Lipid profile V/s. Severity of Cirrhosis: A Child Pugh (CP) Score Based Study

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Original Research Article

ABSTRACT

As it is already known that assessment of prognosis in liver cirrhosis, is currently done by Child–Pugh and Model for End-Stage Liver Disease (MELD) scores. Liver plays a vital role in synthesis, storage and metabolism of lipids. Synthesis, storage and metabolism of lipids is affected with development of cirrhosis. The important lipids in human are cholesterol, high density lipoproteins, very low density lipoproteins, low density lipoproteins and triglycerides. It is reasonable to expect an abnormal lipid profile in those with severe liver dysfunction. Hence the aim of this study was to find out of lipid profile in patients with liver cirrhosis and its correlation with severity of cirrhosis.

A brief history was taken and per abdomen examination was done of all Suspected Patients.Ultrasonography (USG) abdomen was also done to look for cirrhotic changes in the liver. A Prospective cross sectional study was done on 50 patients with cirrhosis of liver. We also did Liver function test (LFT) and Serum Fasting Lipid Profile. Child pugh scoring was done in all cirrhotic patients. Severity of liver cirrhosis by child pugh score was correlated with serum lipid profile of cirrhotic patients. Mean serum total cholesterol (TC), Low density lipoprotein(LDL), Very low density lipoprotein(VLDL), High density lipoprotein (HDL) and Triglyceride (TGs) were lower in patients with cirrhosis of liver. Serum lipid progressively decreased with increasing severity of cirrhosis by child pugh score. Except Low density lipoprotein LDL, all the four parameters (High density lipoprotein HDL, Triglyceride, total cholesterol and Very low density lipoprotein VLDL) had statistically significant association with the severity of cirrhosis by chlid pugh class, while Low density lipoprotein (LDL) had not statistically significant association with severity of cirrhosis.

KEY WORDS: cirrhosis, lipid profile, lipoproteins, severity

INTRODUCTION:

Liver Cirrhosis is a major health problem worldwide. It is the 12th leading cause of death by disease[1]. The disease progresses gradually. In cirrhosis patients, healthy liver tissue is replaced by scar tissue, ultimately stopping liver from functioning correctly.

Cirrhosis is a common hepatological disorder ,seen in clinical practice .Cirrhosis is defined by the WHO- as a diffuse process, characterized by, fibrosis and the conversion of normal liver architecture, into structurally abnormal nodules[2].

According to the latest WHO data published in may 2014 Liver Disease Deaths in India reached 216,865 or 2.44% of total deaths. The age adjusted Death Rate is 21.96 per 100,000 of population. India ranks 61 in the world. (3)

Liver plays an essential role in lipid metabolism, several stages of lipid synthesis and transportation. Therefore, it is reasonable to expect, an abnormal lipid profile ,in those with severe liver dysfunction[3].

The aim was to study the Lipid profile (Total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, Triglycerides) in cirrhosis of liver patients and to determine the correlation between severity of cirrhosis (on the basis of child pugh

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Annex Table (A)

To evaluate the severity of cirrhosis, Child-Pugh (CP) criteria can be used. Severity of cirrhosis by Child-Pugh score: The score employs five clinical measures of liver disease. Each measure is scored 1-3 with 3 indicating most severe derangement.

Measure	1 Point	2 Point	3 Point
Total Bilirubin ? mol/L (Mg/Dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
S.Albumin Gm/Dl	>3.5	2.8-3.5	<2.8
Prothrombin Time Prolongation (Secs)	<4	4-6	>6
Ascites	None	Mild	Moderate To Severe
Hepatic Encephalopathy	None	Grade I-Ii (Or Suppressed With Medication)	Grade Iii-Iv (Or Refractory)

Annex Table (B): Child-Pugh (CP) scoring classification (class A to C), is useful to assess liver disease severity in patients with established cirrhosis.

Points	Class	One year survival	Two year survival
5-6	A	100%	85%
7-9	B	81%	57%
10-15	C	45%	35%

classification score (A,B,C) & serum lipid profile in patient with liver cirrhosis.

MATERIALS AND METHODS:

A prospective cross sectional study was done on 50 cirrhotic patients, both males and females, presented to the OPD or getting admitted in the people's hospital Bhopal, during the study period (from November 2015 to April 2017). Inclusion criteria were (a) age more than 18 years; and (b) known and established cases of Cirrhosis of liver by ultrasound abdomen. Exclusion criteria were (a) patients who had used cholesterol lowering drugs within previous 30 days; (b) patients with Diabetes Mellitus, Nephrotic syndrome, Hypertension, chronicsmokers, chronicalcoholic, malignancy, thyroid problem; and (c) patients who were not willing for study.

After obtaining the informed consent, patient details are obtained. By aseptic precautions , 7 ml venous blood is collected after 8-12 hours of fasting. Blood is collected in sodium EDTA citrate(3.2%) added vacutainer (2ml) and plain vacutainer (5ml).

Blood collected in plain vacutainer is processed immediately to obtain serum and following parameters are estimated:

Serum Total Cholesterol was estimated by enzymatic method (CHOD-PAP). Serum HDL Cholesterol was estimated by enzymatic method. Serum LDL Cholesterol was estimated by Friedewald formula.

[Friedewald formula: [LDL cholesterol]=
[Total cholesterol] – [HDL cholesterol] – [VLDL];
where VLDL = Triglyceride/5

Serum triglyceride was estimated by enzymatic method (GPO-ESPAS). Serum total bilirubin was estimated by Acid Diazo method. Albumin Quantative determination was done using Bromocresol green reagent (BCG). 2 ml of blood collected in Sodium EDTA citrate(3.2%) added vacutainer is used for estimation of Prothrombin time: By Electrome-chanical method. Statistical tests employed in our study were: Chi-Square Test, Analysis of Variance (ANOVA), Spearman's Correlation, p value.

RESULTS:

Total 50 liver cirrhosis cases were selected to find out the correlation between lipid profile and severity of liver cirrhosis by child pugh score.

Most of the cases i.e. 26(52.0%) were 41-60 year old and 13(26%) were less than 40 year of age. Severity of liver cirrhosis assessed by child pugh score and total 50 cases were divided in to three classes. Class A, B & C. Most of 25(50%) cases were of class

Table 1(A): Distribution of study subjects (Liver Cirrhosis cases) according to age.

		Number	Percentage
Age Groups	= 40 Year	13	26.0%
	41-60 Year	26	52.0%
	>60 Year	11	22.0%
Mean Age		50.92 Year	
Age Range		26-67 Year	

Table 1(B): Distribution of study subjects (Liver Cirrhosis cases) according to Child Pugh Class.

		Number	Percentage
Child Pugh Class	Class A	5	10.0%
	Class B	25	50.0%
	Class C	20	40.0%
	Total	50	100.0%

Table 2: Etiology of liver cirrhosis.

Etiology		Number	Percentage
Viral Cause			
HbsAg Status	Positive	23	46.0%
HCV Status	Positive	10	20.0%
Viral Cause (Total)		33	66.0%
Non Viral Cause		17	34.0%

Chi Square Value: 7.64; Significance 'p' value: 0.006(S)

B, 20(40%) cases were of class C severity and 5(10.0%) were of class A. All the cases were 26-67 year old with the mean age of 50.92 year. There was statistically no significant difference in distribution of study subjects (Liver Cirrhosis cases) according to gender, age & Child Pugh Class. (p>0.05) (Table 1).

Out of 50 cases of liver cirrhosis, 33(66.0%) were having viral cause for cirrhosis and 17(34.0%) had non viral etiology for cirrhosis of liver. HbsAg (Hepatitis B) was found positive among 23(46.0%) cases and HCV (Hepatitis C) was found positive among 10(20%) cases. There was statistically significant association of viral cause with liver cirrhosis. (p=0.006) (Table 2).

As severity of liver cirrhosis was increasing lipid profile concentration level was decreasing. Mean lipid profile level was highest among patients with child pugh class A and it was least among class C patients. Mean total cholesterol level was 157.60±47.5, 125.68±37.3 & 98.05±39.1 among class A, B & C respectively. Mean Triglyceride level was 124.40±53.3, 103.68±50.2 &76.55±35.1 among class A, B & C respectively. Mean VLDL level was 24.88±10.6, 20.77±10.1 &15.26±6.9 among class A, B & C respectively. Mean LDL was 83.32±41.8, 67.33±26.7 &59.84±31.1 among class A, B & C respectively. Mean HDL was 49.40±21.8, 36.72±12.2 & 22.85±14.9 among class A, B & C respectively. There was statistically significant association or difference in mean lipid profile level (Except LDL) and severity of cirrhosis by chlid pugh class ($p<0.05$) while LDL had not significant association with severity of cirrhosis. (p=0.290) (Table 3).

Child Pugh score (Severity of cirrhosis) had negative correlation with complete lipid profile. It means lipid profile is decreasing as severity of liver cirrhosis increases. T. Cholesterol & Triglyceride had Negative Moderate highly Significant correlation with severity while VLDL & HDL had Negative Strong highly Significant correlation with severity of liver cirrhosis. LDL had Negative Weak Not significant correlation with severity of liver cirrhosis (Table 4).

Mean bilirubin level was increasing as severity of cirrhosis was increases. It was highest among class C & lowest among class A grade of severity. It was 0.916±0.33 among class A patients, 1.937±1.77 among class B and 4.929±3.86 mg 5 among class C patients. There was statistically highly significant difference in mean Bilirubin level according to Child Pugh class among Liver cirrhosis patients (p=0.001) (Table 5). PT Prolongation was less than 4 second among 44(88.0%) cases and it was more than 6 second among 5(10.0%) cases. (Table 6). Mean serum albumin level was decreasing as severity of cirrhosis increases. It was highest among class A & lowest among class C. It was 3.85±0.32 gm % among class A,2.80±0.588 among class B & 2.48±0.54 gm % among class C patients. There was statistically highly significant difference in Mean Serum Albumin level according to Child Pugh class among Liver cirrhosis patients. (p=0.001) (Table 7). 25(50.0%) patients had moderate to severe Ascites, 18(36.0%) had mild Ascites and 7(14%) had no Ascites (Table 8). 31(62.0%) had no Hepatic Encephalopathy. 13(26%)

Table 3: Association of severity of liver cirrhosis by child Pugh score with lipid profile.

	Lipid Profile (mg%)				
	T. Cholesterol	Triglyceride	VLDL	LDL	HDL
Child Pugh Class	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD
Class A	157.60 ±47.5	124.40 ±53.3	24.88 ±10.6	83.32 ±41.8	49.40 ±21.8
Class B	125.68 ±37.3	103.68 ±50.2	20.77 ±10.1	67.33 ±26.7	36.72 ±12.2
Class C	98.05 ±39.1	76.55 ±35.1	15.26 ±6.9	59.84 ±31.1	22.85 ±14.9
Total	117.82 ±42.6	94.90 ±46.9	18.97 ±9.4	65.93 ±30.2	32.44 ±16.5
ANOVA'F'Vale	5.668	3.212	3.284	1.273	9.128
Sig. 'P' Value	0.006(S)	0.049(S)	0.046(S)	0.290(NS)	0.001(HS)

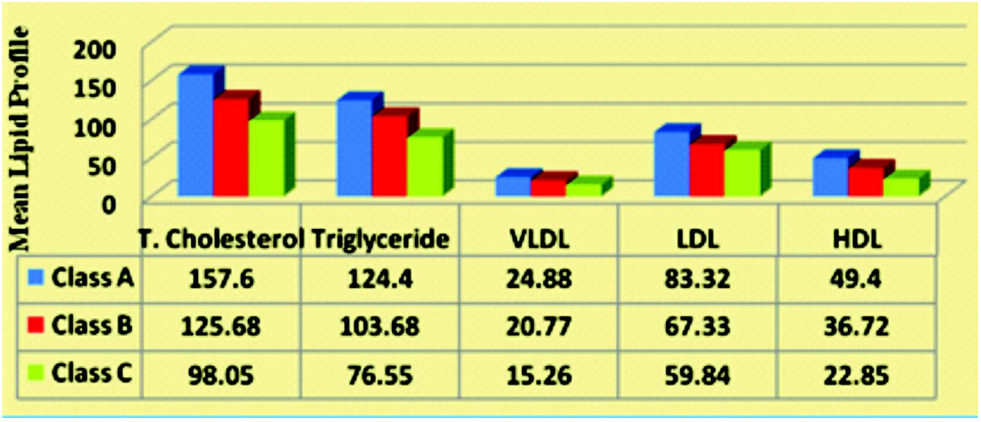

Figure 1: Association of severity of liver cirrhosis by child Pugh score with lipid profile.

Table 4: Spearman's Correlation of child Pugh score (severity of cirrhosis) with lipid profile.

Lipid Profile	Child Pugh score (Severity of cirrhosis)		
	Correlation Coefficient (r)	*p-value*	Inference
T. Cholesterol	-0.491**	0.001(HS)	Negative Moderate Significant
Triglyceride	-0.498**	0.001(HS)	Negative Moderate Significant
VLDL	-0.501**	0.001(HS)	Negative Strong Significant
LDL	-0.238	0.096(NS)	Negative Weak Not significant
HDL	-0.558**	0.001(HS)	Negative Strong Significant

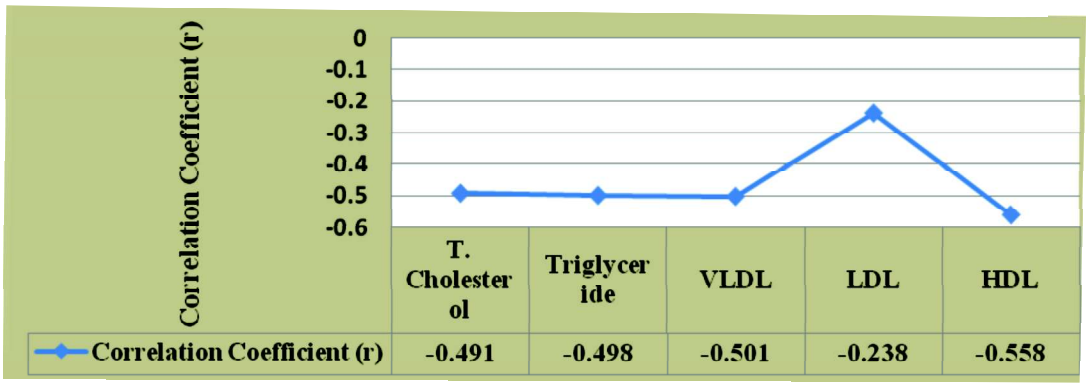

Figure 2: Spearman's Correlation of child Pugh score (severity of cirrhosis) with lipid profile.

Table 5: Mean Bilirubin level according to Child Pugh class among Liver cirrhosis patients.

	Bilirubin level (mg %)	
Child Pugh Class	Mean	SD
Class A	0.916	0.33
Class B	1.937	1.77
Class C	4.929	3.86
Total	3.032	3.14
ANOVA 'f' value	8.105	
p value	0.001(HS)	

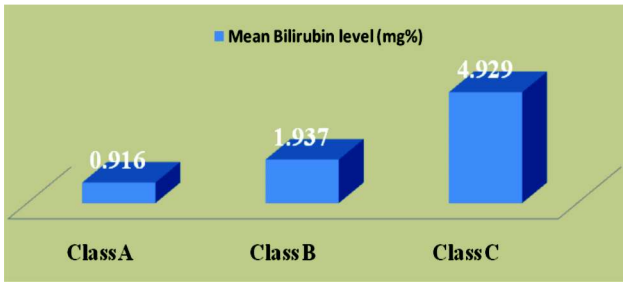

Figure 3: Mean bilirubin level according to Child Pugh class among liver cirrhosis patients.

had grade I-II hepatic encephalopathy and 6(12%) had grade III-IV hepatic encephalopathy.

In our study, males were 56% and females were 44%. 41 to 60 years was most common age group (52%). Thirty three cases (66.0%) were having viral cause for cirrhosis which was most common and 17(34.0%) had non viral etiology for cirrhosis of liver. HbsAg (Hepatitis B) was found positive among 23(46.0%) cases and HCV (Hepatitis C) was found positive among 10(20%) cases. Sequence of child's pugh class was B>C>A (50%, 40% and 10% respectively). Except LDL, All the four lipid parameters (HDL, Triglyceride, total cholesterol and VLDL) had statistically significant association with the severity of cirrhosis by chlid pugh class. while LDL had not significant association with severity of cirrhosis.

Table 6: PT Prolongation among Liver cirrhosis patients.

PT Prolongation level (Second)	Number	Percentage
<4	44	88.0 %
4-6	1	2.0%
>6	5	10.0%

Table 7: Mean Serum Albumin level according to Child Pugh class among Liver cirrhosis patients.

	Serum Albumin level (gm%)	
Child Pugh Class	Mean	SD
Class A	3.85	0.324
Class B	2.80	0.588
Class C	2.48	0.541
Total	2.77	0.667
ANOVA 'f' value	12.415	
p value	0.001(HS)	

DISCUSSION:

In our study 56% were males and 44% were female. That is ratio of male and female was 1.3:1. Most of 26(52.0%) were 41-60 year old and 13(26%) were less than 40 year of age and 11(22%) were above 60 year of age. Most of 25(50%) cases were of class B, 20(40%) cases were of class C severity and 5 (10.0%) were of class A. These results were similar to those of

Table 8: Severity of Ascites among Liver cirrhosis patients.

Severity of Ascites	Number	Percentage
None	7	14.0%
Mild	18	36.0%
Moderate to Severe	25	50.0%

Table 9: Hepatic Encephalopathy among Liver cirrhosis patients.

Hepatic Encephalopathy Grades	Number	Percentage
None	31	62.0%
Grade 1-II	13	26.0%
Grade III-IV	6	12.0%

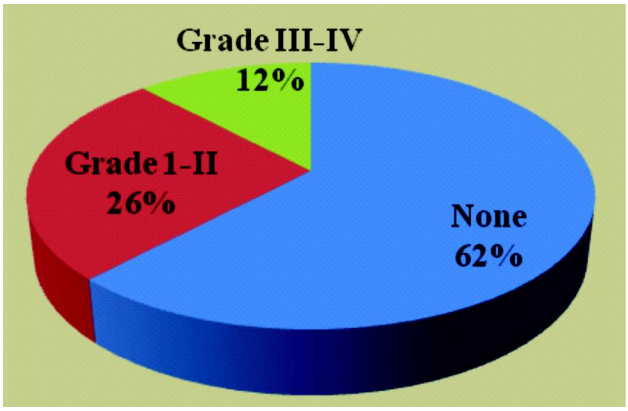

Figure 4: Hepatic Encephalopathy among liver cirrhosis patients.

study conducted by Mohammad Reza Ghadir[4] in which the most affected age group was 41 to 50 years so that 90% of cirrhotic patients were over 41 years of age as seen in our study. There was a significant (p=0.03) difference in the frequency of cirrhotic patients among different age groups but no statistical significance was found in our study (p >0.05).

Fifty-eight percent of patients were male and 42% were female, which was approximately similar to our study in which males were more in number. According to Child criteria, 11 (22%) patients had score "A," 14 (28%) score "B," and 25 (50%) had score "C" which was opposite to those found in our study.

In study conducted by Muhammad Israr Ul Haq[5] screening of 133 patients with cirrhosis was done. Male/female ratio was 66:34 which was similar to our study, in which males were more in number. The most affected age group was 39-45yrs which was some about similar because most of the cirrhotics in our study were of age group 41-60 years. Out of enrolled patients in study group, 17 (17%) patients were in CTP class A,35 (35%) were in CTP B , and 48% were in CTP C, contrary to our study in which maximum were of CTP class B i.e 50 %. The results of previous studies were similar to our study in relation to gender and age because most of the alcoholics were adult males. Exposure to various viruses can be seen more in males because most of the females were housewives and males were daily workers.

This may attribute to the delayed presentation of cirrhosis of liver of various etiologies due to their complications .The most affected age group was supported by the epidemiological studies. The three independent factors were associated with an increased rate of fibrosis: age at infection older than 40 years, daily alcohol consumption and male gender.

In our study most common etiological agent was virus i.e. 66% and non viral cause was less 34%, which was contrary to study conducted by C. Suman et al[2] in which the most common cause for cirrhosis in the study was alcohol (64 %). Other common causes were Hepatitis B and Hepatitis C.

In study conducted by Vijay Laxmi Nangliya[6] 42.6% percent of the patients had Cirrhosis of alcoholic etiology, 20% had NASH, 20.7% had HBV, 6.7% had HCV and 10 % with other etiologies (Autoimmune, PBC, PSC). These results were also opposite to those of our study. Similarly in study conducted by Hashik P Muhammed[9] the results were contrary to our study. Among the total patients, 63 % were using alcohol in study done by Hashik . But in our study viral causes were more. The reason for such contrasting result can be the composition of study population. Because most of the participants were younger and adult age group, they have more exposure to viral causes. So prevalence of viral causes was more than non viral causes.

The result of Hashik Muhhamed study revealed that more number of patient were in class C. All the parameters of lipid profile were lower in the severe form of liver disease irrespective of the etiologies. Furthermore, the amount of decrement in the serum HDL, LDL, TC and TG had a negative correlation with the severity of liver disease. This indicated an inverse correlation of lipid parameters with the severity of the disease. The result was consistent to the previous studies. As in study conducted by Hashik P Muhhamed[9] and Fazle Subhan[12] they found a reduction in all parameters of lipid profile with severity of chronic liver disease. Their study showed that patients with liver diseases had lower lipid levels and all four studied variables (HDL, LDL, total cholesterol and TG) were significantly lower in cirrhotic patients than in the

comparison group. Besides, the amount of decrement in the serum HDL and total cholesterol was significant with increasing severity of disease. This was similarly significant in our study. But in our study LDL was not significant, which was contrary to study conducted by Hashik Muhhamed.

However, there is conflicting of observations on this regard. Previous study by Warun Kumar et al[8] and PJ Meikle et al[16] found that reduction in serum VLDL level did not correlate with severity of liver cirrhosis, which was contrasting to those found in our study.

In this study, the final results showed that liver damage is correlated with total cholesterol, HDL and TG but not with LDL levels (p value 0.290). Sanjay kumar[13] found that HDL level is lower in Child-Pugh B than Child-Pugh A and apo-A level is the most affected factor in those with liver damage similar to our study in which HDL of class B is36.72 mg%. In this study, the change in HDL level was higher in Child A than B, and higher in Child B than C which shows that is the severity of liver function that causes HDL level to decline.

In study conducted by Mohhamed Raza, et al it was found that as the severity of liver damage proceeds, the more decline in lipid levels is detected, especially in LDL and total cholesterol levels. No association between TG and liver damage was there. Concluding that HDL, LDL, total cholesterol and TG were significantly lower in cirrhotic patients than in the comparison group[4] which was contradictory to that of our study because we got LDL levels not significant while triglycerides as significant with severity of disease.

In study conducted by Mohhammed Idrar Ul Haq et al[5] Significant negative correlation was seen between CTP class and serum cholesterol, HDL and LDL, but no such correlation was observed between CTP class and Serum triglycerides. Higher the CTP class, Lower the HDL, LDL and Serum Cholesterol level. However, the results obtained in our study showed that exept the reduction of LDL levels, the other 4 variable (HDL, Serum total cholesterol, Triglycerides and VLDL)which was significantally correlated with the severity of cirrhosis (by CTP class).

In the study conducted by Vijay Laxmi Naghliya et al[6]there was a significant decrease in total cholesterol, LDL and HDL cholesterol levels compared to the control, but not triglycerides level. Serum total, LDL and HDL cholesterol level were significantly decreased with advancement of liver disease (Child A to C). Serum triglyceride level decrease with advancement of liver disease but it was not statistically significant. In contrast to that, in our study in which triglyceride level was significantally correlated with CTP class severity of cirrhosis while LDL levels had not significant association with severity of cirrhosis.

We excluded smokers & alcoholics in our study, which was not done in the previous studies. As smoking and alcoholism increases S.TGs. This may also have contributed to the difference in the results.

In our study there was PT Prolongation observed among Liver cirrhosis patients. PT Prolongation was less than 4 second among 44(88.0%) cases and it was more than 6 second among 5(10.0%) cases. Similar results were seen in study conducted by Yousfi MM et al[19]. This prolonged prothrombin time can be a consequence of an intravascular activation of coagulation during sepsis. Overall, the individual components of the Child-Pugh score encompass a broader spectrum of conditions than the single impairment of "liver function." Child-Pugh score as a whole is also a marker of the multiorgan changes resulting from cirrhosis.

Several studies have shown that Child-Pugh score is an independent prognostic marker in the settings of ascites as in study conducted by Fernández-Esparrach G et al[17] which was contrary to our study in which Severity of) Ascites among Liver cirrhosis patients was deciding factor as 25(50.0%) patients had moderate to severe Ascites, 18 (36.0%) had mild Ascites and 7(14%) had no Ascites.

In our study mean bilirubin level was increasing as severity of cirrhosis was increases. It was highest among class C & lowest among class A grade of severity. The results were similar to the study conducted by E Christensen et al[14]. Hepatic encephalopathy had no association with liver cirrhosis in our study.62.0% had no Hepatic Encephalopathy. Because, the limits for qualitative variables (ascites and encephalopathy) are vague. They may be influenced by subjective interpretation.

Prognostic evaluation of patients with liver cirrhosis is an important topic often challenging clinicians. Correct timing of liver transplantation can reduce the mortality of patients on waiting lists and improve post-transplant survival[18]. Predicting prognosis is important for further plan of treatment, especially in patients with esophageal variceal bleeding.

The Child-Pugh score is an important component of the prognostic evaluation of cirrhotic

patients, although this traditional score has several shortcomings such as subjectivity of some parameters and a limited discriminatory ability. In order to overcome the limits of the Child- Pugh score, previous studies have evaluated a 'combined score' with quantitative liver function tests, or have applied the scores that were originally formulated to evaluate multiorgan insufficiency in critically ill patients to cirrhotic patients[20].

CONCLUSIONS:

As the severity of cirrhosis increases from Child class A to child class C, mean lipid levels had decreased i.e inverse correlation is found between the severity of cirrhosis by Child pugh and mean lipid profile level.

Hypolipidemia is a common finding in cirrhosis of liver and has got significant association with Child-Pugh class. It may increase the reliability of Child-Pugh classification in assessment of severity and prognosis in the cirrhotic patients.

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Cite this article as: Jaiswal P, Choubay PP: Lipid profile V/s. Severity of Cirrhosis: A Child Pugh (CP) Score Based Study. PJSR ;2018:11(1):28-35.
Source of Support : Nil, Conflict of Interest: None declared.