

Review Article

GALL BLADDER DISEASE IN PAKISTAN

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Gall Bladder Disease produces considerable morbidity and is a common cause of hospitalization. Complications of this disease have also been reported (Ahmad 1974; Chaudry 1960). Ahmad (1974) while operating on 15 selected cases of acute cholecystitis encountered 2 cases of free perforation and 4 of impending perforations. Chaudry (1960) reported one case of intestinal obstruction caused by gallstone.

In Karachi operations on biliary tract constitute 33.3% of all the abdominal operations performed at a local hospital from 1971-1976 (Yaqin et al., 1976) and 34.9% of 149 abdominal operations carried out at Jinnah Postgraduate Medical Centre during the last 6 months (Hassan et al., 1978). Amiruddin (1964) from Lahore reported an increase from 20 to 400 cholecystectomies a year which could hardly be accounted for by improved methods of diagnosis and more people seeking medical advice. Being a common and serious problem, an attempt was made to define its clinical and biochemical features by reviewing the work of various workers from different provinces of Pakistan.

Clinical Pattern

Cholelithiasis appears to be a disease of young multiparous females (Table I), 75-80 per cent of the cases were between 20-50 years of age in all 3 provinces. Average age varied between 39.4-40.3 years (Yaqin et al., 1976; Hassan and Zuberi, 1977). Average age reported from the West was between 47.5 years to 53.6 years (Gunn and Kedde, 1972; Yaqin and Hadfield, 1970).

Occurrence of disease at younger age may be due to early marriages and multiple pregnancies (Hassan et al., 1976). Mean parity being 5-6.1 (Yaqin et al., 1976; Hassan et al., 1976). High female to male ratio was noted in all 3 series (Table I). Diabetes was reported in 8% from Karachi (Hassan et al., 1976) and family history of gallstones was obtained

from 3% and 11% of patients from Lahore (Amiruddin 1964) and Karachi (Hassan et al. 1976) respectively.

Table I: Preexisting Symptoms of Gallbladder Disease

Symptoms	Karachi (Hassan et al., 1976)	Karachi (Yaqin et al., 1976)	Lahore (Amirud- din 1964)
Age (Years)	40.3 (15-80)	39.4 (20-70)	— (9-85)
Cases between 20-50 yr.	75%	78%	80%
Parity	6.1	5	6
F : M	7:1	5.7:1	4.7:1
F/H/O Gall- stones	11%	—	3%
H/O Diabetes	8%	—	—

Obesity was not a prominent feature in our patients, average weight, being 113 lbs (Hassan et al., 1976). In Karachi only 25%—30% of the patients were overweight (Hassan et al., 1976; Yaqin et al., 1976). In Lahore too where females are generally obese only 40% of the patients were overweight (Amiruddin 1964). Jaundice was detected in 15-16% of the cases (Yaqin et al., 1976; Hassan et al., 1976). A high frequency of palpable gall bladder was reported in one of the Karachi series (Hassan et al., 1976) and they attributed this to mæcocolic or adhesions of the omentum to the gall bladder due to repeated acute attacks of cholecystitis.

Biochemical Pattern

Biochemical pattern reported from Karachi (Hassan et al., 1976) shows slight disturbances of transaminases and a significant elevation of alkaline phosphatase (Table II).

Table II: Cholelithiasis Biochemical Investigations

Investigations	Mean $\pm$ S.E. (Range)
Bilirubin total mg%	2.22 $\pm$ 0.31 (0-32.75)
Bilirubin conjugated mg%	1.5 $\pm$ 0.28 (0-23)
Alkaline Phosphatase B.L.U.	4.8 $\pm$ 0.30 (0-2.3)
SGOT mu/ml	21.26 $\pm$ 2.02 (1-100)
SGPT mu/ml	14.22 $\pm$ 1.88 (3.0-8.2)
Calcium mcq/L	5.51 $\pm$ 0.61 (3.0-8.2)
Cholesterol mg%	237.44 $\pm$ 5.77 (100-461)
Total lipids mg%	715 $\pm$ 17.7 (300-990)
Phospholipids mg%	160 $\pm$ 5 (80-250)
Triglycerides mg%	189 $\pm$ 10.1 (80-250)

Lipid Pattern

Total lipids, triglycerides, cholesterol and phospholipid levels were estimated by Hassan et al. (1979) in the serum of patients and control subjects. A significant elevation was observed in serum triglycerides and cholesterol. Phospholipid values were the same in both the groups (Table III).

Table III: Lipid Values in Controls and Patients

Investigations	Controls Mean $\pm$ S.E. (Range)	Patients Mean $\pm$ S.E. (Range)	P Value
Total Lipids	579 $\pm$ 19.0 (390-800)	715 $\pm$ 17.7 (380-990)	< .001
Cholesterol	205 $\pm$ 8.3 (130-250)	238 $\pm$ 6.0 (145-390)	< .01 < .001
Phospholipids	167 $\pm$ 7.2 (100-250)	160 $\pm$ 5.0 (80-250)	< insignificant
Triglycerides	90.5 $\pm$ 10.4 (20-230)	194 $\pm$ 9.8 (30-300)	< .001

Note: All values are expressed as mg/100 ml of sera. Ranges are expressed in parenthesis.

Plasma triglycerides and cholesterol are responsive to changes in diet (Fredrickson 1976). High consumption of carbohydrate and saturated fat and low intake of protein was reported from Lahore (Amiruddin 1964) and Karachi (Hassan et al., 1979).

Biliary Lipids

While comparing the Lipids in hepatic and gall bladder bile Hassan et al. (1979) noted no significant difference in the composition of the two. Gall bladder bile was low in cholesterol (Table IV). This may be due to precipitation of cholesterol which probably is facilitated by biliary stasis, delayed gall bladder emptying due to repeated pregnancies and infection, as majority of the stones were of mixed infective type (Maqsood et al., 1976).

Table IV: Biliary Lipids

Investigation	Total No	Gall bladder bile Mean $\pm$ S.E. (Range)	Hepatic Bile Mean $\pm$ S.E. (Range)
Total lipid	29	119.85 $\pm$ 10.76 (40-260)	144 $\pm$ 10.42 (60-280)
Cholesterol	29	7.80 $\pm$ 0.42 (2.5-12)	9.25 $\pm$ 0.58 (3-13.5)
Phospholipid	29	17.7 $\pm$ 0.90 (1.4-25)	16.47 $\pm$ 0.67 (10-24)
Triglycerides	29	1.22 $\pm$ 0.13 (0-2.5)	0.97 $\pm$ 0.15 (0.3-3)

Note: All values are expressed as mg/ml of bile.

Stones

Morphological typing of stones was reported in two series. In Karachi study majority of the stones were of mixed type (Maqsood et al., 1976) while that in Lahore 57.5% were mixed and 40.6% of cholesterol type (Amiruddin 1964) as shown in Table V. Simultaneous estimation of cholesterol, calcium and bilirubin was done in serum and gallstones of 47 cases by Maqsood et al. (1976). An inverse relationship was observed between serum and stone cholesterol level and a direct relationship between bilirubin level of the two (Maqsood et al., 1976). Composition of various types of calculi was determined by Microchemical (Table VI) and Histochemical analysis (Table VII) as reported by Maqsood et al. (1977) and Sadrudin and Zuberi (1977) to highlight the probable etiology of lithogenesis. Centre was composed chiefly of calcium, bilirubin and protein and the periphery of cholesterol, fat and mucoprotein. Composition of centre indicates infective (Maqsood et al., 1977) and peripheral deposition of cholesterol is probably influenced by dietary habits or some abnormalities of lipid metabolism (Hassan et al., 1978).

Culture of Gallbladder Wall,

To determine the frequency and type of infection, Gall bladder wall, bile and gallstones were cultured by Yaqin et al. (1978) and Amiruddin (1964) and stones alone by Farooki (1971) as shown in Table VIII.

Positive cultures were obtained in 9(25.7%) by Yaqin and Sultan (1978) 28(28%) by Amiruddin (1964) and 8(23%) by Farooki (1971). Percentage of positive cultures would probably have increased if anaerobic cultures were also performed. Commonest organism identified in all 3 studies was E. Coli. Other organisms are given in Table IX.

Table V: Type of Stones

Stones	Karachi Maqsood et al. (1976)	Lahore Amiruddin (1964)
	No. (%)	No. (%)
Mixed	41(87.5)	92(57.5)
Cholesterol	4(8.5)	65(40.6)
Pigment	2(4.2)	2(1.25)
Calcium Carbonate	—	1(0.62)

Table VI: Microchemical Analysis of Gallstones

Constituents	Mixed, Stones (26)		Cholesterol Stones (2)		Pigment Stones (3)
	Centre No. (%)	Periphery No. (%)	Centre No. (%)	Periphery No. (%)	Powder
Protein	22(84.62)	11(42.31)	Nil	Nil	1(33.33)
Calcium	18(69.23)	26(100)	2(100)	1(50)	2(66.67)
Bilirubin	26(100)	26(100)	1(50)	—	3(100)
Cholesterol	16(61.54)	26(100)	2(100)	1(150)	1(33.33)

Table VII: Histochemical Analysis of Gallstones

Constituents	Mixed infective stones (26)			Cholesterol Stones (2)		
	Centre No. (%)	Intermediate No. (%)	Periphery No. (%)	Centre No. (%)	Intermediate No. (%)	Periphery No. (%)
Cholesterol	7(26.9)	25(96)	25(96)	2(100)	2(100)	2(100)
Calcium	26(100)	2(98.6)	13(50)	2(100)	1(50)	1(50)
Mucoproteins	11(42.3)	18(96.2)	18(96.2)	1(50)	1(50)	1(50)
Fat	Nil(0.0)	18(96.2)	21(80.8)	Nil(0.0)	1(50)	2(100)

Table VIII: Results of Culture in Gallbladder Bile and Stones

Growth	Karachi (Yaqin et al., 1978) No. (%)	Lahore (Amiruddin 1964) No. (%)	Peshawar (Farooqi 1971) No. (%)
Sterile	26(74.2)	72(72)	10(28.5)
Pathogenic growth	9(25.7)	28(28)	8(23)
Gallbladder	9(100)	28(100)	—
Bile	9(100)	26(98)	—
Stones	7(77.7)	21(100)	8(100)
Pathogenic growth	—	—	17(48.5)

Identical organisms were isolated from

Table IX: Carcinoma of Gall Bladder

Studies	Total Cases	Adenocarcinoma Sq.	Cell Carcinoma	Carcinoma	Total Cancer	Age	P:M
Karachi (Yaqin & Parmar, 1976)	94	4(66.6)	1(16.6)	1(16.6)	6(6.3)	44.5 (32 - 55)	5:1
Karachi (Hassan et al., 1978)	118	7(70)	2(20)	1(10)	10(8.4)	45.4 (30 - 60)	9:1
Karachi (Jafarey 1978)	482	22(68.7)	6(18.8)	4(12.5)	32(6.6)	—	—

gall bladder bile and stones and are therefore unlikely to be contaminant (Yaqin & Sultan, 1978).

The incidence of post operative complications is significantly higher in patients with positive cultures. As reported by Yaqin and Sultan (1978), 4 patients out of 9 developed post operative complications which responded well to appropriate antibiotic therapy. Routine bile culture may therefore help to reduce the morbidity and complications in patients undergoing operations for Gall bladder disease (Yaqin and Sultan, 1978).

Cancer

A high association of Gallstones and Gall-bladder cancer was observed by Yaqin and

Parmar (1976) and Hassan et al. (1978). No remarkable difference was observed in the clinical and biochemical pattern of benign and malignant disease of the Gallbladder (Hassan et al., 1978). Average age of the cancer patient varying between 44.5—45.4 year and majority of the patients being female (Yaqin and Parmar, 1976; Hassan et al., 1978) as shown in Table X.

Table X: Hepatic Abnormalities

Liver Changes	Hassan et al. (88) No. (%)	Yaqin et al. (100) No. (%)
Normal	48(54.5)	62(62)
Minimal Change	5(5.6)	2(2)
Cholestasis	12(13.6)	4(4)
Fatty change	8(9.1)	7(7)
Hepatitis	7(8.0)	6(6)
Cholangitis	1(1.2)	11(11)
Cirrhosis	1(1.2)	2(2)
Acute Biliary Obstruction	1(1.2)	—
Tuberculosis	1(1.2)	—
Biliary Infarction	—	1(1)
Supra Capsular Oedema	—	1(1)
Metastatic Carcinoma	4(4.6)	5(5)

A remarkably high frequency of gall-bladder cancer was reported from Karachi. Hassan et al. (1978) studying 188 cases operated for gallbladder disease at Jinnah Post-graduate Medical Centre encountered 10(8.4%) cases of histologically confirmed cancer. Same workers on retrospective analysis of 6 year record from Pathology Department of the same Centre detected 32 cancers among 482 surgically removed gallbladder sent to this department from various hospitals of Karachi, giving a frequency of 6.6% (Hassan et al., 1978). Of these 32 cancers 68.7% were squamous cell carcinomas, 18.8% adeno carcinomas and 12.5% of anaplastic variety (Jafarey 1978).

Yaqin and Parmar (1976) reported a frequency of 6.3%.

Early detection and removal of gallstones irrespective of the age might help to reduce the frequency of Gallbladder cancer.

Hepatic Abnormalities

Yaqin (1978) and Hassan et al. (1979) while studying associated hepatic abnormalities in cholelithiasis observed changes varying from minor to gross structural disturbances (Table X).

Normal liver was observed in approximately 50% of cases in both the series. According to Hassan et al. (1979) duration of symptoms and age of the patients seem to influence the severity of histological changes in liver indicating early surgical intervention as an important step in reducing the morbidity of the disease.

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