

TRANSPORT AND TISSUE IRON IN PATIENTS WITH LIVER DISEASE

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Abstract

Serum iron, total iron binding capacity and liver iron was estimated in 54 liver biopsy specimens of subjects with various liver diseases (hepatitis, cirrhosis, cancer and thalassemia with jaundice).

Liver iron was significantly raised in thalassemic patients. No significant difference in liver iron was found in hepatitis, cirrhosis and liver cancer.

Serum iron was elevated in hepatitis and cirrhosis and almost normal in liver cancer. Transferrin saturation was high in hepatitis and thalassemia and normal in liver cancer.

Introduction

The internal redistribution of iron in the body occurs through the serum iron compartment, with the liver playing an important role. Several workers have found changes in serum iron levels in liver disease. It has been reported that serum iron level is helpful in the differential diagnosis of jaundice and elevated serum iron levels in acute hepatitis are probably associated with liver cell necrosis (Stone et al., 1955).

The purpose of this study was to report the serum iron levels, total iron binding capacity and liver iron concentration in patients with various types of liver diseases.

Material and Methods

A total of 54 patients suspected of suffering from various liver diseases were investigated. Their liver biopsies were performed by the Menghini technique and a part of liver tissue was taken for liver iron estimation.

Blood samples were also drawn from these subjects at the same time, usually in the morning, for the estimation of hemoglobin, serum iron and total iron binding capacity. Liver iron concentration in biopsy specimens was estimated by the method of Barry and Sherlock (1971). This method measures total liver iron concentration expressed as ug/100 mg dry weight.

Results

Fifty Four subjects in this study included 32 males and 22 females. Their ages ranged from 12 to 78 years and 17 to 80 years respectively.

Of the 54 patients, 18 had hepatitis, 8 had cirrhosis and 13 were of cancer, four subjects with thalassemia who had jaundice were also investigated. Amongst the five subjects listed in the miscellaneous group one each was found to have hepatosplenomegaly, tuberculosis, fatty changes, amoebic liver abscess and lymphatic leukemia. Six subjects, including 4 males and 2 females, whose biopsy report revealed no significant changes and biochemical investigations were normal, were grouped as controls. Their ages ranged between 35 and 70 years.

Subjects with various liver diseases are listed in Table I.

Table I: Number of Cases with Various Liver Diseases

Groups	Males	Females	Total Cases
Hepatitis	12	6	18
Cirrhosis	4	4	8
Cancer	6	7	13
Thalassemia	1	3	4
Miscellaneous	5	—	5
Controls	4	2	6
Total:	32	22	54

Of the 18 patients of hepatitis, 12 had acute hepatitis, 5 had minor changes of acute hepatitis and one had chronic persistent hepatitis. Their ages were between 18 and 65 years. Jaundice was present in 15 cases.

Of the 8 patients with cirrhosis 2 had jaundice and 3 had ascites. Their ages ranged between 38 to 63 years.

Of the 13 cancer patients, 8 had jaundice, 3 had ascites and in 3 cases gastrointestinal bleeding was present. Their ages were between 45 and 80 years.

Of the 4 thalassemic patients, 2 had thalassemia major, one thalassemia trait and one had thalassemia—Hb-E. Their biopsies revealed, acute hepatitis, cholestatic hepatitis and mild cholestasis. All the cases had jaundice. Their ages ranged between 13 to 20 years.

Table II shows the mean liver iron, serum iron, total iron binding capacity and transferrin saturation in various groups studied.

Table II: Mean $\pm$ S.E. of Liver Iron, Serum Iron, TIBC, % Saturation of Transferrin and Hemoglobin in Various Liver Diseases

	<i>Hepatitis</i>	<i>Cirrhosis</i>	<i>Cancer</i>	<i>Thalassemia</i>	<i>Normals</i>
Liver Iron (ug/100 mg dry wt.)	205 $\pm$ 36 (18)	118 $\pm$ 12 (8)	102 $\pm$ 25 (13)	720 $\pm$ 214 (4)	86 $\pm$ 15 (6)
Serum Iron (ug %)	139 $\pm$ 18 (16)	145 $\pm$ 31 (8)	68 $\pm$ 7 (9)	176 $\pm$ 36 (4)	63 $\pm$ 10 (4)
TIBC (ug %)	339 $\pm$ 21 (13)	309 $\pm$ 36 (6)	277 $\pm$ 29 (8)	226 $\pm$ 21 (4)	275 $\pm$ 56 (3)
% Saturation of Transferrin	43 $\pm$ 5 (13)	38 $\pm$ 7 (6)	26 $\pm$ 3 (8)	77 $\pm$ 12 (4)	24 $\pm$ 1.3 (3)
Hb: (g %)	13.7 $\pm$ 0.5 (18)	12.7 $\pm$ 0.6 (7)	10.2 $\pm$ 0.7 (11)	6.8 $\pm$ 0.5 (4)	12.3 $\pm$ 0.4 (6)

The mean liver iron concentration was significantly increased in thalassemic patients. No significant difference in liver iron was found in hepatitis, cirrhosis and liver cancer. Mean serum iron was high in hepatitis and cirrhosis, while in liver cancer it was almost normal. Thalassemia patients had raised mean serum iron.

The highest mean for transferrin saturation was found in thalassemic patients. In acute hepatitis it was also elevated while it is found to be normal in liver cancer. The mean hemoglobin was significantly low in thalassemia and liver cancer.

The mean values for liver iron, serum iron, TIBC and transferrin saturation in males and females is separately shown in Table III.

Table III: The Mean $\pm$ SE Values for Liver Iron, Serum Iron, TIBC and Transferrin Saturation in Males & Females in Hepatitis Group

	<i>Males</i>	<i>Females</i>
Liver Iron (ug/100 mg)	238 $\pm$ 47 (12)	138 $\pm$ 49 (6)
Serum Iron (ug %)	167 $\pm$ 18 (11)	79 $\pm$ 29 (6)
TIBC (ug %)	351 $\pm$ 20 (9)	311 $\pm$ 56 (4)
Transferrin Saturation (%)	51 $\pm$ 6 (9)	25 $\pm$ 18 (4)
Hemoglobin (G %)	14.8 $\pm$ 0.3 (12)	11.6 $\pm$ 0.8 (6)

The mean values for serum iron and hemoglobin were significantly lower in females. The mean for liver iron, TIBC and transferrin saturation was lower in females though not significant. In majority of hepatitis patients, serum iron was elevated and transferrin saturation was above 30%.

In males, values for serum iron over 200 ug% were found in 5 patients and in females only in one case. Values below 100 ug% were found in 2 males and in 4 females. Values between 100 and 200 ug% were found in 4 cases.

Low serum iron in females was usually associated with low hemoglobin levels and transferrin saturation between 13-21%.

In Cirrhosis, values for serum iron above 200 ug% were found in only one patient. In 5 patients values were between 100 and 150 ug% and in 2 patients they were found below 100 ug%.

In cancer, serum iron ranged between 38 and 100 ug%. In 4 cases the values were between 38 and 50 ug%. In majority of cases transferrin saturation was below 30%. In 2 cases values were found below 15%.

In thalassemia, serum iron ranged between 117 and 277 ug%. The transferrin saturation was also very high and ranged from 54 to 100%.

All cases of thalassemia were severely anemic. Their hemoglobin was between 5.6 and 8.2 G%. They had received numerous blood transfusions. Their liver iron was significantly raised, ranging from 308 to 1116 ug per 100 mg.

Table IV shows the findings of each patient included in the miscellaneous group.

When the serum iron and the liver iron were compared with liver function tests (Serum bilirubin; alkaline phosphatase and transaminases), no clear cut correlation was found in any disease group. However, the more severe the case and the more abnormal the liver function generally, the higher the serum iron.

Table IV: Liver Iron, Serum Iron, TIBC, Transferrin Saturation and Hemoglobin in the Miscellaneous Group

No	Cases	Age	Tissue Iron (ug/100 mg)	Serum Iron (ug %)	TIBC (ug %)	% Transferrin Saturation	Hb (G %)
1.	Hepatosplenomegaly	12	133	—	—	—	12.3
2.	Tuberculosis	35	58	70	210	33	—
3.	Fatty Change	45	42	136	225	60	15.8
4.	Amebic Liver Abscess	30	42	96	171	56	13.2
5.	Lymphatic Leukemia	59	543	56	150	37	9.4

Discussion

Acute hepatitis is characterized by the elevated serum iron levels, which reaches a peak from 12 to 31 days after the onset of jaundice. Elevated serum iron levels in cases of acute hepatitis were also found in this study. It has been shown that this rise is probably associated with liver cell necrosis (Stone et al., 1955). In the subacute and chronic stages of hepatitis the plasma iron is usually normal or low. The majority of females patients in the present study had minor changes of acute hepatitis. The significant difference between males and females in the present study reflects the sex differences in iron stores.

In cirrhosis, the plasma iron is usually normal unless this is associated with liver cell necrosis or with megaloblastic anemia (Peterson 1952). Elevated levels have been found in alcoholic Cirrhosis (Stone et al., 1955). No such cases were observed in this study.

The moderate depression of the serum iron level observed in cancer (Miller et al., 1956), was also found in patients reported in this study.

It is known that high serum iron levels are common finding in patients with thalassemia. The striking rise in liver iron in these cases may be due to the abnormal mechanism of iron utilization for Hb-Synthesis or increased absorption and repeated blood transfusions in cases of thalassemia major.

References

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