Original Articles

FATTY LIVER — CLINICAL FEATURES AND POSSIBLE ETIOLOGY

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Abstract

Fifty-nine patients with fatty liver were studied. Severe fatty changes were observed in 28.8% and mild in 47.5% of cases. Varying degrees of fatty change was observed in the remaining patients.

There were 28 males and 13 females and their mean age was 45.3 years. Hepatomegaly was the main presenting symptom. Seven had a history of diabetes and 8 took alcohol. Hepatitis Bs Antigenaemia was observed in 7.14% of cases.

In this series very few patients took alcohol and only a few had diabetes. It is, therefore, likely that imbalance of intake of essential food factors may be the main cause of fatty liver seen in this series (JPMA 29:138, 1979).

Introduction

Etiology of fatty liver differs in different parts of the world. In the developing countries nutritional imbalance due to economic factors are responsible for this disease while in developed countries alcohol is the main etiological factor.

The observations on 59 patients with fatty liver demonstrated by liver biopsy are recorded in this communication.

Material and Methods

Fifty-nine cases referred from the Department of Medicine, Jinnah Postgraduate Medical Centre, Karachi, for investigation of their liver diseases were included in this study. The study commenced in March 1973 and concluded in June 1977.

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History and clinical features were recorded on a proforma and the morphological diagnosis of fatty liver was obtained in every case.

Hematological investigations included Hemoglobin, total and differential leukocytes count, platelet count and prothrombin time.

Biochemical investigations were total and conjugated bilirubin, alkaline phosphatase, transaminases and serum proteins. Serum protein electrophoresis was also carried out. Hepatitis Bs antigen was done using crossover immnoelectrophoresis.

Results

A total of 59 subjects were investigated. Of these 28(47.4%) were males and 31(52.5%) were females. Their ages ranged between 12 and 79 years with a mean of 45.3 years.

The symptoms and signs in order of frequency are shown in Table I and II. The most frequent symptoms were abdominal pain, anorexia, weight loss and fever.

Table I: Symptoms

Symptoms	*No. of cases*	*Percentage*
Abdominal pain	32	54.24
Anorexia	21	35.59
Loss of weight	19	32.2
Fever	17	28.81
Nausea/vomiting	15	25.42
Ascites	7	11.86
Jaundice	7	11.86
Oedema	5	8.47
G. I. Bleeding	4	6.78
Pruritus	3	5.08

Table II. Physical Signs

Physical signs	*No. of cases*	*Percentage*
Hepatomegaly	53	89.83
Jaundice	7	11.86
Splenomegaly	6	10.17
Ascites	6	10.17
Oedema	5	8.47
Clubbing	3	5.08
Palmar Erythema	3	5.08
Sparse body hair	2	3.39
Angular stomatitis	2	3.39
Glossitis	2	3.39
Spider naevi	1	1.69

Hepatomegaly was the commonest (89.8%) clinical sign, jaundice was present in 12% of the patients and the fluid retention in 10.2%. Splenic enlargement was observed in 10.2% of patients.

Signs of vitamin deficiency like peripheral neuritis, glossitis, angular stomatitis, petichae and hyperkeratosis were infrequent.

Of the total of 59 subjects 7(11.86%) had diabetes and 8(13.56%) took alcohol. Of the drugs methyldopa was taken by two subjects.

Laboratory Investigations

The results of haematological investigations are shown in Table III. Haemoglobin levels varied from 5.6-17G%. Seven (13.72%) patients had anaemia (Hb < 11G%). It was mainly microcytic with occasional macrocytoes in peripheral smear. Of 56 patients, 6(10.71%) had leucocytosis and in 3(5.3%) platelet count was below 100,000/cm. Prothrombin time was abnormal in 7% of the patients but returned to normal level after Vit. K therapy.

Table IV shows the biochemical investigations.

A total bilirubin above 1.0 mg was found in 35% of patients, unconjugated bilirubin was raised in 6 and conjugated in 14 cases. Alkaline phosphatase above 3.1 sigma units was observed in 28(51.85%) cases. Levels of SGOT were found to be higher than SGPT in patients with steatosis.

Total proteins were normal in all except 4 cases. Albumin was below 3.5G% in 10 and the globulin above 3.2G% in 20 cases.

Serum protein electrophoretic pattern is shown in Table V. Elevation of mean levels of $alpha_1$ $alpha_2$. Beta and Gamma globulin levels was observed.

Hepatitis Bs antigen was determined in 28 subjects and was found positive in 2(7.14%).

Table III: Haematological Findings

Haematological investigations	*No. of cases*	*Mean*	*±SD*	*±SE*
Haemoglobin G%	51	12.36 ±	2.80 ±	0.39
WBC/cmm	56	8046.75 ±	2875.25 ±	384.22
Platelet count/cmm	56	199750.0 ±	82800.0 ±	11060.0
Prothrombin time (Sec)	57	16.63 ±	4.19 ±	0.56

Table IV: Biochemical Investigations

Biochemical investigations	*No. of cases*	*Mean*	*±SD*	*±SE*
Total bilirubin (mg%)	54	1.66 ±	5.44 ±	0.74
Conjugated bilirubin (mg%)	50	0.85 ±	2.11 ±	0.30
Unconjugated bilirubin (mg%)	50	0.65 ±	0.75 ±	0.11
Total protein (G%)	48	7.13 ±	0.93 ±	0.13
Albumin (G%)	47	3.87 ±	0.86 ±	0.13
Globulin (G%)	47	3.27 ±	0.89 ±	0.13
SGOT (mu/ml)	50	25.0 ±	37.8 ±	5.34
SGPT (mu/ml)	52	20.5 ±	51.9 ±	7.18
Alkaline phosphatase (Sigma units)	54	4.5 ±	2.43 ±	0.33
Thymol turbidity (Mac. units)	25	5.9 ±	4.78 ±	0.96

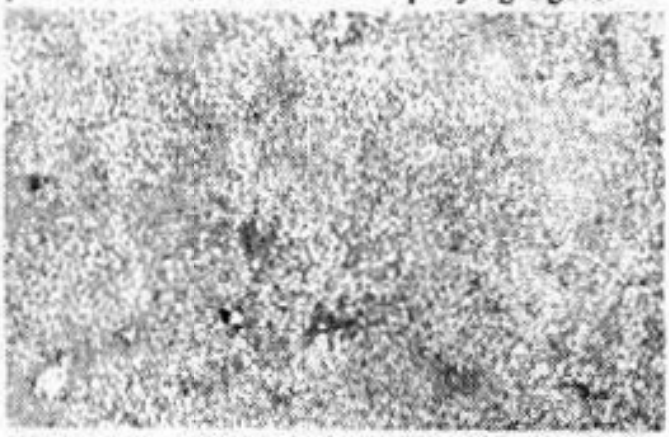
Table V: Electrophoretic Pattern of Protein in Fatty Liver

Proteins	*No. of cases*	*Mean*	*±SD*	*±SE*
Total protein	22	7.31 ±	1.00 ±	0.21
Albumin	22	3.55 ±	1.03 ±	0.22
$Alpha_1$	22	0.29 ±	0.10 ±	0.02
$Alpha_2$	22	0.69 ±	0.24 ±	0.05
Beta	22	0.85 ±	0.32 ±	0.07
Gamma	22	1.82 ±	0.97 ±	0.21

Table VI: Types of Fatty Changes

Types of fatty changes	No. of cases	Percentage
Mild fatty change	28	47.46
Fatty change with cholestasis	03	5.08
Fatty change with liver cell Necrosis	03	5.08
Moderate fatty change	08	1.69
Severe fatty change	17	28.81

The various types of fatty changes found by histological assessment of liver biopsy are shown in Table VI. In majority of cases (47.4%) the fatty change was of mild type while the severe change was found in 28.8% of subjects as shown in the accompanying figure.



Fatty liver — Diffuse infiltration of liver parenchyma with fat vaccuoles (H&E:X20)

Discussion

Dietary imbalance of fat, carbohydrate or alcohol along with inadequate intake of lipotropic factors, proteins and certain of the B-vitamins are the most important factors in the production of fatty livers and cirrhosis.

In children, the imbalance of proteins in relation to calories as in Kwashiorkar appears to be the most common nutritional cause of liver injury. Induction of uncomplicated protein deficiency in rhesus monkeys produced similar morphological changes as seen in human Kwashiorkar. Earlier fatty change was seen in the liver cells at the periphery of hepatic lobule. The parenchymal cells are laden with Sudanophylic fat globules giving a vacuolar appearance with eccentric nuclei. Changes gradually progress towards the centre of the lobule and thus increased number of cells are involved and the fatty change becomes diffuse. In severe cases fat cysts are encountered especially in the periportal zones. Fibrosis, cellular infilteration and necrosis are usually inconspicuous (Deo et al., 1965). Effects of protein deficiency has not been clearly delineated in human adults (Lieber 1972).

Protein deficiency results in reduction in plasma triglyceride and phospholipids and a rise in free fatty acid and fatty liver due to accumulation of triglyceride associated with a reduction in hepatic phospholipids. It, therefore, appears that fatty liver of protein deficiency is mainly due to a defect in secretion of hepatic triglycerides (Kumar et al., 1972).

Even when the diet contains adequate amount of lipotropes and all known essential food factors imbalance in the chief sources of energy, carbohydrate or fat are associated with some degree of fatty liver. However, the complication of cirrhosis does not ensue unless the diet is also low in protein and choline (Porta and Hartroft, 1970).

Another important source of calorically imbalanced diet is alcohol. Consumption of alcohol with lipid containing diet results in the deposition of dietary fatty acids in the liver, whereas alcohol taken with low fat diet leads to the deposition of endogenously synthesized fatty acids in the liver (Lieber and Spritz, 1966; Lieber et al., 1966 and 1969).

Depending on the metabolic state of the animal decreased lipid oxidation and enhanced lipogenesis can be linked to ethanol oxidation and the associated increase generation of NADH (Lieber 1972).

Human beings with or without history of alcoholism, given a variety of non-deficient diets with alcohol either as a supplement or an isocalorie substitution for carbohydrates developed fatty liver (Lieber and Rubin, 1968, Lieber et al., 1963; Lieber et al., 1965).

Morphologically fatty livers are classified into type A and B (Hartroft and Porta, 1967).

In type 'A' fatty liver the lobular distribution of fat is usually nonportal initially but becomes diffuse at later stages. In such liver ruptured fatty cysts, fibrosis and cirrhosis have been reported. Type 'A' fatty liver is encountered in all instances in which lipotropic deficiency is known or suspected to play a role. It is classically the type found in human alcoholics.

In type 'B' fatty livers, the lobular distribution of fat has consistantly been observed to be periportal, and no ruptured fatty cysts, fibrosis and cirrhosis is seen. This type of fatty livers are seen at both extremes of calorie intake (inanition and obesity), and in fatty

livers associated with hormonal imbalances as seen in diabetes (Hartroft, 1973). This is the type more frequently seen in this series.

As far as liver function is concerned no impairment was seen in severe stages of type B fatty change. Changes in the liver function tests in this study were minimal. A progressive type 'A' change may however presage cirrhosis and its complications.

In this study, alcohol was taken by only a few subjects and this could not be a factor in producing fatty liver. Diabetes was also found only in a small number of subjects. It is therefore possible that imbalance of intake of essential food factors may be responsible for the fatty liver seen in this series.

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