SERUM IRON LEVEL IN PATIENTS WITH CHRONIC VIRAL HEPATITIS: *SIX MONTHS HOSPITAL BASED CROSS SECTIONAL DESCRIPTIVE STUDY*

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ABSTRACT: This descriptive type cross sectional study was conducted at Liaquat University Hospital Hyderabad Sindh, Pakistan. All patients above 12 years of age, of either gender and were known (diagnosed) cases of chronic viral hepatitis (B and C) were further evaluated for their serum iron level. One hundred and fourteen (114) patients with chronic viral hepatitis B (37%) and C (63%) with means age 34.523 ± 5.185 and 39.041 ± 7.155 years were enrolled and evaluated. Regarding Hepatitis B, the serum iron was raised in 26/42 (62%) patients while regarding hepatitis C, the serum iron was raised in 53/72 (74%) patients. In both categories (hepatitis B and C) the male population was predominant and majority of patients (77%) belonged to rural areas. The rise in serum iron was observed in patients with chronic viral hepatitis (B and C)

Key words: chronic viral hepatitis, hepatitis B, hepatitis C, serum iron.

INTRODUCTION

The term chronic hepatitis means active, ongoing inflammation of the liver persisting for more than six months that is detectable by biochemical and histological means. It does not imply an etiology. The biochemical hallmark of chronic hepatitis is an increased serum aminotransferase (AST and ALT) with minimal elevation of alkaline phosphatase. When the inflammation is severe and/or prolonged, hepatic dysfunction may become apparent with an increase in serum bilirubin and INR/ prothrombin time, and a decrease in serum albumin. Typically, biochemical tests are used to identify and follow patients with chronic hepatitis, while liver biopsies serve to more precisely define the nature of the chronic hepatitis and provide useful information regarding the extent of damage and prognosis. The commonest cause of chronic hepatitis is viral infections of the liver (hepatitis B and C). Hepatitis C virus was discovered in 1988. This virus has an RNA genome, which is single stranded with a positive polarity, having 10,000 nucleotides. It possesses 30 subtypes. The transmission is parenteral, i.e., commonest by blood transfusion & I/V drug abuse, vertical transmission from mother to child, needle prick, ear piercing, tattooing, barbers', razors, etc (Zuckerman, 1989). More than 3 million Americans and 170 million persons worldwide are chronically infected with hepatitis C virus (HCV) (Armstrong *et al*.,2006 and Di-Bisceglie *et al*., 2008) which can result in progressive hepatic injury and fibrosis, culminating in cirrhosis and end-stage liver disease (Thomas, 2000). In Pakistan the prevalence of hepatitis C is 40.88%, similarly Hepatitis B Virus (HBV) infection is another global health problem with 350 million people being carrier worldwide (Taher *et al*., 2003). The prevalence of hepatitis B in chronic liver diseases is 30.35% (Ali *et al*, 2005).

Iron is a chemical element with the symbol Fe and atomic number 26. It is a group 8 and period 4-element. Viral related liver damage is characterized by increased iron storage (possibly induced by the virus), which elicits a free-radical-mediated peroxidation, with consequent steatosis and activation of glutathione turnover.(Taher *et al*., 2003) The reported prevalence of increase in serum iron level in patients with chronic viral hepatitis is 40%. (Farinati *et al*., 1995 and Bacon, 1997)

Therefore keeping all such important views in mind and by considering the increasing incidence of chronic viral hepatitis in our country, the present study was conducted to evaluate and assess the disturbance in serum iron level in patients with chronic viral hepatitis. The raised serum iron level leads to the development of resistance to the interferon therapy. Therefore, this study help in filling the gap, open new forum of discussion and provide knowledge and information regarding the medical workup of patients with

chronic viral hepatitis, such parameters add some weight in the management protocols of chronic viral hepatitis.

PATIENTS AND METHODS

This descriptive type cross sectional study was conducted in the department of Medicine at Liaquat University Hospital (a tertiary care teaching hospital) Hyderabad Pakistan from August 2008 to January 2009. All patients above 12 years of age, of either gender, were known (diagnosed) cases of hepatitis B or C for ≥ 6 months duration came through outdoor patient department (OPD) for medical / follow up visit were evaluated and enrolled in the study. The detail history of all such patients was taken and complete relevant clinical examination and investigations was performed. All the patients were assessed for their serum iron and ferritin level. The advice of serum iron was made to follow up / OPD / stable patients while for hospitalized hepatitis B and C infected patients the 3cc blood sample was sent to laboratory for the assessment of serum iron. The normal reading of serum iron for female subjects: 37–145 µ/dL and for male subjects: 59–158 µ/dl, the value >158ug/dl (cut off) was considered raised (in males) and the value >145 µd/dL (cut off) was considered raised (in females). The informed consent was taken from every patient or from attendant of patients after full explanation of procedure regarding the study, and all such maneuvers were performed under medical ethics. The data were collected through pre design proforma and demographical parameter was also recorded. The exclusion criteria of the study were (1). Patients who were already on iron therapy, (2) Known cases of haemochromatosis, (3) Known cases of thalassemia (4) patients had history of repeated blood transfusions, (5) known cases of chronic renal failure. (6) History of hemolytic anemia (7) Non cooperative patients who refused and did not have interest to participate in the study. The sample size was calculated according to the formerly estimated prevalence of raised serum iron level in patients with chronic viral hepatitis by Farinati *et al* (1995) and Bacon (1997) with consideration of 9% margin of error.

The collected data were analyzed through SPSS version 11.00. The frequency and percentage of raised serum iron in patients with chronic viral hepatitis and gender distribution was calculated. The chi-square test was applied between categorical variables like normal / raised iron level and gender at 95% confidence interval while the means with standard deviation were calculated for quantitative variables i.e. serum iron levels and age; and the difference between means was compared through t-text ($P<0.05$).

RESULTS

In this study total 114 patients were identified with viral hepatitis, out of which 42(37%) had viral hepatitis B infection and 72 (63%) had viral hepatitis C infection, of which 68 (60%) were males and 46 (40%) were females. The 93 patients attended the medical OPD of Liaquat university hospital Hyderabad, while 21 patients were hospitalized and collected from medical wards of hospital. Eighty eight (77%) belonged to rural areas while twenty six (23%) were from urban areas. The mean age ±SD for hepatitis B and C infected patients was 34.523± 5.185 and 39.041± 7.155, respectively. The mean±SD serum iron level of overall study population was 164.947 ± 17.841 mmol/L. Thirty Five (31%) patients were found to have normal serum iron level (below cut-off value) whereas 79 (69%) patients had raised serum iron levels (above cut-off point). Mean±SD of serum iron levels in patients had raised and normal levels were 174.835±8.347 mmol/L and 138.828 ± 2.884 mmol/L, respectively ($P<0.001$). The majority of viral hepatitis infected patients were males (68, 60%) with male-female ratio of 1.1:1. The 12/42 (29%) patients in hepatitis B group and 17/72 (24%) patients in hepatitis C group had history of alcoholism as well. The 03% patients had both viral hepatitis B and C infection. The gender distribution, frequency, mean and standard deviation of serum iron and ferritin level in patient with hepatitis B and C are shown in **Table**: I, II, III and IV.

Table I: Serum iron level in hepatitis b infected patients with their gender distribution

Gender	Hepatitis B (*n* = 42) Serum Iron		P - value
	Raised	Normal	
Male	20 (74.1%)	07 (25.9%)	0.02*
Female	06 (40%)	09 (60%)	

*P - value is statistically significant

Table II: Mean serum iron level in patients with hepatitis b infection

Gender	n = 42	Mean ± SD (µg/dL)	t - value	P - value

Male	27 (64%)	164.62 ±28.42	2.123	0.04*
Female	15 (36%)	146.26 ± 23.68		

* P-value is statistically significant

Table III: Serum iron level in hepatitis c infection with their gender distribution

Gender	Hepatitis C (*n* = 72) Serum Iron		P - value
	Raised	Normal	
Male	39 (95.1%)	02 (4.9%)	<0.001*
Female	14 (45.2%)	17 (54.8%)	

*P-value is statistically significant

Table IV: Mean serum iron level in patients with hepatitis c infection

Gender	n = 73	Mean ± SD (µg/dL)	t - value	P - value
Male	41(57%)	168.12 ±10.86	3.861	<0.001*
Female	31(43%)	147.09 ± 32.62		

*P-value is statistically significant

DISCUSSION

The present study identified the results shown that the serum iron and ferritin level is increased in patients with chronic viral hepatitis B and C. In our study 72 subjects were HCV positive, the serum iron was raised in 53 (74%) patients p = <0.001, however such observation was also reported (Bolewska *et al*., 2005). Several mechanisms have been proposed to explain the relation between HCV infection and hepatic iron overload and it has been suggested that iron may promote HCV replication. Recently identified hepcidin, exclusively synthesized in the liver, is thought to be a key regulator for iron homeostasis and is induced by infection and inflammation suggesting that hepcidin may play a pivotal role in the pathogenesis of iron overload and hyperferritinemia in patients with chronic hepatitis C (Naoki *et al*., 2007). Although in our study we had not take the management parameters but it has been reported that iron-restricted diet may be an important therapeutic modality for improving liver injury in patients with chronic hepatitis C (Iwasa *et al*., 2002).

The presence of chronic hepatitis B viral infection in association with raised serum iron is due to the break down of hepatic cells and in our study we identified 42 patients, of which 26(62%) had raised serum iron level p = 0.02 (statistically significant) whereas a study published in Journal of gastroenterology and hepatology shown similar findings (Martinelli *et al*., 2004). However in our study we did not observed any treatment response for iron therapy but the decrease in serum iron level was found after an antiviral therapy (Zheng-Wen *et al*., 2004).

In our study the majority of patients were belonging to rural areas, such areas have higher rate for Hepatitis B and C infection because there is lack of medical and awareness facilities and motivational programs, however our such finding resembled with the study conducted by Mujeeb *et al* (2008) who observed hepatitis B and C infection in rural / peripheral areas of province Sindh of Pakistan. Another study has also shown the dominancy of rural population in relation to hepatitis B and C infection (Altaf *et al*., 2007). The mean age of patients with chronic hepatitis B and C infection was 34.523± 5.185 (SD) and 39.041± 7.155 (SD) while this finding approximately correlates with the study conducted by Fayyaz *et al* (2006).

In our study twelve patients with hepatitis B virus infection with raised serum iron level had history of alcoholism, it is well recognized that there is an association between alcohol intake and liver damage but many exceptions can be found, as there are alcoholics who never developed important liver diseases. Therefore, other agents may be involved in the progression of liver damage in alcoholic patients. The discussion on this subject has attracted attention toward hepatitis B virus (HBV) infection. Evidence supporting the hypothesis of HBV involvement has been described; in fact, typical histological features of postviral chronic persistent hepatitis (CPH) and chronic active hepatitis (CAH) were found in liver biopsies of alcoholic patients, in which alcohol appeared to be the only pathogenetic agent. There are still many contrasting opinions concerning the role of HBV in the pathogenesis called "non-alcoholic liver disease in the alcoholic". It has been found an increased incidence of HBV markers in patients with alcoholic liver disease when compared with controls, and this is highly suggestive of a pathogenetic role of HBV in the progression of this chronic liver disease (Calabrese *et al*., 1986). In current study, 17 hepatitis C infected subjects with raised serum iron level had history of alcoholism; infection with hepatitis C virus (HCV) has been proposed as one of the co-factors which contribute to the development of

liver disease in individuals chronically abusing alcohol. Infection due to both i.e. hepatitis B and C virus is more common in alcohol abusers. This association may, in many cases, be related to the patient's lifestyle. Many alcohol abusers with concomitant viral infection have identifiable parenteral risk factors, even in the absence of such risk factors; portal or lobular inflammation in individuals chronically abusing alcohol is strongly associated with an increased prevalence of HCV infection (Grellier *et al*., 1997).The individuals abusing alcohol are known to be susceptible to a variety of infections which may occur more frequently and which may be more severe than in non-alcohol abusers, there is now substantial evidence that chronic HCV infection may accelerate or aggravate the development of liver injury in chronic alcohol abusers resulting in cirrhosis and hepatocellular carcinoma (Anand *et al*., 2000).

Conclusion: It may be concluded that the serum iron level was raised in patients with chronic viral hepatitis B and C. Therefore it is suggested that the serum iron level should be assessed in patients with chronic viral hepatitis B and C infection. This protocol will spare and prevent the patients to develop resistant to interferon therapy.

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