

Original Article

Gall Bladder Polyps : A Paradigm Shift – Need for Reappraisal of Guidelines

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Background : Gall Bladder Polyps are mucosal lesions that project from the Gall Bladder wall into the Gall bladder lumen. They form morphologically distinct lesion/s with internal characteristics different than that of neighboring structures as verified by microscopic examination. About 4-6% are picked up clinically, 2-12% in Cholecystectomy specimens and 4% on Ultrasound.

Materials and Methods : A three calendar year retrospective single surgical unit study comprised of 1442 cholecystectomies performed for benign Gall Bladder Disease. The patient were subjected to Ultrasound of abdomen for diagnosis and routine clinic work up. The Gall Bladders Harboring Polyps were examined grossly for site, number, and microscopy for histological details.

Results : In a total number of 40 cases of Gall Bladder Polyp, females outnumbered males.

This series spreads over age groups of 3rd decade - 9th decade, most of the patients were seen in 6th decade of life. Youngest patients were 27 years old and oldest one was 85 years old. Incidentally, none of the old patients had evidence of malignancy on histopathology in their Gall Bladder Polyp, only 2% were necessitated for a pre-operative diagnosis of Gall Bladder Polyps alone. Rest required it for presence of Gallstones with or without Polyp. None of >10mm size showed any malignant change on histopathological examination. On the Contrary, among the polypoid lesions <10mm size, one polypoid lesion (7mm) showed a malignant change (Carcinoma in situ)

Conclusion : A predictive model for neoplastic potential of Gall Bladder Polyp may support clinical decision to achieve an ideal therapeutic outcome. Hence a need for reappraisal of management guidelines.

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Key words : Gall Bladder Polyp (GBP), Polypoid Lesions of Gallbladder (PLG), Laparoscopic Cholecystectomy (LC), Endoscopic Ultrasound (EUS), Photoacoustic imaging.

Gall Bladder polyps are mucosal lesions that project from the Gall bladder wall into the Gall bladder lumen. By definition Gall Bladder Polyp is a protrusion of mucosa that is clearly recognizable either on the gross bench or by examination of the glass slide and that formed a morphologically distinct lesion with internal characteristics different than that of neighboring structures as verified by microscopic examination.

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Editor's Comment :

- Polypoid Lesions of Gall Bladder (PLG) are benign in nature yet some early carcinomas may resemble benign polyps.
- Since smaller polyps may rarely present as malignancy, it would be worthwhile to closely put polyps smaller than 10 mm (and more than 5-6mm) under a suspicious surveillance.
- A predictive model for neoplastic potential of GBP may support clinical decision to achieve an ideal therapeutic outcome. Hence a need for reappraisal of management guidelines.

These polyps are one of the most common diseases Worldwide¹. Majority are diagnosed as an incidental finding on routine investigation or in Gall Bladder operation, in the specimen. While most Polyps are benign in nature, some early Carcinomas may resemble Benign Polyps. About 4-6% are picked up in clinical practice and 2-12% are picked up in Cholecystectomy specimens and 4% are picked up on Ultrasound examination of Hepatobiliary system in adults². Male sex³ and Dyslipidaemia (a higher non-HDL-c/HDL-c ratio)⁴ have also been reported to be associated with Gall Bladder Polyps.

The Polyps are mostly Benign. Malignant ones are rare (Piechart 1).

GB Polyps

- Neoplastic
 - i) Primary
 - a) Adenocarcinoma
 - b) Clear cell carcinoma
 - c) Melanoma
 - ii) Metastatic
- Non-neoplastic
 - i) Adenomas
 - a) Tubular
 - b) Papillary
 - c) Mixed
 - ii) Mesenchymal Tumors
 - a) Fibroma
 - b) Lipoma
 - c) Haemangioma
 - iii) Pseudotumors
 - a) Cholesterol Polyps
 - b) Cholesterosis
 - c) Inflammatory Polyps
 - d) Hyperplasia and Adenomyometosis

Histologically (Task in *et al* 2020) polyps are classified into :

- Non-neoplastic polyps
 - i) Fibromyoglandular polyps
 - ii) Cholesterol polyps
 - iii) Polypoid pyloric gland metaplasia
 - iv) Inflammatory polyps
- Neo plastic polyps
 - i) Intracholecystic neoplasms
 - ii) “Incipient” intracholecystic neoplasms
 - iii) Polypoid invasive carcinoma
 - iv) Non-neoplastic polyps harboring dysplasia.

The following two facts have to be considered while managing the polypoid lesions of Gall Bladder that :

- (a) while as early cancer in the Polypoid lesions can be treated by Cholecystectomy alone, and
- (b) if neglected or delayed, a resultant Gall Bladder cancer carries a very dismal prognosis.

Therefore a correct diagnosis and a fair surveillance is warranted and mandatory for good outcome⁵.

Not with standing early reports about smoking to be inversely related to presence /occurrence of Gall Bladder Polyps⁶, yet later report⁷ presenting results of a meta-analysis showed increased risks of Gall Bladder Disease in smokers.

However, definite risk factors include: General factors:

- Obesity
- Dyslipidaemia
- Congenital Polyposis Syndroms eg. Peutz-Jeghers, Gardener Syndrome⁸
- Indian ethnicity⁹

Pathological factors :

- Size of the Polyp/s 10 mm
- Single sessile broad based polyp
- Polyps broader than tall
- Polyps with adjacent wall thickening
- 2 mm or more increase in the size of Polyps during surveillance

Transabdominal Ultrasound is the most ideal diagnostic tool with a sensitivity & specificity of 93% and more than 95 % respectively. Generally polyps of >5 mm size are easily demonstrable. In case of many Polyps, largest one decides the plan of management while as Polyps dimensions (size) can be a predictor of tumorous lesion^{10,11}.

Predictions of malignancy in Polypoid lesions of Gall Bladder¹² are scored as given in Table 1.

The sensitivity, specificity and accuracy for the risk of malignancy with scores of 3 or more being 81.6%, 86.7% and 84.4%, respectively. However, Since Trans-abdominal Ultrasound has a high false positive rate (85.1%) for diagnosis of Gall Bladder Polyps, further study of alternative imaging modalities and re-evaluation guideline are warranted¹³.

Endoscopic Ultrasound (EUS) is considered to be superior to the conventional transabdominal Ultrasound, because of its higher resolution of images and its scoring system is as follows :-

- Maximum diameter(in mm)
- +
- Internal Echo Pattern Score (Heterogenous = 4, Homogenous = 0)
- Hyperechoic spot score (Presence = -5, Absence = 0)

Scores of 12 or more are a strong risk factor, the sensitivity; specificity and accuracy being 78%, 83% and 83% respectively¹⁴.

Photoacoustic imaging is an ex-vivo study used in differentiating cholesterol versus Neoplastic Polyps and Benign *versus* Malignant Polyps of the Gall Bladder. A study showed a distinguishable photoacoustic spectral patterns and therefore, suggested this method could be used for differentiating Malignant from Benign Polyps¹⁵.

Table 1 — Ultrasound based scoring system for differential diagnosis of polypoid lesions of Gall Bladder

Feature	0	1
Max. diameter	< 13.9mm	≥ 13.9mm
Base width	<3.4 mm	≥ 3.5mm
Height/width Ratio	>1.05	≤ 1.05
Hyperechoic Spots	Presence	Absence
Blood flow	Absence	Presence

Abdominal CT is incapable of detecting low density lesions and its sensitivity for diagnosis of Gall Bladder Polyps is only between 44% and 77%¹⁶.

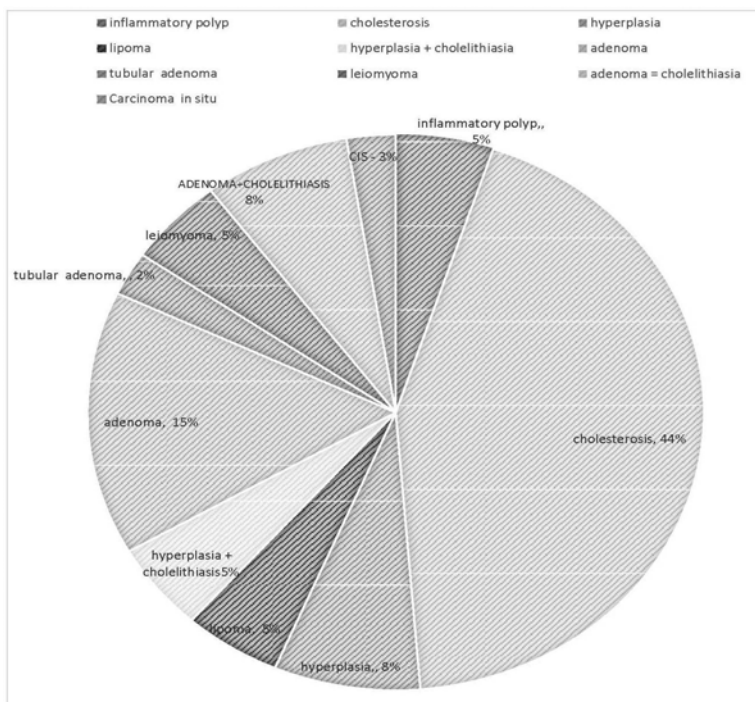
Summing up it is a diagnostic challenge to determine which polyps are likely to be malignant or undergo malignant transformation in order to determine which patients require Cholecystectomy on priority.

AIMS AND OBJECTIVES

To evaluate the pattern of the Gall Bladder Polyp disease in our setup and to authenticate need for change/modification of management guidelines.

MATERIAL AND METHODS

A three calendar year retrospective single Surgical Unit study comprised of 1442 Cholecystectomies performed for Benign Gall Bladder Disease. The patient were subjected to Ultrasound of abdomen



Pie Chart 1 — Histopathological Depiction of various Gall Bladder Polyp Specimens

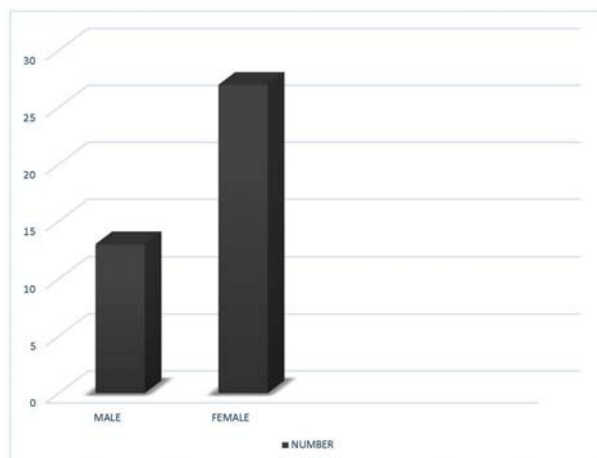


Fig 1 — Illustrating gender pre-disposition of Gall Bladder Polyps in our study

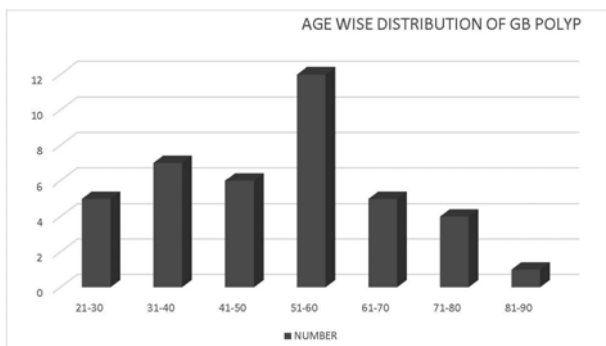


Fig 2 — Agewise Distribution of GB Polyp

for diagnosis and routine clinic work up. After obtaining an informed consent for operation and pre-operative fitness for surgery, Laparoscopic Cholecystectomy (LC) was performed. The specimens retrieved were individually subjected to histopathology examination. The Gall Bladders harboring polyps were examined grossly for site, number and microscopy for histological details.

OBSERVATIONS

In a total number of 40 cases of Gall Bladder Polyp, females outnumbered males (27;13)(Fig 1).

This series spreads over age groups of 3rd decade - 9th decade, most of the patients were seen in 6th decade of life. Youngest patients were 27 years old and oldest one was 85 years old (Fig 2).

Incidentally, none of the old patients had evidence of malignancy on histopathology in their Gall Bladder Polyp (Piechart 1 and Fig 2).

Out of total number of Laparoscopic Cholecystectomies (n=1442), only 2% were necessitated for a pre-operative diagnosis of Gall Bladder Polyps alone. Rest required it for presence of Gallstones with or without Polyp (Piechart 2).

Out of the total number of 40 polypoid lesions, 23 were equal to or more than 10 mm in size and interestingly none of them showed any malignant change on Histopathological Examination (Piechart 3).

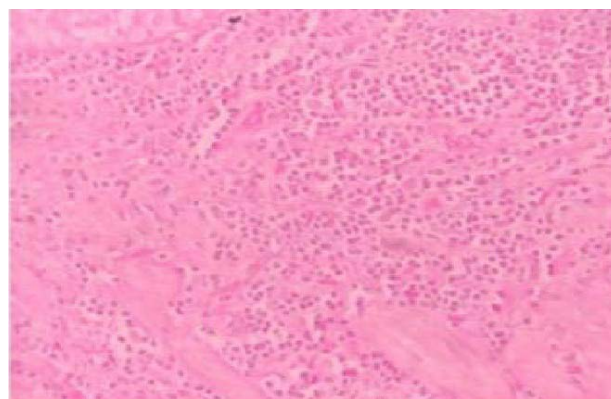
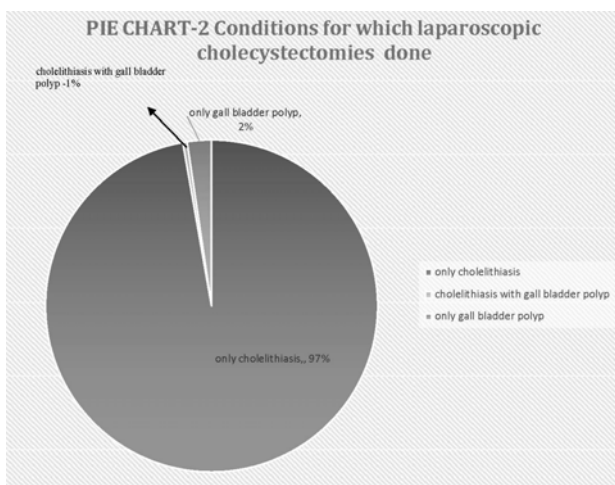


Image 1 — H&E Stained, High power microscopic picture showing carcinoma in situ

On the Contrary, among the polypoid lesions <10mm size, one polypoid lesion (7mm) showed a malignant change (Carcinoma in situ)(Images 1&2).

DISCUSSION

Gall Bladder Polyps (GBP) are found in more than 4% of adult abdominal ultrasounds but their growth pattern and association with gall bladder cancer are poorly defined. Although most are thought to have no malignant potential yet a minority (ie, 4% to 10%) are adenomas which do have a malignant potential³. However distinction between adenomas and non-adenomas is usually made after surgery, so if surgery is not performed the clinician must decide whether

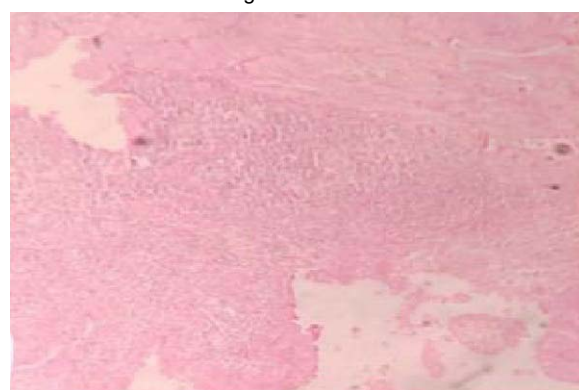
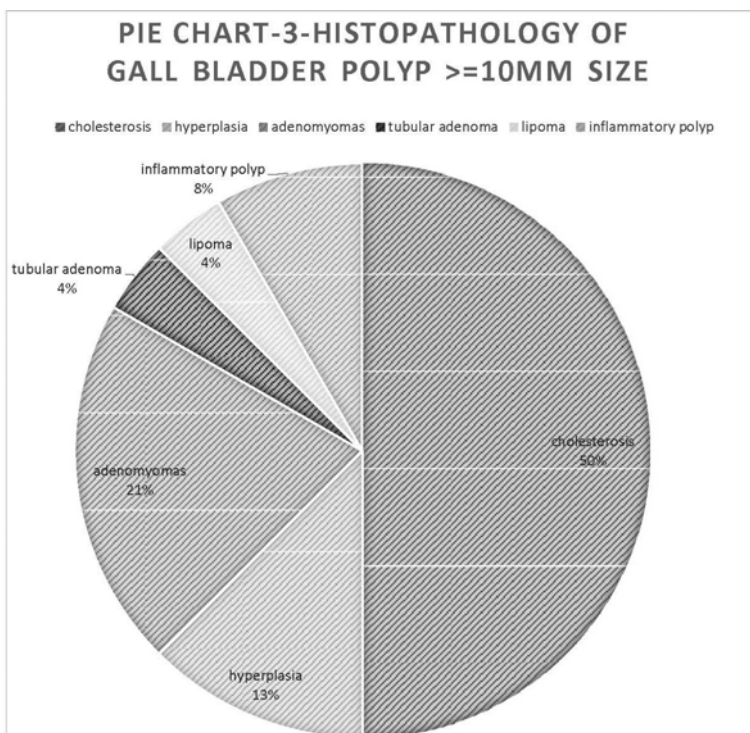


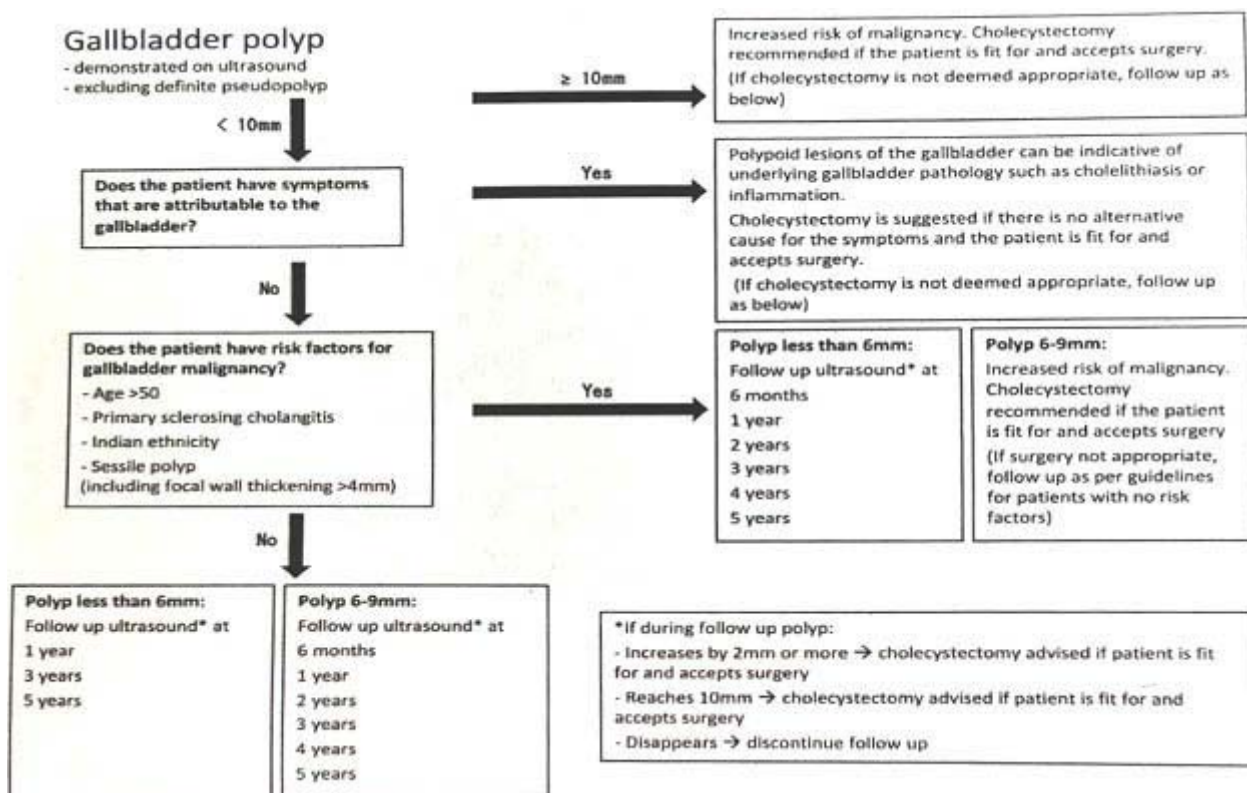
Image 2 — H&E Stained, Low power microscopic picture of gall bladder carcinoma in situ



and how best to perform surveillance, during the wait and watch period. The indications for laparoscopic Cholecystectomy for Gall Bladder cancer prevention are still a matter of discussion¹⁷.

Joint Guidelines (Algorithm 1), regarding management and follow-up of Gall Bladder Polyps, between European Society of Gastrointestinal and Abdominal Radiology (ESGAR), European Association for Endoscopic Surgery and other Interventional Techniques (EAES), International Society of Digestive Surgery-European Federation (EFISDS) and European Society of Gastrointestinal Endoscopy (ESGE), were put forth in 2017¹⁸.

Pre-operative determination of the nature of Gall Bladder lesions is however, fraught with challenges¹. For Gall Bladder Polyps size measurement has been used as the simplest way to estimate the potential nature of the lesion with one centimeter remaining the most commonly



Algorithm 1 — Joint guidelines for management of Gall Bladder Polyp, 2017

used rule of thumb criteria for a polyp (GBP) removal. This cut-off size however, has been debated¹⁹. Generally the opinion prevails that Polypoid Lesions of Gall Bladder (PLG) greater than or equal to 10 mm require Cholecystectomy, if the patient is fit and accepts surgery. Polyps smaller in size than this need a surveillance; bigger the size more strict the surveillance – especially in presence of risk factors viz. old age (age>50 years) increasing polyp size (especially at base), wide based single sessile polyp, absence of echogenicity, concomitant presence of Gall Stones, increased vascularity in the Polyp etc. A polyp that increases by 2 mm during follow up requires Cholecystectomy.

In spite of rigid guidelines, surprises may spring up on histopathology of Polyps by manifesting malignant or pre-malignant pathology. The authors have known one such case, a 56 year old non co-morbid (with no risk factor) women presenting with a 7 mm polyp –advised surveillance. Having been lost to follow up, she presented with an advanced Gall Bladder cancer 9 months later. (not included in this study). Another patient (Fig 3) with only a 7 mm Polyp turned out to be a ca- in situ. David Kastle *et al*²⁰ have drawn the attention towards strong surveillance in Polyps of

even lesser magnitude and suggested a change of practice. Wennmacker *et al*¹ have raised doubts about the threshold of the size of 10 mm in GB Polyps, as lacking evidence.

Even the findings of Szpakowski and Tucker³ call into question the European Societies recommending follow up of Gall Bladder Polyps. Their study suggested that the natural history of these Polyps is to grow over time. This is clearly evident in our series wherein most of the lesion were more than 10 mm, although benign had grown over a period of time. They suggested a pro-active monitoring and changing the threshold to recommend early Cholecystectomy²².

The authors of the guidelines of management, themselves, had hinted at a re-appraisal of these guidelines by September, 2021 or earlier as the need be¹⁸.

CONCLUSIONS

Most Polypoid Lesions of Gall Bladder (PLG) are benign in nature yet some early Carcinomas may resemble benign polyps. It might be difficult to accurately predict or diagnose the pathologic status pre-operatively. Our study highlights 2 important aspects of the management of Gall Bladder Polyps. 60% were large solitary, sessile and some even

associated with presence of stones and of these none showed pre-malignant or malignant nature. On the other hand a small Polyp of 7 mm size showed a pre-malignant change (ca-in situ). Since smaller Polyps may rarely, present malignancy, it would be worthwhile to closely put polyps smaller than 10 mm (and more than 5- 6mm) under a suspicious surveillance, especially if accompanied with any one or more of the risk factors, particularly in view of increasing reports of malignancy in smaller polyps and of otherwise in Polyps of sizes 10mm or more. A predictive model for Neoplastic potential of GBP may support clinical decision to achieve an ideal therapeutic outcome. Hence a need for reappraisal of Management Guidelines.

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