“EVALUATION OF CARDIAC FUNCTION IN PATIENTS WITH CHRONIC LIVER DISEASE”

By:

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DISSERTATION SUBMITTED TO THE

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA,

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

DOCTOR OF MEDICINE (M.D.)

IN

GENERAL MEDICINE

Under the Guidance Of

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Introduction:

Cirrhosis is a condition of liver that leads to a number of complications, some of which may eventually prove fatal.

Chronic liver disease is accompanied by several circulatory changes. In advanced cirrhosis a condition known to be Hyper dynamic circulatory syndrome is seen among cases suffering from Cirrhosis.

It is characterized by splanchnic blood pooling, opening of portal systemic collaterals, arterial vasodilatation and compensatory increase in blood volume. The resultant autonomic regulatory system events result in an increase in the cardiac output along with the reduced peripheral vascular resistance[1].

The involvement of cardiac dysfunction among the cases suffering from Liver disease was first described by Kowalski and Abelmann who noted a higher resting cardiac output and decreased systemic vascular resistance. After this observation numerous studies were done and the existence of hyper dynamic circulation which was characterized by peripheral vasodilatation and increased cardiac output. [2,3]

The Autonomic Dysfunction among the chronic liver cases varies from 8 to 80 % in different studies and its presence is usually irrespective of the causes which leads to chronic liver diseases which is caused by ethanol or non-ethanol related issues. [4]

In the early stages of the cirrhosis, the hyper dynamic type of circulation is not seen frequently or elicited clinically. However, as the disease starts to progress into advanced stages, the overall association between the severity of the disease and the degree of hyper dynamic circulation. The

increase in the cardiac output results in increase in the venous return and Heart rate. Heart rate is circadian variability and disrupted in patients with cirrhosis. impaired chronotropic responses may be exhibited by patients with cirrhosis of any cause and their prevalence increases with disease severity.[5]

Vasodilatation (low systemic vascular resistance), the presence of arteriovenous communications, expanded blood volume and increased sympathetic nervous activity may further raise the cardiac output; most of these pathophysiological mechanisms are active in advanced cirrhosis [6,7].

In the advanced cirrhosis cases, there is will be also raise in blood and plasma volume but the distribution between central and non-central vascular areas becomes unequal .[8]

Other than the hyper dynamic circulation, there will be impaired ventricular contractility among the cirrhotic patients. These cardiovascular function was thought to be a manifestation of latent alcoholic cardiomyopathy but subsequently studies were conducted on alcoholic and nonalcoholic patients which revealed the same type of cardiovascular manifestation among both the groups which subsequently ruled out the alcohol cause and established that the impaired ventricular contractility was due to cirrhotic changes in the liver which was a common etiological factor in both the groups .[9,10,11]. These changes were termed as Cirrhotic Cardiomyopathy.[12]

. The characteristic features of cirrhotic cardiomyopathy include [12]

- an attenuated systolic or diastolic response to stress stimuli,
- structural or histological changes in cardiac chambers,
- electrophysiological abnormalities, and

- serum markers suggestive of cardiac stress.

Hence the cases of Liver cirrhosis are frequently associated with various cardiovascular abnormalities which include hyper dynamic circulation, characterized by higher resting cardiac output and decreased systemic vascular resistance and impaired ventricular contractility.

Hence this study was undertaken to observe the frequency of Diastolic and Systolic dysfunction in cirrhotic.

OBJECTIVES:

1. To study the clinical profile of chronic liver disease cases admitted in R.L.J.H Kolar, tertiary care hospital.

2. To study the cardiovascular structural and functional status in the above patients.

Review of Literature:

Chronic Liver Disease: [13]

The profile of chronic inflammatory disease of liver extends from acute hepatitis to chronic hepatitis and finally to cirrhosis. Chronic hepatitis is defined as chronic inflammation of the liver of more than 3–6 months' duration, demonstrated by persistently abnormal serum aminotransferase levels and characteristic histologic findings.

In many cases, the diagnosis of chronic hepatitis may be made on initial presentation. The causes of chronic hepatitis include HBV, HCV, and HDV as well as autoimmune hepatitis; alcoholic and nonalcoholic steatohepatitis; Wilson's disease; alpha1-antiprotease deficiency; and, rarely, celiac disease.

CIRRHOSIS OF LIVER.[13]

Cirrhosis is a condition which is defined as pathological entity that is associated with a wide range of characteristic manifestations.

The liver transformation was identified by a anatomic pathologist named Gianbattista Morgagni in his literature of 500 autopsies which was published in the year 1761. The name "cirrhosis" was first coined by Laennec in the year 1826. The yellowish tan colour of the liver was the reason for the derivative of such name .

Even though the term “cirrhosis” was used only in 1761, there have been many mentions in world history about the same condition.

The first use of alcohol dates to Neolithic period circa, around 100,000 BC with the discovery of mud jugs which were used for drinking a special brew on special occasions.

As early as 4000 BC in the Egyptian culture the consumption of wine has been reported in the various pictures. The association between amount and duration of alcohol consumed was associated with the distension of abdomen.

In the Egyptian culture it has been mentioned that during the embalmment of the dead bodies there were report of aspiration of clear or straw colored fluid in those people who had distension of adbdomen. This is the earliest mention of ascetic fluid collection. The sentiment towards moderation in drinking was documented in a Chinese imperial edict in 12th century BC. By the 2nd century AD, during the Hung's dynasty rule in china, Chinese medical practioners had already warned public about excessive consumption of wine, which leads to liver damage and eventually insanity, which in modern times is referred to as hepatic encephalopathy.

Buddhist monasteries wrote texts about the severity of the liver disease and the presence of yellow discoloration of the eyes along with distension of abdomen. They were the first to correlate the alcohol consumption with liver disease and severity of the disease. In ancient India, the references to alcoholic liver disease and cirrhosis, appear in the rig Veda and the atharva Veda, where they mention the condition associated to excessive consumption of wine and called it 'abdominal dropsy'.

Only in 1930, however, the first theory regarding the pathogenesis of this disorder was advanced by Roessle: parenchymal degeneration, regeneration and scarring. [13,14,15]

METHODOLOGY

The present study was carried out in the Department of Dermatology at R.L Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka Kolar from January 2017 to July 2018.

One hundred patients who presented with Chronic liver disease and who satisfied the inclusion criteria were included in this study.

The present study was an observational study.

Inclusion criteria:

Patients diagnosed with chronic liver disease above the age of 20 years were included in the study.

Exclusion criteria:

1. Patients With other known etiology of cardiac disease.
2. Patients with severe anaemia.
3. Patients with HIV infection
4. Patients with hepatorenal syndrome

Methods of data collection:

All cases with Chronic liver disease were screened and those satisfying the inclusion criteria were included in the study. After an informed consent, a detailed history regarding symptoms, signs and were noted.

All patients with chronic liver disease were subjected to 2d echocardiography and the findings were noted.

Sample size calculation :

Sample Sample size was estimated by using the proportion of diastolic dysfunction among alcoholic liver disease subjects detected by ECHO as 64% from the study by A.Batra et al et al. using the formula

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.
p = Expected proportion in population based on previous studies or pilot studies.
d = Absolute error or precision – Has to be decided by researcher.

P = 64 or 0.64

q = 36 or 0.36

d = 15% or 0.15

Using the above values at 95% Confidence level a sample size of 40 subjects with Chronic liver disease will be included in the study.

Considering 10% Nonresponse a sample size of 40 + 4 ≈ 44 subjects will be included in the study. However we have considered 100 samples in this study.

STATISTICAL METHODS USED FOR DATA ANALYSIS

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation.

Graphical representation of data: MS Excel and MS Word was used to obtain various types of graph such as bar diagram and pie diagram.

p value (probability that the result is true) of <0.05 will be considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22(IBM SPSS Statistics, Somers NY, USA) was used to analyse the data.

Results:

Table 1: Age distribution of subjects

		Count	%
Age	<40 years	34	34.0%
	41 to 60 years	40	40.0%
	61 to 80 years	26	26.0%
	Total	100	100.0%

In the study 34% were in the age group <40 years, 40% were in the age group 41 to 60 years and 26% were in the age group 61 to 80 years.

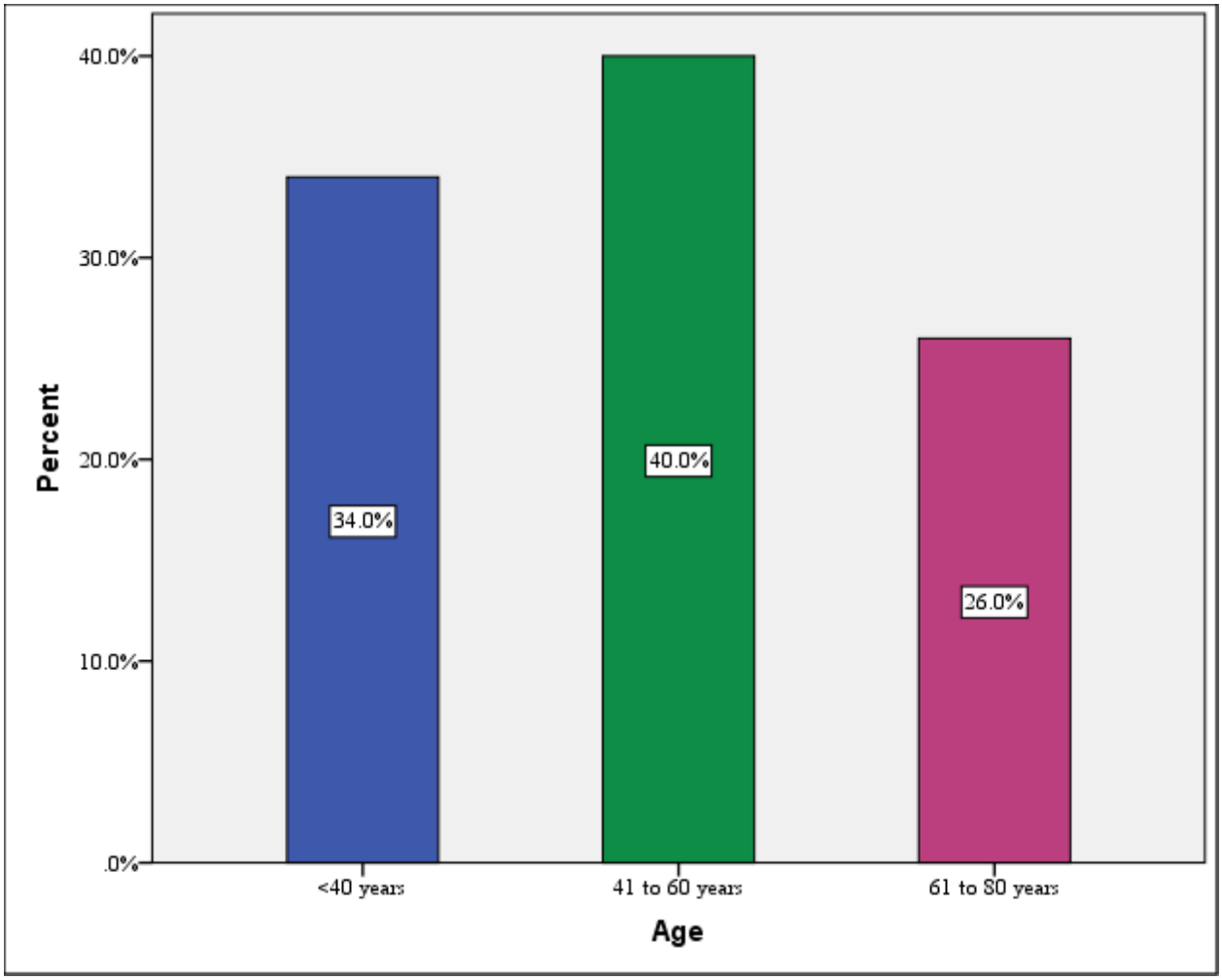

Figure 1: Bar diagram showing Age distribution of subjects

Table 2: Sex distribution of subjects

		Count	%
Sex	Male	96	96.0%
	Female	4	4.0%
	Total	100	100.0%

In the study 96% were males and 4% were females.

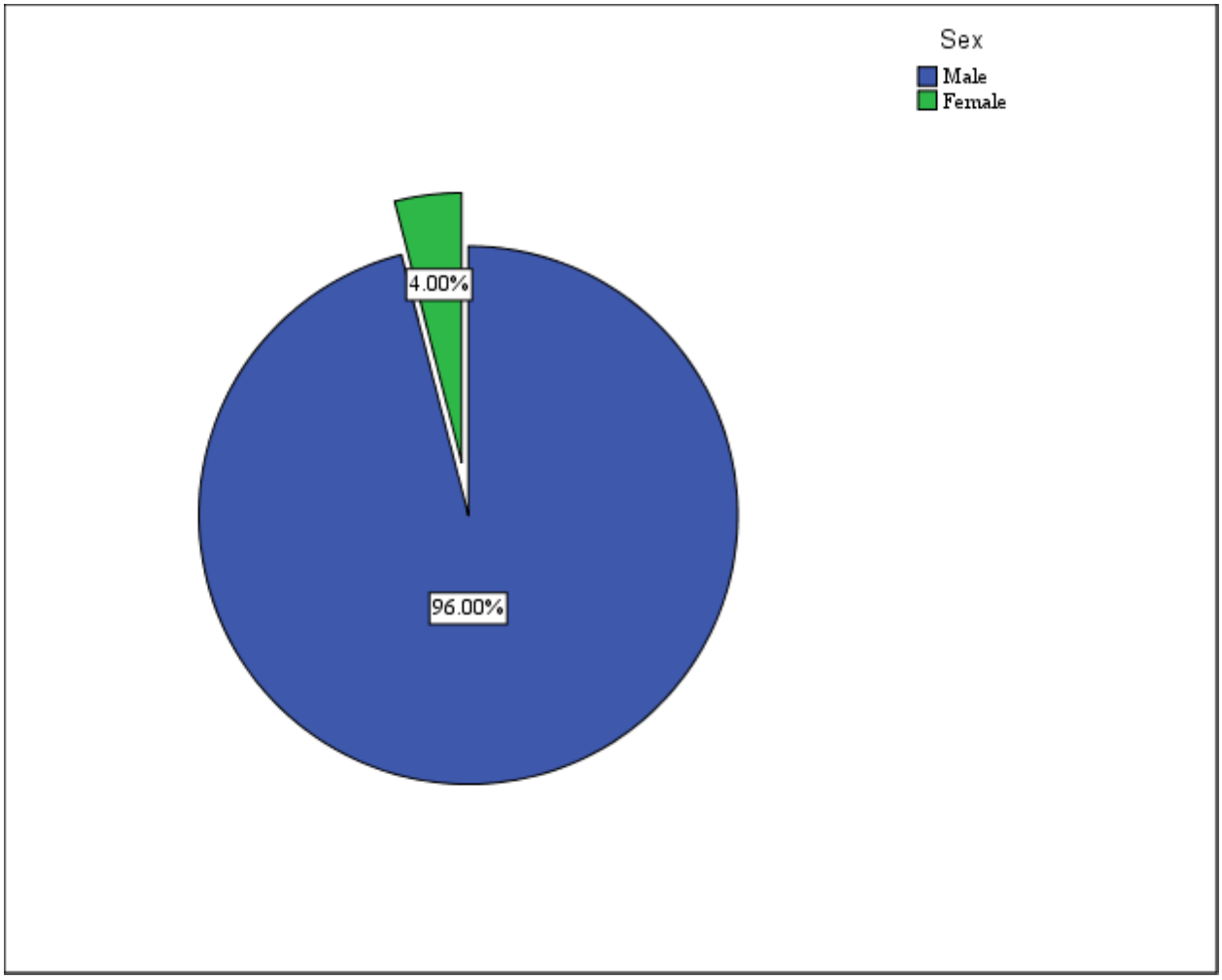

Figure 2: Pie diagram showing Sex distribution of subjects

Table 3: Etiology of cirrhosis in study subjects

		Count	%
Etiology	Alcoholic	80	80.0%
	Alcoholic + HbSAg	6	6.0%
	HBsAg	8	8.0%
	HCV	6	6.0%

In the study most common etiology was Alcoholic (80%), 6% due to Alcoholic + HbSAg, 8% due to HBsAg and 6% due to HCV.

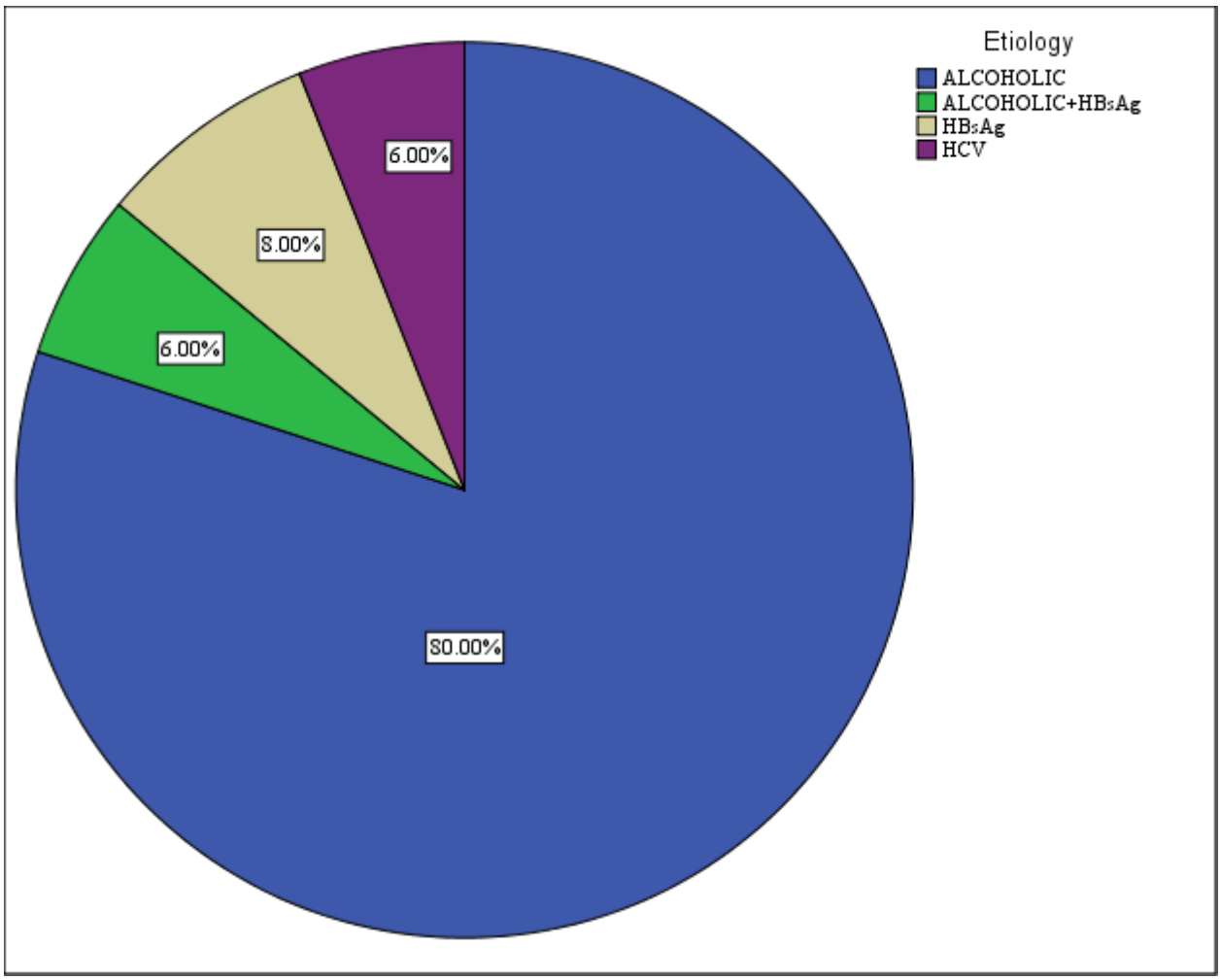

Table 4: Symptoms and signs among subjects

	Absent		Present	
	Count	%	Count	%
Symptoms				
Breathlessness	36	36.0%	64	64.0%
Abdominal distension	20	20.0%	80	80.0%
Lower limb swelling	62	62.0%	38	38.0%
Hematemesis	72	72.0%	28	28.0%
Signs				
Icterus	46	46.0%	54	54.0%
Pedal edema	58	58.0%	42	42.0%
Hepatic Encephalopathy	70	70.0%	30	30.0%

In the study 64% presented with Breathlessness, 80% with Abdominal distension, 38% with Lower limb swelling, 28% with Hematemesis.

54% had Icterus, 42% had pedal edema and 30% had Hepatic Encephalopathy.

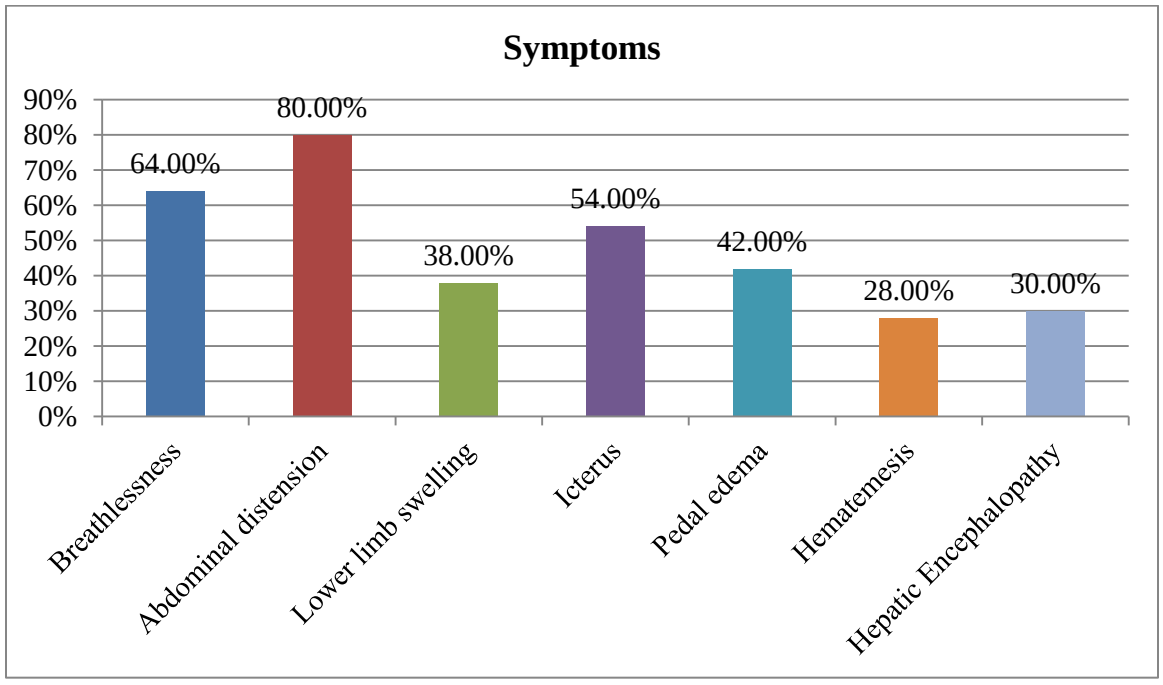

Figure 3: Bar diagram showing Symptoms and signs among subjects

Table 5: Grade of Ascites among subjects

		Count	%
Ascites	Grade 1	2	2.0%
	Grade 2	66	66.0%
	Grade 3	32	32.0%

In the study 2% had Grade 1 Ascites, 66% had Grade 2 Ascites and 32% had Grade 3 Ascites.

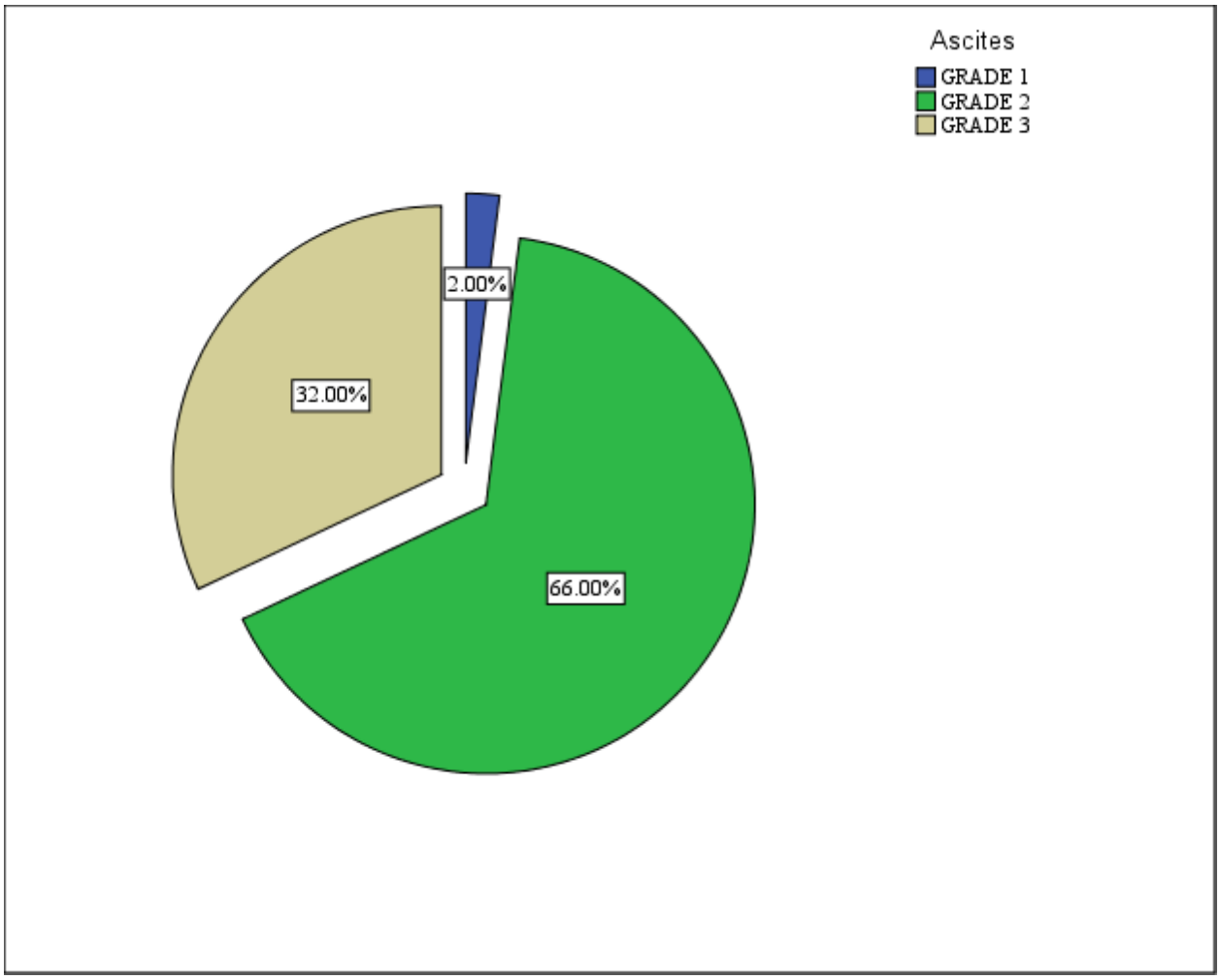

Figure 4: Pie diagram showing Grade of Ascites among subjects

Table 9: Cardiac profile distribution among subjects

		Count	%
IVSd	6 to 11 mm	88	88.0%
	>11 mm	12	12.0%
IVSs	6 to 11 mm	54	54.0%
	>11 mm	46	46.0%
LV Hypertrophy	Absent	48	48.0%
	Present	52	52.0%
LV diameter (Systolic)	23 to 39	100	100.0%
LV diameter diastolic (mm)	36 to 52	100	100.0%
LA diameter	19 to 40 mm	78	78.0%
	>40 mm	22	22.0%
PWd	6 to 11 mm	22	22.0%
	>11 mm	78	78.0%
Diastolic Dysfunction	Absent	30	30.0%
	Present	70	70.0%
EF %	<50 %	26	26.0%
	>50 %	74	74.0%
RWMA	Absent	74	74.0%
	Present	26	26.0%

In the study 12% had increased IV Sd, 46% had increased IV Ss, 52% had LV Hypertrophy, 100% had normal LV diameter both systolic and diastolic, 22% had increased LA diameter, 78% had increased PWd, 70% had diastolic diameter, 26% had decreased Ejection fraction (<50%), 26% had RWMA.

RESULTS:

-In this study 96% were males and 4% were females.

-In this study 64% presented with Breathlessness, 80% with Abdominal distension, 38% with Lower limb swelling, 28% with Hematemesis.

-54% had Icterus, 42% had pedal edema and 30% had Hepatic Encephalopathy.

-In this study 2% had Grade 1 Ascites, 66% had Grade 2 Ascites and 32% had Grade 3 Ascites.

-In this study 79% had increased Total Bilirubin, 92% had increased direct bilirubin, 96% had decreased albumin levels, 84% had increased AST and 56% had increased ALT.

- In this study there was significant association between LV hypertrophy and Etiology, Diastolic dysfunction and Etiology, EF% and Etiology, RWMA and Etiology.

Among those with alcohol as etiology, 45% had LVH, 72.5% had Diastolic dysfunction, 20% had EF <50% and 17.5% had RWMA.

Among those with Alcohol + HBsAg as etiology, 66.7% had LVH, 100% had Diastolic dysfunction, 66.7% had EF <50% and 0% had RWMA.

Among those with HBsAg as etiology, 100% had LVH, 25% had Diastolic dysfunction, 50% had EF <50% and 75% had RWMA.

Among those with HCV as etiology, 66.7% had LVH, 33.3% had Diastolic dysfunction, 66.7% had EF <50% and 100% had RWMA.

CONCLUSION:

Chronic liver disease is a systemic disease with widespread functional consequences affecting almost any other organ including the cardiovascular system. Some systemic complications of cirrhosis, such as HRS, acute and chronic encephalopathy, hepatopulmonary syndrome, are well-defined and specific guidelines have been developed for their diagnosis and treatment. Cardiovascular dysfunction in patients with liver cirrhosis has been documented since 1960 , although only recently has it been well-characterized and defined.

It has been suggested that patients with advanced liver disease have a different risk-factor profile for cardiovascular disease than the general population. However, there are currently no specific guidelines for the diagnosis and treatment of cardiovascular disease in this patient

population. Thus, new prospective studies are needed to identify more specific criteria and standardized procedure for cardiovascular assessment and treatment of cardiocirculatory dysfunction in patients with chronic liver disease.

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ANNEXURES

PROFORMA FOR DATA COLLECTION

NAME: IP NO:

AGE:

SEX:

ADDRES:

OCCUPATION:

DETAILED HISTORY:

ANTHROPOMETRIC MEASUREMENT:

HEIGHT:

WEIGHT:

BODY MASS INDEX:

GENERAL PHYSICAL EXAMINATION:

PULSE:

BLOOD PRESSURE

SYSTEMIC EXAMINATION:

CARDIOVASCULAR EXAMINATION:

RESPIRATORY EXAMINATION:

PER ABDOMINAL EXAMINATION:

CENTRAL NERVOUS SYSTEM EXAMINATION:

LABORATORY DATA:

1. COMPLETE HEMOGRAM

2. LIVER FUNCTION TEST

3. ECG

4. 2D ECHOCARDIOGRAPHY

5. USG ABDOMEN

6. FBS,PPBS

7.HBsAg

8.HIV

CONSENT FORM

Study title: **EVALUATION OF CARDIAC FUNCTION IN PATIENTS WITH CHRONIC LIVER DISEASE**

Chief researcher : DR. SANKETH J

Under the guidance of: DR. VIDYA SAGAR C.R

Name of the subject:

Age :

Address :

a. I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible

risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature

Signature of the witness:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date: