Serum Lipid Profile as an Indicator of Severity of Liver Cirrhosis

Muhammad Mamoon Mujahid, Imran Fazal, Umair Ahmad Siddiqi, Fraz Tahir, Ehtisham Haider, Asma Asghar

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To look for the relationship of deranged lipid profile with severity of liver cirrhosis along with other socio-demographic factors at Pak Emirates Military Hospital Rawalpindi.

Study Design: Cross sectional study.

Setting and Duration of Study: Gastroenterology department, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Sep 2018 to Feb 2019.

Methodology: Eighty patients suffering from cirrhosis admitted in the medical ward or reporting in outpatient department of Pak Emirates Military Hospital were included in this study. Diagnosis of cirrhotic liver was made based on clinical findings and relevant investigations and severity of cirrhosis was established by using the Model for end stage liver disease (MELD) score. Total cholesterol, LDL cholesterol and HDL cholesterol and triglyceride levels were correlated with the severity of cirrhosis in the target population along with other factors.

Results: Out of 82 patients included in the final analysis 49 (59.7%) were male and 33 (40.3%) were female. Most of the patients presented with the chronic liver disease secondary to the hepatitis C virus (HCV). 45 (54.8%) had MELD score >10 while 37 (45.2%) had MELD score <10. Analysis showed total hypo2holesterolemia and hypotrigly ceridemia emerged as strong predictors of severe cirrhotic illness (p-value <0.05).

Conclusion: Low values of lipid parameters were strongly related to the presence of severe cirrhotic illness among the patients suffering from liver cirrhosis. Lipid profile can be used as an indicator to predict the severity of illness among cirrhotic based on our results.

Keywords*:* Cirrhosis, Lipid profile, Model for end stage liver disease.

How to Cite This Article*: Mujahid MM, Fazal I, Saddiqi UA, Tahir F, Haider E, Asghar A. Serum lipid profile as an indicator of severity of liver cirrhosis. Pak Armed Forces Med J 2022; 72(Suppl-2): S110-113. DOI: https://10.51253/pafmj.v72iSUPPL-2.2915*

INTRODUCTION

Burden of hepato-biliary diseases has been on a rise globally.[1] Diseases involving the vital organ of liver rank among the top in affecting the quality of life of patients all over the world.[2] These diseases can be benign or malignant and may lead to temporary or permanent damage to the parenchyma of this vital organ of human body. Chronic or end stage liver disease has been commonly associated with the phenomenon of liver failure. There can be multiple causes for this, which may be primary or secondary. Once cirrhosis of liver has occurred then no medical therapy can reverse this condition and liver transplant remains the only option.[3]

Liver has been regarded as a factory of human body where many products are synthesized or broken down. Various forms of lipids have been processed in liver and their metabolism is dependent upon the proper functioning of this vital organ. It has been an established fact that when liver has structural or functional problems, metabolic capacity becomes altered and many chemicals either get increased or decreased in concentration inside the body.[4,5] This phenomenon has been used to assess the nature and severity of liver disease. Alteration in levels of total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride has been associated with liver damage among the patients suffering from cirrhosis.[6]

Metabolic property of liver has been severely compromised in the patients of cirrhosis. Various studies have been done in past highlighting this fact.[7,8] Therefore it can be concluded that though cirrhosis affects the architecture of liver and seems like a structural deficit, has clear effect on the functioning of this vital organ of the human body.

Relationship of altered lipid profile indices and presence and severity of liver cirrhosis has been discussed by clinicians and researchers at various levels. Ghadir *et al*. concluded that serum triglyceride level, serum lipid levels diminish linearly with progression of liver damage and these indices inversely correlate with severity of cirrhosis.[9] Another similar study done in Brazil revealed that hypocholesterolemia can be

Correspondence: Dr Muhammad Mamoon Mujahid, Appart 3-D, SPD Officer Colony-6 Rafiqui Road, Chaklala Cantt, Rawalpindi-Pakistan

Received: 19 May 2019; revision received: 09 May 2020; accepted: 19 May 2020

used to assess the progression of liver disease, because of the association between lowered cholesterol levels and outcome of the patients suffering from cirrhotic liver.[10] A recent study came up with interesting findings that the serum HDL-Cholesterol and LDL-Cholesterol may be considered as markers of severity of liver damage in non-alcoholic cirrhosis, but the triglycerides only in disease of alcoholic origin. A similar study in our part of the world concluded that hypolipidemia was a consistent finding in patients with cirrhosis secondary to Hepatitis B virus infection. Liver cirrhosis may lead alteration in enzyme function causing derangement in lipid metabolism.

In Pakistan liver cirrhosis has been a common medical diagnosis affecting millions of people of all the age groups. Various researchhas been conducted locally to assess the etiology and severity of cirrhosis among the patients suffering from end stage liver disease.[13,14] As ours is a developing country with limited resources which need to be managed effectively, so this becomes very important to look for the methods which are less expensive and can predict the severity and outcome of the illness. We therefore designed this study with the rationale to look for the relationship of deranged lipid profile with severity of liver cirrhosis along with other socio-demographic factors at Pak Emirates Military Hospital Rwp.

METHODOLOGY

This cross-sectional study was conducted at the Gastroenterology unit of Pak Emirates Military Hospital Rawalpindi Pakistan, from September 2018 to February 2019. Sample was gathered by using the non-probability consecutive sampling technique. Sample size was calculated by using the World Health Organization (WHO) sample size calculator by using population prevalence proportion of 90%.[11]

Inclusion Criteria: All patients between the age of 12 and 60years reported in the gastroenterology department with liver cirrhosis due to any cause and were considered as potential candidates for liver transplant were included in the study.

Exclusion Criteria: Patients with unclear diagnosis regarding the cause of liver failure. Patients who were pregnant or had a diagnosis of hepatocellular carcinoma were also not included from the start. Patients with active psychiatric illness or delirium or dementia were also excluded in the beginning. Patients suffering from uncontrolled diabetes or any other metabolic disorder interfering with lipid metabolism were also excluded. Patients on any type of lipid lowering drugs were not included in the analysis as well.

Diagnosis of chronic liver disease or liver cirrhosis was made on the clinical, laboratory and radiological findings by the consultant gastroenterologist.[12-14] Model for end stage liver disease criteria was used to assess the severity of illness among these patients. MELD For-mula used was: 0.957 x Loge (Creatin -ine [mg/dL]) + 0.378 X Loge (Total Bilirubin [mg/mL] 1.120 x Loge (INR)+ 0.643. Patients with initial MELD score greater than 10 were considered as having more severe illness as compared to those having MELD score less than 10.[15,16]

Pak-Emirates Military Hospital has an ethical review board committee which was approached to get the approval for study. Lipid profile was done from the laboratory of own hospital. Other investigations included all base line investigations (Blood Complete picture, liver function test, renal function test, C-reactive protein, tumor markers etc.) ultrasound abdomen. Mini mental state examination was also done to look for the signs of hepatic encephalopathy or other causes of delirium in these patients.

Intravenous blood samples were collected from the cirrhosis patients with the help of 5ml syringe. Serum was separated and stored at−40°C until analyzed for lipid profile and fatty acids by micro-lab 300 and gas chromatography (GC 8700, Perkin–Elmer Ltd). Lipid profile performed by kit method (Merck, Germany) included total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein–cholesterol (HDL-C), low density lipoprotein–cholesterol (LDL-C), very low-density lipoprotein–cholesterol (VLDL-C) and total lipids. All these investigations were carried out in the laboratory of own hospital under the supervision of consultant chemical pathologist. Hypocholesterolemia in our analysis was defined as: TC <100 mg/dl and/or HDL-cholesterol <40 mg/dl and/or LDL-cholesterol <70 mg/dl and for hypotrigly-ceridemia value of TG <70 mg/dl.[17] All statistical analysis was performed by using the Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Mean and standard deviation for the age of study participants was calculated. Frequency and percentages for gender, causes of liver failure, severity of cirrhosand patients with abnormal lipid profile were calculated.

RESULTS

A total of 90 patients of liver cirrhosis reported in the department in the given period. Three of them were not fulfilling the age criteria of study, three

wereon lipid lowering drugs and diagnosis of two remained unclear. Out of 82 patients included in the final analysis 49 (59.7%) were male and 33 (40.3%) were female. Male to female ratio was 1.5:1. Mean age of patients diagnosed with liver failure in our study was 47.14 ± 2.342 years. Other characteristics of study population have been summarized in Table.

Table: Characteristics of study participants (n=82).

Age (Years)	
Mean ± SD	47.14 ± 2.342 years
Range (min-max)	12-59 years
Mean MELD Score	16.13 (1.231)
Gender	
Male	49 (59.7%)
Female	33 (40.3%)
Severity of cirrhosis	
MELD Score <10	37 (45.2%)
MELD Score > 10	45 (54.8%)
Causes of Cirrhosis	
HCV Infection	55 (67.1%)
HBV Infection	10 (12.2%)
Alcoholic Liver Disease	08 (8.7%)
Autoimmune Hepatitis	03 (3.65%)
Wilsons Disease	03 (3.65%)
Cryptogenic Cirrhosis	02 (2.4%)
Others	01 (1.2%)

Forty five (54.8%) had severe illness (MELD score >10) while 37 (45.2%) had less severe illness (MELD score <10). HCV was the commonest cause of liver failure in our setup followed by HBV.

DISCUSSION

Liver cirrhosis has been a prevalent condition in all parts of the world.[2] Etiology may vary according to the demography of patient. Developing countries like Pakistan has more cases of viral infections which present as cirrhosis or end stage liver disease.[1] Some-times even with the development of hepatocellular carcinoma.[18] Western and developed countries have controlled the spread of these infections but alcoholism become the culprit for cirrhosis in these parts of the world and adds to the burden of hepatobiliary diseases.[19] Cirrhosis can be classified on structural as well as functional basis.[3]Classifying cirrhosis based on severity becomes important due to advent of newer treatments like liver transplant. There are many direct and in direct ways and scoring systems to assess the severity of cirrhosis and predict the prognosis of patient and prioritize them for the liver transplant.[14]

Most of the patients included in our analysis were male with a male to female ratio of 1.5:1. Gender has no role in predicting the severity of illness in our target population. Similar results have been produced in the studies done in the past as well by Bombeck *et al,* where *p*-value was not significant for the gender.[10] Hepatitis C virus (HCV)was the commonest cause of cirrhosis followed by Hepatitis B virus (HBV) in our target population. This is also not a new finding and consistent with the results of other studies done on our population by Salamat *et al,* in which around 80% of the patients suffered from HCV.[13] Type of etiology of cirrhotic liver disease has also been an influencing factors on the metabolic derangement in various studies done in the past but it was not the scope of our study so we did not establish or studied this association.

Reduction in the levels of total cholesterol emerged as strong predictor of severe cirrhotic illness in our target population. Similar studies done on this subject in the past have also shown similar results. Especially studies done by Ghadir *et al,* and Bomeke *et al,* which showed *p*-value less than 0.05 for these parameters.[9,10] Altered metabolic capacity of liver in presence of cirrhosis secondary to alcoholism or viral infections can be an explanation to this finding as this has been replicated in number of studies among all type of populations.

Triglyceride levels were the second component of lipid profile which had a strong link with presence of severe illness in our analysis. Past literature also through light on this association and establishes a link between the two variables.[10,11] Study of Chrostek *et al*. is especially important in this regard. One theory which explains this phenomenon postulates that reduction in the activity of microsomal triglycerides transfer protein (MTTP)may be responsible for decrease in the levels of triglycerides among the patients suffering from liver cirrhosis, especially secondary to viral infections.[6]

LDL cholesterol and VLDL were not significantly liked with the presence of more severe illness in the patients we targeted for our study. Studies published in 2013 and 2017 done in other parts of the world have shown different results and *p*-value <0.05 showing significant association of these variables.[11,12] Possible reasons may be ethnic difference in the study population or difference in etiology of cirrhosis. More studies with a large sample size may show accurate results in this regard.

This study was conducted in the gastroenterology unit of a Military hospital which has limited budget. Free of cost treatment is provided to the entitled patients only. This was the biggest limitation of this

analysis as it cannot be generalized because lipid profile could be done only of entitled patients or those who could afford. Non affording patients who were not entitled as well were unable to afford the cost of this investigation. Another limitation is not following up the patients for a long time as MELD score may vary with the time and condition of the individual. Long term follow up may have generated different results. Further studies addressing these limitations and involving multiple centers may generate generalizable results in this regard.

CONCLUSION

Low values of lipid parameters were strongly related to the presence of severe cirrhotic illness among the patients suffering from liver cirrhosis. Lipid profile can be used as an indicator to predict the severity of illness among cirrhotic-based on our results.

Conflict of Interest: None.

Authors' Contribution

MMM: Study design and statistical analysis, IF: Study design and discussion, UAS: Discussion, FT: Data collection and introduction, EH: Statistical analysis, AA: Abstract.

REFERENCES

1. Butt AS. Epidemiology of viral hepatitis and liver diseases in Pakistan.Euroasian J Hepatogastroenterol 2015; 5(1): 43-48.
2. Wang FS, Fan JG, Zhang Z. The global burden of liver disease: The major impact of China. Hepatol 2014; 60(6): 2099-2108.
3. Perri GA, Khosravani H. Complications of end-stage liver disease. Can Fam Physician 2016; 62(1): 44-50.
4. Albhaisi S, Sanyal A. Recent advances in understanding and managing non-alcoholic fatty liver dis. F1000 Res 2018; 7(1): 1.5.
5. Khan V, Putluri N, Sreekumar A, Mindikoglu AL. Current applications of metabolomics in cirrhosis. Metabolites 2018; 8(4): 67. Published 2018 Oct 22. doi:10.3390/metabo8040067
6. Ipsen DH, Lykkesfeldt J, Tveden-Nyborg P. Molecular mechanisms of hepatic lipid accumulation in non-alcoholic fatty liver disease.Cell Mol Life Sci 2018; 75(18): 3313-3327.
7. Masarone M, Rosato V, Dallio M, et al. Role of oxidative stress in pathophysiology of nonalcoholic fatty liver disease. Oxid Med Cell Longev 2018; 2018(1): 9547613. Published 2018:10.1155/2018/9547613
8. Kumar R. Hepatogenous diabetes: An underestimated problem of liver cirrhosis.Indian J Endocrinol Metab 2018; 22(4): 552-559.
9. Ghadir MR, Riahin AA. Nooranipour M, Habibi-nejad AA. The relationship between lipid profile and severity of liver damage in cirrhotic patients. Hepat Mon 2010; 10(4): 285-288.
10. Boemeke L, Bassani L, Marroni CA, Gottschall CB. Lipid profile in cirrhotic patients and its relation to clinical outcome. Arq Bras Cir Dig 2015; 28(2): 132-135.
11. Chrostek L, Supronowicz L, Panasiuk A, Cylwik B, Gruszewska E, Flisiak R. The effect of the severity of liver cirrhosis on the level of lipids and lipoproteins. Clin Exp Med 2013; 14(4): 417-421.
12. Arain SQ, Talpur FN, Channa NA, Ali MS, Afridi HI. Serum lipid profile as a marker of liver impairment in hepatitis B Cirrhosis patients. Lipids Health Dis 2017; 16(1): 51. Published 2017 Mar 1. doi:10.1186/s12944-017-0437-2
13. Salamat A, Zubair UB, Shafqat H, Saeed F. Assessment of patients with chronic liver disease qualifying for liver transplant. Pak Armed Forces Med J 2012; 62(1), Available at: https://-pafmj.org/index.php/PAFMJ/article/view/3487
14. Zubair UB, Salamat A, Alam MM, Shafqat H, Saeed F. Predictive accuracy of model for end stage liver disease (meld) as a prognostic marker for cirrhosis in comparison with child – pugh score. Pak Armed Forces Med J 2015; 65(1): 22-25.
15. Dumitrascu DL, Neuman MG. Non-alcoholic fatty liver disease: an update on diagnosis. Clujul Med 2018; 91(2): 147-150.
16. Li B, Zhang C, Zhan YT. Nonalcoholic fatty liver disease cirrhosis: A review of its epidemiology, risk factors, clinical presentation, diagnosis, management, and prognosis.Can J Gastroenterol Hepatol 2018; 2018(1): 2784537.
17. Moraes ACO, Fonseca-Neto OCLD. The use of meld score (model for end-stage liver disease) and derivatives in cardiac transplantation. Arq Bras Cir Dig 2018; 31(2): e1370.
18. Pradat P, Virlogeux V, Trépo E. Epidemiology and elimination of HCV-related liver disease. Viruses 2018; 10(10): 545. Published 2018 Oct 6. doi:10.3390/v10100545
19. Liangpunsakul S, Haber P, McCaughan GW. Alcoholic liver disease in Asia, Europe, and North America. Gastroenterol 2016; 150(8): 1786-1797.