increased proliferation of hepatic stellate cells, chemo taxis, fibro genesis, altered degradation of collagen matrix and interaction between hepatic stellate cells and immune system and secretion of inflammatory mediators. The extracellular matrix during fibrogenesis consists of collagen and glycoproteins and hyaluronic acid. TGF beta1 is the central molecule in mediating fibrogenesis and TIMP-1 plays a huge role in initiation, progression and regression of fibrogenesis. The importance of TIMP-1 can be understood from the fact that overexpression of human TIMP-1 in mice increased CCL4 induced fibrosis by seven fold.

ETIOLOGY AND RISK FACTORS:

Alcoholic liver disease is the most common worldwide but in developed countries it is being overtaken by Hepatitis C and Hepatitis B.

NAFLD AND NASH (Nonalcoholic fatty liver disease and Nonalcoholic steatohepatitis): around two to three percentage of those with NAFLD will progress to NASH of which about ten percentages will progress to cirrhosis.

RISK FACTORS:

Heavy alcohol consumption

Health care professionals

Obesity

Tattooing

Unprotected sex

Toxic and chemical exposures

Certain medications

IV drug abusers sharing intravenous needles

ETIOLOGY:

Alcoholic liver disease

Viral:

Chronic hepatitis C

Chronic hepatitis B

Cytomegalovirus

Epstein Barr virus

Metabolic:

NAFLD/NASH

Hemochromatosis

Wilson's disease

Diabetes mellitus

Alpha 1 anti-trypsin deficiency

Cystic fibrosis

Tyrosinosis

Hereditary fructose intolerance

Glycogen storage diseases

Drug induced:

Amiodarone

Methotrexate

Nitrofurantoin

Biliary cirrhosis

Primary biliary cirrhosis

Primary sclerosing cholangitis

Autoimmune cholangiopathy

Cardiac:

Chronic right heart failure

Tricuspid regurgitation

Cryptogenic

CLINICAL FEATURES:

Patient with chronic liver disease may be identified in the following ways⁽³⁾:

1. Patients may be identified on routine clinical examination.
2. They might have undergone laboratory/radiological imaging or some procedures which incidentally found out the presence of chronic liver disease.
3. They may present in a decompensated state.
4. Some patients may never come to clinical attention.⁽⁴⁾

HISTORY:

This should include questions to identify risk factors for chronic liver disease like history of alcohol intake, hepatitis, jaundice, diabetes, illicit drug use, blood transfusion, any surgery, family history of liver diseases and autoimmune conditions.

Questioning should also include those related to symptoms of chronic liver disease like fatigue, pedal edema, weight loss, confusion, bleeding tendency.

Symptoms may vary from asymptomatic to overt features of decompensation. Patients with chronic liver disease due to hepatitis C may have muscle wasting, large ascites and overt hepatic encephalopathy but only mild jaundice while patients with chronic liver disease due to primary biliary cirrhosis may have deep icterus but no muscle wasting. Patients may experience fatigue, anorexia, weight loss. Cutaneous manifestations may include jaundice, spider naevi, paper money skin, palmar erythema, white nails, disappearance of lunulae, and finger clubbing.

Increased conversion of androgens to estrogen occurs in adipose tissue, skeletal muscle which may be responsible for loss of axillary and pubic hair, gynaecomastia, impotence. Anemia may be due to folate deficiency, hemolysis, and hypersplenism. Thrombocytopenia is usually the first marker

of hypersplenism. Coagulopathy results from decreased production of coagulation factors and diminished absorption of vitamin

SYMPTOMS:

Fatigue, weakness

Poor appetite

Muscle wasting

Jaundice

Breast enlargement in men

Ascites

Parotid gland enlargement

Altered sleep pattern, somnolence,

Pruritus

Blood vomiting

Redness of palms

Impotence, loss of libido

SIGNS ⁽⁹⁾

Signs may be classified as those associated with etiology and those associated with decompensation.

SIGNS ASSOCIATED WITH ETIOLOGY:

Alcohol related:

Parotid enlargement

Dupuytren's contracture

Peripheral neuropathy

Cerebellar signs

Testicular atrophy

Wilson's disease:

Kayser Fleischer ring

Hepatomegaly

Dystonia, tremors, involuntary movements

Hemochromatosis:

Increased pigmentation

Hepatomegaly

NASH:

Xanthomas, xanthelesma

Corneal arcus

Viral hepatitis:

Tattoo marks, injection marks

Right heart failure:

Peripheral edema

Elevated JVP

SIGNS OF DECOMPENSATION:

Icterus

Ascites

Peripheral edema

Ecchymosis

Asterixis

Encephalopathy

Bleeding varices

Spider angiomas

Cruveilhier Baumgarten murmur

Fetor hepaticus

Caput medusae

COMPLICATIONS ⁽⁹⁾:

Portal hypertension

Ascites

Hypersplenism

Variceal bleeding

Hepatorenal syndrome

Portopulmonary hypertension

Hepatic encephalopathy

Hepatopulmonary syndrome

Malignant transformation.

DIAGNOSIS:

Many times the presence of chronic liver disease is suggested by laboratory investigations. Common laboratory investigations performed under the label LFT (liver function tests) are

1) Enzyme tests

Serum aminotransferases (AST, ALT)

Serum alkaline phosphatase

Gamma Glutamyl Trans peptidase

2) Serum bilirubin

3) Assess synthetic function

Serum albumin

Prothrombin time and INR

Aminotransferases:

Both aspartate transaminase and alanine transaminase may be elevated but usually <3 times the upper normal limit, but can be normal in advanced

stages of liver disease. Chronic liver disease other than alcohol will have AST/ALT ratio less than one.

Alkaline phosphatase:

Elevated in most forms of chronic liver disease but will be less than three times the upper normal limit. High levels are noted in

- 1) Primary biliary cirrhosis
- 2) Primary sclerosing cholangitis

Gamma Glutamyl Trans peptidase:

It is considered moderately specific for alcoholic liver disease because of two reasons

- 1) Alcohol induces hepatic microsomal GGT synthesis.
- 2) Alcohol causes leakage of GGT from hepatocytes.

Serum bilirubin:

It may be normal in compensated state but elevated bilirubin indicates fairly advanced liver disease.

In primary biliary cirrhosis elevated bilirubin indicates poor prognosis.

Serum albumin:

As liver function deteriorates albumin levels also decreases as it is solely synthesized in liver but hypoalbuminaemia is not specific for chronic liver disease as it may be decreased in other conditions like

- 1) Nephrotic syndrome
- 2) Protein losing enteropathy
- 3) Malnutrition

Prothrombin time:

Increases as liver disease progresses since coagulation factors are produced in liver.

Serum globulin:

Elevated levels of globulin are seen in cirrhosis as various antigens are shunted away from liver, reach systemic circulation and elicit immunological response. Increased levels of IgM are seen in primary biliary cirrhosis, increased IgA is seen in alcoholic liver disease.

Serum sodium:

Hyponatremia in chronic liver disease patients indicates poor prognosis, and is due to high levels of ADH seen in cirrhotic patients.

Hematological investigations:

Anemia:

May be due to blood loss

Folate deficiency

Direct toxicity of alcohol

Hemolysis

Anemia of chronic disease

Hypersplenism

Thrombocytopenia:

Due to hypersplenism, but the platelet count doesn't drop below 50000 cells/mm³. May cause bleeding if associated with coagulopathy.

Leucopenia, neutropenia:

Due to hypersplenism and splenic margination.

INVESTIGATIONS TO DETERMINE THE ETIOLOGY OF CHRONIC LIVER DISEASE:

Alcoholic liver disease:

History of alcohol abuse

AST: ALT ratio > 2 due alcohol induced deficiency of pyridoxal phosphate

Liver biopsy may show features typical of alcoholic hepatitis, Mallory's hyaline, liver cell necrosis.

Chronic hepatitis C:

Anti HCV antibody

HCV RNA quantification

Liver biopsy to establish the severity of liver disease.

Chronic hepatitis B:

HBsAg

HBeAg

HBV DNA Quantification

NASH:

associated features of metabolic syndrome like hyperglycemia, hyperlipidemia.

Liver biopsy

Primary biliary cirrhosis:

Elevated alkaline phosphatase

Anti-mitochondrial antibody is considered to be the hallmark of primary biliary cirrhosis

ERCP

Primary sclerosing cholangitis:

Associated with inflammatory bowel disease.

Contrast cholangiography shows diffuse, focal strictures and dilatation of bile ducts giving it a beaded appearance.

Anti-smooth muscle antibody (ASMA)

Anti-nuclear antibodies

Anti-neutrophilic cytoplasmic antibody (ANCA)

Autoimmune hepatitis:

Increased gamma globulin levels

Anti-LKM1 antibody

Anti-ALC antibody

Hemochromatosis:

Family history of cirrhosis

Increased skin pigmentation

Fasting transferrin saturation

More than 60% in men

More than 50 % in women

Plasma ferritin

>300mg/dl in men

>200mg/dl in women

Genetic testing

Liver biopsy

Wilson's disease:

Kayer Fleisher rings on slit lamp examination.

Decreased serum ceruloplasmin.

24 hour urinary copper >100mg

Copper content >200mg/g of liver tissue in liver biopsy.

Haplotype analysis.

Alpha 1 anti-trypsin deficiency:

Decreased serum alpha1 anti-trypsin levels.

Genetic testing

Right sided heart failure:

Electrocardiogram

Echocardiogram

RADIOLOGICAL IMAGING

Ultrasound abdomen:

Provide useful information regarding liver size, echo texture.

Useful screening to identify development of HCC (hepatocellular carcinoma) in a patient with preexisting cirrhosis.

Doppler ultrasound:

Provides information regarding blood flow in portal vein, hepatic veins.

Assess size of portal vein, splenic vein.

Identify presence of collaterals.

Computed tomography Abdomen:

To assess liver size, shape.

To identify liver nodule.

To detect HCC.

MRI Abdomen:

Most useful in evaluating the biliary tree

To detect malignancy.

Transient elastography⁽⁹⁾ (Fibro scan):

Noninvasive method to assess the stiffness and evaluate liver fibrosis and cirrhosis.

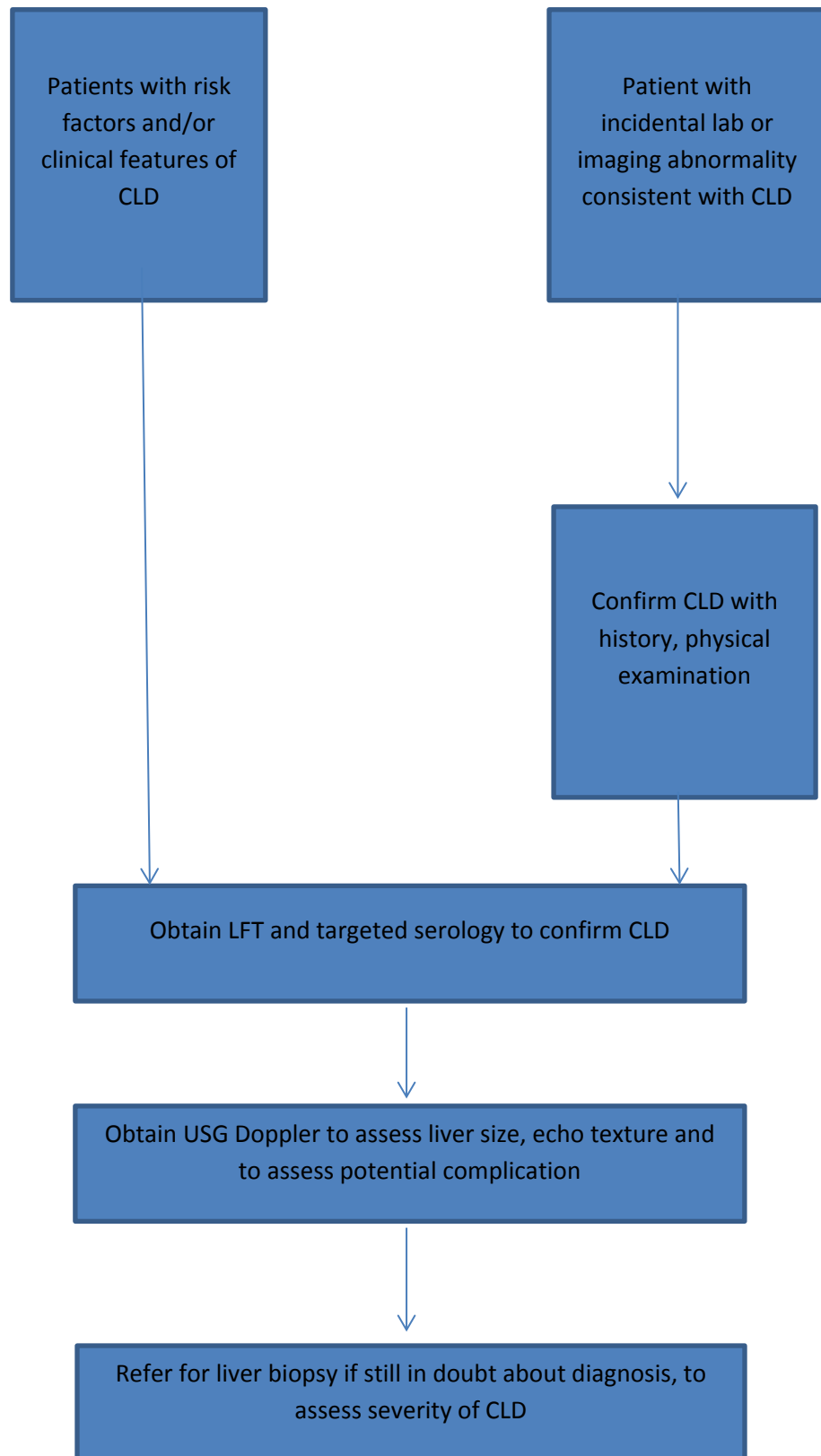
Liver biopsy:

The gold standard test to aid in identifying the etiology of chronic liver disease.

To grade the disease activity.

To assess the severity of chronic liver disease.

DIAGNOSTIC ALGORITHM: CHRONIC LIVER DISEASE



ASSESSMENT OF SEVERITY AND PROGNOSIS

Severity may be assessed by

- 1) Child Pugh's scoring system
- 2) MELD scoring system
- 3) Liver biopsy

CHILD PUGH'S SCORING SYSTEM:

Clinical and Lab Criteria.	Points		
	1	2	3
Ascites	None	Slight (diuretic responsive)	Moderate (diuretic unresponsive)
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Bilirubin (mg/dl)	<2	2-3	>3
Encephalopathy	None	Grade 1 and 2	Grade 3 and 4
Prothrombin time INR	<1.7	1.7-2.3	>2.3

Class A: 5-6 survival at one and two year 100% and 65%, Class B: 7-9 survival at one and two year 80% and 60%, Class C: 10-15 survival 45% and 35%.

MELD SCORING SYSTEM:

MELD (model for end stage liver disease) was initially developed to assess short term prognosis in patients with chronic liver disease who undergo TIPS^(2,5) (Trans jugular intra-hepatic Porto systemic shunt) but its usefulness to assess the prognosis and severity of chronic liver disease has been well validated. It consists of three variables

- 1) Serum bilirubin
- 2) Serum creatinine
- 3) Prothrombin time INR (International Normalized Ratio)

SCORE	THREE MONTH MORTALITY (%)
>40	71.3
30-39	52.6
20-29	19.6
10-19	6
<9	5

MANAGEMENT OF CHRONIC LIVER DISEASE

GENERAL MANAGEMENT⁽⁹⁾:

As the patient once lands in cirrhosis, liver will never regain its normal structure, but symptomatic measures can go a long way in improving the quality of life. Liver has such a regenerative capacity that even though structurally abnormal its functional capacity may be achieved.

MANAGEMENT IN A COMPENSATED STATE:

Adequate diet⁽⁶⁾:

30-40 Kcal/kg body weight

1.2-1.5g of protein per kg of body weight

Abstinence from alcohol.

Weight loss if obese.

Early detection and treatment of complications.

Treatment of specific cause:

Antiviral therapy for chronic hepatitis B and C

Steroids and immunosuppressant for autoimmune hepatitis.

Ursodeoxycholic acid in early stages of primary biliary cirrhosis.

Chelation therapy for Wilson's disease.

Venesection for hemochromatosis.

DECOMPENSATED STATE:

Treatment is aimed at

Identification of precipitating factors

Early detection and management of complications.

Hepatic encephalopathy⁽⁹⁾:

Avoidance of precipitating factors.

Lactulose 40-120 ml daily

Lactitol 20-40g daily

Rifaximin 400mg three times a day.

Liver transplantation.

Portal hypertension:

Propranolol 40-80 mg two times a day.

Ascites and peripheral edema:

Sodium restriction <2 g per day.

Fluid restriction if there is Hyponatremia.

Spirolactone starting dose 100 mg , maximum dose 400mg per day

Furosemide 40 mg per day, maximum 160 mg per day

Large volume paracentesis with intravenous salt poor albumin

Hepatorenal syndrome:

Avoidance of nephrotoxins

Intravenous albumin

Midodrine

Octreotide

Spontaneous bacterial peritonitis

Cefotaxime 2 g IV tds

Norfloxacin 400 mg twice daily

EMERGING ANTIFIBROTIC STRATEGIES:

The ever increasing understanding of mechanisms leading to fibrogenesis has led to development of anti fibrotic therapy a reality in near future. The potential approach includes

Decrease and or modify host response to stellate cell activation

Down regulate stellate cell activation.

Stimulate programmed cell death of stellate cell.

Increase the degradation of scar matrix.

ROLE OF LIVER TRANSPLANTATION:

Liver transplantation is considered when liver no longer has its ability to do its various functions. The following are the most common indication for liver transplantation

Hepatitis C, B

Alcoholic liver disease

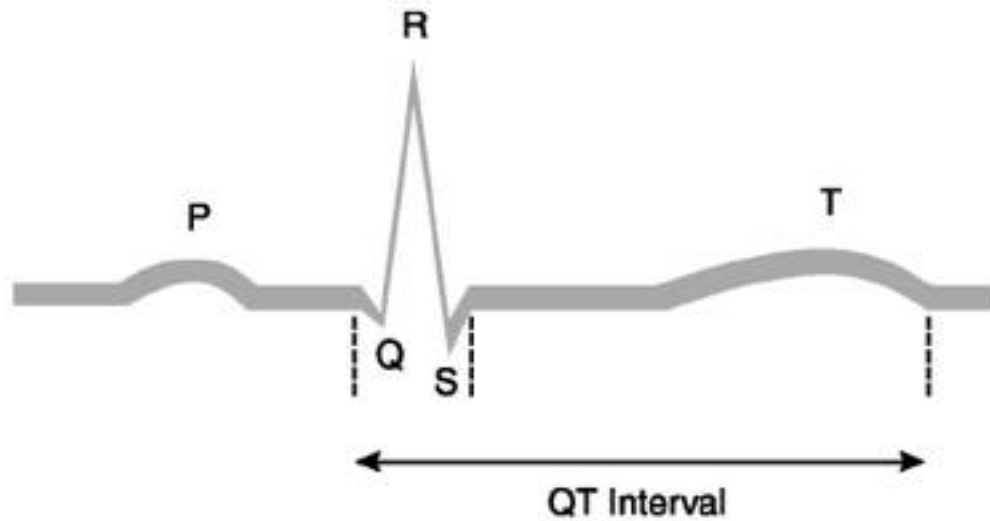
Autoimmune liver disease

Primary biliary cirrhosis

QT DISPERSION

QT interval:

In a standard surface electrocardiogram the QT interval includes the QRS complex, ST segment and the T wave corresponding to phases 0 to 3 of action potential.



QT dispersion:

QT dispersion has been defined as inter lead variability (difference between maximum and minimum QT interval) Increased QT dispersion is a direct reflection of disparity in myocardial recovery. Thus determination of QT dispersion may help to predict arrhythmogenicity in patients with chronic liver disease.

Homogeneity of ventricular recovery is considered to be protective against ventricular arrhythmias on the contrary dispersion of recovery is considered to be arrhythmogenic.

Historical background of QT dispersion:

It was in the year 1990, a report was published by Prof Campbell et al which re introduced an old concept of inter lead differences in QT interval. It was termed “QT dispersion” and it was considered to be an index of spatial dispersion of ventricular recovery time. In electrocardiogram different leads accentuate the ECG signals of different part of myocardium, so that QT dispersion is a mean of heterogeneity of myocardial repolarization. Since the idea was first mooted, the cardiology community has been flooded with articles measuring and discussing QT dispersion in various cardiac and non-cardiac conditions.

Measurement of QT interval⁽¹⁰⁾ and QT dispersion:

QT interval is measured from beginning of QRS complex to the end of T wave. The presence of a U wave is not included in measuring QT interval.

Corrected QT interval:

The QT interval is affected by heart rate. It is longer when the heart rate is slow and shorter when the heart rate is fast, so the QT interval should be corrected for heart rate.

The most frequently used formula for correcting QT interval for heart rate is the Bazett's formula. Corrected QT interval is QT interval (in seconds) divided by the square root of preceding RR interval (in seconds)

The American college of Cardiology/American Heart Association recommendation is that the QT interval should be measured in at least three different leads and longest should be taken as QT interval.

Otherwise QT interval should be measured in all the 12 leads and the longest value should be taken as the QT interval for that ECG.

PROLONGATION OF QT INTERVAL:

A prolonged QT interval is defined as

>0.44 seconds in men

>0.46 seconds in women and children

>0.50 seconds if there is bundle branch block or intraventricular conduction delay.

The standard method for measuring QT dispersion is to measure QT interval in a simultaneous twelve lead ECG recording during a sinus rhythm but recording of six or three lead ECG recording is also accepted.

Various studies have found that QT dispersion varies between 30 and 60 milliseconds in normal population. A QTcd of more than 70 milliseconds is considered abnormal.

CLINICAL APPLICATION OF QT INTERVAL AND QT DISPERSION

QT interval and dispersion were increased in various cardiac and non-cardiac diseases⁽¹³⁾

Cardiac diseases:

Inherited diseases-congenital long QT syndrome

Systemic hypertension

Coronary artery disease

Acute myocardial infarction

Chronic heart failure

Hypertrophic obstructive cardiomyopathy

Drug induced-antiarrhythmics

Non-cardiac diseases:

Athletes

Chronic liver disease

Diabetes mellitus

Peripheral vascular disease

Chronic obstructive pulmonary artery disease

CARDIAC DISEASES

Systemic hypertension:

QT dispersion is related to resting systolic hypertension but not diastolic hypertension. Patients with QT dispersion >80 milliseconds are five times more likely to die suddenly.

Coronary artery disease:

QT dispersion is used to predict cardiac arrhythmias in patients with coronary artery disease.

Acute myocardial infarction:

It is difficult to measure QT dispersion in patients with acute myocardial infarction as electrocardiogram is often abnormal and changes rapidly. However increased QT dispersion after myocardial infarction predicts ventricular fibrillation. Decrease in QT dispersion following reperfusion may indicate that it is successful.

QT dispersion may be used to stratify patients with chest pain who are at risk for developing acute coronary events.

Heart failure:

Most patients with chronic heart failure die of sudden cardiac death and the underlying event is thought to be cardiac arrhythmia which may be related to left ventricular systolic function. So QT dispersion could be used as a prognostic marker.

NON-CARDIAC DISEASES

Sports persons and athletes:

QT dispersion is increased in athletes with symptomatic ventricular tachycardia, so it is used to identify sports persons at risk of developing sudden ventricular tachycardia and sudden death and to identify those with undiagnosed hypertrophic obstructive cardiomyopathy.

Diabetes:

Diabetes itself is high risk factor for cardiovascular disease and the risk is increased many fold if it occurs in the presence of hypertension, micro-albuminuria, smoking, hyperlipidemia. QT dispersion can be used to predict sudden death in this population.

Peripheral vascular disease:

QT dispersion is increased in patients with peripheral vascular disease even in the absence of overt coronary artery disease.

Drug induced:

Increased QT dispersion has been noted with the use of following drugs

- 1) Quinidine
- 2) Propafenone
- 3) Disopyramide

Beta Blockers have been shown to decrease QT dispersion.

Recently QT dispersion has been shown to be prolonged in patients with chronic obstructive pulmonary disease and Duchene muscular dystrophy.

CHRONIC LIVER DISEASE AND QT DISPERSION

CARDIOVASCULAR CHANGES IN CHRONIC LIVER DISEASE:

Cardiovascular changes in chronic liver disease ranges from subclinical alterations in early stages to hyper dynamic circulation in cirrhotic cardiomyopathy in advanced stages of chronic liver disease. The most common electrocardiogram abnormality is prolongation of QT interval. Previously many studies have proven that chronic liver disease patients have increased QT interval and QT dispersion when compared with normal population. This particularly holds true for alcoholic liver disease⁽¹⁴⁾ and QT interval have been shown to regress following liver transplantation^(15,16). The cause for this prolongation is unclear.

There is high risk of cardiac arrhythmias and sudden death in those patients whose electrocardiogram shows increased QT interval.

FACTORS INFLUENCING QT INTERVAL IN CHRONIC LIVER DISEASE

Autonomic dysfunction

Anemia

Electrolyte imbalance

Hyperbilirubinemia

Hypertestosteronaemia

QT prolongation is independent of etiology of chronic liver disease but still alcoholic etiology has been shown to be clearly associated with prolonged QT.

Relationship between severity and prolongation of QT interval has been established that those with severe and advanced liver have increased chance of prolonged QT interval. Testosterone has been shown to shorten QT interval and as expected in chronic liver disease decrease in testosterone leads to prolonged QT interval, and QT dispersion. There are evidence for direct relationship between long QT syndrome and sympathetic activity and adrenergic hyperactivity has been identified in cirrhosis which leads to prolonged QT in these patients.

MATERIAL AND METHODS

SETTING:

This study was conducted at the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, and Madras Medical College.

ETHICAL COMMITTEE APPROVAL:

Obtained.

STUDY DURATION:

This study was conducted over a period of six months.

STUDY POPULATION:

Patients admitted with chronic liver disease at medical wards, Institute of Internal medicine.

SAMPLE SIZE:

Sixty cases admitted with chronic liver disease.

TYPE OF STUDY

Cross sectional study.

INCLUSION CRITERIA

- Known case of chronic liver disease
- Newly detected chronic liver disease

EXCLUSION CRITERIA:

- Heart failure.
- Systemic hypertension.
- Structural heart disease.
- Coronary artery disease.
- Arrhythmias and conduction disturbances.
- Electrolyte abnormalities.
- Diabetes.
- Renal and lung diseases.
- Patients on drugs known to prolong QT interval.

DATA COLLECTION AND METHODS

Informed consent will be obtained from each patient.

Patients have their history taken according to a Questionnaire and subjected to clinical examination.

Patients are subjected to routine blood investigations like renal function tests, liver function tests, PT-INR.

Chest X-ray, Echocardiography and USG abdomen will be done

Patients will be classified based on Child-Pugh's classification.

Standard 12 lead electrocardiogram will be done for all patients on admission. QT interval will be measured manually in all leads and corrected by Bazett's formula. Corrected QT dispersion >70 milliseconds is considered abnormal.

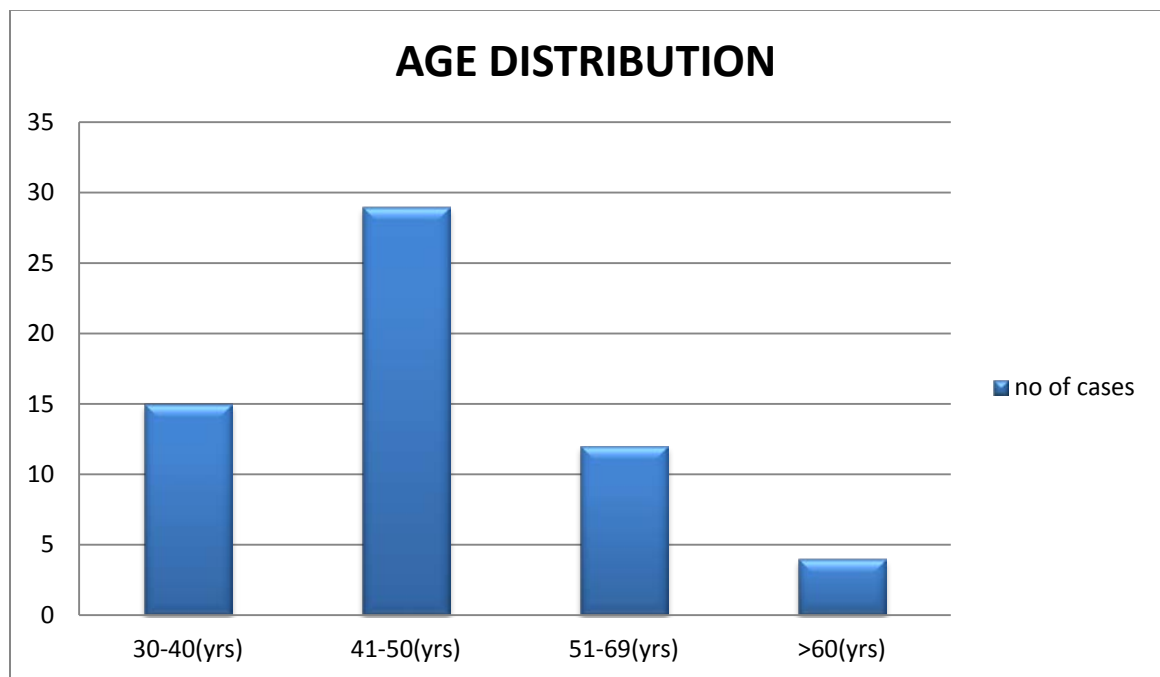
All the data will be entered in proforma(enclosed).

Data will be analyzed using SPSS package and ANOVA.

OBSERVATION AND RESULTS

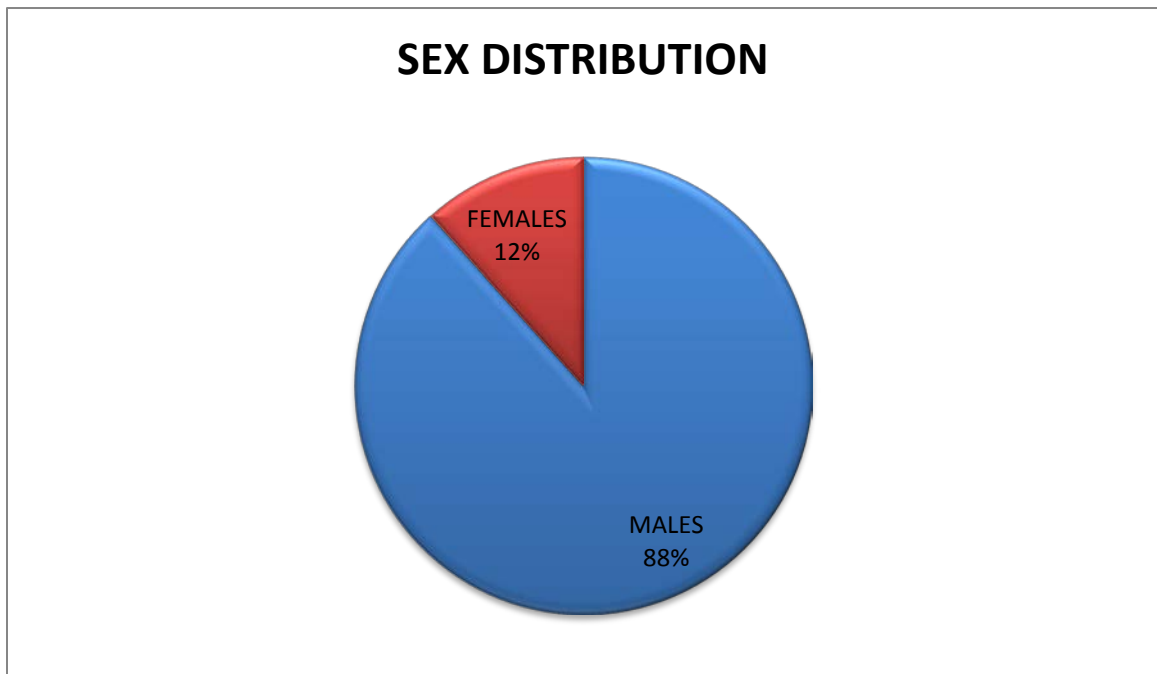
AGE DISTRIBUTION

AGE GROUP(years)	NO OF CASES	PERCENTAGES
30-40	15	25
41-50	29	48
51-60	12	20
>60	4	7



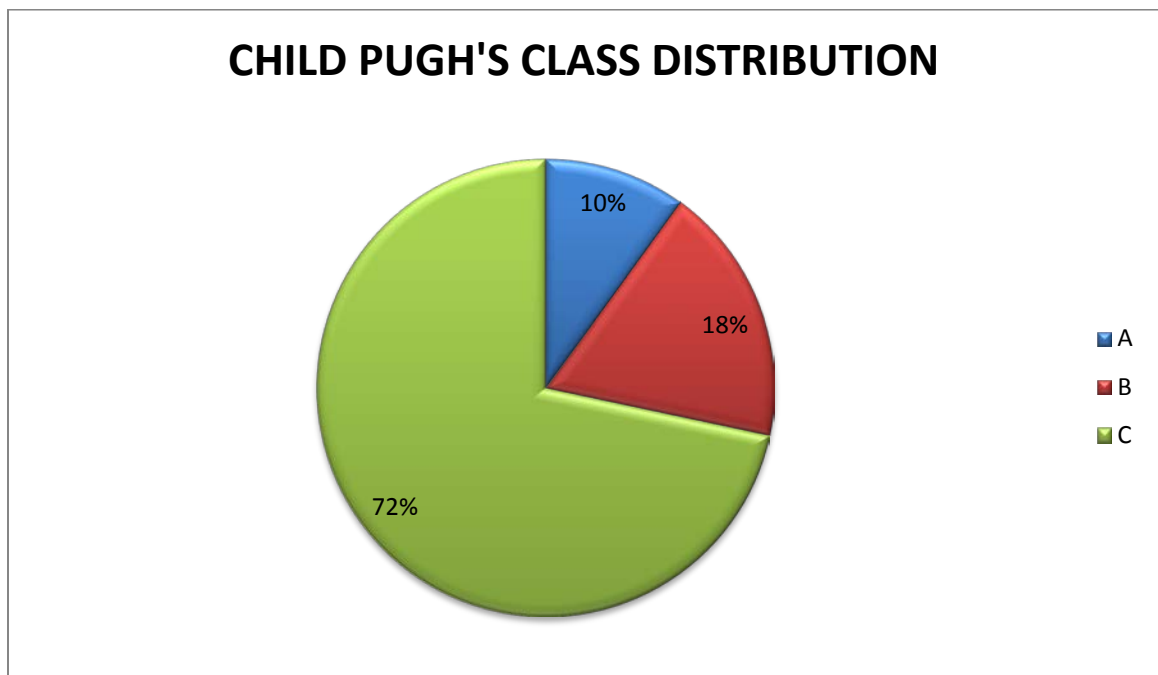
SEX DISTRIBUTION

SEX	NO OF CASES	PERCENTAGES
MALE	53	88
FEMALE	7	12



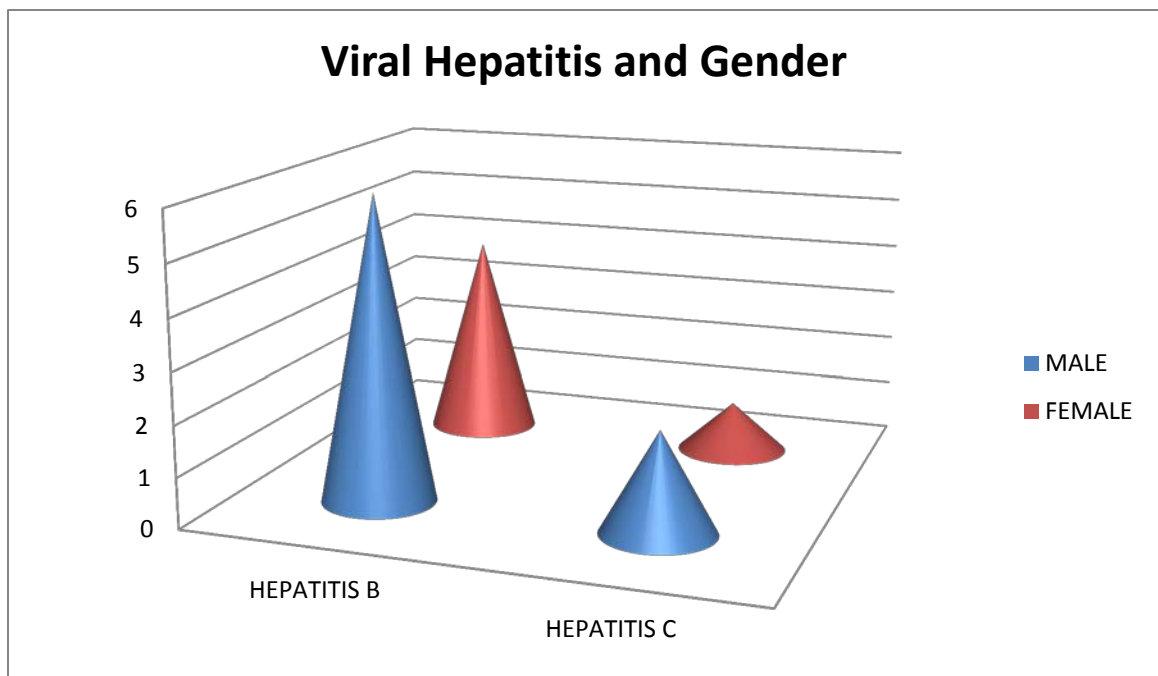
CHILD PUGH'S CLASSIFICATION

CHILD PUGH'S CLASS	NO OF CASES	PERCENTAGE
A	6	10
B	11	18
C	43	72

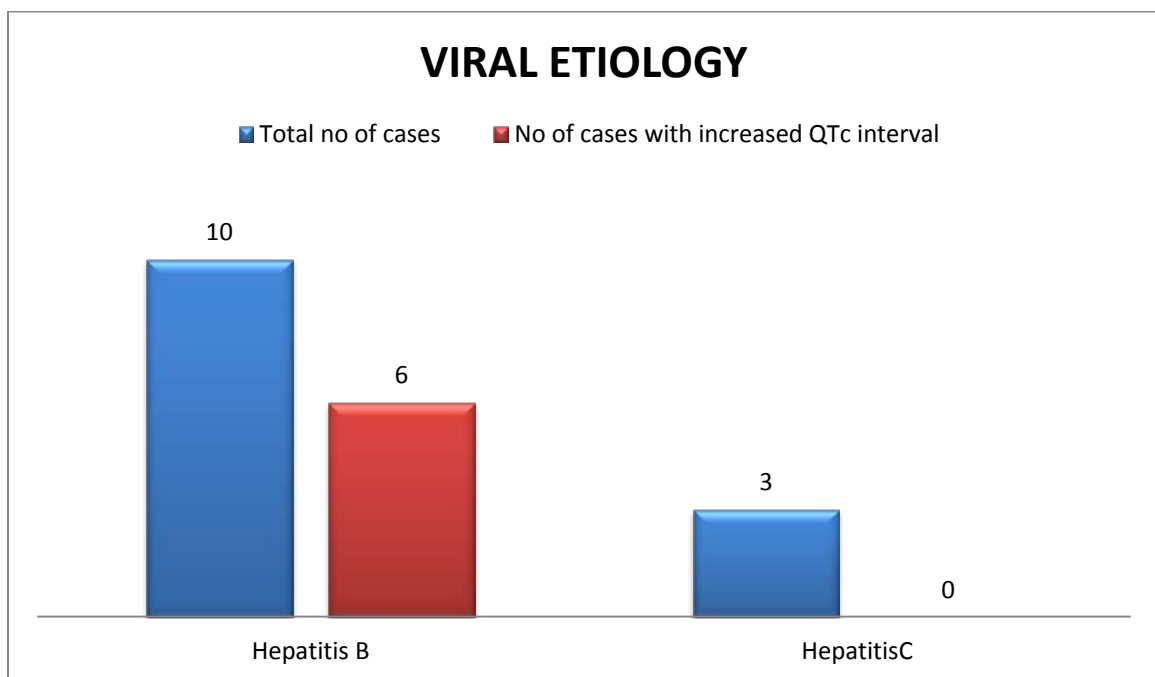


VIRAL ETIOLOGY: SEX DISTRIBUTION

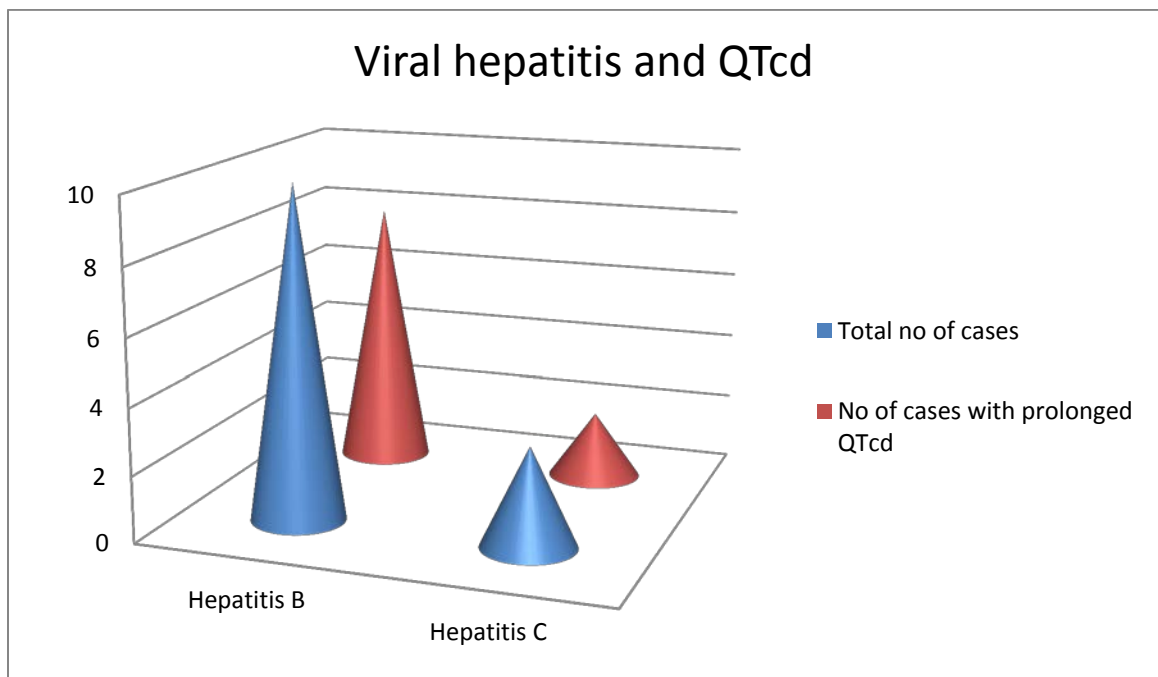
VIRAL ETIOLOGY	MALE	FEMALE
HEPATITIS B	6	4
HEPATITIS C	2	1



VIRAL HEPATITIS	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QT _c INTERVAL
HEPATITIS B	10	6
HEPATITIS C	3	0



VIRAL HEPATITIS	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTcd
HEPATITS B	10	8
HEPATITS C	3	2

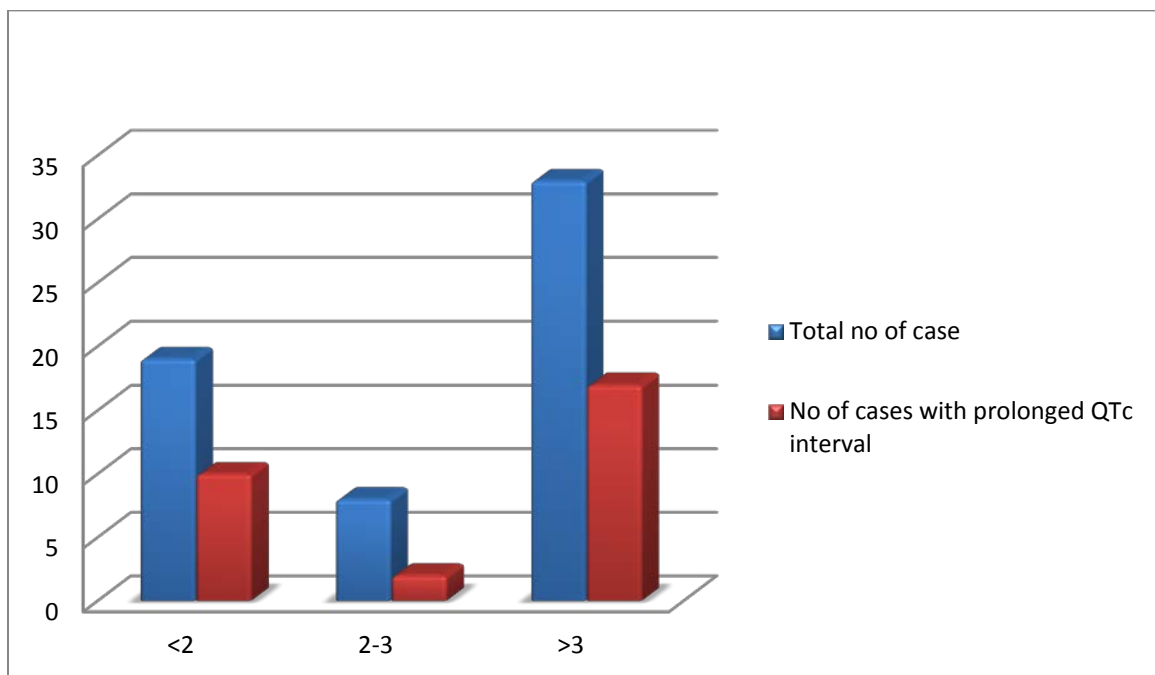


VIRAL HEPATITIS	MEAN QTc INTERVAL(in milliseconds)	MEAN QTcd(in milliseconds)
HEPATITIS B	450±44.63	79±22.44
HEPATITIS C	387±37.98	82±30.11

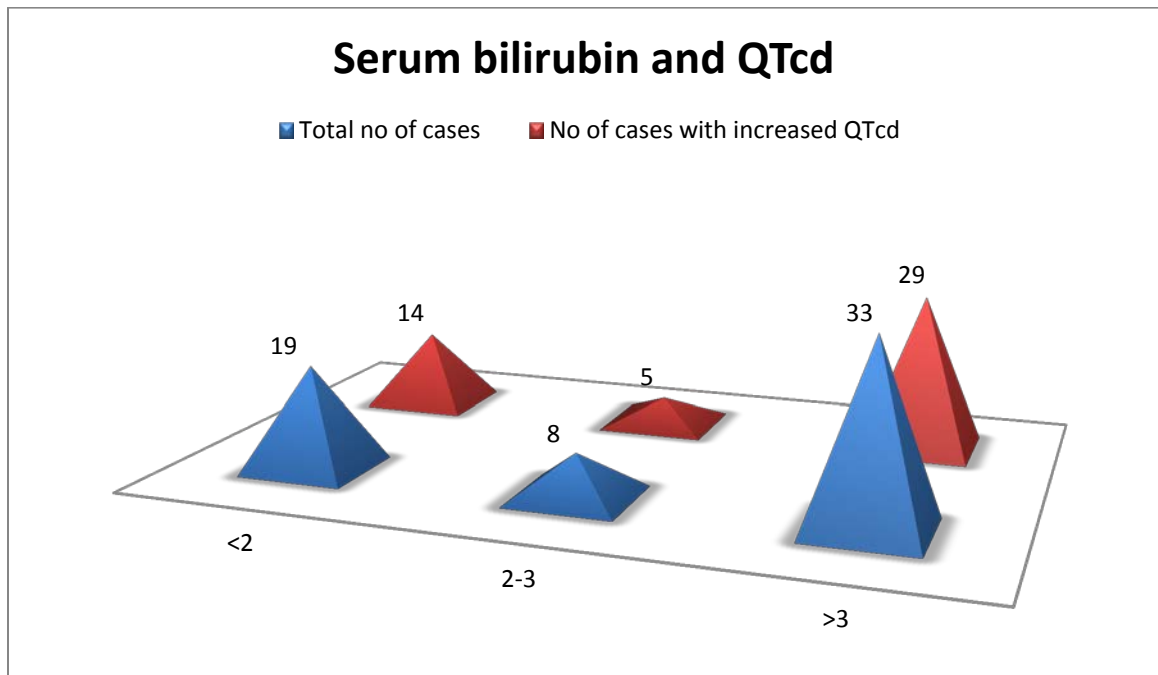
TOTAL BILIRUBIN(mg/dl)	MEAN QTc INTERAVL(in milliseconds)	MEAN QT cd(in milliseconds)
<2	79.36±24.43	449.94±36.69
2-3	78.5±23.4	429.5±40.69
>3	89.45±20.2	443.12±39.99

TOTAL BILIRUBIN(mg/dl)	TOTAL NO OF CASES	NO OF CASE WITH PROLONGED QTc INTERVAL
<2	19	10
2-3	8	2
>3	33	17

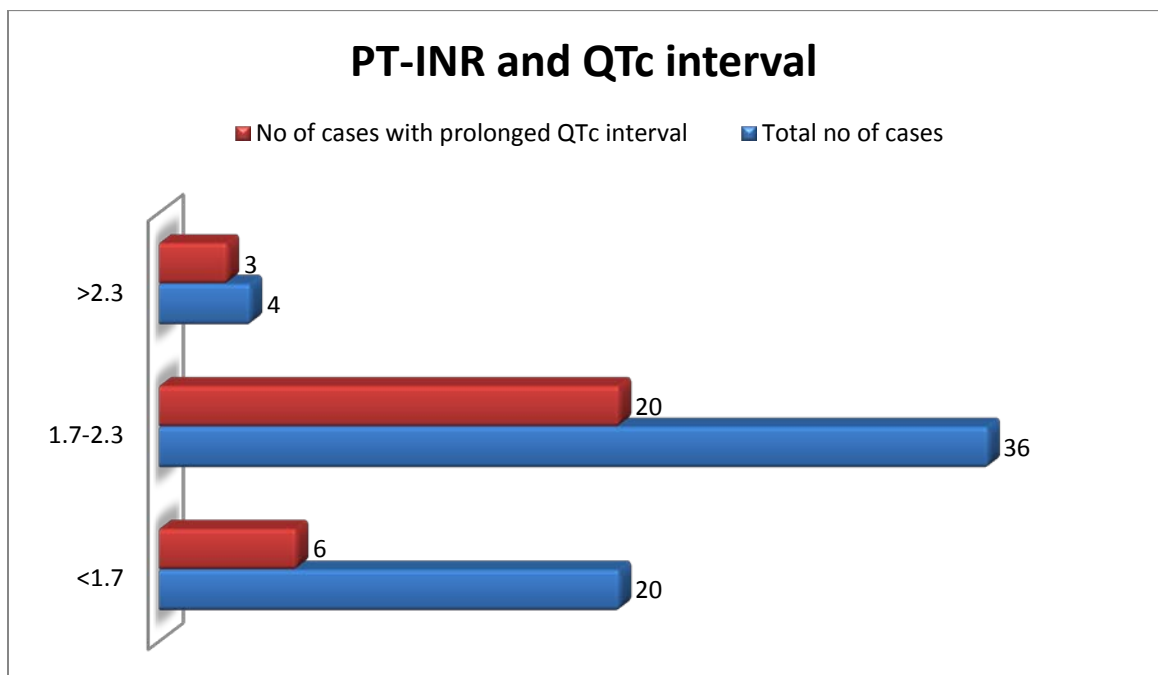
SERUM BILIRUBIN AND QTc INTERVAL



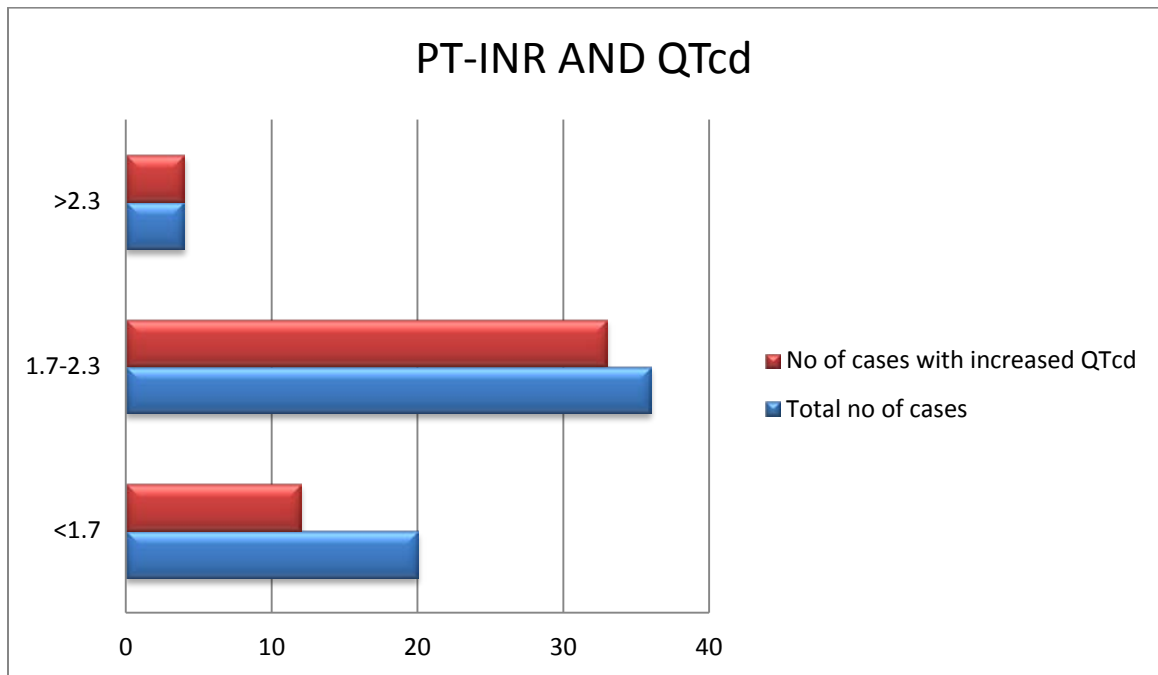
TOTAL BILIRUBIN(mg/dl)	TOTAL NO OF CASES	NO OF CASE WITH INCREASED QTc d
<2	19	14
2-3	8	5
>3	33	29



PT-INR	TOTAL NO OF CASES	NO OF CASES WITH PROLONGED QTc INTERVAL
<1.7	20	6
1.7-2.3	36	20
>2.3	4	3



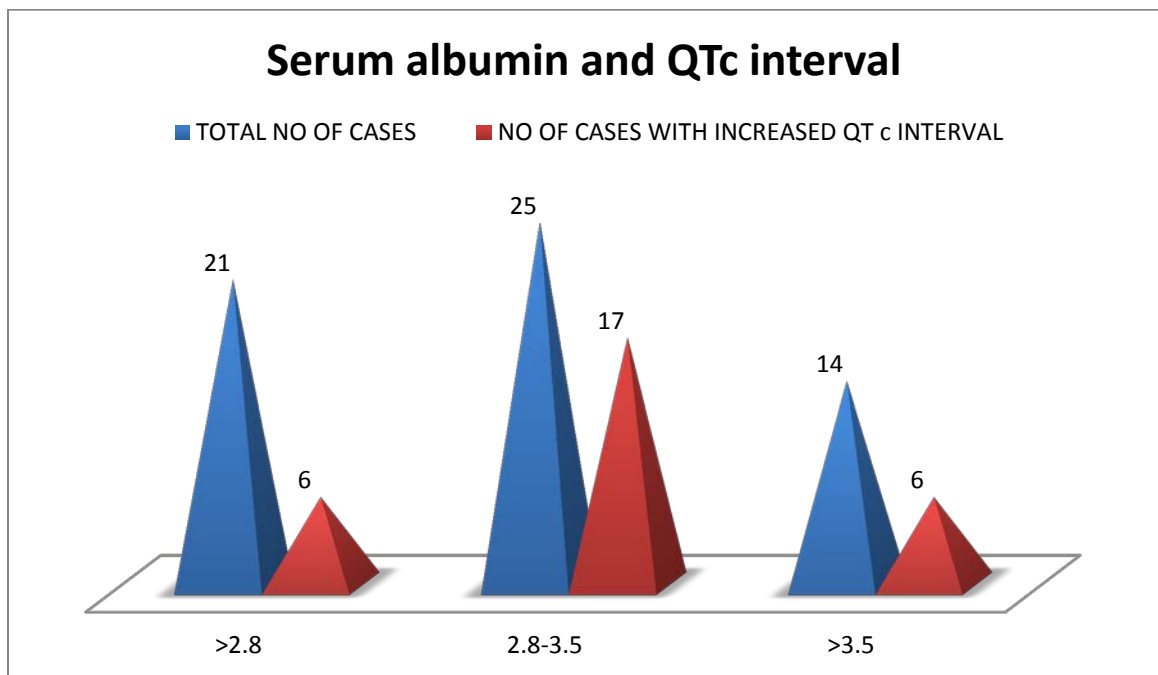
PT-INR	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTcd
<1.7	20	12
1.7-2.3	36	33
>2.3	4	4



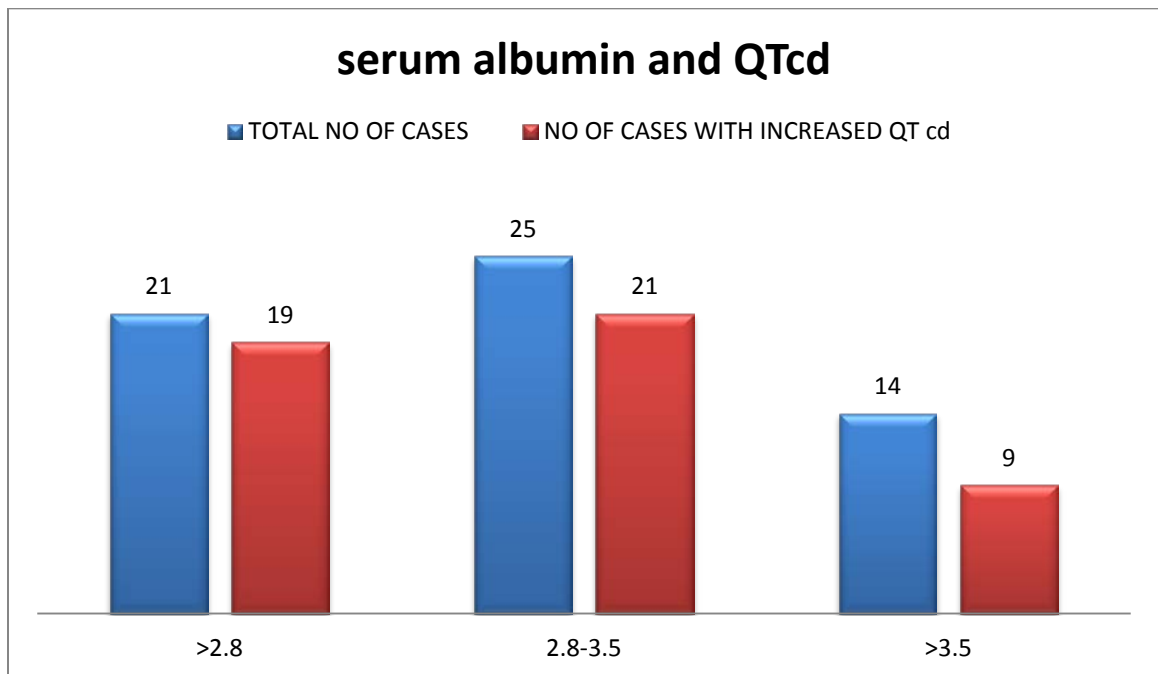
PT-INR	MEAN QT _c INTERVAL(ms)	MEAN QT _{cd} (ms)
<1.7	429.6±37.06	72.1±24.06
1.7-2.3	448.47±38.88	91.41±19.06
>2.3	467.75±32.93	88.75±11.87

SERUM ALBUMIN(g/l)	MEAN QT _c INTERVAL(ms)	MEAN QT _{cd} (ms)
<2.8	425.5±39.01	90.42±21.17
2.8-3.5	457.16±33.59	89.04±21.89
>3.5	449.85±39.56	68.78±17.16

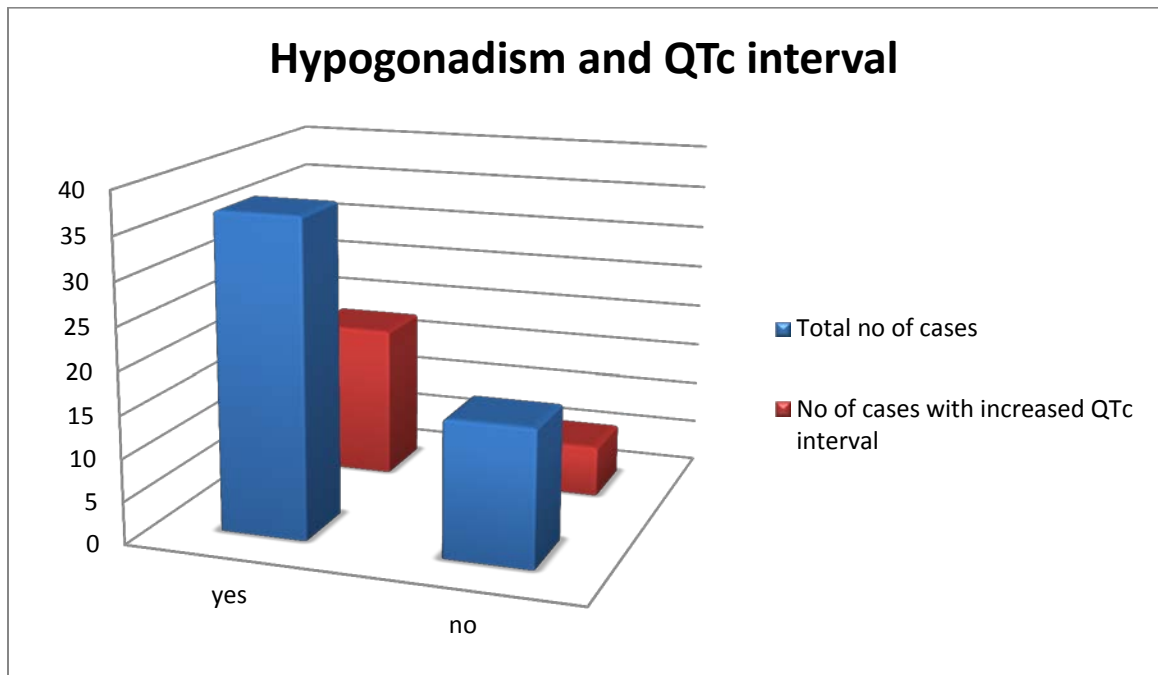
SERUM ALBUMIN(g/l)	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QT _c INTERVAL
<2.8	21	6
2.8-3.5	25	17
>3.5	14	6



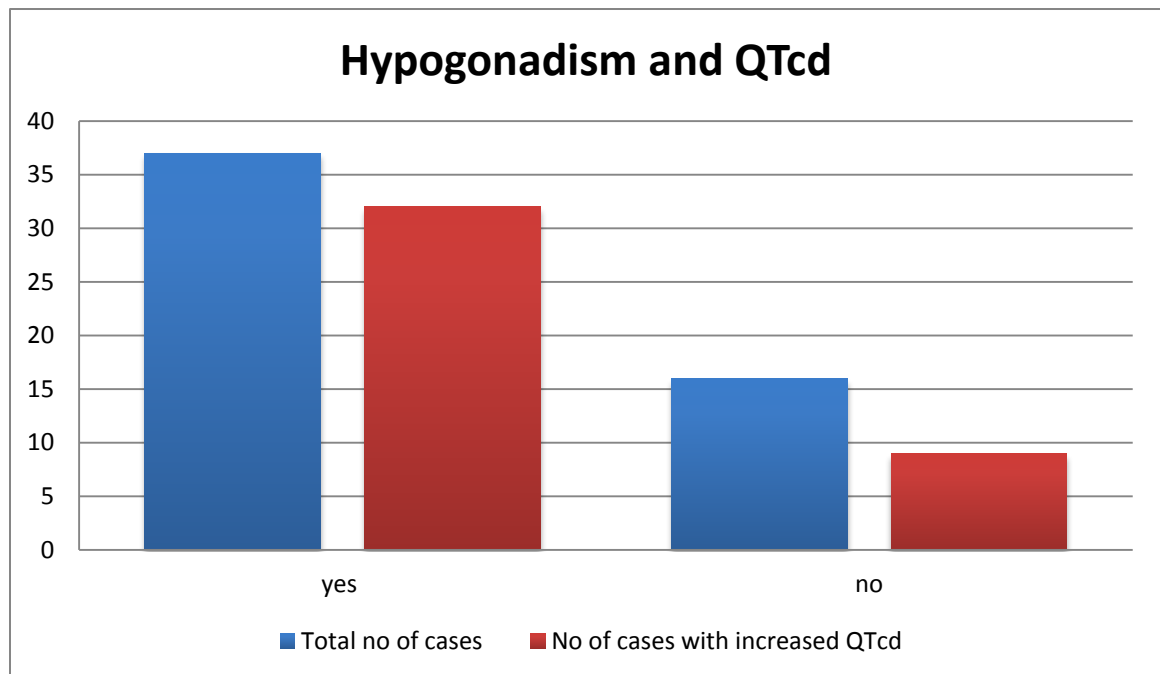
SERUM ALBUMIN(g/l)	TOTAL NO OF CASES(ms)	NO OF CASES WITH INCREASED QTcd(ms)
<2.8	21	19
2.8-3.5	25	21
>3.5	14	4



HYPOGONA DISM	TOTAL NO OF CASES	NO OF CASES WITH PROLONGED QTc INTERVAL
YES	37	18
NO	16	6



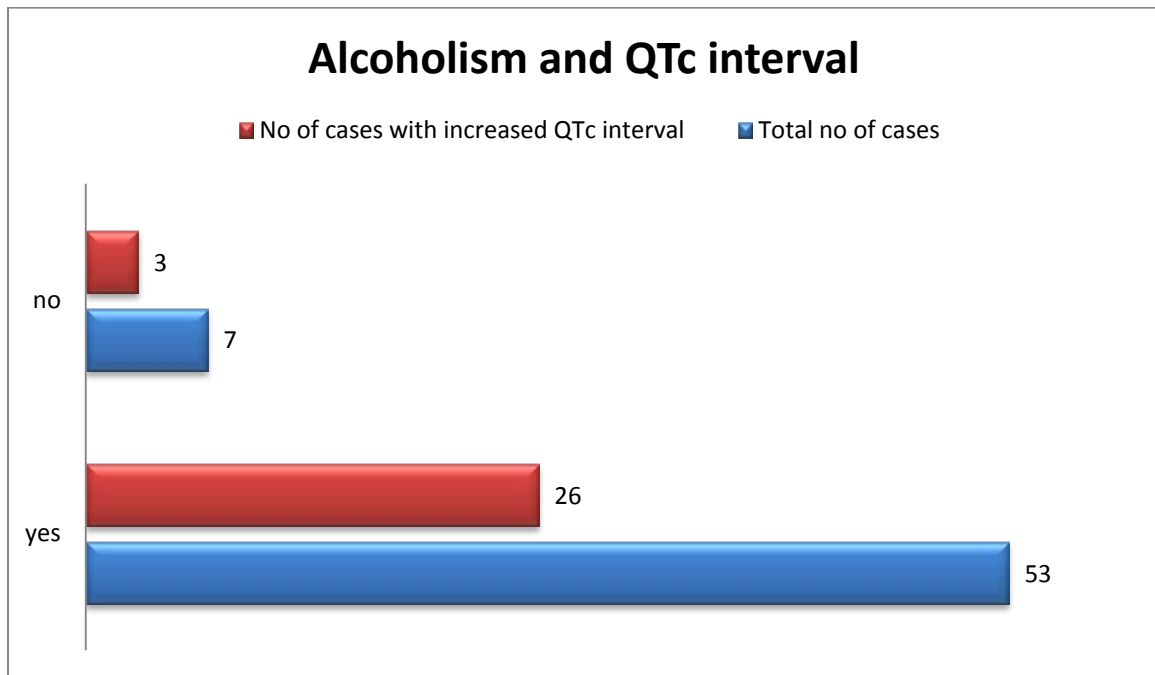
HYPOGONADISM	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTcd
YES	37	32
NO	16	9



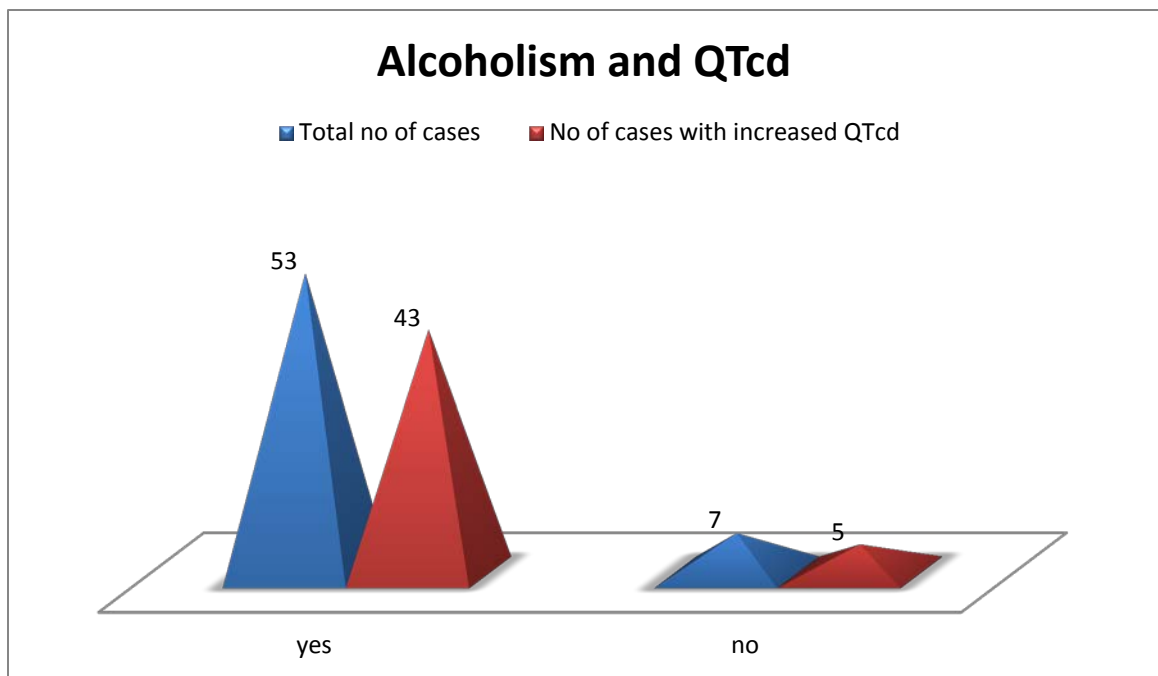
HYPOGONADISM	MEAN QTc INTERVAL(in ms)	MEAN QTcd(in ms)
YES	445.13±39.23	88.35±20.66
NO	437.93±32.02	76.75±27.12

H/O ALCOHOLISM	MEAN QTc INTERVAL(in ms)	MEAN QTcd(in ms)
YES	446±35.98	86.5±21.82
NO	424±56.46	71.57±21.7

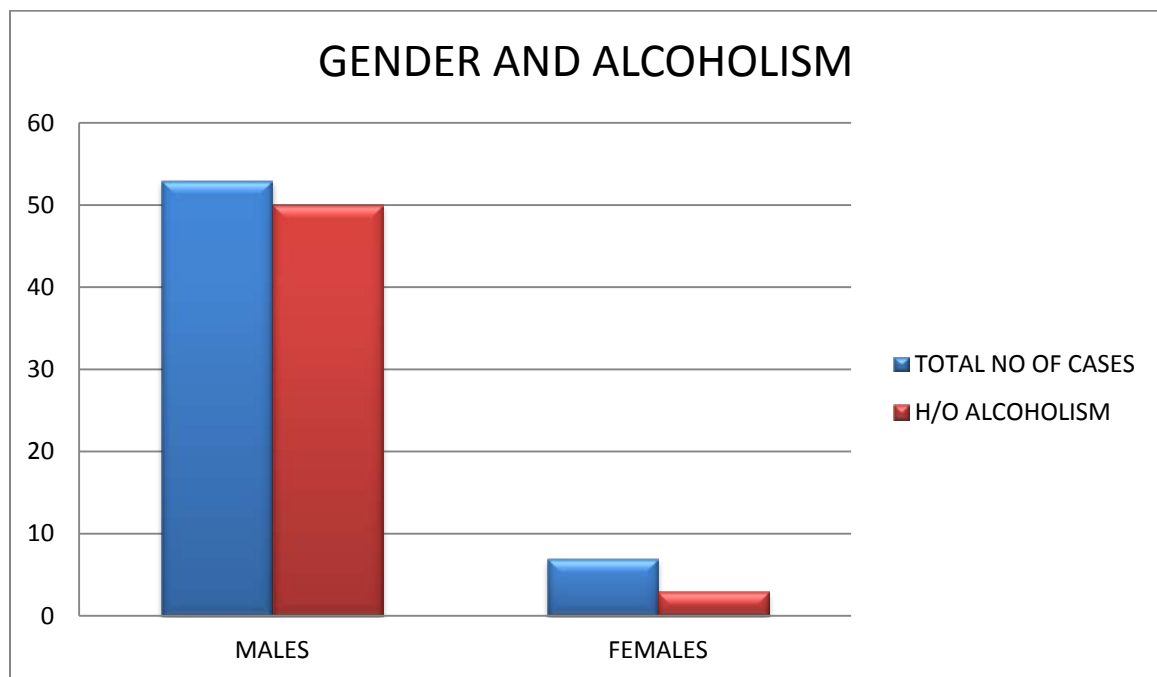
ALCOHOLISM	TOTAL NO CASES	NO OF CASES WITH PROLONGED QTc INTERVAL
YES	53	26
NO	7	3



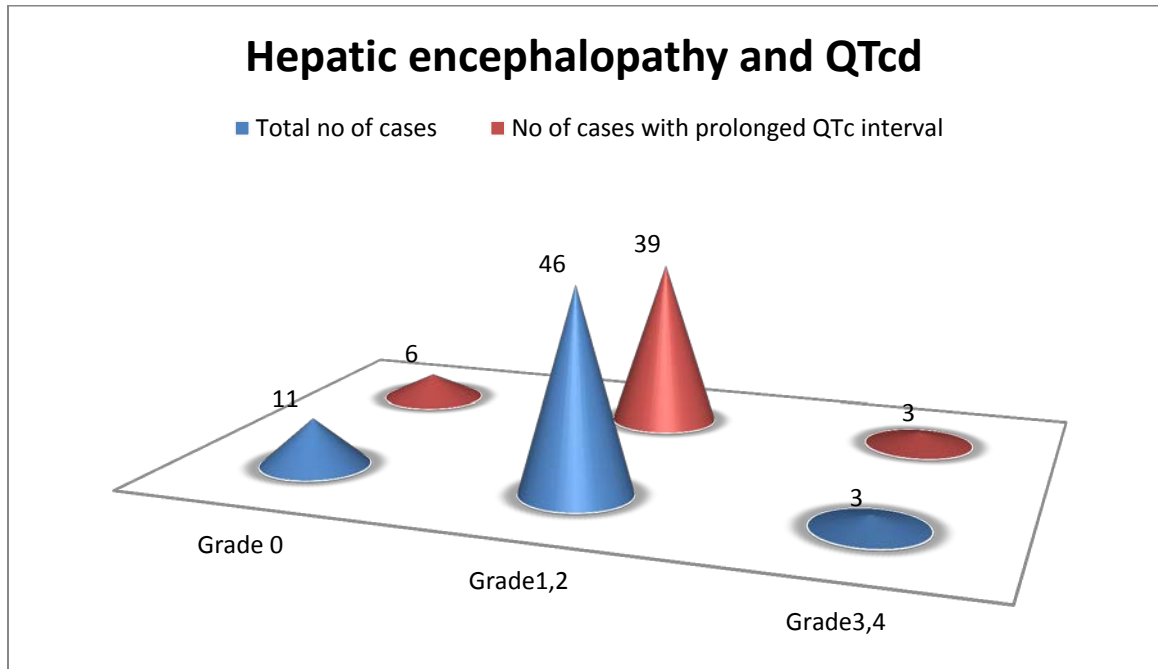
ALCOHOLISM	TOTAL NO CASES	NO OF CASES WITH INCREASED QTcd
YES	53	43
NO	7	5



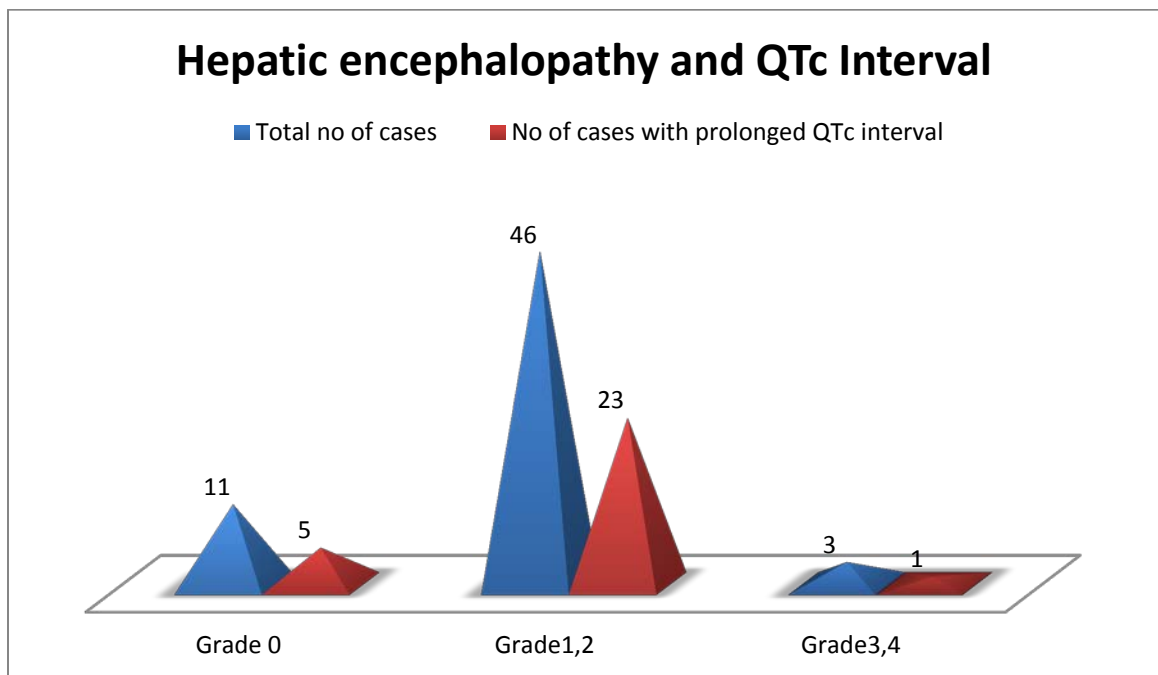
SEX	TOTAL NO OF CASES	H/O ALCOHOLISM
MALES	53	50
FEMALES	7	3



HEPATIC ENCEPHALOPATHY	TOTAL NO OF CASES	NO OF CASES WITH PROLONGED QTcd
GRADE 0	11	6
GRADE1,2	46	39
GRADE3,4	3	3



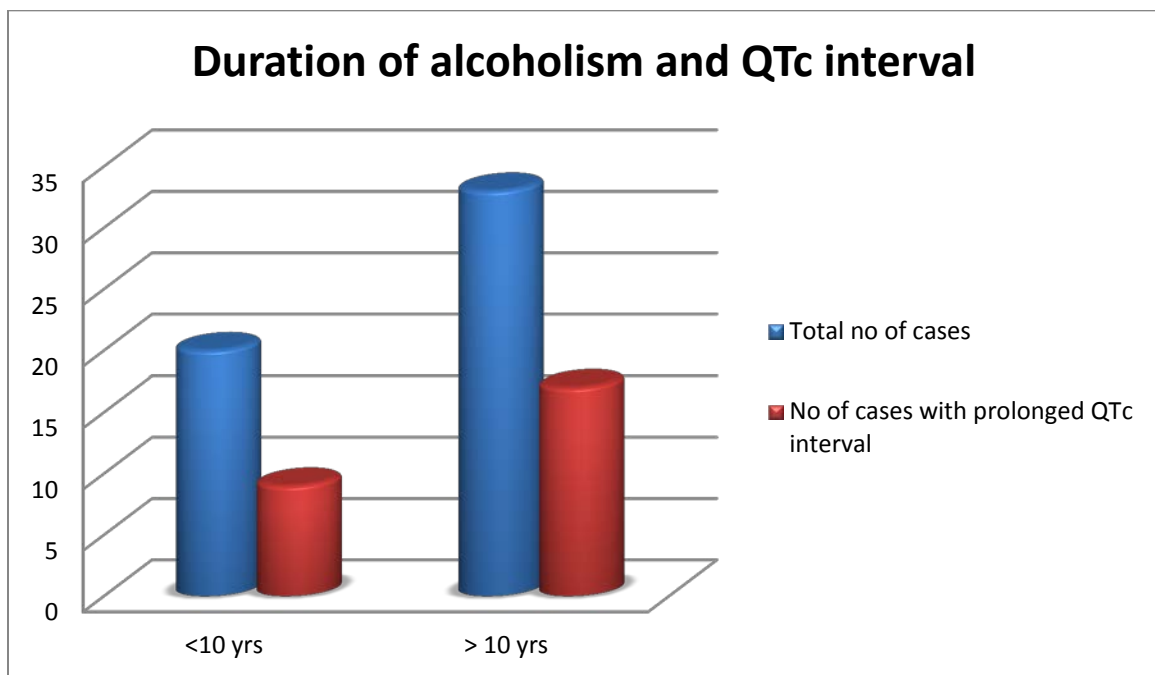
HEPATIC ENCEPHALOPATHY	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTc INTERVAL
GRADE 0	11	5
GRADE1,2	46	23
GRADE3,4	3	1



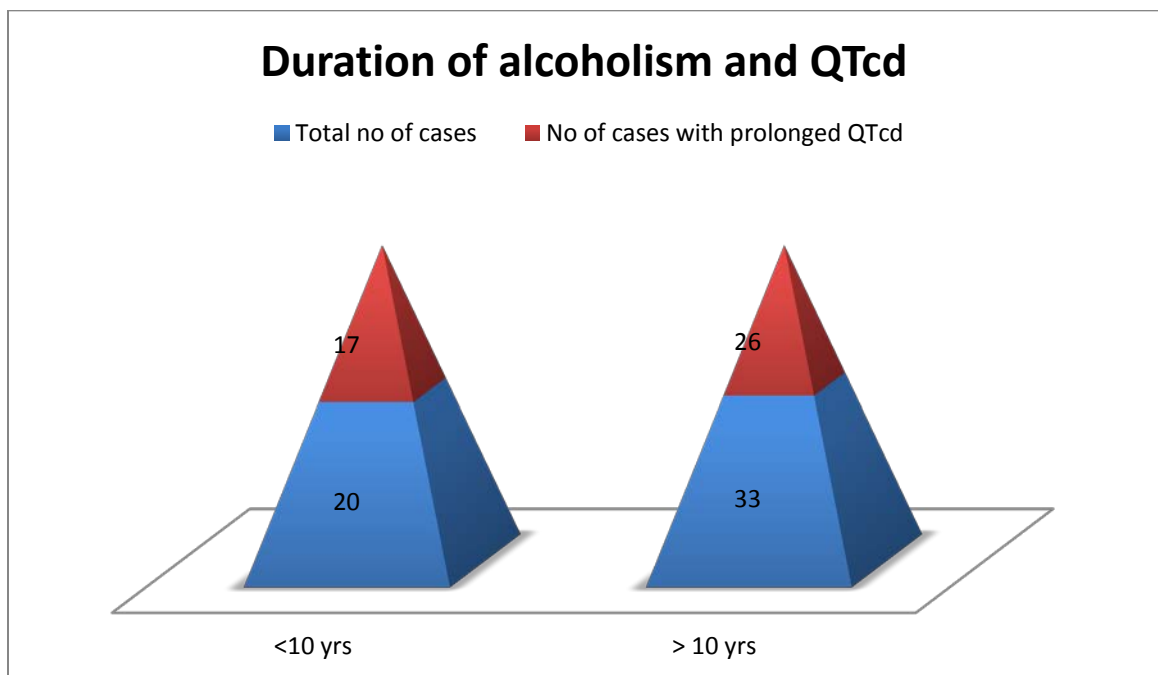
HEPATIC ENCEPHALOPATHY	MEAN QTC INTERVAL(in milliseconds)	MEAN QTcd(in milliseconds)
GRADE 0	448.9±37.22	81.27±31.93
GRADE1,2	444.82±37.04	85.93±20.26
GRADE3,4	402.66±64.59	80.33±6.11

DURATION OF ALCOHOL INTAKE(years)	MEAN QTc INTERVAL(in ms)	MEAN QTcd(in ms)
<10	444.15±36.55	89.2±18.10
>10	447±36.16	84.93±23.93

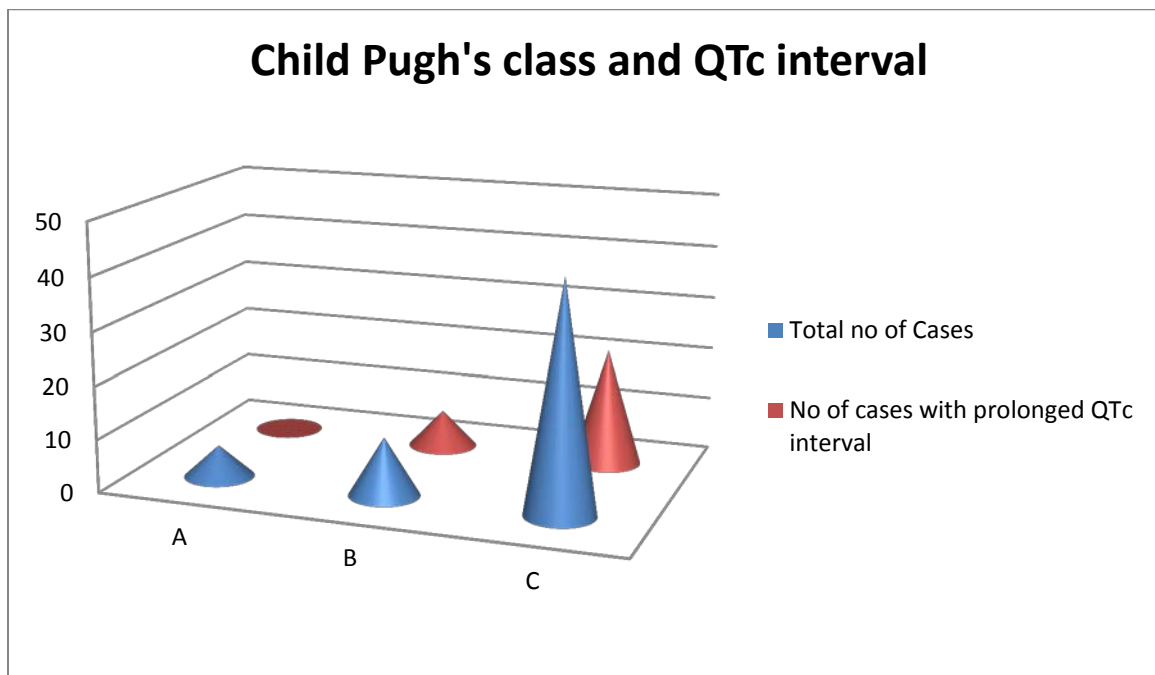
DURATION OF ALCOHOL INTAKE(years)	TOTAL NO OF CASES	NO OF CASES WITH PROLONGED QTc INTERVAL
<10	20	9
>10	33	17



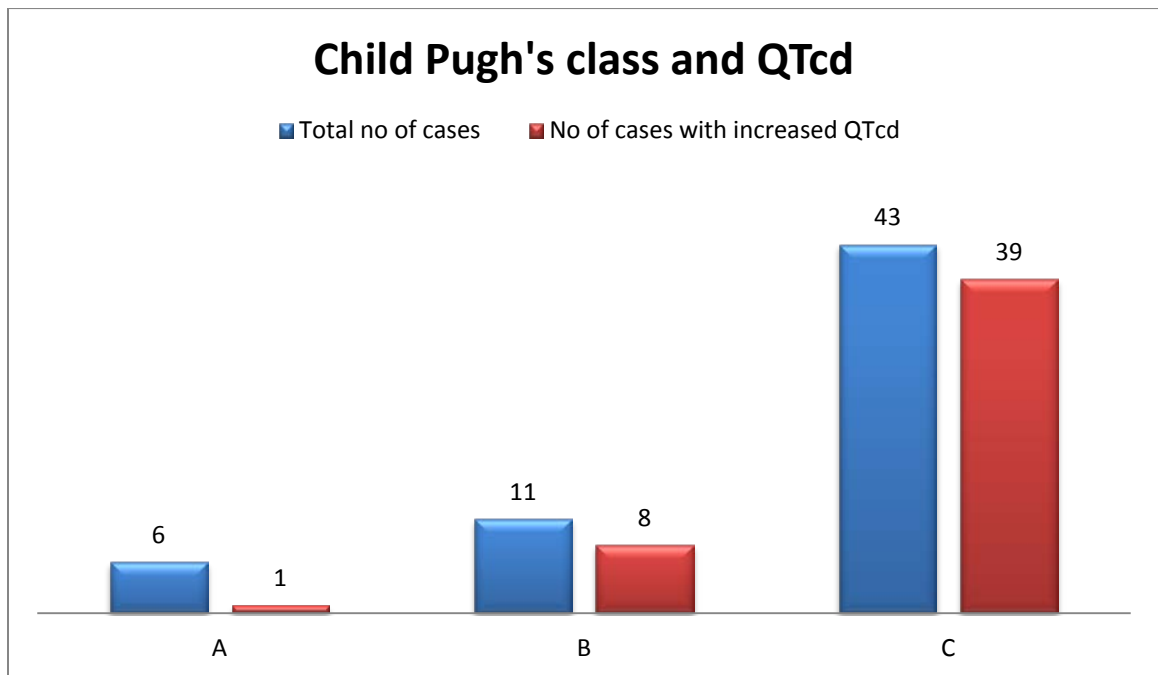
DURATION OF ALCOHOL INTAKE(years)	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTcd
<10	20	17
>10	33	26



CHILD PUGH'S CLASS	TOTAL NO OF CASES	NO OF CASES WITH PROLONGED QTc INTERVAL
A	6	0
B	11	7
C	43	22



CHILD PUGH'S CLASS	TOTAL NO OF CASES	NO OF CASES WITH INCREASED QTcd
A	6	1
B	11	8
C	43	39



CHILD PUGH'S CLASS	MEAN QTc INTERVAL(in milliseconds)	MEAN QTcd(in milliseconds)
A	415±4.92	54.66±19.85
B	457±36.53	74.36±16.69
C	443.88±40.6	91.67±11.25

Multiple Comparison:Dependent Variable: QT cd

Tukey HSD

(I) Child pugh class	(J) Child pugh class	Std. Error	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
A	B	9.562	.107	-42.71	3.31
	C	8.211	.000	-56.86	-17.34
B	A	9.562	.107	-3.31	42.71
	C	6.366	.022	-32.72	-2.08
C	A	8.211	.000	17.34	56.86
	B	6.366	.022	2.08	32.72

* The mean difference is significant at the .05 level.

RESULTS

Age distribution:

In this present study about 25% were in the age group 30-40 years, 48% were in the age group of 41-50 years, 20% were in the age group of 51-60 years and 7% were in the group of >61 years. The mean age is 46.56 ± 7.5 years

Sex and QTcd:

In our study about 88% were males and 12% were females. About 77% of males had increased QTcd and mean QTcd is 84.84ms. All of the female patients had prolonged QTcd and the mean QTcd is 84.42ms.

Viral hepatitis:

Hepatitis B was positive in 17% of cases and Hepatitis C was positive in 6% of cases. Among those with Hepatitis B 80% had increased QTcd and the mean QTcd was 79 ± 22.44 . 66% of those with hepatitis C had increased QTcd and the mean QTcd was 82ms.

Serum bilirubin QTcd:

Out of 60 patients serum bilirubin was <2 in 19 patients, between 2-3 in 8 patients and >3 in 33 patients. 74 % of those with bilirubin had increased QT interval and the mean QTcd in them was 79.36ms. 63% of those with serum bilirubin between 2-3 had increased QTcd and the mean QTcd was 78.5ms. 88% of those with serum bilirubin >3 had prolonged QTcd and their mean QTcd was 89.45ms.

Serum albumin and QTcd:

Out 60 patients 21 had serum albumin below 2.8 g/dl, 90 % of them had prolonged QTcd and their mean QTcd was 90.42ms. 25 patients had albumin level between 2-3, 84 % of them had increased QTcd and their mean was 89.14ms. 14 patients had serum albumin >3 , 64% of them had increased QTcd and their mean was 68.78ms.

Hypogonadism:

Out of 60 patients, 37 had features of Hypogonadism, 86% of these had prolonged QTcd and their mean QTcd was 88.35ms. About 56% of those without hypogonadism had increased QTcd and the mean QTcd was 76.75ms.

Alcoholism and QTcd:

In this present study, 88% were alcoholic and 12% were nonalcoholic. Among those with alcoholism 81% had prolonged QTcd and their mean QTcd was 86.5 ms, while 71% of those without alcoholism had increased QTcd and their mean QTcd was 71.57ms.

Child Pugh's class and QTcd:

In this study 10% of patients were in Child Pugh's class A, 18% were in Child Pugh's class B and 72% belonged to Child Pugh's class C. Increased QTcd was noted in 17% of those in Child Pugh's class A, 73% of those in Child Pugh's class B, 91% of those in Child Pugh's class C. The mean QTcd in A, B, C class were as follows 66ms, 74.36ms, 91.67ms. and the difference between class A and B, C was statistically significant as shown by ANOVA.

DISCUSSION

Number of patients taken up for study:

Study groups	Total number of cases
Bernadi et al	94
Mozos et al	38
Kosar et al	33
Present study	60

But no controls were used in this present study.

AGE:

Mean age of patients in various studies

Kosar et al 53 ± 11 years

Bernardi et al 53.1 ± 1.4 years

Present study 46.5 ± 7.5 years

The mean age of patients in this present study was lower than that of previous studies.

Mean QTc interval and QTcd:

Study group	Mean QTc interval(in milliseconds)	Mean QTcd(in milliseconds)
Bernardi et al	462±4.2	-
Kosar et al	448±96	71±39
Present study	443.5±38.9	84.8±22

In this present study QTcd is higher than previous studies, while QTc interval though prolonged is lower than previous studies.

Etiology and QT variables:

Mean QTc interval in alcoholics was 527±50 ms in a study by Kosar et al, while it is 446±35.98 ms in our study. And our study showed difference in mean QTcd between alcoholics and non-alcoholics

Alcoholics: 446±35.9 ms

Non alcoholics: 424±56.4 ms

But this was not statistically significant p value 0.161.

The mean QTc interval among patients with viral etiology

Mozos et al 481 ± 57 ms

Present study 418.5 ± 44 ms

Our study has lower mean QTc interval than previous study

Child Pugh's class and QT variables:

	Child Pugh's class		
Study group	A	B	C
Genovesi et al	425 ± 24	452 ± 30	465 ± 24
Mozos et al	462 ± 25	493 ± 62	520 ± 45
Kosar et al	437 ± 49	444 ± 40	468 ± 66
Present study	415 ± 4.9	457 ± 36.5	443.8 ± 40.6

In this present study QTc interval was increased in both child Pugh's class B and C, but was less than 440ms in class A as was the results of Genovesi et al and Kosar et al.

Many studies had previously demonstrated prolonged QT variables in patients with alcoholic liver disease and child Pugh's class C⁽⁷⁾. In this present study though mean QT variables were increased among alcoholics it was not statistically significant as was the result with Bernardi et al.

Mean QTcd (in milliseconds)

	Child Pugh's class		
Study group	A	B	C
Kosar et al	65±33	67±24	83±43
Present study	54.7±19.9	74.4±16.7	91.7±19.2

QT variables were significantly increased in class B and C when compared with class A, as shown by ANOVA , as was the findings of Bernardi et al, Kosar et al, Mozos et al.

LIMITATIONS OF STUDY

- One limitation of this study is low number of female patients, patients with nonalcoholic etiology, and the results should be confirmed in large group of patients.
- Bazett's formula was used to correct QT interval, it may under correct if heart rate is lower than 60 and over correct if heart rate is more than 110.
- Though thorough history, physical examination, ECG and echocardiogram were done to rule out coronary artery disease, coronary angiogram was not done to rule out occult coronary artery disease.

CONCLUSION

- QTcd (corrected QT dispersion) correlates well with the severity of chronic liver disease based on Child Pugh's class.
- QTcd is independent of etiology of chronic liver disease.
- QTcd can be used to assess the severity of chronic liver disease.

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PROFORMA

CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE

Name :

Patient ID No:

Age/Sex :

IP No :

Patient characteristics		Drugs
Duration of CLD		<input type="checkbox"/> Antibiotics
<input type="checkbox"/> Smoking		<input type="checkbox"/> Furosemide
<input type="checkbox"/> Alcoholism		<input type="checkbox"/> Spironolactone
		<input type="checkbox"/> Propranolol

CLINICAL PARAMETERS			
Pulse		Blood Pressure	
<input type="checkbox"/> Pallor		<input type="checkbox"/> Ascites	
<input type="checkbox"/> Icterus		<input type="checkbox"/> Dilated veins over the abdomen	
<input type="checkbox"/> Oedema		<input type="checkbox"/> Splenomegaly	
<input type="checkbox"/> Features of hypogonadism		<input type="checkbox"/> Hepatic flap	

Investigations:

RFT			LFT		
Glucose		mg/dl	Total bilirubin		mg/dl
Urea		mg/dl	Direct bilirubin		mg/dl
Creatinine		mg/dl	SGOT		U/l
Na ⁺		mEq/l	SGPT		U/l
K ⁺		mEq/l	ALP		U/l
HBsAg			Total protein		g/dl

Anti-HCV		Albumin		g/dl
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Chest X-ray:

Echocardiography:

Ultrasound abdomen:

ECG:

Heart rate	
QTc max	
QTc min	
QTcd	

Child-Pugh classification

Parameter	1	2	3
Ascites			
Bilirubin (mg/dL)			
Albumin (g/dL)			
PT-INR			
Encephalopathy			
GRADE			

PATIENT CONSENT FORM

Study Detail : Corrected QT dispersion and its correlation with
severity of chronic liver disease

Study Centre : Rajiv Gandhi Government General Hospital,
Chennai.

Patient's Name :

Patient's Age :

Identification :

Number

Patient may check (☒) these boxes

I confirm that I have understood the purpose of procedure for the above
study. I have the opportunity to ask question and all my questions and
doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am
free to withdraw at any time without giving reason, without my legal
rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms.

☐

I hereby consent to participate in this study.

☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

☐

Signature/thumb impression

Signature of Investigator

Patient's Name and Address:

Study Investigator's Name:

Dr. A. VIGNESH

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. A. Vignesh
PG in MD General Medicine
Madras Medical College, Chennai -3

Dear Dr. A. Vignesh

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Corrected QT dispersion and its correlation with severity of chronic liver disease" No.25042012.


The following members of Ethics Committee were present in the meeting held on 19.04.2012 conducted at Madras Medical College, Chennai -3.

- | | |
|----------------------------------------------------|---------------------|
| 1. Dr. S.K. Rajan. M.D.,FRCP.,DSc | -- Chairperson |
| 2. Prof. Pregna B. Dolia MD | -- Member Secretary |
| Director , Institute of Biochemistry, MMC, Ch-3 | |
| 3. Prof. B. Kalaiselvi MD | -- Member |
| Prof. of Pharmacology ,MMC, Ch-3 | |
| 4. Prof. C. Rajendiran, MD | -- Member |
| Director , Inst. of Internal Medicine MMC, Ch-3 | |
| 5. Prof. Md. Ali. MD.DM | -- Member |
| Prof & HOD, Dept. of MGE, MMC, Ch-3 | |
| 6. Prof.P.Karkuzhali MD | -- Member |
| Director i/c, Prof., Inst. of Pathology, MMC, Ch-3 | |
| 7. Prof. S. Deivanayagam MS | -- Member |
| Prof of Surgery, MMC, Ch-3 | |
| 8. Prof. A. Radhakrishnan MD | -- Member |
| Prof of Internal Medicine, MMC, Ch-3 | |
| 9. Thiru. S. Govindsamy. BABL | -- Lawyer |
| 10. Tmt. Arnold Soulina MA MSW | -- Social Scientist |

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.


Member Secretary, Ethics Committee



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Assignment title	Medical
Author	Vignesh 20101021 M.D. General Medicine
E-mail	mails2maverick@gmail.com
Submission time	19-Dec-2012 07:05PM
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First 100 words of your submission

DISSERTATION TITLED "CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE" Submitted in partial fulfilment of Requirements for M.D.DEGREE EXAMINATION BRANCH-I INTERNAL MEDICINE THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY CHENNAI INSTITUTE OF INTERNAL MEDICINE MADRAS MEDICAL COLLEGE CHENNAI - 600003. APRIL 2013 CERTIFICATE This is to certify that the dissertation entitled " A STUDY ON CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE " is a bonafide work done by DR. A.VIGNESH , Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for...

KEY WORDS

M	MALE
F	FEMALE
Y	YES
N	NO
P	POSITIVE
N	NEGATIVE
SERUM BILIRUBIN	UNITS IN mg/dl
ALBUMIN	UNITS IN g/dl
QTcmax	maximal QT interval in milliseconds
QTcmin	minimum QT interval in milliseconds
QTcd	corrected QT dispersion in milliseconds

S.NO	AGE	SEX	DURATION OF ALCOHOL INTAKE (IN YEARS)	DRUG INTAKE	ICTERUS	HYPOGONADISM	ASCITES	ENCEPHALOPATHY (GRADE)	HBsAg	ANTI-HCV	SERUM BILIRU BIN	ALBUMIN	PT-INR	CHILD PUGH CLASS	QT cmax	QT cmin	QT cd
1	38	M	5	N	Y	Y	1	0	N	N	7.2	2.5	1.8	C	481	374	107
2	63	M	10	Y	Y	Y	1	2	N	N	3	3.2	1.9	C	481	374	107
3	45	M	6	Y	Y	Y	1	0	P	N	2	3.4	1.8	C	503	391	112
4	47	M	10	N	Y	N	1	0	N	N	6.7	2.9	2	C	498	374	124
5	36	M	10	Y	N	Y	0	1	N	N	0.9	3.5	1.8	C	498	427	71
6	48	F	20	N	Y		0	0	N	N	1.8	3	1.8	C	481	374	107
7	36	M	10	N	Y	N	1	2	N	N	4.5	3.1	1.9	C	465	398	67
8	48	M	12	Y	N	Y	2	2	N	P	1.2	3.4	1.4	C	394	279	115
9	64	M	20	Y	Y	N	0	2	N	N	9.7	3.1	1.6	B	470	423	47
10	40	M	10	N	Y	Y	1	2	N	N	8.8	3	2	C	470	423	47
11	46	M	12	Y	Y	Y	0	1	N	N	3.8	2.4	1.8	C	421	374	147
12	42	M	8	Y	Y	N	1	2	N	N	2.8	2.4	1.6	C	410	365	45
13	52	M	6	N	Y	Y	1	2	N	N	4.3	2.9	1.9	C	498	398	100
14	47	M	10	N	N	Y	1	2	N	N	1.8	3.1	2	C	479	383	96
15	39	M	9	N	Y	Y	1	2	N	N	5.2	2.4	2.3	C	498	427	71
16	50	F	0	N	N		0	2	P	N	0.8	3.5	1.2	B	465	374	91
17	46	M	12	N	Y	Y	1	1	N	N	3.8	2.4	1.8	C	416	323	93
18	45	M	0	N	N	N	0	0	P	N	1.2	3.8	1.1	A	416	370	42
19	34	M	11	N	Y	Y	1	2	N	N	5.6	2.9	2.3	C	479	383	96
20	43	M	15	N	Y	N	1	2	N	N	9.8	3.4	2.4	C	421	327	94
21	48	M	0	Y	Y	Y	0	2	P	N	3.2	2.4	1.9	C	365	319	46
22	54	M	12	N	Y	Y	1	1	N	N	8.8	2.5	2	C	410	319	91
23	39	F	0	N	N		1	3	N	P	6.4	2.6	1.4	C	346	302	75
24	52	M	9	N	Y	Y	1	2	N	N	7.4	3.4	1.9	C	431	327	104
25	49	M	10	N	Y	Y	1	2	N	N	8.9	3.2	2	C	484	410	74
26	45	M	12	N	N	Y	1	1	N	N	1.8	3.5	1.8	B	498	427	71
27	64	M	19	N	N	N	0	0	N	N	1.8	3.6	1.5	A	421	327	94
28	46	M	6	N	N	Y	1	2	N	N	1.4	2.5	1.4	C	436	327	109
29	54	M	0	Y	Y	N	1	2	P	N	3.1	2.3	1.8	C	410	308	102
30	43	F	0	N	N		0	2	P	N	1	3.5	1	B	498	427	71
31	38	F	0	N	N		0	2	P	N	0.9	3.5	1.2	B	470	396	74
32	49	M	10	N	N	N	0	2	N	N	0.8	2.4	1.9	C	410	313	97
33	56	M	12	Y	Y	N	0	1	N	N	3.8	3.5	1.2	B	421	327	94

S.NO	AGE	SEX	DURATION OF ALCOHOL INTAKE (IN YEARS)	DRUG INTAKE	ICTERUS	HYPOGONADISM	ASCITES	ENCEPHALOPATHY (GRADE)	HBsAg	ANTI-HCV	SERUM BILIRU BIN	ALBUMIN	PT-INR	CHILD PUGH CLASS	QT cmax	QT cmin	QT cd
34	48	M	10	N	N	N	0	0	N	N	1.2	3.8	1	A	410	365	45
35	54	M	8	Y	Y	Y	1	2	N	N	3.8	2.4	1.8	C	479	380	99
36	36	M	20	Y	Y	Y	1	2	P	N	4	2.5	2	C	421	327	94
37	49	M	12	N	Y	Y	1	2	N	N	3.6	2.8	1.5	C	501	401	100
38	61	M	12	N	N	N	0	0	N	N	1.8	3.6	1	A	421	365	56
39	39	M	8	Y	Y	Y	0	1	N	N	3.6	2.1	1.8	C	431	342	89
40	34	M	10	Y	Y	Y	0	1	N	N	1.2	3.8	1	A	410	365	45
41	52	M	8	Y	Y	N	0	0	N	N	1.2	2.9	2	B	470	365	105
42	41	M	17	N	N	N	0	0	N	N	1.6	3.4	1.2	A	416	370	46
43	48	M	9	Y	Y	Y	1	2	N	N	3.4	2.8	1.8	C	431	342	89
44	48	M	8	N	N	Y	0	0	N	P	2.5	2.9	1.5	B	421	365	56
45	53	M	8	N	Y	Y	1	2	N	N	3	3.4	2	C	416	333	83
46	32	M	16	Y	Y	Y	1	2	P	N	3.8	2.6	1.9	C	479	394	79
47	38	M	6	N	Y	Y	1	3	N	N	2	2.6	2	C	389	302	87
48	54	F	7	N	N		2	3	P	N	3.4	2.8	1.8	C	473	394	79
49	49	M	12	Y	Y	Y	0	1	N	N	4.2	2.1	2.1	C	410	315	95
50	46	M	14	N	Y	Y	2	2	N	N	4.5	2.9	2.2	C	450	360	90
51	38	M	8	Y	Y	Y	0	1	N	N	2.6	3.5	1.6	B	421	354	67
52	52	M	9	N	Y	N	2	2	N	N	9.7	3.1	1.4	C	450	351	99
53	56	M	12	Y	Y	Y	0	2	N	N	3.5	2.2	1.8	C	410	312	96
54	49	M	10	Y	Y	Y	0	1	N	N	3	3.5	1.4	B	395	327	71
55	45	M	5	N	Y	Y	2	1	N	N	8.8	2.9	1.8	C	389	302	87
56	42	F	8	N	N		2	2	N	N	4.2	2.6	2	C	398	304	94
57	48	M	6	N	N	Y	1	2	N	N	0.8	3.2	2	C	458	356	102
58	39	M	11	N	Y	Y	2	2	N	N	7.2	2.5	2.5	C	473	379	94
59	41	M	10	N	N	N	1	1	N	N	1.8	3.5	1.7	B	498	427	71
60	56	M	12	N	Y	Y	1	2	N	N	3.5	2.6	1.8	C	444	355	89