HISTOPATHOLOGICAL STUDY OF POST-SURGICAL GALLBLADDER TO ESTABLISH TRUE HISTOPATHOLOGY PROVEN CHRONIC INFLAMMATION

Tania Khattak¹, Almas Khattak², Susan Kakakhel³, Anwar Ul Haque⁴

ABSTRACT:

OBJECTIVES:
The aim of this study was to establish true histopathology proven diagnosis of chronic cholecystitis.

METHODOLOGY:

A cross-sectional study was conducted on 51 post-surgical gallbladders was done to assess their histopathological patterns in a single centered tertiary care hospital. The specimens were studied for chronic cholecystitis, fibrosis, hypertrophy and presence of Rokitansky-Aschoff sinuses. Descriptive analysis was done and associations of the histopathological changes with demographic data of patients were analyzed through Chi-squared test.

RESULTS:

Fifty-one post cholecystectomy samples of gallbladder were analyzed for histopathological changes with 82.4% showing chronic cholecystitis, 84.3% fibrosis, 64.7% congestion, and more than 60% mild or moderate hypertrophy. Moreover, 49% of the specimens showed Rokitansky-Aschoff sinuses. All these changes suggest chronic inflammation.

CONCLUSION:

Chronic cholecystitis, fibrosis, and Rokitansky-Aschoff sinuses are the most common histopathological findings in specimens of patients undergone cholecystectomy for cholelithiasis.

KEYWORDS: Cholelithiasis, Chronic Cholecystitis, Cholecystectomy, Rokitansky-Aschoff sinuses

INTRODUCTION:

Gallbladder is small organ of the digestive tract situated between the two lobes of the liver having three parts namely the fundus, corpus and infundibulum. Its main function is collecting, storing and transporting bile produced by liver. The histological pattern of gallbladder shows a mucosa of epithelial cells, a lamina propria and a muscle and serosal layer. The gallbladder is prone to a spectrum of diseases. Cholelithiasis is the medical term used for gallstone disease (hard deposits of digestive fluids in the gallbladder commonly presenting with right abdominal pain associated with nausea and vomiting, indigestion, heartburn and flatulence. It is the most commonly presenting health issue in
emergency medicine. Gallstones can occur in any age and gender but most commonly it affects female patients after their forties. Most of the cases of gallstones are asymptomatic which are usually found incidentally requiring no treatment. However, over time symptoms can appear leading to complications such as acute and chronic cholecystitis, pancreatitis, and carcinomas. About 3-10% of patients presenting with abdominal pain are usually diagnosed as acute cholecystitis mostly in those above 50 years of age. A number of genetic and environmental factors are attributed to the formation of gallstones. These include female gender (up to 60%), increasing age, use of contraceptives and pregnancy as cholesterol level is increased by estrogen, family history, fatty food and inactivity etc. although more common in females, the gallstone disease is more severe in males.

The most common and preferred treatment of choice for gallstones disease is surgical excision of gallbladder. Many cases of early gall bladder carcinoma are missed because of not sending the specimen for histopathology. 0.3-12% of the carcinoma of the gall bladder is associated with gall stones. Therefore, every specimen should be sent for histopathology to avoid any mis-diagnosis. The morphologies of gall bladder vary vastly, from being muscular hypertrophy to fibrosis. But are these frequencies benign or malignant it is still unclear. We assume that cholecystectomies are frequently done for cholelithiasis-induced inflammation based on clinical features of patients for cholecystitis. Therefore, we conducted this study to establish the true histopathological proven chronic inflammation of the gallbladder after surgery.

METHODOLOGY:

A descriptive cross-sectional study on 51 histopathological examinations of postoperative gallbladders cholecystectomy for gallstones and their individualized reports from year 2018 to 2020. The requests for the examinations and reports were placed by different surgeons from Northwest General Hospital and Research Centre after they operated the patients. After the operation, the operating surgeon conducted the gross examination, and the specimen was then sent for histopathological examination in a container with formalin solution. At arrival in the laboratory, each specimen was carefully grossly examined and properly treated to prepare slides. Several slides were prepared after going through the long routine histopathological slide preparation process and finally stained with haematoxylin and eosin. These slides were examined under microscope. The following histopathological changes were studied: presence of acute and chronic cholecystitis, cholelithiasis, lymphocytes, smooth muscle hypertrophy or atrophy, presence of sinuses, congestion, fibrosis, neutrophils and other cells and the evidence for malignancy. The demographic data of patients in terms of age and gender was collected. Descriptive analysis was performed to determine association between the histopathological changes and patients’ age and gender. The ethics committee of Northwest General Hospital and Research Centre approved the study.

RESULTS:

Fifty-one histopathological reports were analyzed, 33 (64.7%) from females and 18 (35.3%) from male patients having undergone cholecystectomy for cholelithiasis induced inflammation. The mean age of patients was 40.06 ± 16.640 years, with 28 (54.9%) patients under 40 years and 23 (45.1%) above 40 years of age.
### Table 1: Frequency Distribution of Histopathological Diagnoses and Changes after Cholelithiasis

| Histopathological Changes       | Number | %  |
|---------------------------------|--------|----|
| Chronic Cholecystitis           | 42     | 82.4 |
| Acute Cholecystitis             | 5      | 9.8  |
| Cholesterosis                   | 6      | 11.8 |
| Presence of Lymphocytes         |        |     |
| Excess                          | 3      | 5.9  |
| Many                            | 27     | 52.9 |
| Few                             | 7      | 13.7 |
| None                            | 14     | 27.5 |
| Atrophy/Hypertrophy            |        |     |
| Atrophy                         | 11     | 21.6 |
| Mild Hypertrophy                | 20     | 39.2 |
| Moderate Hypertrophy            | 18     | 35.3 |
| Severe Hypertrophy              | 2      | 3.9  |
| Rokitansky-Aschoff Sinuses     | 25     | 49   |
| Congestion                      | 33     | 64.7 |
| Fibrosis                        | 43     | 84.3 |
| Additional Findings             |        |     |
| Neutrophils                     | 5      | 9.8  |
| Macrophages                     | 7      | 13.7 |
| Eosinophils & Multinucleated Giant Cells | 1 | 2 |
| Hypertrophic Nerves             | 1      | 2    |
| Thick Arterial Wall             | 1      | 2    |
| Plasma Cells                    | 1      | 2    |
| Massive Haemorrhage             | 1      | 2    |
| Necrosis                        | 1      | 2    |
| Autolyzed Epithelium            | 1      | 2    |

### Table 2: Association of Predominant Histopathological Changes with Demographic Information of Patients

| Characteristics | <40 years (N) | >40 years (N) | P-value | Female (N) | Male (N) | P-value |
|-----------------|---------------|---------------|---------|------------|----------|---------|
| Chronic Cholecystitis (N=42) Present | 22            | 20            | 0.434   | 28         | 14       | 0.527   |
| Absent          | 6             | 3             |         | 5          | 4        |         |
| Fibrosis (N=43) Present | 23            | 20            | 0.638   | 28         | 15       | 0.887   |
| Absent          | 5             | 3             |         | 5          | 3        |         |
| Rokitansky-Aschoff Sinuses (N=25) Present | 14            | 11            | 0.877   | 18         | 7        | 0.285   |
| Absent          | 14            | 12            |         | 15         | 11       |         |
DISCUSSION:

This study was conducted to establish histopathological reports the true diagnosis of chronic cholecystitis (42 out of 51 samples) after cholelithiasis and other histopathological changes. The findings suggest that chronic cholecystitis was the most frequent diagnosis proved from the histopathologic reports of 51 gallbladders after cholecystectomy for cholelithiasis. Acute cholecystitis and cholesterolosis were least observed. Other histopathological findings show that fibrosis was the most prominent finding in 43 out of 51 samples. Other prominent findings were presence of lymphocytes, hypertrophy, congestion and Rokitansky-Aschoff sinuses in majority of the samples. All these findings suggest evidence of chronic inflammation induced by cholelithiasis indicating cholecystectomy. No age or gender related statistically significant differences were seen among patients. A study conducted in India also found chronic cholecystitis to be the most frequent histopathologic diagnosis established after cholecystectomy for cholelithiasis. In another study the most common age group affected was between 40-49 years corresponding with our findings. Another study in a tertiary care hospital to study histopathological spectrum of gallbladder disease also found chronic cholecystitis to be the most frequent post surgically established histopathologic diagnosis after cholelithiasis. A study with large sample size of 1278 samples of gallbladder studied for histopathological proven cholecystitis also found that almost 98% of the samples had chronic cholecystitis on histopathologic reports. These findings suggest that cholecystectomies done for cholelithiasis induced chronic inflammation are justified as all these studies including ours established the true chronic inflammation proved by the gold standard histopathology reports. As with all other studies, our study also showed female patients to be predominant in number having diverse spectrum of gallbladder disease. In contrast, other studies also found incidental malignancies in their specimens while this study did not find any evidence of malignancy. The reports found no evidence of malignancy and very few numbers of other cells as shown in the tables.

LIMITATIONS:

We had some limitation concerning this study as we had a small sample of only 51 surgically excised gallbladders limiting our ability to generalize our findings and establish cause-effect relationship between the variables. We anticipate conducting prospective multicentre study in future to make up for the limitation.

CONCLUSION:

Chronic cholecystitis induced by cholelithiasis is the most common clinical indication for cholecystectomy. Our research in agreement with other studies concluded that chronic cholecystitis is the most common histopathological proven diagnosis in post-surgical gallbladders excised for cholelithiasis, with female predominance. Other histopathological findings such as fibrosis, hypertrophy, and Rokitansky-Aschoff sinuses were also predominantly seen suggesting chronic inflammation of the gallbladder warranting cholecystectomy.

CONFLICT OF INTEREST: None

FUNDING SOURCES: None

REFERENCES:

1. Afghani E, Lo SK, Covington PS, Cash BD, Pandol SJ. Sphincter of Oddi function and risk factors for dysfunction. Frontiers in nutrition. 2017 Jan 30;4:1.
2. Wang CC, Tsai MC, Sung WW, Yang TW, Chen HY, Wang YT, Su CC, Tseng MH, Lin CC. Risk of cholangiocarcinoma in patients undergoing therapeutic endoscopic retrograde cholangiopancreatography or cholecystectomy: A population based study. World journal of gastrointestinal oncology. 2019 Mar 15;11(3):238.
3. Tanaja J, Lopez RA, Meer JM. Cholelithiasis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
4. Navuluri R, Hoyer M, Osman M, Fergus J. Emergent treatment of acute cholangitis and acute cholecystitis. Seminars in interventional radiology.
HISTOPATHOLOGICAL STUDY OF POST-SURGICAL GALLBLADDER

2020 Mar (Vol. 37, No. 01, pp. 014-023). Thieme Medical Publishers.

5. Afamefuna S, Allen SN. Gallbladder disease: pathophysiology, diagnosis, and treatment. US Pharm. 2013;38(3):33-41.

6. Bansal A, Akhtar M, Bansal A. A clinical study: prevalence and management of cholelithiasis. Int Surg J. 2014;1(3):134

7. Tan Z, Xie P, Qian H, Yao X. Clinical analysis of prophylactic cholecystectomy during gastrectomy for gastric cancer patients: a retrospective study of 1753 patients. BMC surgery. 2019 Dec;19(1):7.

8. Histopathology of Gallbladder After Cholecystectomy [Internet]. [cited 2021 May 10]. Available from: https://www.medscape.com/viewarticle/810696_2

9. Khan MM, Mohammed AT, Behan RB, Yousif S. Frequency of Gall Bladder Carcinoma among Patients of Cholelithiasis at Tertiary Care Hospital. Journal of Pharmaceutical Research International. 2020 Aug 29:20-4.

10. Terada T. Histopathologic features and frequency of gall bladder lesions in consecutive 540 cholecystectomies. Int J Clin Exp Pathol [Internet]. 2013 Nov 20 [cited 2021 May 10];6(1):91–6. Available from: www.ijcep.com/

11. Rawla P, Sunkara T, Thandra KC, Barsouk A. Epidemiology of gallbladder cancer. Clinical and experimental hepatology. 2019 May;5(2):93.

12. Butti AK, Yadav SK, Verma A, Das A, Naeem R, Chopra R, Singh S, Sarin N. Chronic calculus cholecystitis: Is histopathology essential post-cholecystectomy?. Indian journal of cancer. 2020 Jan;57(1):89.

13. Sing A, Singh G, Kaur K, Goyal G, Saini G, Sharma D. Histopathological changes in gallbladder mucosa associated with cholelithiasis: a prospective study. Niger J Surg. 2019;25(1):21.

14. Suzuki T, Asahi Y, Sawada A, Umemoto K, Kina M, Shinohara M, et al. Laparoscopic cholecystectomy for a cholelithiasis patient with an aberrant biliary duct of B5: a case report [Internet]. Surg Case Reports. 2020;6(1). Available from: https://doi.org/10.1186/s40792-020-00981-z

15. Khan DM, S.C A. Histopathological spectrum of gallbladder diseases in a tertiary care centre. IP Arch Cytol Histopathol Res. 2020;3(4):206-9.

16. Hasan A, Nafie K, Aldossary MY, Ismail A, Monazea K, Baheeg M, Rady K, Elhawary R, Ibrahim AA. Unexpected histopathology results following routine examination of cholecystectomy specimens: How big and how significant?. Annals of Medicine and Surgery. 2020 Dec 1;60:425-30.

17. Holanda AKG, Lima Júnior ZB. Gallbladder histological alterations in patients undergoing cholecystectomy for cholelithiasis. Rev Col Bras Cir. 2019;46(6):1-8.

18. Jha V, Sharma P, Mandal KA. Incidental gallbladder carcinoma: Utility of histopathological evaluation of routine cholecystectomy specimens. South Asian journal of cancer. 2018 Jan;7(1):21.

CONTRIBUTORS

1. Tania Khattak - Concept & Design; Data Acquisition; Drafting Manuscript; Critical Revision; Final Approval
2. Almas Khattak - Data Analysis/Interpretation; Critical Revision; Final Approval
3. Susan Kakakhel - Data Analysis/Interpretation; Critical Revision;
4. Anwar Ul Haque - Concept & Design; Supervision; Final Approval

LICENSE: JGMDS publishes its articles under a Creative Commons Attribution Non-Commercial Share-Alike license (CC-BY-NC-SA 4.0). COPYRIGHTS: Authors retain the rights without any restrictions to freely download, print, share and disseminate the article for any lawful purpose. It includes scholarly networks such as Research Gate, Google Scholar, LinkedIn, Academia.edu, Twitter, and other academic or professional networking sites.