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Evaluation of the clinical profile of patients diagnosed with gallstones from Bihar region

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Abstract
In recent years, potential precursors of gallbladder carcinoma have been identified, making their recognition by diagnosticians clinically relevant. Gallbladders are common surgical specimens and most procedures are performed for cholecystitis and cholelithiasis. Hence based upon the above literature findings the present study was planned to assess the clinical profile of the Gallstones.
The present study was planned on 50 cases of any age and either gender with gall stones. The patients were referred to Department of Surgery in IGIMS, Patna from Dec 2007 to Jun 2008. All sonographically diagnosed patients of gallstone admitted into the department. Clinical presentation like pain, vomiting, dyspepsia, fever and preoperative ultrasound findings of all patients were noted on predesigned performa.
Gallbladder is a rare identity with silent progression thus present in advanced stage carrying high rate of mortality and morbidity. It is more common in female than in male. Presence of gallstone has higher risk of malignancy. The present study concludes that femininity and obesity are strongly associated with gallstones formation presumably due to excess cholesterol in bile which eventuates in cholecystectomy.

Keywords: cholecystitis, cholesterol stone, gallbladder, gallstone disease, mixed stone

1. Introduction
A gallstone is a stone formed within the gallbladder out of bile components. The term cholelithiasis may refer to the presence of gallstones or to the diseases caused by gallstones. Most people with gallstones (about 80%) never have symptoms. When a gallstone blocks the bile duct, a cramp-like pain in the right upper part of the abdomen, known as biliary colic (gallbladder attack) can result. This happens in 1–4% of those with gallstones each year. Complications of gallstones may include inflammation of the gallbladder (cholecystitis), inflammation of the pancreas (pancreatitis), jaundice, and infection of a bile duct (cholangitis). Symptoms of these complications may include pain of more than five hours duration, fever, yellowish skin, vomiting, dark urine, and pale stools.
Risk factors for gallstones include birth control pills, pregnancy, a family history of gallstones, obesity, diabetes, liver disease, or rapid weight loss. The bile components that form gallstones include cholesterol, bile salts, and bilirubin. Gallstones formed mainly from cholesterol are termed cholesterol stones, and those mainly from bilirubin are termed pigment stones. Gallstones may be suspected based on symptoms. Diagnosis is then typically confirmed by ultrasound. Complications may be detected on blood tests [1].
The risk of gallstones may be decreased by maintaining a healthy weight with exercise and a healthy diet. If there are no symptoms, treatment is usually not needed. In those who are having gallbladder attacks, surgery to remove the gallbladder is typically recommended. This can be carried out either through several small incisions or through a single larger incision, usually under general anesthesia. In rare cases when surgery is not possible, medication can be used to dissolve the stones or lithotripsy to break them down [2].
In developed countries, 10–15% of adults have gallstones. Rates in many parts of Africa, however, are as low as 3%. Gallbladder and biliary related diseases occurred in about 104 million people (1.6%) in 2013 and they resulted in 106,000 deaths. Women more commonly have stones than men and they occur more commonly after the age of 40. Certain ethnic groups have gallstones more often than others. For example, 48% of Native Americans have gallstones. Once the gallbladder is removed, outcomes are generally good [1].
Gallstones may be asymptomatic, even for years. These gallstones are called "silent stones" and do not require treatment. The size and number of gallstones present does not appear to influence whether people are symptomatic or asymptomatic. A characteristic symptom of gallstones is a gallstone attack, in which a person may experience colicky pain in the upper-right side of the abdomen, often accompanied by nausea and vomiting. The pain steadily increases for approximately 30 minutes to several hours. A person may also experience referred pain between the shoulder blades or below the right shoulder. Often, attacks occur after a particularly fatty meal and almost always happen at night, and after drinking. In addition to pain, nausea, and vomiting, a person may experience a fever. If the stones block the duct and cause bilirubin to leak into the bloodstream and surrounding tissue, there may also be jaundice and itching. This can also lead to confusion. If this is the case, the liver enzymes are likely to be raised [3].
Gallstone risk increases for females (especially before menopause) and for people near or above 40 years; the condition is more prevalent among both North and South Americans and among those of European descent than among other ethnicities. A lack of melatonin could significantly contribute to gallbladder stones, as melatonin

inhibits cholesterol secretion from the gallbladder, enhances the conversion of cholesterol to bile, and is an antioxidant, which is able to reduce oxidative stress to the gallbladder [4]. Researchers believe that gallstones may be caused by a combination of factors, including inherited body chemistry, body weight, gallbladder motility (movement), and low calorie diet. The absence of such risk factors does not, however, preclude the formation of gallstones.

Nutritional factors that may increase risk of gallstones include constipation; eating fewer meals per day; low intake of the nutrients folate, magnesium, calcium, and vitamin C; low fluid consumption; and, at least for men, a high intake of carbohydrate, a high glycemic load, and high glycemic index diet. Wine and whole-grained bread may decrease the risk of gallstones [5].

Rapid weight loss increases risk of gallstones. The weight loss drug orlistat is known to increase the risk of gallstones. Cholecystokinin deficiency caused by celiac disease increases risk of gallstone formation, especially when diagnosis of celiac disease is delayed. Pigment gallstones are most commonly seen in the developing world. Risk factors for pigment stones include hemolytic anemias (such as from sickle-cell disease and hereditary spherocytosis), cirrhosis, and biliary tract infections. People with erythropoietic protoporphyria (EPP) are at increased risk to develop gallstones. Additionally, prolonged use of proton pump inhibitors has been shown to decrease gallbladder function, potentially leading to gallstone formation [6].

Cholesterol modifying medications can affect gallstone formation. Statins inhibit cholesterol synthesis and there is evidence that their use may decrease the risk of getting gallstones [29, 30]. Fibrates increase cholesterol concentration in bile and their use has been associated with an increased risk of gallstones [7].

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 overconcentrated 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 duct [8]. 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.

In recent years, potential precursors of gallbladder carcinoma have been identified, making their recognition by diagnosticians clinically relevant. Gallbladders are common surgical specimens and most procedures are performed for cholecystitis and cholelithiasis. Hence based upon the above literature findings the present study was planned to assess the clinical profile of the Gallstones.

2. Methodology

The present study was planned on 50 cases of any age and either gender with gall stones. The patients were referred to Department of Surgery in IGIMS, Patna from Dec 2007 to Jun 2008. All sonographically diagnosed patients of gallstone admitted into the department. Clinical presentation like pain, vomiting, dyspepsia, fever and preoperative ultrasound findings of all patients were noted on predesigned performa.

All the patients were informed consents.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Patients of any age and either gender with gall stones, had approval for general anesthesia and consented for the study.

Exclusion criteria: Patients unfit for general anesthesia, pregnant ladies and those having suspicion of carcinoma gall bladder, acute pancreatitis, obstructive jaundice and acute cholecystitis were excluded.

3. Results & Discussion

Though considered a worldwide medical problem there is a wide variation in the magnitude of gallstone disease in different geographic areas. In North American Indians, the disease is epidemic with up to 60% of women being affected. Annually 600,000 cholecystectomies are performed in the American adult population. However, the true magnitude is not known as most of the patients are asymptomatic. Studies indicate that only 10-18% of patients with gallstone disease become symptomatic.

Gallstone formation results from many complex factors working together. The pathologic factor related to gallstone formation is still the hot debate. Bile stasis secondary to gallbladder dyskinesia is the most widely accepted theory. The study demonstrated that mixed type of gallstones account for about 46% of stones found in cholecystectomy patients, mainly in females and the ratio of male & female was 1:3. It is consistent with the reports of Bruce W. Trotman *et al*., [9] and Harshi T W Weerakoon *et al*., [10] and Aslam H.M. *et al*., [11]. Raised values of SGPT and Alkaline phosphatase were observed in present study which is as similar as the findings of Aslam H.M. *et al*, 2003,04 so, the occurrence of gallstones was positively correlated with rise in SGPT levels. It is also proved that obese women secretes more cholesterol into their bile then a non obese female [12].

Three types of stones are identified [13] as

a. **Cholesterol stone:** Radiolucent light yellow to dark green color stone, 2 to 3 cm in length oval shaped. They are more likely to respond to non surgical management than is pigment or mixed stones.
b. **Pigment stone:** They are formed by the crystallization of calcium bilirubinate, black and brown colored, usually multiple, small and hard in consistency associated with infection in the gall bladder, commonly found in Asian descent.
c. **Mixed stone:** Radio graphically visible, commonest type formed by calcium carbonate, palmitate phosphate, bilirubin and other bile pigments

Table 1: Type of Stones

Type of Stones	No. of Cases
Cholesterol	12
Mixed	23
Pigmented	15
Total	50

Table 2: Distribution of Cases

Type of Stones	Cholesterol	Mixed	Pigmented	Total
Total Cases	12	23	15	50
Age	32-45 years	34-42 years	30 – 46 years	
Weight	58 – 79 kg	60 – 77 kg	61 – 74 kg	
Sex (male)	2	5	5	
Sex (Female)	10	18	10	
Alcoholism	2	5	3	
Non Veg Diet	3	8	5	

Table 3: Clinical Feature

Feature	No. of Cases
Site of Pain:	
Right hypochondria (RHC)	35
Epigastrium	6
RHC + Epig	9
Nature of pain:	
Colicky	41
Dull/constant	9
Nausea + vomiting	29
Dyspepsia	24
Fever	3
Number of stones:	
Single	11
Multiple	39

The study done by chandran *et al.* [14] reported quantitative chemical analysis of total cholesterol bilirubin, calcium, iron and inorganic phosphate in 120 gallstones from haryana. To extend this chemical analysis of gall stones by studying more cases and by analyzing more chemical constituents. A quantitative chemical analysis of total cholesterol, total bilirubin, fatty acids, triglycerides, phospholipids, bile acids, soluble proteins, sodium potassium, magnesium, copper, oxalate and chlorides of biliary calculi (52 cholesterol, 76 mixed and 72 pigment) retrieved from surgical operation of 200 patients from Haryana state was carried out. Total cholesterol as the major component and total bilirubin, phospholipids, triglycerides, bile acids, fatty acids (esterified), soluble protein, calcium, magnesium, iron, copper, sodium, potassium, inorganic phosphate, oxalate and chloride as minor components were found in all types of calculi.

Jaraari AM *et al.* [15] study was conducted to determine the composition of gallstones and their possible etiology in a Libyan population. The chemical composition of gallstones from 41 patients (six males and 35 females) was analyzed. The stones were classified into cholesterol, pigment, and mixed stones (MS). Cholesterol stones (CS) showed a significantly higher cholesterol content than pigment stones (PS) (p=0.0085) though not significantly higher than MS, which is similar to our study.

Ramana Ramya J *et al.* [16] found Representative gallstones from north and southern parts of India were analyzed by a combination of physicochemical methods: X-ray diffraction (XRD), infrared spectroscopy (IR), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), CHNS analysis, thermal analysis and Nuclear Magnetic Resonance (NMR) spectroscopy (1H and 13C). The stones from north Indian were predominantly consisting of cholesterol monohydrate and anhydrous cholesterol which was confirmed by XRD analysis. FTIR spectroscopy confirmed the presence of cholesterol and calcium bilirubinate in the south Indian gallstones.

Jayanthi V *et al.* [17] Gallstones (GS) in south India (SI) are predominantly pure pigment or mixed, while in North India (NI), these are either pure cholesterol or mixed. While cholesterol rich gallbladder (GB) bile predicts cholesterol GS, constituent of bile in primary pigment GS is not known. Gallbladder bile in controls and patients with GS from north India had significantly high cholesterol concentration. In south India, patients with mixed GS had cholesterol rich bile while pigment GS had higher concentrations of bile salts.

Mofti AB *et al.* [18] reporting the frequency of developing adhesions around the gallbladder, wall thickness, mucocele, empyema, gallbladder perforation and postoperative complications were significantly higher in the group with solitary stones than those with multiple gallstones. Jalali SA *et al.* [19] reporting incidence of developing gallbladder changes like adhesions, wall thickness, mucocele, empyema, perforation were significantly found in group with solitary stones and those with multiple gallstones.

Gallstone disease appeared to be increasing in incidence over past couple of decades in India and western world due to increased intake of fatty and high calorie diet and increased consumption of alcohol [20]. It was observed that despite the diverse mechanism of stone induction and the differences before in stone composition, there is a quantitative increase in the epithelium mucus production in the period stone formation.

4. Conclusion

Gallbladder is a rare identity with silent progression thus present in advanced stage carrying high rate of mortality and morbidity. It is more common in female than in male. Presence of gallstone has higher risk of malignancy. The present study concludes that femininity and obesity are strongly associated with gallstones formation presumably due to excess cholesterol in bile which eventuates in cholecystectomy.

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