HEPATIC ABNORMALITIES IN CHOLE-LITHIASIS

Talat J. Hassan, Sarwar J. Zuberi and Rashida Maqsood

Abstract

Preoperative clinical and biochemical investigations were done in 88 cases undergoing cholecystectomy for Cholelithiasis. Liver biopsy was taken at the time of surgery. Normal liver was obtained in 48 cases (54.6%). Abnormalities in liver varied from minimal structural changes to biliary cirrhosis.

Clinical and biochemical investigations were not useful in predicting the histological appearance of the liver with the exception of duration of illness which was longest (21 years) in patient who had cirrhosis.

PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi-35.

Introduction

Abnormalities in the hepatic structure and the function have been described in the patient with Cholelithiasis (Mateer et al., 1948; Dunlap et al., 1954; Poulson and Christoffersen, 1970; Shorter and Baggenstoss, 1959). Liver function tests reflect only gross hepatic dysfunction (Raven 1975) but the exact structurel changes in the liver can only be determined by liver biopsy (Dunlap et al., 1954; Weisbrod et al., 1950). This study presents the correlation of histological changes in the liver with the clinical and biochemical findings in patients with cholelithiasis.

Material and Method

Preoperative clinical examination and biochemical investigations were done in 88 cases undergoing cholecystectomy for gallbladder disease.

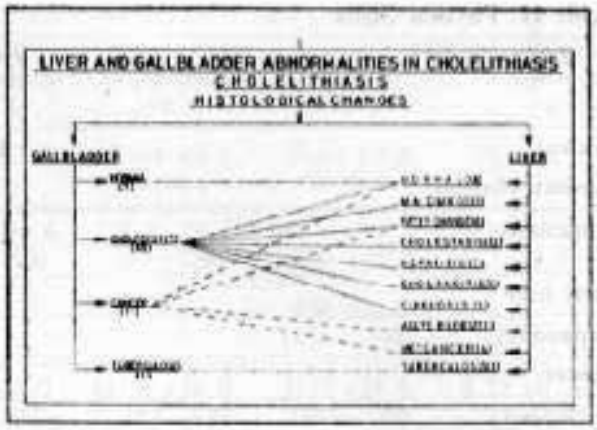

Fig: Liver and Gallbladder abnormalities in Cholelithiasis.

Table I shows the age and sex distribution and clinical findings in patients in different histological groups. Patients with normal liver or minimal changes were younger than those with more advanced changes. Average age of females was 38 years, and that of males 53.8 years. Majority of the patients were females.

Table 1: Age, Sex and Symptoms

Liver histology	*Total No.*	*Age in years*	*F:M*	*Abdominal pain No. (%)*	*Nausea and vomiting No. (%)*	*Duration of illness (years)*
Normal	41	37.97	19:1	38 (92.6)	36 87.8	2.5
Minimal changes	3	33.7	3:0	3 (100)	2 66.6	2.2
Cholestasis	10	42.6	3:2	10 (100)	8 80	4.3
Fatty changes	4	44	4:0	4 (100)	4 100	2.18
Hepatitis	7	41.2	6:1	7 (100)	4 58	2.4
Cancer	7	49	5:2	6 (85.7)	6 85.7	3.3
Cirrhosis	1	45	1:0	1 (100)	1 100	21
Tuberculosis	1	40	1:0	9 (100)	1 100	5
Cholangitis	1	30	1:0	1 (100)	1 100	4

Table II: Physical Signs

The laboratory tests included haemoglobin, total leucocyte count, serum bilirubin, alkaline phosphatase, transaminases (SGPT, SGOT) calcium, cholesterol, total lipids, phosphlipid and triglycerides. Specimen of glallbladder and needle biopsy of the liver obtained at the time of surgery were submitted for histological examination.

Analysis of clinical and biochemical data was done according to histological findings in the liver.

Results

Histological findings in the gallbladder and liver are shown in the accompanying figure. Chronic inflammatory changes were observed in most of the gallbladder specimens and from no structural change to cirrhosis in liver biopsies.

The main presenting symptoms were pain in the abdomen with nausea and vomiting. Duration of symptoms correlated well with the histological changes in the liver.

History of longer duration was associated with gross structural abnormalities in the liver. Hepatomegaly and palpable gallbladder were more frequently seen in patients with cholestasis and carcinoma of gallbladder with hepatic metastasis. Jaundice was more frequent in patients with hepatitis and cholestasis (Table II).

Patients with normal liver associated with normal or diseased gallbladder showed no difference in the clinical presentation with the exception of jaundice which was more frequent in patients with cholecystitis (Table III).

Table II: Physical Signs

Liver histology	*Total*	*Jaundice* No. (%)	*Hepatomegaly* No. (%)	*Palpable gall bladder* No. (%)	*Type of stones*
Normal	41	4 (9.75)	9 (21.9)	8 (19.5)	Mixed
Minimal changes	3	1 (33)	2 (66)	1 (33)	Mixed
Cholestasis	10	4 (40)	6 (60)	4 (40)	Mixed 7 Pigment 2 Cholesterol 1
Fatty liver	4	0 (0)	0 (0)	0 (0)	Mixed 2 Pigment 2
Hepatitis	7	3 (42.8)	5 (71.4)	3 (42.8)	Mixed 6 Pigment 1
Cancer	7	3 (42.8)	3 (42.8)	5 (71.4)	Mixed
Cirrhosis	1	1 (100)	1 (100)	0 (0)	Mixed
Tuberculosis	1	0 (0)	0 (0)	1 (100)	Mixed
Cholangitis	1	0 (0)	0 (0)	1 (100)	Mixed

Table III: Signs and Symptoms

Signs and symptoms	*Gall bladder histology*		
	Normal (7)	*Cholecystitis* (34)	*Cancer* (2)
	Positive cases No(%)	*Positive cases* No(%)	*Positive cases* No(%)
Abdominal pain	7 (100)	31 (91.1)	2 (100)
Nausea vomiting	5 (71.4)	32 (94.1)	2 (100)
Jaundice	0 (0)	4 (11.7)	0 (0)
Hepatomegaly	1 (14.3)	9 (26.4)	1 (50)
Age (Years)	41.14	37.45	44
Duration of illness (Years)	2.8	2.9	4
Type of stone	Mixed	Mixed	Mixed

Liver function tests were normal or slightly disturbed in patients with a normal liver biopsy or minimal structural changes. Serum bilirubin, alkaline phosphatase and transaminases were all disturbed in cases with fatty liver and cholestasis. Serum transaminases were markedly raised in patients with associated Hepatitis. Alkaline phosphatase was high in all patients with histological abnormalities (Tables IV, V).

Serum cholesterol was elevated in patients with fatty changes and metastatic cancer. Total lipids, phospholipids and triglyceride showed no correlation with histological findings (Table VI).

Liver function tests with normal liver irrespective of pathology in the gallbladder were within normal range with only slight rise of alkaline phosphatase and SGOT. Total lipids, phospholipids triglyceride and cholesterol were also within normal limits (Table V, VI).

Table IV: Biochemical Investigations

Liver Histology	*Total No.*	*Bilirubin mg%* Mean ±S.E. (Range)	*Bilirubin Conj.* Mean ±S.E. (Range)	*Alk. phosp.* Mean ±S.E. (Range)	*SGOT m/ml* Mean ±S.E. (Range)	*SGPT m/ml* Mean ±S.E. (Range)
Normal	37	0.89 ±0.15 (0.2—4.75)	0.55 ±0.11 (0.1—4)	3.82 ±0.37 (1.4—11.6)	16.88 ± 2.65 (7—67)	9.68 ±2.55 (0—63)
Minimal change	3	3.36 ±0.17 (0 —47)	0.5 ±0.12 (0—2.8)	3.89 ±0.39 (1.4—11.6)	17.43 ± 2.82 (7—67)	9.78 ±2.43 (3—63)
Cholestasis	10	4.5 ± 2.0 (0.3—18.6)	3.34 ±1.6 (0.1—14.6)	5.6 ±0.95 (1.9—9.9)	21.3 ± 3.9 (5—31)	14.6 ±4.8 (2—39)
Fatty changes	5	3.2 ±2.4 (0.6—10.5)	2.71 ±2.18 (0.3—9.25)	7.4 ±1.82 (3.1—11.6)	32.6 ± 1.82	11.5 ±4.53 (4.5—20)
Hepatitis	7	4.1 ±1.4 (0.5—9.5)	2.66 ±0.89 (0.2—5.9)	5.45 ±1.12 (2.3—9.0)	55.5 ±12.6 (18—98)	61.66 ±15.8 (18—108)
Cancer	7	8.25 ±3.99 (8.3—23.7)	6.11 ±2.45 (0.2—18)	6.17 ±2.45 (1.8—18)	30.7 ±13.22 (7—100)	16.07 ±8.5 (7—100)
Cirrhosis	1	1.8	—	2.8	15	% 17
T.B.	1	0.3	0.11	—	8	8.3

Table V: Lipid Pattern

Liver Histology	*Total No.*	*Total Lipids mg%*	*Phospholipids mg%*	*Triglycerides mg%*	*Cholesterol mg%*	*Calcium mg%*
		Mean ±S.E. (Range)	*Mean ±S.E. (Range)*	*Mean ±S.E. (Range)*	*Mean ±S.E. (Range)*	*Mean ±S.E. (Range)*
Normal	37	639.2 ±70.4 (270—980)	117.5 ±14.6 (80—110)	178.8 ±26.33 (55—290)	254 ± 9.8 (160—380)	4.8 ±0.06 (3.9—5.9)
Minimal Changes	3	—	—	—	256 ±30.8 (142—380)	5.4 (5—5.9)
Cholestasis	10	700 ±68.31 (203—300)	154.1 ±16.7 (85—200)	187.5 ±36.0 (95—300)	2577 ±29.5 (142—380)	4.72 ±0.23 (4—5.8)
Fatty Changes	5	744.5 ±55.5 (689—800)	155 ±25 (100—130)	240 ±50 (190—290)	234.3 ±23.77 (200—400)	5.15 ±0.2 (4.5—5.8)
Hepatitis	7	640 ±10 (630—650)	155 ±7 (150—160)	175 ±55 (120—230)	260.6 ±13.2 (220—290)	4.13 ±0.55 (3.1—5.6)
Cancer	7	—	—	—	300.4 ±36.5 (190—385)	4.77 ±0.25 (4.1—5.8)
Cirrhosis	1	—	—	—	—	—
T.B.	1	—	—	—	245	4.3

Table VI: Biochemical Investigation

Investigation	*Gall Bladder Histology*		
	Normal Mean ±S.E. Total No.	*Cholecystitis Mean ±S.E.*	*Cancer Mean ±S.E. Total No.*
Bilirubin Total mg%	0.5 ±0.52 (5)	0.9 ± 0.15 (31)	0.75 (2)
Bilirubin Conjugated mg%	0.25 ±0.04 (5)	0.63 ±0.13 (26)	6.25 (2)
Alkaline Phosphatase SU	3.28 ±1.14 (5)	3.9 ±0.4 (31)	2.25 (2)
SGOT mu/ml	10 (1)	17.4 ±2.8 (24)	8 (2)
Total lipids mg mg%	672.5 (4)	722.75 ±39.1 (12)	—
Phospholipids mg%	166.33 (4)	160.8 ±14.0 (12)	—
Triglycerides mg%	320 (4)	196.6 ±24.5 (12)	—
Cholesterol mg%	272.5 ±9.99 (6) 3	237.09 ±9.2 (32)	201 (2)

Discussion

The age and sex distribution in this series is typical of biliary tract diseases in Karachi (Hassan et al., 1976). Similar pattern has been reported from England (Triger et al., 1976).

Duration of symptoms and the age of the patient influences the pattern of histological changes in the liver. Liver biopsies were normal in 54.6% of patients in the present study, same as 52.6% reported by Raven (1975).

While in studies reported from England normal liver biopsy was reported in 22.8% by Triger et al. (1976) and 6% by Mateer et al. (1948). In the series reported by Triger et al. (1976), 40 patients out of 57 were above 50 years of age, while all the patients in this series were below 50 years. Majority of our patients were females, their average age being 38 years. The length of history here was 2.5 years in patients with normal liver biopsies.

Correlation of clinical features with micro-

scopic appearances is not significant with the exception of length of history, which was longer (21 years) in patients with marked structural abnormalities as cirrhosis.

Among liver function tests, alkaline phosphatase was most sensitive being invariably raised in all patients with associated liver changes (Triger et al., 1976; Raven et al., 1975).

Transaminases were markedly disturbed in patients with associated hepatitis.

Liver functions were not disturbed in patients with normal liver irrespective of pathology in the gallbladder.

It is possible that structural abnormalities in liver produce biochemical changes in bile which may precede the gallstone formation.

A direct relationship has been observed between hepatic bile cholesterol and serum triglycerides levels. Hypertriglyceridemia in our patients may be the cause of increased prevalence of stones where major constituent is cholesterol (64.4 mg%). The concentration of cholesterol in hepatic bile is more than that of gallbladder bile and this may be due to increased synthesis or decreased conversion of cholesterol to bile acids. These observations have tended to shift the blame for gallstone formation from gallbladder to the liver.

Liver abnormalities are more common in patients with gallbladder disease than those with normal gallbladder (Dunlap et al., 1954). Conversely in all patients with abnormal liver, possibility of presence of gallstones is higher irrespective of clinical and biochemical findings.

A cause and effect relationship, therefore, appears to exist between pathological states of liver and gallbladder. But with the present knowledge it is difficult to presume whether a diseased liver produces the lithogenic bile or the calculous disease of gallbladder causes structural damage to the liver or both are coincidental findings.

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