

ASSOCIATION OF GALLSTONE DISEASE RISK WITH SERUM LEVEL OF ALKALINE PHOSPHATASE

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ABSTRACT

OBJECTIVE: To see the relationship between personal history and blood chemistry of preoperative gallstone patients with gallstone disease.

DESIGN: A Cross sectional study.

SETTING: Liaquat University Hospital Jamshoro for a period of three years.

PATIENTS AND METHODS: Gallstone patients admitted for the treatment during January 1999 to December 2001 were studied with the help of a predesigned proforma for recording the personal history and blood chemistry results of the individual patients.

RESULTS: A total of 172 patients was studied. Majority (85.33%) of the gallstone patients was females. Females under 45 years age (65.38%) and females having more than three children (70.55%) were more prone to develop gallstones than the respective female group of over 45 years age (34.62%) and having upto three children (29.45%). Past history of the gallstone patients revealed that 53.5%, 23.2%, and 9.3% of the cases had jaundice, diabetes mellitus and renal stones respectively. Blood chemistry of the patients showed that 18.2%, 2.8%, 3.44% and 4.1% had respectively hyperbilirubinemia, hyperuremia, hyperglycemia and hypoglycemia. Alkaline phosphatase and alanine aminotransferase levels in plasma and total leucocyte count in blood were raised in 17%, 39.7% and 9% cases respectively. However, low plasma alkaline phosphatase levels were also found in 31.1% gallstone patients. The levels of plasma alkaline phosphatase were significantly high ($p < 0.01$) in females than in males, and in females over 45 years age than under 45.

CONCLUSION: Risk of gallstone disease in females is associated with serum alkaline phosphatase level.

KEY WORDS: Cholelithiasis. Blood. Chemistry. Cholesterol. Bilirubin. Sex.

INTRODUCTION

Gallstone disease is a common gastrointestinal problem in day to day practice. Cholesterol and bilirubin, either singly or together in various proportions, are the main constituents of human gallstones which are formed when these constituents precipitate in bile¹⁻³, possibly aided by certain promoting agents⁴⁻⁷.

The epidemiological aspects of cholelithiasis and the clinical presentation of gallstone patients treated at our setup have not yet been reported. Although, clinical history is taken and blood variables such as bilirubin, alanine aminotransferase (ALT), alkaline phosphatase (liver function tests), haemoglobin (Hb), erythrocyte sedimentation rate (ESR), total leukocyte count (TLC), urea and sugar are routinely measured for every gallstone patient treated in this hospital, the association of these parameters in gallstone disease has not been assessed.

Thus, present study was designed to investigate the relationship between the personal history and blood

chemistry of preoperative gallstone patients with gallstone disease.

PATIENTS AND METHODS

A total of 172 gallstone patients admitted for treatment at Liaquat University Hospital Jamshoro, Sindh, Pakistan during 1999 – 2001 were studied with respect to clinical history and blood chemistry of the cases.

Clinical history and examination of every patient was taken and recorded in a proforma developed for that purpose. Preoperative evaluation of blood parameters of patients included measurement of TLC, Hb, ESR, urea, sugar, bilirubin, alanine aminotransferase and alkaline phosphatase which were measured by Neubar Chamber Counting Method, Sahli's Method, Wester Green Method, Sentinel Kit (Italy), Centronic Kit (Germany), Kit of Roche company (Switzerland) and BIO MT Diagnostic Kit respectively⁸⁻¹².

Data (Mean \pm SEM) for comparison of blood

parameters between two groups (females versus males, females having up to 3 children versus females having more than 3 children and females under 45 years age versus females over 45 years age groups) were calculated by using standard methods. Student's t- test was used to estimate the level of significance at 95% confidence interval between the groups¹³.

RESULTS

Personal history of the cases revealed that 53.5% patients had jaundice and 9.3% had renal stones (**Table I**). There appeared to be no clear relationship between gallstone disease and addiction of patients with smoking, tea, chewing of Paan/ Supari/ Ghutka and use of Nass / Naswar (**Table II**).

Figure I shows gender wise comparison of gallstone patients treated at Hospital. No change was observed in blood parameters between two sexes except ALP which was higher in females than males (**Table III**). Since after 45 years age females experience menopause, hence, to see the effect of menopause (if any) on the frequency of occurrence of gallstones, females were divided into two age groups; under 45 years and over 45 years (**Figure II**). Females before menopause could be seen to be at higher risk for formation of gallstones than the females who had experienced menopause. However, amongst the females of under 45 years age, the risk for formation of gallstones increased with the number of pregnancies (**Figure III**). Of the gallstones patients, 18.2% had hyperbilirubinemia (serum bilirubin level greater than 1.0 mg/dl), 2.8% had hyperuremia (blood urea level greater than 50mg/dl), 3.44% hyperglycemia (blood glucose level greater than 110 mg/dl) and 4.1% had hypoglycemia (blood glucose level less than 80 mg/dl). Forty percent of the female

and 36% of the male gallstone patients were anemic. Blood TLC and plasma enzyme levels for ALT and alkaline phosphatase were raised in 9%, 39.7% and 17% gallstone patients respectively.

Tables IV and **V** respectively show the comparison of blood parameters between female gallstone patients divided on the basis of two age groups, and on the basis of number of children. The two patient age groups were comparable except for the levels of alkaline phosphatase which was found to be significantly higher ($p < .003$) in females over 45 years age as against the females under 45 and higher in females having more than three children than the females having up to three children.

Factor	Number of Patients (n=172)	Percentage
Jaundice	92	53.5
Typhoid	12	7
Hernia	12	7
Diabetes	40	23.2
Renal Stones	16	9.3

TABLE I: FACTORS ASSOCIATED WITH PATIENTS HAVING GALLSTONES

Addiction Type	Number of Patients (n=172)	Percentage
Smoking	24	14.0
Paan/ Chalia/Ghutka	21	12.2
Nass/Naswar	7	4.1
Tea	3	1.7
Non-addicted	117	68.0

TABLE III: GENDER WISE COMPARISON OF BLOOD PARAMETERS IN GALLSTONE PATIENTS

Variable	Females		Males		*P-Value
	N	Mean \pm SEM	N	Mean \pm SEM	
Bilirubin (0 - 1mg/dl)	117	1.32 \pm 0.23	20	1.16 \pm 0.30	0.67
ALT (4 - 24U/L)	95	35.8 \pm 2.9	17	35.4 \pm 5.9	0.95
ALP (100 - 290U/L)	94	178 \pm 14	13	120.1 \pm 17	0.014
Hemoglobin (14-18g/dl males, 11.5-16 females)	128	11.13 \pm 0.13	22	11.60 \pm 0.36	0.24
ESR (0-9mm/hour males, 0-15 females)	123	32.9 \pm 2.4	22	25.2 \pm 3.7	0.09
TLC (4000-11000cum)	123	9540 \pm 570	22	9760 \pm 870	0.84
Urea (10 - 50mg/dl)	113	29.1 \pm 1.1	16	32.5 \pm 3.2	0.32
Sugar (75 - 110mg/dl)	125	108.5 \pm 3.3	21	105.4 \pm 75	0.71

* Significant when $P < 0.05$

TABLE IV: COMPARISON OF BLOOD PARAMETERS BETWEEN FEMALE GALLSTONE PATIENTS OF TWO AGE GROUPS

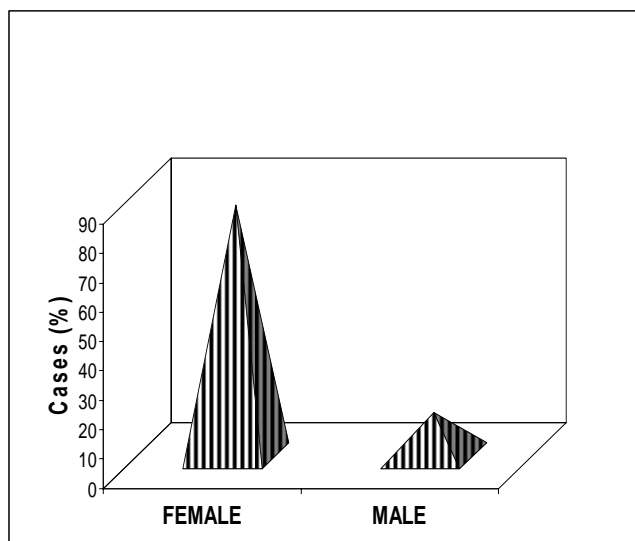
Variable	Under 45 years age group		Over 45 years age group		P – Value
	N	Mean ± SEM	N	Mean ± SEM	
Bilirubin (0 - 1mg/dl)	75	1.03 ± 0.15	42	0.79 ± 0.08	0.88
ALT (4 - 24U/L)	66	43.8 ± 5.3	32	33.4 ± 5.2	0.74
ALP (100 - 290U/L)	61	144 ± 9.3	34	168.9 ± 15	0.003
Hemoglobin (11.5-16g/dl)	85	11.02 ± 0.18	45	11.47 ± 0.16	0.33
ESR (0-15mm/hour)	81	33.2 ± 2.9	42	32.1 ± 4.5	0.63
TLC (4000-11000cum)	79	9370 ± 650	44	9860 ± 1100	0.89
Urea (10 – 50mg/dl)	73	27.6 ± 1.3	40	31.9 ± 2.1	0.70
Sugar (75 – 110mg/dl)	81	106.3 ± 3.5	44	112.6 ± 6.7	0.08

TABLE V: COMPARISON OF BLOOD PARAMETERS BETWEEN FEMALE GALLSTONE PATIENTS WITH UPTO 3 OR MORE THAN 3 CHILDREN

Variable	Females having up to 3 children		Females having more than 3 children		P – Value
	N	Mean ± SEM	N	Mean ± SEM	
Bilirubin (0 - 1mg/dl)	38	0.94 ± 0.22	85	0.81± 0.06	0.54
ALT (4 - 24U/L)	31	32.1 ± 4.8	72	34.5 ± 2.8	0.66
ALP (100 - 290U/L)	32	142.7 ± 15	68	184 ± 18	0.079
Hemoglobin (11.5-16g/dl)	43	10.91 ± 0.36	100	11.36 ± 0.11	0.23
ESR (0-15mm/hour)	41	31.9 ± 3.5	93	28.9 ± 2.5	0.49
TLC (4000-11000cum)	43	10780 ± 1200	94	9150 ± 540	0.21
Urea (10 – 50mg/dl)	36	27.56 ± 1.5	84	31.2 ± 1.4	0.084
Sugar (75 – 110mg/dl)	43	106.8 ± 7.4	94	110.2 ± 3.1	0.67

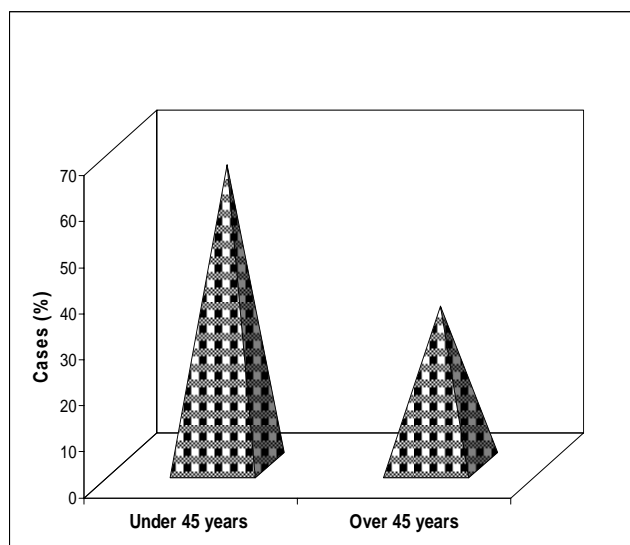
TABLE II: ADDICTION AND GALLSTONE RELATIONSHIP

FIGURE I: GENDER WISE COMPARISON OF



GALLSTONE PATIENTS TREATED AT LIAQUAT UNIVERSITY HOSPITAL DURING 1999 TO 2001

FIGURE II: COMPARISON BETWEEN



TWO AGE GROUPS OF FEMALE GALLSTONE PATIENTS

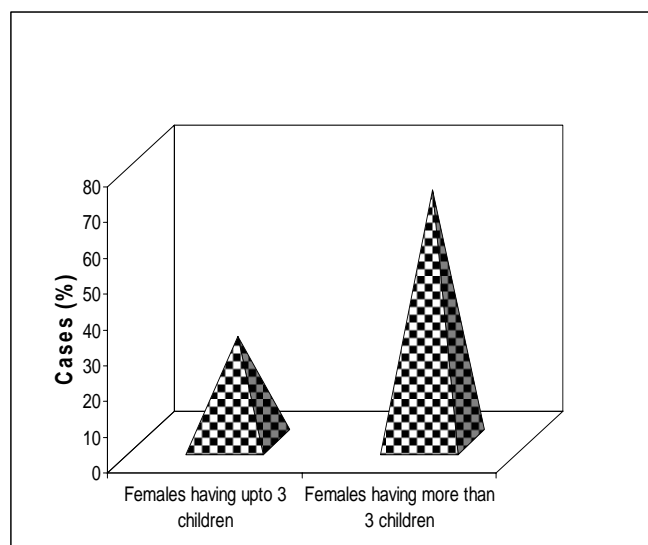


FIGURE III: COMPARISON BETWEEN TWO GROUPS OF FEMALE GALLSTONE PATIENTS DISCUSSION

Females are far more prone to develop gallstones than the males, and our this finding is in full agreement with the reports available in literature¹⁴⁻¹⁶. Several workers have reported two to three fold increase in the incidence of gallstones in diabetic patients, whereas others have failed to find a significant association¹⁷⁻²¹. Gallbladder emptying abnormalities found in diabetic patients may predispose to gallstone formation²².

The significant increase in the levels of alkaline phosphatase in females in our study might be owing to increased bone turn over or simultaneous formation of osteoid in these females than males²³.

Present study showed that the risk for formation of gallstones in females increased with the number of pregnancies. This finding is consistent with the report of Tsimoyiannis et al²⁴ and supports the suggestion that during pregnancy the levels of body mass index, low density lipoproteins, serum cholesterol and triacylglycerols increase which in turn increase the chance for the formation of gallstones. Moreover, there are reports, which suggest that gallbladder emptying becomes poor during pregnancy owing to the effect of progesterone^{25,26}. This sex-related difference in the incidence of cholelithiasis could also be explained on the basis of pregnancy and female sex hormones. As female sex hormones are known to increase blood cholesterol level, hence, females of child-bearing age have higher cholesterol levels than

males of same age group²⁶⁻³¹. This is also supported by the previous finding³² for this area that pure cholesterol stones were more common in females than males.

CONCLUSION

Alkaline phosphatase levels in blood correlate well with the increased risk for the formation of gallstones in females versus males. Females with the increased risk are of under 45 years age and those having more than three children.

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