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FREQUENCY OF LOW SERUM FERRITIN LEVEL IN PATIENTS OF DECOMPENSATED CHRONIC LIVER DISEASE SECONDARY TO HEPATITIS C VIRUS INFECTION

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Abstract:

Objectives*: To determine the frequency of low serum ferritin level in patients of decompensated chronic liver disease secondary to hepatitis C virus infection.*

Place of study: *This descriptive cross-sectional study was conducted in Department of General medicine, Fauji Foundation Hospital Rawalpindi during 1st Jan,2017 to 1st Jun 2017.*

Study design: *The sampling technique we used for this purpose was non-probability consecutive sampling. After taking all aseptic measures blood was taken and stored in a serum bottle. The bottle was clearly marked with the name and hospital number of the patients. The serum bottle was sent to the hospital laboratory in order to check serum iron, ferritin, TIBC, and LFT, s. The sample was sent to the hematology department in order to check for the serum iron and ferritin reports were verified by consultant. The results were recorded on proforma accordingly.*

Results: *Data was entered and analyzed in SPSS version 16.0. Total 165 patients were included according to the inclusion criteria of the study. Descriptive statistics of age (years) of patient was also calculated in terms of mean and standard deviation. Mean age (years) in the study was 53.74+8.66 with ranges from 20 to 60 years. Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. There were 03 (1.8) male and 162 (98.2) female patients who were included in the study according to the inclusion criteria.* ***Conclusion:*** *The study concludes that elevated serum ferritin worsened liver injury. Hence it represents early marker for the severity of chronic liver disease, related both to the degree of liver fibrosis and to the necroinflammatory activity.*

Key Words: *Chronic, Liver, Patients, Fibrosis.*

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INTRODUCTION:

Liver fibrosis and its end-stage cirrhosis resulting from chronic liver injury are major causes of morbidity and mortality worldwide. Among the etiologies of hepatic cirrhosis, viral infection is most common (e.g. hepatitis B and C), and currently affects 1–2% of the US population, with cirrhosis projected to reach 45% of those infected with hepatitis C virus (HCV) in 2030. In Pakistan more, people die of liver disease due to chronic hepatitis every day than terrorism in a year [1].

Hepatic fibrosis was historically thought to be a passive and irreversible process due to the collapse of the hepatic parenchyma and its substitution with a collagen-rich tissue. Currently, it is considered a model of the wound-healing response to chronic liver injury. Early clinical reports in the 1970s suggested that advanced liver fibrosis is potentially reversible [2]. However, liver fibrosis received little attention until the 1980s, when hepatic stellate cells (HSCs), formerly known as lipocytes, Ito cells, or perisinusoidal cells, were identified as the main collagen-producing cells in the liver [3]. This cell type, first described by von Kupffer in 1876, undergoes a dramatic phenotypic activation in chronic liver diseases with the acquisition of fibrogenic properties [4]. Methods to obtain HSCs from both rodent and human livers were rapidly standardized in the 1980s, and prolonged culture of HSCs on plastic was widely accepted as a model for the study of activated HSCs. Key signals that modulate HSCs' fibrogenic actions were delineated. Experimental models for studying liver fibrogenesis in rats and in transgenic mice were developed, which corroborated the cell culture studies and led to the identification of key fibrogenic mediators [5]. Besides HSCs, portal myofibroblasts and cells of bone marrow origin have been recently shown to exhibit fibrogenic potential. At the clinical level, the natural history of liver fibrosis, from early changes to liver cirrhosis, was delineated in patients with chronic HCV infection. Rapid and slower fibrosers were identified, and genetic and environmental factors influencing fibrosis progression were partially uncovered. Since the demonstration, in the 1990s, that even advanced liver fibrosis is reversible, researchers have been stimulated to identify antifibrotic therapies. Biotechnology and pharmaceutical companies are increasingly interested in developing antifibrotic programs, and clinical trials are currently underway [6]. However, the most effective therapy for treating hepatic fibrosis to date is still to remove the causative agent. A number of drugs are able to reduce the accumulation of scar tissue in experimental models of chronic liver injury [7].
To determine the frequency of low serum ferritin level in patients of decompensated chronic liver disease secondary to hepatitis C virus infection.

PATIENTS AND METHODS:

This descriptive cross-sectional study was conducted in Department of General medicine, Fauji Foundation Hospital Rawalpindi during 1st Jan,2017 to 1st Jun, 2017. The sampling technique we used for this purpose was non-probability consecutive sampling.
Inclusion criteria: All adult and middle age 20-60 years patients of both genders, diagnosed case of chronic liver disease (previously or recently diagnosed having features of decompensated disease) were included in the study.
Exclusion criteria: First exclude other causes of anemia like;

- Aplastic Anemia was diagnosed by doing CBC.
- Megaloblastic Anemia diagnosed by peripheral film, Folic Acid and Vitamin B_{12} levels.
- Hemolytic Anemia's; that was excluded by doing serum indirect bilirubin, LDH, uric acid, Coombs test and retics count.
- Upper gastrointestinal malignancy, that was excluded clinically
- Acute liver failure, that was excluded clinically and by doing LFT,s
- Chronic liver disease secondary to Wilson disease that was excluded by serum ceruloplasmin.

Data Collection Procedure: Before initiating study enrolment, an ethical approval for the study was gained from the hospital ethics committee. All patients fulfilling the inclusion criteria were enrolled for study. After taken an informed consent from the patients, the patients were enrolled in study. History was taken in detail and thorough examination was performed. After receiving patient in Gastroenterology department, all patients were assessed clinically. After clinical examination, the diagnosis of chronic liver disease was made. After taking all aseptic measures blood was taken and stored in a serum bottle. The bottle was clearly marked with the name and hospital number of the patients. The serum bottle was sent to the hospital laboratory in order to check serum iron, ferritin, TIBC, and LFT, s. The sample was sent to the haematology department in order to check for the serum iron and ferritin reports were verified by consultant. The results were recorded on proforma accordingly.

Data Analysis Procedure: The data was analysed by SPSS software version 16. Descriptive statistics was calculated for all variables like age, gender, low serum ferritin. Descriptive analysis was used for measuring mean, standard deviation for numerical variables like age, haemoglobin, MCV, serum ferritin. Frequency and percentages were measured for categorical variables like sex, education, duration, socio economic status and low ferritin. Effects modifiers like age, gender was controlled by stratification. Post stratification chi-square test was applied, and p value was less than 0.05 and was significant.

RESULTS:

Data was entered and analysed in SPSS version 16.0. Total 165 patients were included according to the inclusion criteria of the study. Descriptive statistics of age (years) of patient was also calculated in terms of mean and standard deviation. Mean age (years) in the study was 53.74+8.66 with ranges from 20 to 60 years, as shown in Table. No. 01

Table. No. 01: Descriptive statistics of Age (years) of patients

	n	Minimum	Maximum	Mean	Std. Deviation
Age (years)	165	20	60	53.74	8.66

Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. There were 03 (1.8) male and 162 (98.2) female patients who were included in the study according to the inclusion criteria. There were 03 (1.8) patients have low serum ferritin level (< 20 ng/ml) and decompensated chronic live disease secondary to hepatitis C virus infection, as shown in Table. No. 02.

Table. No. 02: Frequency and percentage of Low Serum Ferritin (< 20 ng/ml)

		Frequency	Percentage
Low Serum Ferritin level (< 20 ng/ml)	yes	3	1.8
	no	162	98.2
	Total	165	100.0

Effect modifier like age was stratified and compared with frequency low serum ferritin level in patients of decompensated chronic live disease secondary to hepatitis C virus infection. There were 03 (100.0) patients who age 50 – 60 years with low serum ferritin level in patients of decompensated chronic live disease secondary to hepatitis C virus infection which was statistically not significant (p-value 0.242), as shown in Table. No. 03.

Table. No. 03: Effect modifier like Age stratification with low Serum Ferritin (< 20 ng/ml)

		Low Serum Ferritin level (< 20 ng/ml)		P-value
		Yes	**No**	
Age group	**20 - 50 years**	0	51	
		0.00%	31.50%	
	50 - 60 years	3	111	0.242
		100.00%	68.50%	
Total		**3**	**162**	
		100.00%	**100.00%**	

Table. No. 04: Effect modifier like Gender stratification with Low Serum Ferritin Level (< 20 ng/ml)				
		Low Serum Ferritin Level (< 20 ng/ml)		P-Value
		Yes	No	
Gender	male	0	3	0.812
		0.00%	1.90%	
	female	3	159	
		100.00%	98.10%	
Total		**3**	**162**	
		100.00%	**100.00%**	

DISCUSSION:

Chronic hepatitis C (CHepC) is frequently associated with hepatic iron overload. Elevation of serum iron indices or stainable hepatic iron has been shown in 40 to 70% of patients with CHepC. From these observations, iron-induced oxidative stress has been considered to be an underlying mechanism of liver injury and of development of hepatocellular carcinoma [8].

The mechanisms of hepatic iron overload in CHepC have not yet been elucidated. However, hepcidin has attracted much attention as an important factor in the disease process. Hepcidin is exclusively produced in the liver and regulates body iron stores [9]. Hepcidin causes internalization and degradation of iron-transporter ferroportin on duodenal enterocytes and macrophages, thereby blocking iron absorption and iron recycling, respectively [10]. In hereditary hemochromatosis (HH), defective hepcidin synthesis results in a subsequent increase in body iron stores. In CHepC, hepatic iron overload has been attributed to the mutation of the hemochromatosis protein (HFE) gene, since several reports have found an association between HFE genotypes and iron overload in patients with CHepC [11]. Another possible mechanism is the direct effect of the hepatitis C virus (HCV) on hepcidin synthesis. Transgenic mice expressing HCV polyprotein have been shown to have decreased hepatic expression of hepcidin due to HCV-induced oxidative stress [12].

When hepatic iron overload develops, stainable iron can be seen either in hepatocytes (HC), reticuloendothelial cells (REC), or both cell types. Recently, patterns of hepatic iron distribution have attracted a considerable attention in chronic liver diseases, since the patterns would predict the histological progressions [13]. In particular, nonparenchymal iron deposition has been associated with advanced stages of alcoholic liver disease (ALD) and nonalcoholic steatohepatitis (NASH). The positive relationship was reported between histological activity and iron deposition either in REC or mixed HC/REC in patients with CHepC [14].

CONCLUSION:

The study concludes that elevated serum ferritin worsened liver injury. Hence it represents early marker for the severity of chronic liver disease, related both to the degree of liver fibrosis and to the necroinflammatory activity. Massive iron supplements therapy in patients already having high ferritin level may further induce liver injury. It is mandatory to check serum ferritin level in order to diagnose iron deficiency anemia in patients with chronic liver disease due to hepatitis C in order to prevent judicious use of iron supplements. Iron supplements can only be given if serum ferritin is low.

CONFLICT OF INTEREST:

There is no conflict of interest.

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PROFORMA

FREQUENCY OF LOW SERUM FERRITIN LEVEL IN IRON DEFICIENCY ANEMIA OF DECOMPENSATED CHRONIC LIVER DISEASE SECONDARY TO HEPATITIS C INFECTION

Serial No. _____
Hosp No. _____
Date: _____
Name: _____
Age: _____ (yrs)
Sex: □ Male □ Female
Address:_____
Phone: _____
Duration: _____
Education: no / yes
If yes: primary/ middle / matric / inter / graduation
Socio Economic Status: Monthly Income
< 20,000 / 20-50,000 / > 50,000

Iron Studies

Hb<14g/dl in males and< 12g/dl in females. Yes/No _____

Serum ferritin <20ng/ml Yes/No _____

MCV<78fl Yes/No _____