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Profile of Histomorphological Changes of Gall Bladder with Special Focus on Pre-Neoplastic and Neoplastic Lesions in a Tertiary Care Centre In Eastern India

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ABSTRACT: Background: Cholelithiasis and associated gall bldder diseases are on the rise worldwide and pose to be a major health concern . The diverse histopathological manifestations including inflammatory and noninflammatory lesions, particularly the pre-neoplastic and neoplastic lesions like epithelial hyperplasia, metaplasia, dysplasia, carcinoma-in-situ and carcinoma gall bladder exhibit wide discrepancies in reported frequencies and their significance in various studies. The present study is undertaken to understand the spectrum and frequency of these morphological changes in post-cholecystectomy gall bladder specimens in a tertiary care centre in Eastern India.

Materials and Methods:A total of 230 postcholecystectomy gall bladder specimens received at Department of Pathology, SCB Medical College, Cuttack, India over a period of two years were studied. The clinical history and morphology of associated gall stones were noted and the gall bladder specimen was studied for various histopathological lesions after proper sampling and processing by routine histological techniques.

Results : Cholelithiasis and associated gall bladder diseases were observed to be more common in females (F:M ratio-3.7:1) with maximum number of cases in the age groups of 4th decade(35.22%) and 5thdecade(28.69%). Out of the total 230 gall bladder specimens, 208 (90.43%) had associated gall stones and rest 22(9.57%) were without any gall stones. Histopathologically, the most common lesion was chronic cholecystitis (82.6%) followed by acute cholecystitis (9.13%), acute on chronic cholecystitis (6.52%), chronic follicular cholecystitis (1.74%), xanthogranulomatous cholecystitis (2.17%), adenomyomatosis of gall bladder(4.78%), cholesterolosis (3.04%), adenomatous hyperplasia(5.65%), dysplasia(1.74%), pyloric metaplasia(12.6%), intestinal metaplasia(3.1%) and primary adenocarcinoma gallbladder (3.04%).

Conclusion: Incidence of gall bladder diseases, particularly malignant gall bladder diseases are on the rise. Detailed and vigilant histopathological examination of gall bladder specimens will bring to the fore more of these lesions.

KEYWORDS: - Adenocarcinoma of gall bladder, Cholecystitis, Dysplasia, Metaplasia

I. INTRODUCTION

Cholelithiasis and associated gall bladder diseases have continued to hunt the mankind worldwide with huge morbidity and mortality, affecting approximately 10-20% of the world population.[1] Indian population particularly has witnessed over last decades a significant increase in number of cases of cholelithiasis and associated gall bladder diseases including gall bladder cancers. The estimated prevalence of cholelithiasis in India is being reported to range from 2-29%, North India reporting as high as 7 times more cases than South india [2],[3] and Eastern and Western states registering more and more number of cases. The gall bladder in response to the offending gall bladder stones and other factors manifests a series of diverse histomorphological changes including inflammatory changes like acute and chronic cholecystitis, follicular cholecystitis and xanthogranulomatous cholecystitis; non-inflammatory changes like cholesterolosis, adenomyomatosis; pre-neoplastic changes like adenomatous hyperplasia, metaplasia, dysplasia and carcinoma in-situ and neoplastic changes like invasive carcinoma of gall bladder.[4],[5] In view of the rising incidence of gall bladder cancers, there has been a surge of interest in further studies of the pre-neoplastic lesions of gall bladder with diverse reporting of their frequency and their significance including malignant potential.

The present study has been undertaken to asses the profile of various such histomorphological changes in the gall bladder reflective of Eastern India as there is a paucity of data from this region of the

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country despite exhibiting increasing number of gall bladder diseases, particularly gall bladder cancers.

II. MATERIALS AND METHODS

The present study was conducted in the Department of Pathology, SCB Medical College Hospital, Cuttack which is a premiere tertiary health care institute in eastern India. The objective of the study was to analyse the spectrum of histopathological changes of gall bladder diseases, their incidences, malignant potential and to find any causal relationships. The study material included a total of 230 Post-Cholecystectomy specimens received from Department of Surgery for histopathological study during the period from January 2018 to December 2019. The clinical details and relevant investigations were recorded. All cholecystectomy specimens were fixed in 10% formalin. Gross features of specimens were observed and presence of stones and their morphological types were recorded . Routine sections were taken from fundus, body and neck of all gall bladders and additional representative sections were taken from abnormal appearing areas. Sections were stained with Haematoxylin and Eosin stain after the processing. The stained slides were then studied meticulously for various histopathological changes with special focus on search for pre-neoplastic and neoplastic lesions and the findings were analyzed in correlation with presence or absence of gall stones.

III. RESULTS

Over the study period of 2 years, a total of 230 cholecystectomy specimens from patients of gall bladder diseases were analysed. Females constituted the majority of patients(181 cases, 78.7%) whereas Males accounted for 49 (21.3%)of cases with a F:M ratio of 3.7:1**(Table/Fig-1).** The patients included most age groups, the youngest being a 16 year old girl and the oldest being a 82 years male. The number of patients in various age groups are depicted in **Table/Fig -2,3**. The most common age groups for gall bladder diseases were 31-40 years (81 cases, 35.22%) and 41-50 years (66 cases-28.69%). The mean age of presentation was 40.7. Three patients in the 8th and 9th decades were males, aged 79, 80 and 82.

Out of the total 230 gall bladder specimens, 208 (90.43%) had associated gall stones and rest 22(9.57%) were without any gall stones. Mixed stones comprised the most common type (184, 88.46%) followed by pigment stones(14,6.73%) and cholesterol stones(10, 4.80%)**(Table/Fig -4).**

On microscopic examination, an array of histomorphological changes were observed, the most common lesions being Chronic cholecystitis (190 cases, 82.6%) followed by Acute cholecystitis (21 cases, 9.13%)**(Table/Fig -5).** Out of the 190 cases of Chronic cholecystitis, 172 cases(74.78%) were Chronic calculus cholecystitis and 18 cases(7.82%) were Chronic acalculus cholecystitis. Fifteen cases(6.52%) had features of acute on chronic cholecystitis and all were associated with stones. Other distinct histopathological entities observed are summarised in Table/Fig -5. Significant epithelial changes like metaplastic changes in gall bladder epithelium were observed in 36(15.7%) cases, 29 (12.6%) cases being of pyloric type and 9(3.1%) cases of intestinal variety. Dysplasia of gall bladder epithelium was seen in 4 cases; 3cases of low grade and 1 case of high grade dysplasia. Primary carcinoma of gall bladder was diagnosed in 7(3.04%) cases and were of well differentiated adenocarcinoma type. Most of these lesions

were seen on a background of chronic inflammation and were associated with presence of stones. The association of gall stones with various morphological lesions is highlighted in **Table/Fig -6**.

IV. DISCUSSION

Gall bladder diseases are increasingly afflicting the society worldwide with diverse manifestations of non-neoplastic and neoplastic lesions. Females continue to be the preponderant victims though more and more number of male patients are being affected. In our study, we observed a F:M ratio of 3.7:1 which closely correlates with findings of Goyal S et al.[6] When some studies observed a very high F:M ratio (7.4:1 by Srivastav AC et al[7] , 7:1 by Agrawal R et al[8]and 6.5:1 by Tyagi et al[9]), others reported involvement of more males with much lower F: M ratio (2.1 :1 by Vahini G et al[10],1:0.86 by Beena D et al[11]). We noticed more number of male patients in the 6th, 7th and 8th decades compared to females. Female sex hormones and their metabolites have been incriminated as the primary contributing factors for most of the gall bladder diseases and stone formation. Maximum number of cases in our study were found in the 31-40 years of age group. Most of the recent studies also show high incidence of gall bladder diseases in younger age groups.[2],[7],[12],[13] This is in contrast to other studies where maximum number of gall bladder diseases occurred in the 5th and 6th decades.[9],[11]

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The reported age distribution of gall bladder diseases in various studies is given in **Table/Fig -7**. Gall bladder disease is almost synonymous with gall stone disease as gall stones are associated with gall bladder diseases in more than 90% of cases. In our study , 90.4% of cases were associated with gall stones (calculus gall bladder disease) and 9.57% of cases were without any stones (acalculus gall bladder disease). These observations are in agreement with various large series studies.[3],[6],[9] Mixed type of gall stones constitute the most common type of stones as has been noted in most of the studies. [13],[14] In our study, mixed stones accounted for 88% followed by pigment stones of 7% and cholesterol stones of 5%. However in contrast, some authors have observed a very high incidence of pigment stones compared to mixed and cholesterol stones.[2],[11] Bashir MJ et al[15] from Saudi Arabia and Taher MA et al[16]from University of Baghdad reported pure cholesterol stones as the predominant type of stones, 54.3%, and 49.3% respectively. A comparative report of type of stones in various studies is given in **Table/Fig -8**.

The wide spectrum of histopathological lesions in gall bladder has been very intriguing and has evoked interest in detailed microscopic study of resected gall bladder specimens. Though chronic cholecystitis and acute cholecystitis are the most overwhelmingly reported lesions, significant lesions like xanthogranulomatous cholecystitis(XGC), adenomyomatosis, pre-neoplastic lesions like metaplasia and dysplasia and primary carcinoma of gall bladder are being increasingly recognised in the background of chronic cholecystitis. A comparative data of incidence of various histomorphological lesions of gall bladder in different study reports is presented in **Table/Fig -9**.

In the present study, chronic cholecystitis was observed in as high as 82.6% of total cases and majority (74.78%) were associated with gall stones (calculus cholecystitis) . Only 7.82% of total cases were acalculus cholecystitis. These findings are similar to large number of studies.[13],[18],[19] Though gall bladder stones are incriminated as the direct aetiological factor for development of chronic cholecystitis, both the processes of stone formation and chronic inflammation are believed to be parallel processes due to supersaturation of bile and consequent stasis.[14]

The next common reported histopathological presentation of gall bladder diseases is acute cholecystitis, majority of which are associated with gall stones. The incidence of acute cholecytitis varies widely in various studies.[10],[13],[18] In present study, acute cholecystitis was observed in 9.13% cases and all were associated with gall stones. Acute on chronic cholecystitis was observed in 6.57% of cases in our study. This closely resembles with the incidence reported by Kulkarni M et al[2]-6.21%. This entity has also been described by some authors as chronic active cholecystitis.[17],[19]

Follicular cholecystitis, a severe variant of chronic cholecystitis was observed in 6 cases (2.6%) in our study and was characterised by presence of lymphoid aggregates and follicles in the lamina propria and muscularis layers of gall bladde. The findings are similar to the findings of Mohan H et al[4] (2.3%)and Gupta K et al[12](2.53%). Tyagi et al[9] and Kini H et al[17] recorded higher incidences of 6.2% and 5.75% respectively. A strong association with gall stones has been reported.[6][19] All four cases(100%) in our study were associated with gall stones .

Xanthogranulomatous cholecystitis (XGC), an unusual variant of chronic destructive cholecystitis was observed in 5 cases in our study (2.17%) which is similar to the incidence in various other studies(Gupta K et al[12] -2.07%, Jokhi C et al[13] -2.3%).The lesion is characterised grossly by focal or diffuse thickening of the gall bladder wall with yellowish tumor like nodular masses and microscopically by accumulation of lipid-laden macrophages (Xanthoma cells) in a background of chronic inflammatory cells, histiocytes, foreign body giant cells and fibroblasts. Tyagi et al[9] reported a high incidence of 6.2%. Xanthogranulomatous cholecystitis is being increasingly recognised of late because of it's close mimic with gallbladder cancer preoperatively.[9],[20] Though authors have observed association of XGC with carcinoma of gall bladder (Tyagi et al[9]), no causal relationship is established yet (Mohan H et al.[4]

Adenomyomatosis is a variant of hyperplastic cholecystoses characterised by benign proliferation of surface epithelium of gall bladder invaginating through muscularis layer into the hyperplastic muscle layer and forming glandular and cystic structures within the wall.[21] The motility disorders of the gall bladder cause functional obstruction to the flow of bile and increase intraluminal pressure producing invagination of the mucosal epithelium. The cholelithiasis and chronic inflammation provoke the myoepithelial proliferations.[22] The lesions are being identified in 1-8.5% of cholecystectomy specimens. In our study we observed the lesion in 4.78% of cases. The varying incidence rates by other authors are as follows: Terada T et al[20] -

3.68%, Gupta K et al[12] -3% and Tyagi et al-8.2%[9]. Though some (Nabatame N et al[23]) describe it as a precancerous lesion, majority consider it as an incidental finding without any intrinsic malignant potential.[21],[22] Frequent coexistence with cholelithiasis is seen; however, no causative relationship has been established. Nine out of 11 cases (81.8%) in our study had associated gall stones. Cholesterolosis is another benign variant of hyperplastic cholecystoses characterised by deposition of lipids, especially cholesteryl esters in the gall bladder mucosa and aggregation of lipid laden macrophages in the lamina propria of the gall bladder. Cholesterolosis was encountered in our study in 7 cases (3.04%) which was similar to the findings of Rashmi HK et al[24] -3.8% and Tyagi et al[9] -2.7% but in contrast to the high frequencies observed in other studies(Aggarwal S et al[5] -18%, Dattal DS et al[19] -15.7%, Mohan et al[4] - 10.1%). Cholesterol stones are the most frequent type of gall stones accompanying cholesterolosis.[4] Four out of 7 cases in our study were associated with cholesterol gall stones.

Cholelithiasis with chronic cholecystitis manifest a spectrum of pathological surface mucosal changes of gall bladder including hyperplasia, metaplasia and dysplasia, all with inherent potential to evolve into in-situ carcinoma and invasive carcinoma.[25] With increasing incidence of gall bladder cancers being encountered recently, pre-neoplastic lesions are being recognised with reported high incidence in various studies. The chronic irritation and inflammation have been unequivocally considered as the precipitating factors for these pre-neoplastic mucosal changes.[26]

Adenomatous hyperplasia is microscopically described as hyperplastic proliferation of the surface epithelium and is characteristically of two distinct morphological types, villous hyperplasia and spongioid hyperplasia.[26] The reported frequency of adenomatous hyperplasia varies widely from as low as 0.09%(Mohan et al[4]) to as high as 83%(Saavedra JA et al[27]). In the present study, adenomatous hyperplasia was observed in 5.65% of total cases which closely resembled the incidence reported by Dattal DS et al[19] (7.4%) . Out of the 13 cases of adenomatous hyperplasia in our study, 9 cases (69.3%) were of villous type and 4 cases (30.7%) were of spongioid variety. This correlates with findings of Stancu M et al[25] who reported a total incidence of 7.8% of epithelial hyperplasia with papillary and spongioid variety contributing 73.3% and 26.7% respectively. Tyagi et al[9] encountered 10.1% of adenomatous hyperplasia; villous hyperplasia in 52.4%, spongioid hyperplasia in 33.3% and combined type in 14.3%. Saavedra JA et al[27] in their study of 200 gall bladder specimens observed 83% of epithelial hyperplasia along with 13.5% atypical hyperplasia and 3.5% carcinoma in situ .The authors proposed that a small number of hyperplasias of the gall bladder evolves towards atypical hyperplasia, in situ carcinoma and ultimately to invasive carcinoma.

Metaplastic changes in gallbladder epithelium are frequently underestimated (Agrawal R et al[8]-3.2%, Stancu M et al[25]-5%, Singh P et al[13]-8.4%) though these can be harbingers of more ominous invasive carcinomas of gall bladder. These are reactionary changes to the chronic irritation by gall stones and associated chronic inflammation and include various types like pyloric or antral metaplasia, intestinal metaplasia and uncommonly squamous cell metaplasia. Pyloric metaplasia is the most frequently observed variety and very often coexists with other types of metaplasia. Various other authors have emphasized on these changes and have recognised very high frequencies of these lesions. Martinez-Guzman et al[28]recorded high incidence of 50% pyloric and 16% intestinal metaplasia. Patil M et al[18] observed 21% of of gastric metaplasia and 17% 0f intestinal metaplasia. The present study observed total 36 cases (15.7%) of metaplasia; 29 (12.6%) cases being of pyloric type **(Table/Fig-10)**. and 7(3.1%) cases being of intestinal type**(Table/Fig-11)**. This correlates closely to the observations of Dattal et al[19] (Pyloric-13.4%, Intestinal-2.1%). Thirty two out of the 36 cases of metaplasia in our study were associated with gall stones. Seretis C et al[29] reported metaplastic changes in the gallbladder epithelium in 25.6% of cases which were accompanied in 45.5% of cases with dysplastic or cancerous lesions. Current literature unambiguously acknowledge metaplastic changes as preneoplastic lesions.[27]

Gall bladder dysplasia is a disordered proliferation of mucosal epithelium in response to the chronic injury by gall bladder calculi and associated inflammation and is universally recognised as a precursor lesion of gall bladder cancer. Majority of studies report frequency of gall bladder dysplasia between 1-3.5%[30]. The present study noted a frequency of dysplasia**(Table/Fig-12,13)** of 1.74% which is very similar to that reported by Kini H et al[17] (1.75%) and Beena D et al[11](1.5%). Higher frequencies have been noted by Khanna R et al[31] (8.5%) and Duarte I et al[32](16%). Various authors have observed very high incidence of dysplasia adjacent to the site of invasive carcinoma (Khanna R et al[31] in 25% of cases, Martinez Guzman et al[28]-low-grade

dysplasia in 40% and high-grade in 16% of cases). Duarte I et al[32]recommended extensive sampling of the proximal, middle and distal segments of the specimen with at least 2-3 routine sections from each part keeping in view the focal and/or patchy distribution of the precursor lesions. The present authors also strongly recommend for such extensive sampling.

Primary carcinoma of gall bladder is the commonest cancer of the biliary tract and the 3rd most common cancer of the gastrointestinal tract. Western countries report higher incidence of gall bladder cancers [29]) while in India, northern and north eastern states encounter greater number of cases compared to southern states. The overall incidence reported for gall bladder cancers varies from 0.4 to 3%, females being 2-6 times more frequently affected as compared to males. In the present study, we observed 7 cases (3.04%) of primary carcinoma of gall bladder, all being of well differentiated adenocarcinoma variety **(Table/Fig - 14).** Similar incidences of gall bladder cancer have been reported by Jokhi et al[14](3.0%) and Duduyemi BM et al[33](3.8%) . Few studies from North India however have recorded much higher frequencies (Tyagi et al-6.8%[9], Agrawal R et al[8] - 10%, Gupta SC et al[34]-12.4%). Studies across board confirm association of gall stones with gall bladder cancer in 70-100% of cases and incriminate gall stones as the most important risk factor in development of gall bladder cancer. In our study, all 7 cases (100%) of gall bladder carcinoma were associated with gall stones. The observation of frequent occurrence of epithelial changes like metaplasia, dysplasia and carcinoma in situ in tissues adjacent to the invasive carcinoma has lent support to the plausible concept of sequence of events like chronic irritation and inflammation, induction of changes like hyperplasia, metaplasia, dysplasia and carcinoma in situ and development of overt invasive carcinoma.[27],[28],[32] The average duration of cholelithiasis and chronology of epithelial changes culminating in invasive carcinoma is estimated at approximate 10 years and average age of occurrence is reported as 6th and 7th decades.[30] In our study however, all cases of carcinoma gall bladder were females in the 5th and 6th decades pointing towards an earlier occurrence. The most common histologic type of gall bladder carcinoma is adenocarcinoma (80-95%) followed by other less common types like adenosquamous carcinoma(1-4%), squamous carcinoma (1-6%) and anaplastic carcinoma(2-7%).[17],[35]

V. CONCLUSION

Cholelithiasis and associated gall bladder disease continue to inflict significant morbidity and mortality worldwide, particularly India witnessing a significant increase in the number of gall bladder diseases. The age profile of gall bladder disease affliction is swinging towards more younger age groups(3rd and 4th decades) and males are also more often being affected. Cholelithiasis plays the key agent in 70-90% of all gall bladder diseases producing various inflammatory and noninflammatory changes including the pre-neoplastic and neoplastic lesions. The incidence of gall bladder cancers is on the rise in India, spreading over from the old stone belt of north India to more of eastern and other states. Hence it is imperative to subject all cholecystectomy specimens for histomorphologial examination with a more open and vigilant approach. Including larger number of sections and focussing on the search for pre-neoplastic and neoplastic lesions along with other morphological changes would improve the overall outcome of gall bladder diseases including morbidity and mortality.

BIBLIOGRAPHY

[1]. Weedon D. Diseases of the gallbladder. In: McSween RMN, Antony PP, Bua AD, et al, eds. Pathology of the Liver, 3rd edition. New York: Churchill Livingstone; 1994:514-534.

[2]. Kulkarni AM, Jadhav ED, Ramteke RV. Histopathological spectrum of gall bladder lesions. Int J Res Med Sci. 2020 Mar;8(3):1056-1060

[3]. Prakash A. Chronic cholecystitis and cholelithiasis in India.IntSurg 1968;49:79-85.

[4]. Mohan H, Punia RP, Dhawan SB, Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in north India. Indian J Surg 2005;67:140-2.

[5]. Savita Agarwal , Pinki Pandey , Megha Ralli , Ranjan Agarwal , Priyanka Saxena. Morphologic Characterisation of 1693 Cholecystecomy Specimens- A Study from Tertiary Care Center in Northern India. Journal of Clinical and Diagnostic Research. 2018 Jan, Vol-12(1): EC05-EC09

[6]. Goyal S, Singla S, Duhan A. Correlation between gallstones characteristics and gallbladder mucosal changes: A retrospective study of 313 patients. Clin Cancer Investigation J. 2014;3(2):157-61.

[7]. A.C.Srivastav, Manglesh Srivastava, Rajesh Paswan. Spectrum of clinico-pathological presentations of gall bladder diseases in

eastern UP. International Journal of Contemporary Medicine Surgery and Radiology. 2019;4(1):A18-A23.
[8]. Agrawal R, Srivastava A, Mohan N, Arya A, Sharan J, Singh A. Histo-morphological study of mucosal changes in gall bladder a tertiary care centre. Ind J Pathol Oncol, 2018;5(3):398-404.
[9]. Tyagi SP, Tyagi N, Maheshwari Y, Ashraf SM, Sahoo P. Morphologic changes in diseased gall bladder: a study of 415 cholecystectomies at Aligarh. J Indian Med Assoc 1992; 90: 278181.
[10]. Vahini G, Premalatha P, Mathi A, Krishna R, Renuka I.V. A Clinicopathological Study of Gallbladder Lesions. IOSR-JDMS 2015;14(2)III:15-20
[11]. Beena D, Shetty JP, Jose V. Histopathological Spectrum of Diseases in Gallbladder. National Journal of Laboratory Medicine. 2017 Oct, Vol-6(4): PO06-PO096
[12]. Gupta K, Faiz A, Thakral RK, Mohan A and K Sharma VK. The spectrum of histopathological lesions in Gallbladder in cholecystectomy specimens. International Journal of Clinical and Diagnostic Pathology 2019; 2(1): 146-151
[13]. Singh P, Jaiswal VK, Verma N, Rathi M, Sharma B, Saroj AK. Histopathological spectrum of gall bladder lesions and association with cholelithiasis. International Journal of Medical and Health Research, Volume 4; Issue 9; September 2018; Page No. 134-138
[14]. Cyrus Jokhi, R Kanetkar and V Vohra . Study of histopathological findings in gallbladder diseases. Indian Journal of Pathology and Oncology 2019;6(4):627–635
[15]. Bashir M Jarrar, Meshref A al-rowaili . Chemical Composition of Gallstones from Al-Jouf Province of Saudi Arabia. Malaysian J Med Sci. Apr-Jun 2011; 18(2): 47-52
[16]. Mohammed A. Taher. Descriptive study of cholelithiasis with chemical constituents' analysis of gallstones from patients living in Baghdad, Iraq . Int. J. Med. Med. Sci. Vol. 5(1), pp. 19-23, January 2013
[17]. Kumar H, Kini H,Tiwari A. Histological evaluation of 400 cholecystectomy specimens.Journal of Pathology of Nepal, (2015) Vol. 5, 834-840.
[18]. Patil M, Londhe MM, Margam S, Iqbal J. Spectrum of Lesions of Gall Bladder: Experience of Five Years at Tertiary Care Hospital. Ann Pathol Lab Med. 2018;5(9):779–784.
[19]. Digvijay Singh Dattal, Rajni Kaushik, Anchana Gulati, V. K. Sharma. Morphological spectrum of gall bladder lesions and their correlation with cholelithiasis. Int J Res Med Sci. 2017 Mar;5(3):840-846.
[20]. Tadashi Terada. Histopathologic features and frequency of gall bladder lesions in consecutive 540 cholecystectomies . Int J Clin Exp Pathol 2013;6(1):91-96
[21]. Jutras A, Longtin JM, Levesque HP. Hyperplastic cholecystoses. Am J Roentgenol. 1960;83:795–827.
[22]. Pang L, Zhang Y, Wang Y, Kong J. Pathogenesis of gallbladder adenomyomatosis and its relationship with early-stage gallbladder carcinoma: An overview. Braz J Med Biol Res. 2018;51:e7411
[23]. Nabatame N, Shirai Y, Nishimura A, Yokoyama N, Wakai T, Hatakeyama K. High risk of gallbladder carcinoma in elderly patients with segmental adenomyomatosis of the gallbladder. J Exp Clin Cancer Res. 2004;23:593-8.
[24]. Rashmi H K, Shivamurthy Y L, Suresh K K, Chatura K R. Histopathological study to establish the association of gallstones with cholecystitis and carcinoma of gallbladder. MedPulse International Journal of Pathology. March 2018; 5(3): 56-59.
[25]. Manuela Stancu, Irina-Draga Căruntu, Simona Giuşcă, Gioconda Dobrescu. Hyperplasia, metaplasia, dysplasia and neoplasia lesions in chronic cholecystitis – a morphologic study. Romanian Journal of Morphology and Embryology 2007, 48(4):335–342
[26]. Elfving G, Teir H, Degert H, Mäkelä V. Mucosal hyperplasia in the gallbladder demonstrated by plastic models. Acta Pathol Microbiol Scand 1969;77:384‑8
[27]. Albores-Saavedra J, Menck HR, Scoazec JC, Soehendra N, Wittekind C, Sriram PV J, Spira B. Carcinoma of the gall bladder and extrahepatic bile ducts. In: Mamilton SR and Aaltonen LA editors. WHO Classification of tumours. Pathology and genetics of tumours of the digestive system. Lyon: IARC Press. 2000. pp: 203214
[28]. Martinez-Guzman-e, de-la Rosa-Bayan J. Neoplasma and dysplasia of the gallbladder and their relationship with lithiasis. A case

control clinic pathological study. Rev Gastroenterol Mex 1998;63:82-8.

[29]. Charalampos Seretis, Emmanouil Lagoudianakis , George Gemenetzis , Fotios Seretis , Apostolos Pappas , Stavros Gourgiotis. Metaplastic Changes in Chronic Cholecystitis: Implications for Early Diagnosis and Surgical Intervention to Prevent the Gallbladder Metaplasia-Dysplasia-Carcinoma Sequence. J Clin Med Res. 2014;6(1):26-29

[30]. Katabi N. Neoplasia of gallbladder and biliary epithelium. Arch Pathol Lab Med 2010;134:1621-7.

[31]. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in gallbladder due to stone disease. Indian J surg. 2006; 68(4):201-4.

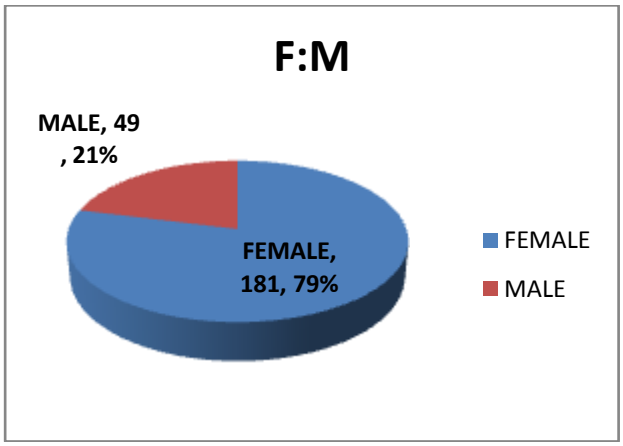
[32]. Duarte I, Llanos O, Domke H, Harz C, Vicente Valdivieso. Metaplasia and precursors lesion of gallbladder carcinoma. Cancer 1993;72:1878-84. Crossref

[33]. Duduyemi M, Aboagye E,Titiloye NA. Histopathological review of cholecystectomy specimens in a tertiary hospital in Ghana. June 2019, Journal of Gastroenterology and Hepatology Research Vol.11

[34]. Gupta SC, Misra V, Singh PA, Roy A, Misra SP, Gupta AK. Gall stones and carcinoma gall bladder. Indian J Pathol Microbiol. 2000;43:147-54

[35]. Hamdani NH, Quadri SK, Aggarwala R, Bhartia VK, Chaudhuri S, Debakshi S, Baig Sj, Pal NK. Clinicopathological study of gall bladder carcinoma with special reference to gallstones: our 8-year experience from eastern India. Asian Pac J Cancer Prev . 2012;13(11):5613-7.

TABLES/FIGURES



Table/Figure-1: Gender Distribution of all Post-cholecystectomy Cases (Total Cases-230)

Age group	No. Of cases	Female- Male Distribution of Cases		% of cases
		Female	Male	
11-20	4	4	0	1.74
21-30	33	33	0	14.35
31-40	81	69	12	35.22
41-50	66	51	15	28.69
51-60	36	21	15	15.65
61-70	7	3	4	3.04
71-80	2	0	2	0.87
81-90	1	0	1	0.43
Total	230	181	49	100

Table/Figure-2:: Age and Gender Distribution Of Post-cholecystectomy Cases (Total Cases-230)

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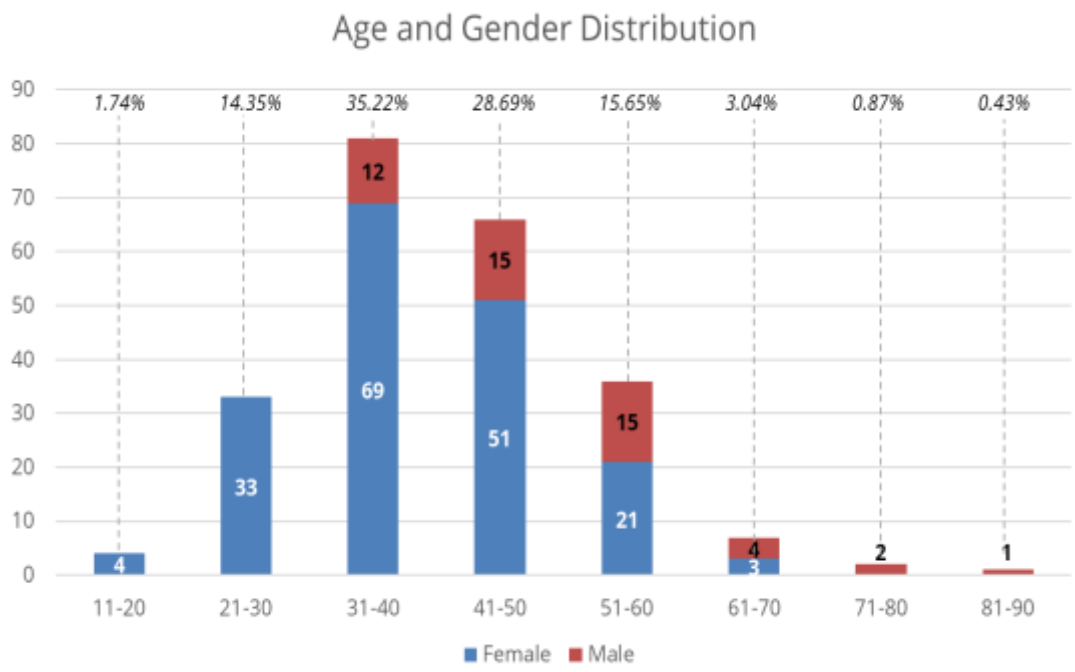
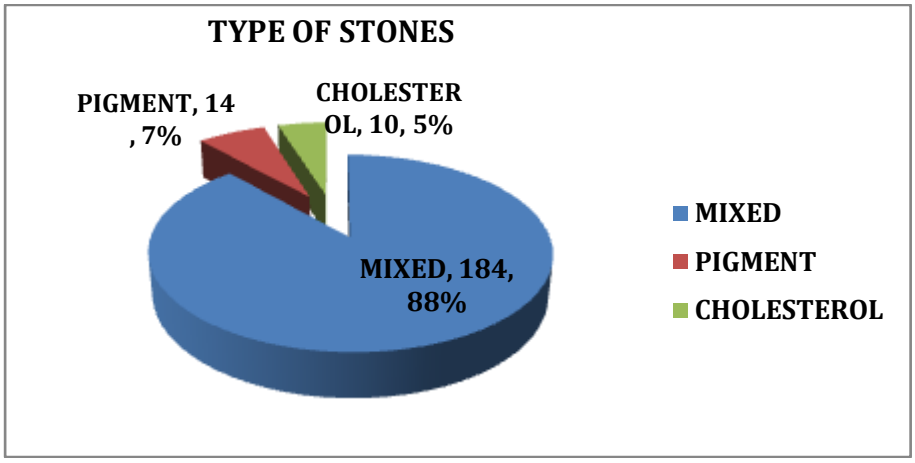


Table/Fig-3: Age and Gender Distribution of all Post-cholecystectomy Cases.



Table/Fig.-4: Morphological types of stones in all Post-cholecystectomy Cases

Histomorphological Changes of Gall Bladder		**No. Of cases**	**% of Cases (Frequency)**
Chronic Cholecystitis:		190	82.6
	Chronic Calculus Cholecystitis	172	74.78
	Chronic Acalculus Cholecystitis	18	7.82
Acute Calculus Cholecystitis		21	9.13

Acute on Chronic Calculus Cholecystitis		15	6.52
Chronic Follicular Cholecystitis		6	1.74
Xanthogranulomatous Cholecystitis		5	2.17
Adenomyomatosis of Gall bladder		11	4.78
Cholesterolosis of Gall Bladder		7	3.04
Adenomatous hyperplasia		13	5.65
Dysplasia		4	1.74
Metaplasia	Pyloric Metaplasia	29	12.6%
	Intestinal Metaplasia	7	3.1%
Primary carcinoma of Gall bladder		7	3.04

Table/Figur-5: Histomorphological Changes of Gall Bladder observed in 230 Post-cholecystectomy Cases

Histomorphological Changes	**No.of cases with Stones**	**No.of cases without Stones**
Chronic Cholecystitis:	172	18
Acute Calculus Cholecystitis	21	0
Chronic Follicular Cholecystitis	6	0
Xanthogranulomatous Cholecystitis	5	0
Adenomyomatosis	9	2
Cholesterolosis	4	3
Adenomatous Hyperplasia	10	3
Dysplasia	4	0
Metaplasia	32	4
Primary carcinoma of Gall bladder	7	0

Table/Figure-6: Histomorphological Changes of Gall Bladder in association with Gall Stones

Age Group	**Present study**	**Kulkarni AM et al[2]**	**Devi B et al[11]**	**Gupta K et al[12]**	**Singh P et al[13]**
11-20	1.74%	1.86%	1.5%	2.76%	3.24%
21-30	14.35%	10.56%	12.5%	22.58%	28.0%

31-40	35.22%	30.43%	23%	26.49%	32.63%
41-50	28.69%	17.39%	26%	24.65%	19.44%
51-60	15.65%	12.42%	22%	15.20%	11.34%
61-70	3.04%	18.63%	15%	7.37%	4.16%

Table/Figure-7: Comparison Of Age Group Distribution in various studies

Type of stones	**Present Study**	**Srivastav et al.[7]**	**Singh P et al[13]**	**Jokhi C et al[14]**	**Mohan et al[4]**	**Kulkarni et al[2]**	**Beena D et al[11]**
Mixed stones	88%	78.69%	82.5%	84.1%	62.3%	-	2%
Pigment stones	7%	8.63%	6.5%	12.4%	17.3%	83.02%	58.5%
Cholesterol stones	5%	5.33%	11%	3.5%	3.2%	14.15%	4.5%

Table/Figure-8: Types of Gall stones observed in Various studies

Histopathological Lesions	**Present Study**	**Kulkarni AM et al[2]**	**Tyagi et l[9]**	**Kini H et al[17]**	**Singh P et al[13]**	**Patil M et al[18]**	**Mohan H et al[4]**
Chronic Calculus Cholecystitis	74.78%	57.76%	50.8%	66.7%	73.5%	93.1%	-
Chronic Acalculus Cholecystitis	7.82%	22.36%	-		7.25%		-
Acute Cholecystitis	9.13%	-	4.1%	6%	8.7%	2.91%	
Acute on Chronic Cholecystitis	6.57%	11.17%	10.8%				
Follicualr Cholecystitis	2.6%	1.24%	6.2%			0.72%	2.3%
Xanthogranulomatous Cholecystitis	2.17%	1.24%	4.1%	0.5%	1%	1.1%	2.3%
Cholesterolosis	3.04%		2.7%		4.6%	0.45%	10.1%
Adenomyomatosis	4.78%	-	8.2%			0.27%	
Adenomatous hyperplasia	5.65%	-	10.1%	31.5%	2.5%	8%	0.09%
Dysplasia	1.74%	-	-	1.75%	0.8%		

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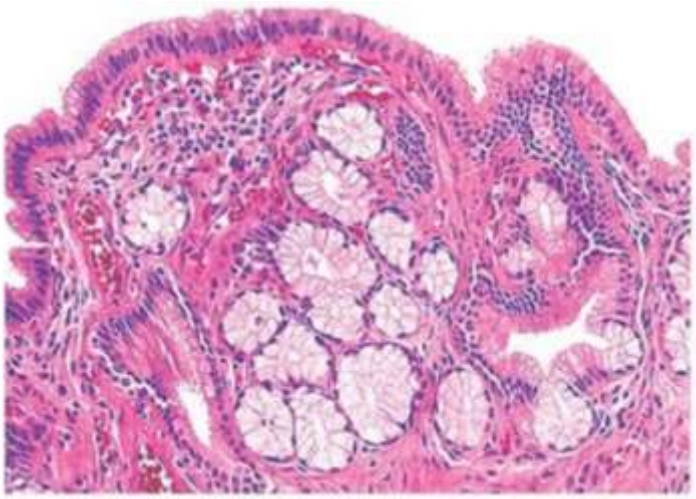
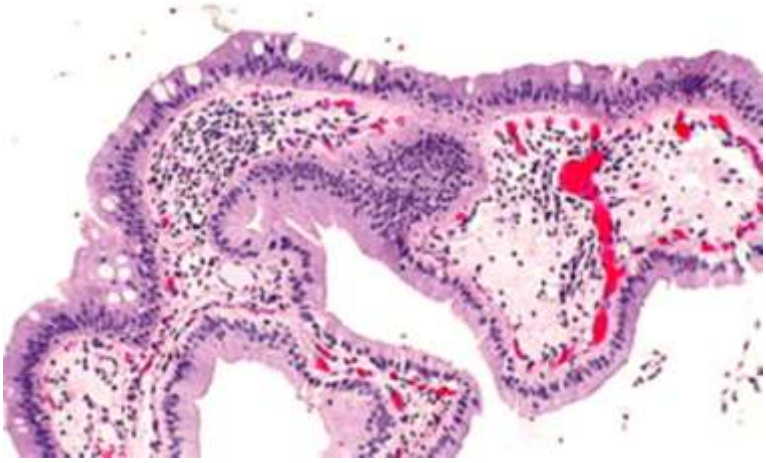
Metaplasia	15.7%	-	-	23.7 %	7.7%		
Primary Carcinoma Gall bladder	3.04%	1.24%	6.8%	1.25 %	0.4%	1.09%	1.09%

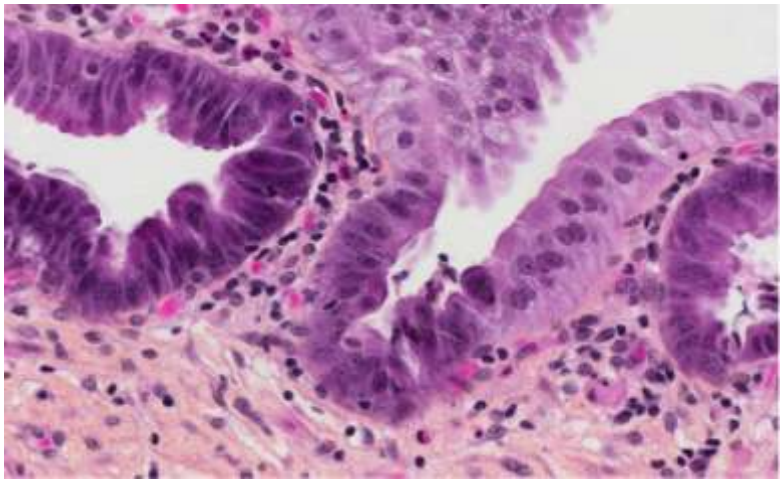
Table/Figure-9: Comparative Study of Incidence of Histomorphological lesions of Gall Bladder in Different Studies



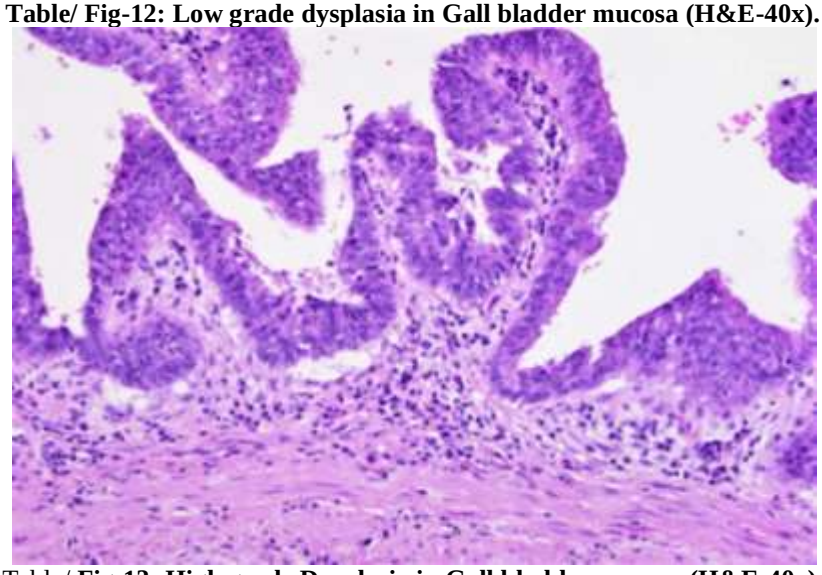
Table/Fig-10: **Pyloric Metaplasia in Gall bladder mucosa(H&E-40x).**



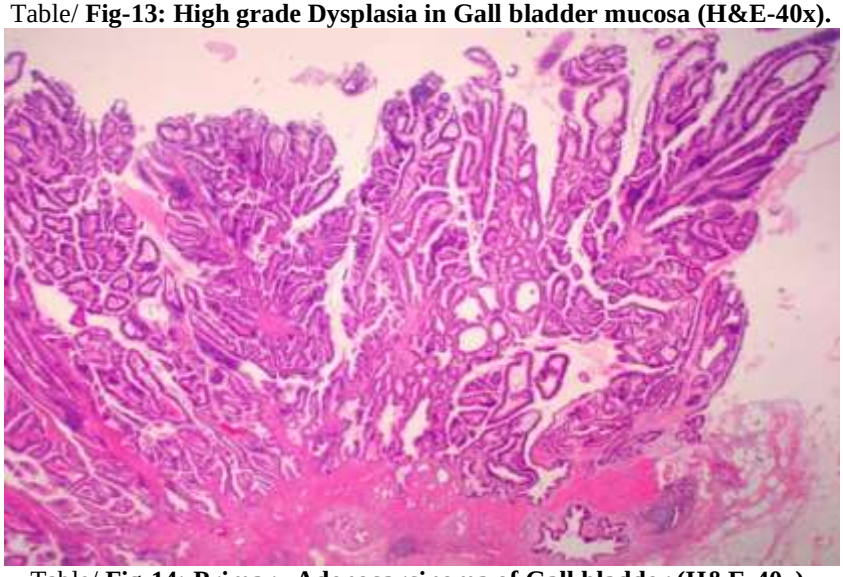
Table/Fig-11: Intestinal Metaplasia in Gall bladder mucosa (H&E-40x).



Table/ Fig-12: Low grade dysplasia in Gall bladder mucosa (H&E-40x).



Table/ **Fig-13: High grade Dysplasia in Gall bladder mucosa (H&E-40x).**



Table/ **Fig-14: Primary Adenocarcinoma of Gall bladder (H&E-40x).**