

MORPHOLOGICAL STUDY OF GALLSTONE- A REVIEW

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ABSTRACT:

Gall stone disease is a common health problem and carcinoma of gall bladder is the fifth commonest GI malignancy world wide. Gallstones afflict 10% to 20% of adult populations in developed countries. Gallstone disease is a common surgical problem requiring cholecystectomy. It is known to produce diverse histopathological changes in the gallbladder ranging from acute or chronic inflammation to metaplasia and even malignancies. The aim of the present study is to estimate various gallstone characteristics like morphological type, number, size and volume association with age and sex ratio. These parameters have been reviewed and analyzed in detail as a part of Ph.D thesis work of the second author under first author. Our objective is to find out the morphology of cholelithiasis.

Keywords: Gallbladder, Cholecystectomy, Cholelithiasis, Bile.

1. INTRODUCTION:

1.1 GALL BLADDER (cholecyst or biliary vesicle):

It is a flask (pear) shaped blind-ending diverticulum or hollow viscus (sac), with a muscular wall. In life, it is grey-blue in colour, situated obliquely in a non peritoneal fossa on the under surface of the right lobe of the liver. It extends from the right end of porta hepatis to the inferior border of liver. It is 7 - 10 cm (3 to 4 inches) long, 3-4 cm broad at its widest part and about 30 to 50ml in capacity¹. The gallbladder is divided into the following regions: fundus, body and neck. The portion of body that joins the neck is referred to the infundibulum; sometimes there is a small bulge in this region, known as Hartmann pouch¹. Neck continues as cystic duct and is marked by a constriction. The gallbladder varies in size and shape. The fundus may be elongated and highly mobile. Rarely, the fundus is folded back upon the body of the gallbladder and is called Phrygian cap, on ultrasound this may be wrongly interpreted as an apparent septum within the gallbladder¹.

1.2 FUNCTION:

Reservoir of bile.

Concentrates bile (5to10 times).

Bile helps in emulsification and absorption of fats.

Bile helps in eliminating bilirubin, a product of haemoglobin metabolism.

1.3 HISTOLOGY:

Inside out gallbladder presents 4 layers:

1. Mucosa layer-

The lining epithelium presents single layer of tall columnar cells having basal nuclei and lightly stained cytoplasm with occasional small apical vacuoles². Ultrastructurally these cells have numerous apical microvilli with filamentous glycocalyx and core rootlets.³ Epithelium also shows pencil cells (smaller, darkly staining columnar cells) and basal cells and myoepithelial cells are absent.

The lamina propria contains loose connective tissue, fenestrated capillaries, small vessels, nerves, some diffuse lymphatic tissue and a scattering of IgA containing plasma cells⁴.

Muscularis mucosa is absent.

The mucosa exhibits numerous interlacing tiny temporary irregular folds which are varying in size and shape gives honeycomb appearance and disappears when the gallbladder is distended with bile. In the neck of the gallbladder, these folds (containing smooth muscle) coalesce to form the spiral valves of Heister, where gallstones are commonly gets stuck.

2. Sub mucosa layer is absent.

3. **Muscle layer-** Large amount of elastic fibers are intermingled with the smooth muscle fibers which

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are arranged in circular, longitudinal and in oblique manner so this layer is also called fibromuscular layer.

4. Serosa layer- Covers its entire surface except the hepatic, where an adventitia attaches it to the liver. The gallbladder has a wide layer of perimuscular loose connective tissue which contain blood vessels, lymphatic and nerves.

1.4 HISTORY OF GALLBLADDER:

Roman anatomist Galen – He identified the gall bladder and spleen as the two crucial subsidiary organs of the liver. All three organs worked together to produce and store three of the four humors of the body: blood (liver), yellow bile (gall bladder) and black bile (spleen).

Berengario - Suggested that the gallbladder regulated the emotions by being a repository for gall.

Harvey described the liver as a "noble organ" in 1653 and the spleen as an "ignoble organ" the gall bladder as "a very long pear compressed from base into neck".

Ayurveda - The doshas are biological energies found throughout the human body and mind. Three Doshas: Vata, Pitta, and Kapha. Pitta of Fire and Water translates as "the energy of digestion and metabolism in the body"

1.5 SOCIETY AND CULTURE:

To have 'gall' is associated with bold behaviour, whereas to have 'bile' is associated with bitterness⁵. In the China, the gallbladder is associated with courage and a plethora of related idioms, including using terms such as "a body completely of gall to describe a brave person, and "single gallbladder hero" to describe a lone hero⁶.

1.6 COMPARATIVE ANATOMY:

Most vertebrates have gallbladders, whereas invertebrates do not. However, its precise form and the arrangement of the bile ducts may vary considerably. Several species of mammals (including horses, deer, rats, and various laminiis)⁷ and several species of birds lack a gallbladder altogether, as do lampreys⁸.

2. REVIEW OF LITERATURE:

Cholelithiasis: Gallstones are hard; pebble like deposits in the gallbladder. The word cholelithiasis derived from greek word (chol = bile + lith = stone + iasis = process). Gallstones generally form because the bile is saturated with either cholesterol or bilirubin then

bile undergoes supersaturation, nucleation and precipitation of cholesterol monohydrate crystals and growth to stone-size aggregates⁹. Initially there is always the formation of a biliary sludge which contains mucus gel, hydrophobic bile pigment, cholesterol- lecithin liquid crystals and solid cholesterol monohydrate crystals. The basic constituents being cholesterol, calcium bilirubinate and calcium carbonate. (Number of gallstones, Type of Gall Stone, Sex Ratio and Sample size are summarized in Table 1). On the basis of their composition, gallstones can be divided into the following types:

1) Pure gallstones (10%) -

Cholesterol stones- are single, large (2- 3 cm long), spheroidal to oval in shape and vary from light yellow to dark green or brown to bluish white in color, each often having a tiny, dark, central spot. To be classified as such, they must be at least 80% cholesterol by weight or 70%, according to the Japanese- classification system¹⁰ (Figure1: A). In the literature the reported incidence of this type of stone varies between 5.43 % to 17.3% (Table 1).

Pigment stones- are multiple, small (2-5 mm) and brown to jet black (dark) in color and comprise bilirubin and calcium salts that are found in bile. They contain less than 20% of cholesterol or 30%, according to the Japanese-classification system¹⁰ (Figure1: B). In the literature the reported incidence of this type of stone varies between 1.62 % to 20% (Table 1).

2) Mixed gallstones (80%) –

These are typically consists of 20–80% cholesterol or 30–70%, according to the Japanese- classification system¹⁰, calcium carbonate, calcium bilirubinate, palmitate phosphate and other bile pigments. Because of their calcium content, they are often radiographically visible. These are usually multiple, faceted, laminated and vary in size & numbers (Figure1: C). In the literature the reported incidence of this type of stone varies between 59 % to 90.8% (Table 1).

3) Combined gallstones (10%) –

These are characteristically large and single. They may have a pure nucleus with a mixed shell or the reverse. Barrel stones, a type of combined stone, are usually two in number, large and faceted on one surface and the thick walled gallbladder is closely wrapped around them (Figure1: D). In the literature the reported incidence of this type of stone varies between 0.54% to 25% (Table 1).

Pathophysiology-

Cholesterol gallstones develop when bile contains too much cholesterol and not enough bile salts. Besides a high concentration of cholesterol, two other factors are important in causing gallstones. The first is how often and how well the gallbladder contracts. Incomplete and infrequent emptying of the gallbladder may cause the bile to become over concentrated and contribute to gallstone formation. This can be caused by high resistance to the flow of bile out of the gallbladder due to the complicated internal geometry of the cystic duct¹¹. The second factor is the presence of proteins in the liver and bile that either promote or inhibit cholesterol crystallization into gallstones. In addition, increased levels of the hormone estrogen, as a result of pregnancy or hormone therapy, or the use of combined (estrogen-containing) forms of hormonal contraception, may increase cholesterol levels in bile and also decrease gallbladder movement, resulting in gallstone formation. Sequential cholecystographic studies and carbon-14 dating suggest that gallbladder stone grow at a rate of approximately 1-2 mm/ year and that they are usually present for 5-20 years before they are removed¹².

Number of stones: Gallstones are present in single, double and multiple numbers. In the available literature the incidence of single stone varied from 7 % to 39.6% cases, double stones in 8.8% cases and multiple stones from 51.6% to 93% cases. (Table 1)

Sex ratio: All the available studies suggest that the females are more prone to gallstone than males. In the

review male and female ratio (M: F) range between 1:1.4 to 1:7.3 (Table 1).

Size: The maximum gallstone size of 4.0 cm was observed in cases of malignancy (Narang et al 2014)¹³. Mathur et al 2012 has reported the gallstone size to be 2.147 cm in cases with carcinoma, followed by hyperplasia 1.187 cm, metaplasia 1.145 cm and cholecystitis 1.136cm¹⁴.

Volume: The average volume of the gallstone was 2.664 ml in cholecystitis, 3.742 ml in hyperplasia, 4.532ml in metaplasia and 19.178 ml in carcinoma as reported by Mathur et al 2012¹⁴.

Age: Stones are found in patients with age range between 23 to 76 years.

3. CONCLUSION:

Based on the review of morphology of gallstone (types, number, size and volume) association with age and sex. It has been found that:

- Multiple gallstones are more common than solitary and double stones.
- Mixed type of gallstones are the most common stone reported by previous studies followed by combined stones and cholesterol stones where as pigmented stone were reported to be minimum.
- Largest sizes of gallstones were usually associated with carcinoma of gall bladder.
- Females had a predilection for the gallstone diseases as compared to males.

Table1: Comparative Chart of Number, Types of Gall Stone, Sex Ratio and Sample size.

MORPHOLOGY		Baig et al 2002 ¹⁵ (%)	Mohan et al 2005 ¹⁶ (%)	Mathur et al 2012 ¹⁴ (%)	Byna et al 2013 ¹⁷ (%)	Goyal et al 2014 ¹⁸ (%)	Narang et al 2014 ¹³ (%)
TYPES	Cholesterol	10	17.3	7	-	5.43	7.03
	Pigmented	20	3.2	9	-	5.75	1.62
	Mixed	70	62.3	59	-	68.0	90.8
	Combined	-	14	25	-	20.8	0.54
NUMBER	Single	-	-	39.6	16.7	30.4	7
	Double	-	-	8.8	-	-	-
	Multiple	-	-	51.6	83.3	69.4	93
SEX RATIO (M/F)		1/ 2.6	1/ 6.4	1/6.6	1/ 1.4	1/ 4.2	1/ 7.3

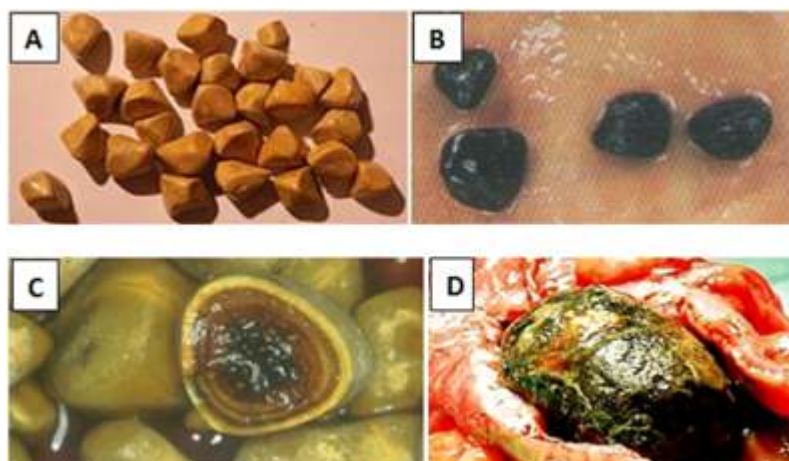


Figure: 1. A- Cholesterol stones, B- Pigmented stone, C- Mixed stone, D- Combined stone

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