

PATHO-MORPHOLOGIC CLASSES OF GALLSTONES, THEIR FREQUENCY AND ETIOLOGICAL FACTORS IN PESHAWAR, KP, PAKISTAN

Rubbia Afridi,^a Faryal G Afridi,^a Zufishan Batool^b

ABSTRACT

Introduction: Gallstones are a common clinical condition, presenting as acute or chronic cholecystitis. Various risk factors have been implicated in the development of a variety of gallstones in different populations. The present study aimed to determine the frequency of various morphologic forms of gallstones in relation to age, sex, occupational status and lifestyle of patients presenting at a tertiary care teaching hospital of Peshawar.

Materials & Methods: This descriptive study was conducted at the Surgical Unit, Khyber Teaching Hospital, Peshawar, KP, Pakistan, from October 2011 to June 2012. Gross morphologic aspects (including the number, size, color, shape, consistency and surface) of gallstones were studied in gallstones retrieved from 150 patients over a period of 9 months and were classified on the basis of their morphology.

Results: A total of 150 patients were included. 114(76%) were admitted through emergency and 36(24%) through clinic. Based on stone morphology, cholesterol based stones (pure cholesterol stones, mixed stones and combined stones) were the most common type (47.33%) closely followed by pigment stones (46%). A majority of our patients (84%) were in the age bracket of 30-50 years with a clear female predominance (92%).

Conclusion: Pigment stones are as frequently prevalent as cholesterol stones in our population indicating infection to be a factor as common and important as diet and sedentary lifestyle.

Key words: Cholecystitis; Cholecystectomy; Gallstones; Cholesterol; Gall Bladder.

Author Designation & Affiliation

^a Department of Surgery, Khyber Teaching Hospital, Peshawar, KP, Pakistan

^b Department of Pathology, Rehman Medical College, Peshawar, KP, Pakistan

INTRODUCTION

Gall stone disease is a common pathologic condition causing significant morbidity worldwide.¹ The overall reported prevalence of gallstone disease is 10-15%; however there is

geographical variation, the prevalence being higher in the western population such as >10% reported in one study focusing on medium income socioeconomic groups,² 7.9% vs 16.6% in American men and women respectively,³ 5.4 % in the Thai population⁴ and 9.1% men versus 8.6% women in China.⁵

Etiology of these stones is a complex interaction between environmental factors, genetic predisposition⁶ and ethnic background.³ Strong association is reported with obesity, female sex, increasing age and family history.⁷ Similar results are reported by Schafmayer et al⁸ where female sex and higher BMI were found to be associated closely with the presence of cholesterol as a main substrate. Other factors include pregnancy, oral contraceptive or hormone replacement therapy, cholesterol lowering drugs, gallstones via increased biliary cholesterol elimination, rapid weight loss (increased fat mobilization from body with subsequent increased cholesterol secretion into bile) and fasting.⁷ Pregnancy however, was ruled out as an important risk factor for gallstone disease in a study by Walcher T et al⁹ conducted in Germany although this needs further investigation.

Biochemistry of Gallstones

Gallstones are broadly classified into cholesterol and pigment stones with a further subdivision into pure, mixed and/or combination stones.¹⁰ Pigment stones are further classed into black stones and brown (calcium bilirubinate) stones.¹⁰ Cholesterol gallstones are composed of cholesterol, calcium, phosphate, carbonate and proteins⁷ and result from concretion of normal or abnormal bile constituents especially if bile is

supersaturated with cholesterol and/or bilirubin or deficient in bile salts. Biliary stasis due to any cause may also cause these stones to develop. Defective bilirubin conjugation is the major underlying mechanism of pigment stone deposition.¹¹ These stones may contain a proportion of both heavy and trace metals.¹²

Appearance of microscopic crystals of cholesterol monohydrate in supersaturated bile is thought to be the initiation event in gallstone formation, followed by growth into cholesterol plates eventually aggregating to form a stone nidus. This leads to subsequent stone growth by cholesterol accretion in an orderly fashion particularly influenced by pro or anti-nucleating proteins.¹³

Patterns of growth differ among different sets of stones governed by the nature of the underlying surface although these factors remain unclear.¹⁴ It is probably a process of many years whereby any appreciable mass (grams) of single or multiple gallstones is formed; the growth rate seems to depend on the lipid contents and the Cholesterol Saturation Index (CSI) of the bile. Arachidonic acid metabolites play a significant role in gall bladder physiology and disease via influencing muscle contraction and controlling mucous secretion and water transport.¹⁵

Gross morphology of Gallstones

Cholesterol stones are usually solitary, large stones with a yellow or yellowish brown color and a finely granular hard external surface. They are usually radiolucent but increasing calcium carbonate, phosphates and bilirubin may render them radio-opaque. Pigment stones occur as small multiple hard stones and can range from being dark brown to black depending on the percentages of unconjugated bilirubin, calcium carbonate, calcium phosphate and mucin glycoproteins. Up to 75% of these are radio opaque. When black they are harder with a rough spiculated exterior; however the browner

ones are softer and laminated. They may even be greasy or soap like. Gallstones occur in various combinations, there may be just one large stone or several tiny stones or almost any combination. Singly occurring stones are usually larger and harder than multiple and smaller stones.

Gallstone disease is common in Pakistan comprising of a significant load of patients seen in the emergency department and the elective setting. Although prevalence data is insufficient for our country, a previous study from Sindh has reported an overall incidence of 9%.¹⁶ No study reports a clear correlation between the various morphological classes of gallstones and patient factors. This study is aimed at investigating the correlation between gallstone morphology and patient factors especially age, sex and lifestyle in patients presenting to a major tertiary teaching hospital of Peshawar.

MATERIALS & METHODS

This descriptive study was conducted in surgical unit of Khyber Teaching Hospital (KTH) from October 2011 to June 2012 and includes 150 cholecystectomies performed over this time period. Patient demographics and clinical details (mode of presentation, presenting complaints, duration of complaints and examination for finding gallstones), investigative results and per-operative finding of gallstones were recorded on pre-designed Performa. Gallstones were collected per-operatively. Gross morphologic features of the retrieved stones were noted. These stones were then classified on the basis of their morphology. Data were analyzed for frequencies and percentages.

RESULTS

Out of the 150 patients included in this study 114 (76%) were admitted through emergency and only 36 cases (24%) were admitted through the out-patient departments showing a clear majority of emergency presentations. A total of

138 (92%) out of the 150 patients studied were females (Table 1). Male to female ratio was 1:11. One hundred and twenty (86.5%) of these 138 were housewives with sedentary life styles, 18 (13.04%) being working ladies. All male patients were full time employed. One hundred

and twenty six (84%) patients were in the 30-50 year age bracket. Twelve (8%) patients were aged less than 30 years with a similar number above 50 years. Only 6 patients (4%) were in their teens.

Table 1: Age and sex distribution of patients (n=150)

S #	Variables		Frequency	Percentage
1.	Gender	Male	12	08
		Female	138	92
2.	Age (Years)	<30	12	08
		30-50	126	84
		>50	12	08

Forty eight cases (32%) of solitary stones were encountered (Table 2). The rest 102(68%) were multiple. Solitary stones were mostly large in size i.e. 24(50%) being 2cm to an inch in size, 6(12.5%) being less than 2cm and 18(37.5%) being more than an inch in size. Of the 102 cases of multiple stones 87(85.29%) were multiple small stones and in 15(14.70%) cases a combination of large and small stones was

noted. Multiple stones were all very small in the majority of cases, with 60 cases (58.82%) having all stones less than 1cm in size. Twenty seven (26.47%) were 1-2cms in size whereas 15(14.70%) of the multiple stones were of varying size combinations. The multiple stones which existed in combinations varied greatly in size from 5mm-1.5cm small stones present with large stones an inch or more in size.

Table 2: Gallstone Characteristics (n=150)

Variables		Frequency	Percentage	
Types	Solitary	48	32.0	
	Multiple	102	68.0	
Sizes	Solitary n=48	> 1 inch	18	37.5
		2 cms - 1 inch	24	50.0
		< 2 cms	6	12.5
	Multiple n=102	<1 cm	60	58.82
		1-2 cms	27	26.47
		Varying Size Combinations	15	14.70

Of the 48 cases of singly occurring stones 12 (25%) were small yellow rounded with smooth surfaces and regular contours and were grouped into the mixed variety of gallstones (Table 3). Nine (18.75%) stones were large yellow rounded with rough surfaces and irregular contours and were classified as pure cholesterol stones,

27(56.25%) stones were small black hard with irregular contours and rough surfaces and were thus labeled pigment stones.

Of the multiply occurring stones 15(14.7%) were classified as combined (Table 3), 32(31.37%) as mixed (yellow or greenish yellow triangular faceted stones with smooth surfaces

and regular contours), 49(48.03%) as pigment stones. Six cases (5.88%) were small hard grains classified as calcium stones. The interior of all

yellow stones was found to be lamellate and cream/whitish cream in color.

TABLE 3: Distribution of morphologic classes of types of Gallstones (n=150).

Type of stones	Class	Frequency	Percentage
Solitary (n=48)	Pure Cholesterol Stones	09	18.75
	Mixed Stones	12	25.0
	Pigment Stones	27	56.25
Multiple (n=102)	Combined Variety	15	14.7
	Mixed Stones	32	31.37
	Pigment Type	49	48.03
	Calcium	06	05.88

Twenty one (43.75%) of the solitary stones were yellow/creamy yellow in color (cholesterol based stones) and 27(56.25%) were black/brown (pigment stones) (Table 4). Multiple stones were yellow in 30(29.41%) out of a total of 102 cases, 09 of 102(8.82%) were brown/greenish black (mixed or pigment stones) and 48 of 102(47.05%) were black in color. The stones occurring in combinations were mostly black i.e. 10/102(9.80%) with the remaining 5(4.90%) having varying colors of the comprising multiple

stones. The consistency of these stones varied considerably (Table 4).

Eighteen of twenty one (85.71%) yellow single stones were hard, only 3 being soft and easily breakable (14.28%). In contrast all twenty seven (100%) solitary black stones were very hard and rough in texture. The multiple yellow stones were soft and easily crumbling in all of the 30 (100%) cases whereas multiply occurring black stones were soft in only 6 out of forty eight (12.5%) cases (Table 4).

Table 4: Distribution of the Gallstones on the basis of Color and Texture

Type	Color	Frequency	Percentage	Consistency		
				Hard	Soft	
Solitary (n=48)	Yellow/Creamy	21	43.75	18	3	
	Black/Brown	27	56.25	27	0	
Multiple (n=102)	Multiple in one size (n=87)	Yellow	30	29.41	0	30
		Brown/Greenish Black	09	08.82	6	3
		Black	48	47.05	42	6
	Varying Size Combinations (n=15)	Black	10	9.80	Varying	
		Varying Colors	5	4.90		

DISCUSSION

Unlike the results of this study, in the west the majority of gallstones are cholesterol stones (80%) and the remaining being mixed, combined and pigment types.¹⁷ In a study conducted by Schafmayer et al⁸ in Germany only 2% stones were found to be pigment as against 95% of stones containing cholesterol as the main substrate. Bilirubin and bilirubinate were present in 30% and calcium was detected in 10% of the cases in their study. This is in contrast to the current study which shows a similar prevalence of pigment and cholesterol stones as discussed above. Ho CY et al report a similar high occurrence of common bile duct pigment stones¹⁸ advocating bacterial infection to be a very important cause of gallstone disease in the Far East.

The present study also showed that in our setup infection leading to pigment stones is as important a causative factor as is cholesterol supersaturation and gall bladder hypomotility. Infection was also found to be a leading cause of gallstones in South India as evidenced by predominance of pigment calcium stones, in a study conducted by Amin et al.¹⁹

A majority of patients in our study were between 30-50 years showing that the average age of our gallstone patients, like that in the subcontinent, is at least a decade younger than the western population.⁵ Male to female ratio in our study was 1:11 which is in accordance with the results published elsewhere in the world showing a clear female preponderance.²⁰ Female sex hormones, sedentary habits and lifestyles of most women may be the factors responsible for this predominance.^{21,22} In addition with established association of infective causes, e.g. hepatitis and *H. pylori* reported elsewhere, it is imperative to exclude these causes in a patient presenting with Cholecystitis.⁵

CONCLUSION

Gallstones and related pathologies accounted for a large number of elective as well as emergency presentations in the hospitals studied. Although genetic factors may play a role in etiopathogenesis of gallstones, patient and environmental factors are as important. Steps for primary prevention of gallstone formation in susceptible individuals through lifestyle changes and dietary modifications remain a major challenge, especially in our people with limited knowledge and resources.

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Corresponding Author

Dr. Rubbia Afridi, Department of Surgery, Khyber Teaching Hospital, Peshawar, KP, Pakistan.

Email: rubbiaafridi@gmail.com

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