

 <p>ISSN NO. 2320-5407</p>	<p>Journal Homepage: - www.journalijar.com</p> <p>INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)</p> <p>Article DOI: 10.21474/IJAR01/2883 DOI URL: http://dx.doi.org/10.21474/IJAR01/2883</p>	 <p>INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR) ISSN 2320-5407</p> <p>Journal Homepage: http://www.journalijar.com Journal DOI: 10.21474/IJAR01</p>
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RESEARCH ARTICLE

HISTOPATHOLOGY OF GALLBLADDER IN IRON DEFICIENCY ANEMIA PATIENTS UNDERGOING CHOLECYSTECTOMY: A PROSPECTIVE STUDY

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Manuscript Info

Manuscript History

Received: 21 November 2016
Final Accepted: 21 December 2016
Published: January 2017

Key words:-

S. Ferritin, Anemia, Cholecystitis,
Laparoscopic Cholecystectomy

Abstract

Gall stones may be said to be contributing to varied pathology affecting gall bladder ranging from chronic cholecystitis to carcinoma. Cholelithiasis produces diverse histopathological changes in gall bladder mucosa namely acute inflammation, chronic inflammation, cholestasis, hyperplasia and carcinoma. The study was performed on a group of 118 patients who were admitted in department of surgery for cholecystectomy (laparoscopic) during period of 1 year and 16 days. Patients were divided in two groups based on S.Ferritin levels and histopathological examination of these patients was done. In both the groups, majority of subjects were diagnosed as chronic cholecystitis on histopathology. There is one interesting finding that acute cholecystitis is more prevalent in iron deficient cases. A finding suggesting higher prevalence of acute cholecystitis in iron deficient case might indicate if acute cholecystitis may be prevented using iron supplements. To establish this correlation a study with large sample size may be done.

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Introduction:-

A gallstone is a stone formed within the gallbladder out of bile components. Most people with gallstones (about 80%) never have symptoms. Complications of gallstones include inflammation of the gallbladder, inflammation of the pancreas, and liver inflammation. In those who are having gallbladder attacks surgery to remove the gallbladder is typically recommended. This can be either done through several small incisions or through a single larger incision. Surgery is typically done under general anesthesia. Among gastroenterological diseases, Gallstone disease is one of the world's most expensive medical conditions¹. In the United States, there are more than 500 000 cholecystectomies, the total cost of which exceeds 5 billion dollars².

Women are three times more likely to develop gallstones than men, and first-degree relatives of patients with gallstones have a twofold greater prevalence.³

Many conditions affecting gall bladder are characterized by finding of associated gallstones. Gall stones may be said to be contributing to varied pathology affecting gall bladder ranging from chronic cholecystitis to carcinoma. Cholelithiasis produces diverse histopathological changes in gall bladder mucosa namely acute inflammation, chronic inflammation, cholesterosis, hyperplasia and carcinoma. The prevalence of gallstone disease varies with age, sex and ethnic group. In India, gallstone disease is 7 times more common in the north as compared to the south. It is mainly due to dietic influence. ⁴The histopathological diagnosis in most of the cholecystectomy specimens is chronic cholecystitis. However, other diverse, but benign histopathological changes of gallbladder mucosa are also seen namely acute inflammation, cholesterosis, metaplasia and hyperplasia. Very rarely cholecystectomy specimen may reveal an unexpected gallbladder carcinoma. Similarly, surgery is performed in clinically suspected (often supported by radiological and other investigational corroborative findings) cases of Gall bladder malignancy. Still in many cases cholecystectomy performed with provisional diagnosis of benign diseases based on clinical, ultrasonological and computerized tomographic scanning misses a significant number of early malignant lesions of gallbladder. ⁵

Material and Methods:-

This prospective study was conducted in the Department of Surgery in collaboration with Department of Pathology at tertiary care hospital, Lucknow, India. The ethical committee of the institute approved the study protocol.

The study was performed on a group of 118 patients who were admitted in department of surgery for cholecystectomy (laproscopic) during period of 1 year and 16 days

Patients suffering from cholelithiasis confirmed by Ultrasonography and admitted in the surgical ward for cholecystectomy were included in the study irrespective of their age, sex and parity. Both laparoscopic and open cholecystectomies were the procedures advocated for treatment. Patients suffering from empyema and mucocele of the gall bladder were excluded from this study.

Serum iron was estimated by time end point method with ferroZine reagent¹²⁵. The normal reference values were supplied with the kit, for males (60-158 µg/dl) and for females (35-145 µg/dl).

All the gallbladder specimens collected during laproscopic cholecystectomy were submitted for histopathological examination in department of pathology. These specimens were analysed for histopathological changes in relation to gall stone disease.

Observation:-

A total of 86 (72.9%) patients comprised Group I which comprised of patients having Serum ferritin levels within normal range (>60 µg/dl for males and >35 µg/dl for females). Remaining 32 (27.1%) subjects were anemic subjects with serum ferritin levels below normal range (<60 µg/dl for males and <35 µg/dl for females). Thus the ratio of iron deficient to non iron deficient patients in present study was 0.37:1

Distribution of subjects according to Histopathological findings.

S.No.	HPE Findings	Total		Group I (n=86)		Group II (n=32)	
		No.	%	No.	%	No.	%
1.	Cholesterosis	1	1.2	1	1.2	0	0
2.	Acute Cholecystitis	16	13.5	11	12.8	5	15.6
3.	Chronic Cholecystitis	82	69.4	58	62.8	24	75.1
4.	Chronic cholecystitis with Pericholecystitis	5	4.2	3	3.5	2	6.3
5.	Chronic granulomatous cholecystitis	8	6.7	7	8.1	1	3.1
6.	Xanthocholecystitis	6	7.0	6	7.0	0	0

$$\chi^2=4.219(df=5); p=0.518$$

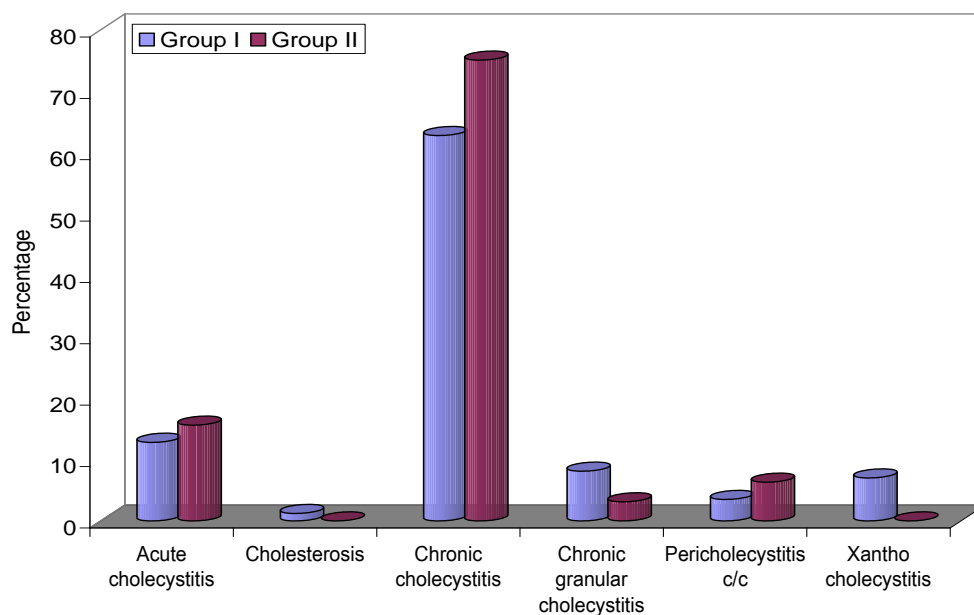


Fig.1. Distribution of subjects according to Histopathological findings.

Histopathological findings in 118 cases were studied. Of these 86 cases belong to group I and 32 belong to group II.

Acute cholecystitis was found in 16 cases, chronic cholecystitis in 86 cases, chronic cholecystitis with pericholecystitis in 5 cases, chronic granumatoscholecystitis in 8 cases and xanthocholecystitis in 6 cases.

In both the groups, majority of subjects were diagnosed as chronic cholecystitis on histopathology. Statistically, the difference between two groups was not significant ($p=0.636$).

There is one interesting finding that acute cholecystitis is more prevalent in iron deficient cases.

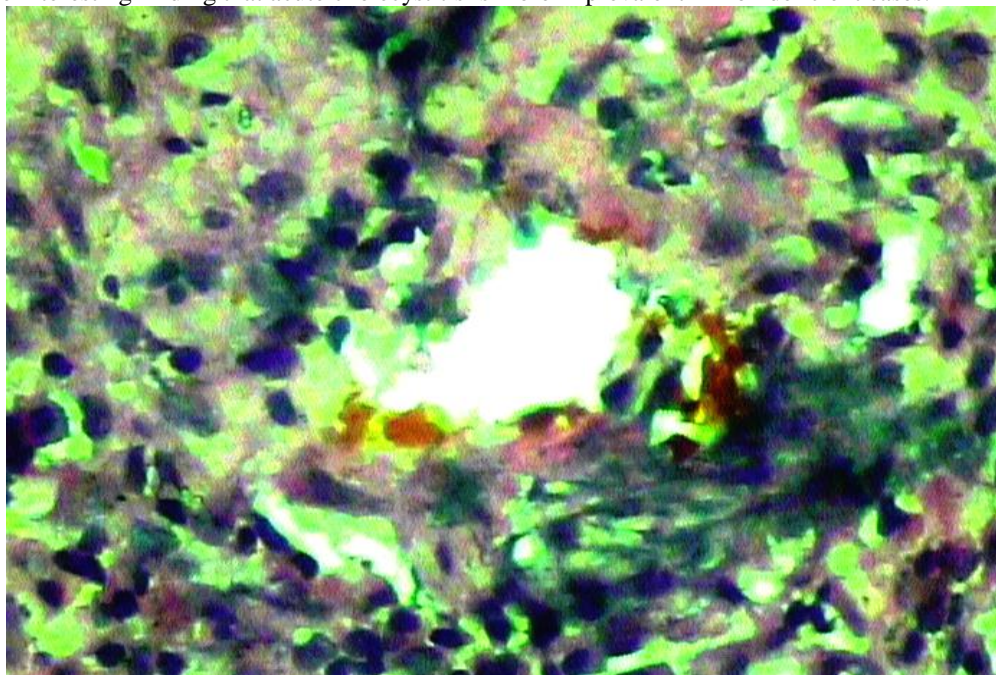


Image 1:- Cholesterosis with biliary sludge.

Cholesterosis was seen in 1 case only (image.1). There was no inflammatory reaction in the wall of gallbladder. Foamy macrophages seen in lamina propria and epithelium, mucosal hyperplasia.



Image 2:- Acute cholecystitis

Acute cholecystitis was found in 16 cases (image.2). There are signs of inflammation present in gallbladder wall. The microscopic features are classical for acute inflammation and include hyperemia, polymorphonuclear leukocyte infiltration, edema and necrosis of the wall of the gall bladder.

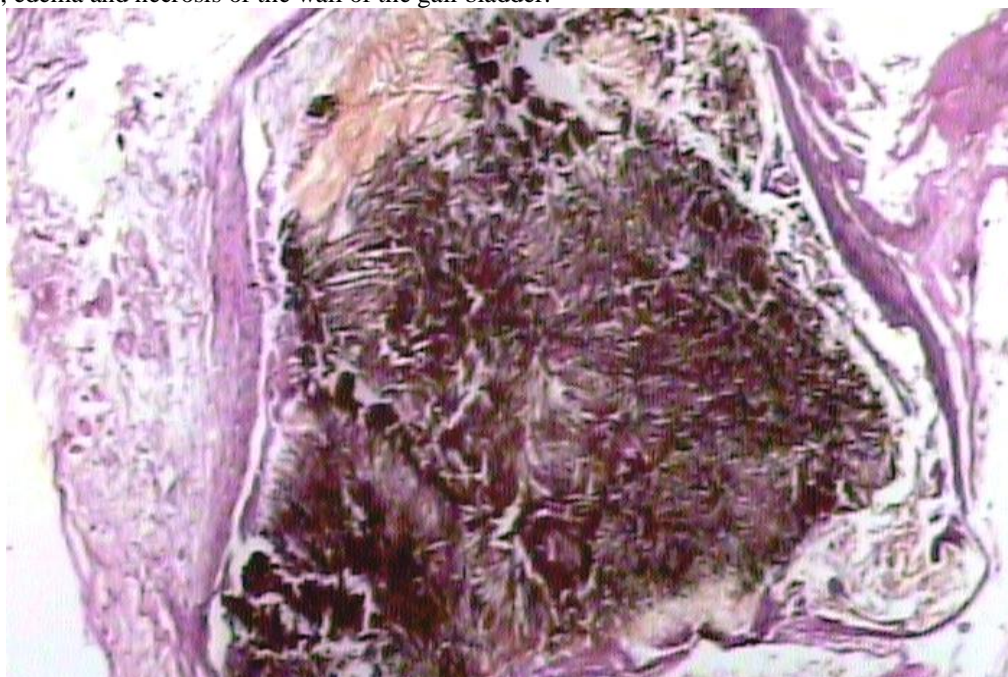


Image 3:- Chronic cholecystitis with impacted stone.

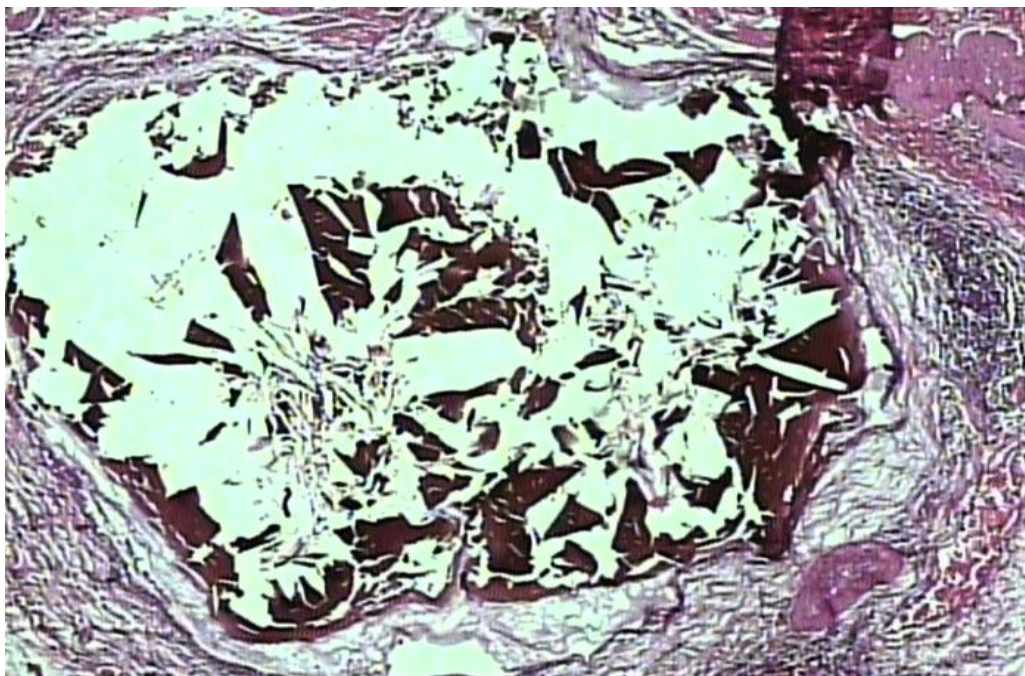


Image 4:- Chronic cholecystitis with impacted cholesterol stone

Chronic cholecystitis was found in 86 cases (image.3, image.4). The gallbladder wall has mild chronic inflammation with rokitansky-Aschoff sinuses, smooth muscle hypertrophy, hyalinized collagen, lymphoid aggregates, variable mucosal changes.

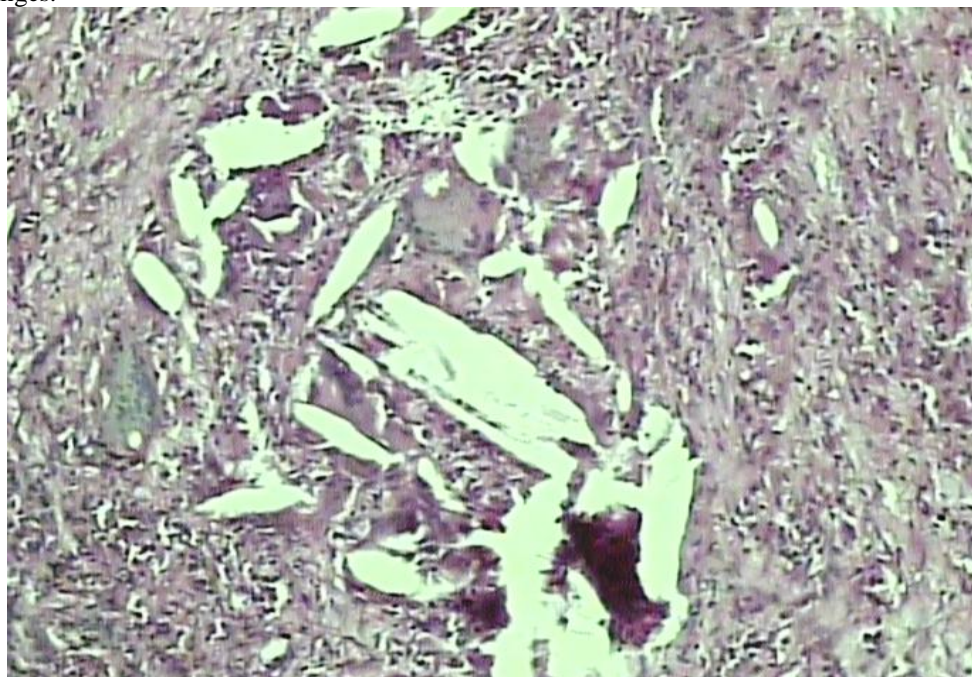


Image 5:- Chronic granulomatous cholecystitis (cholesterol granuloma)

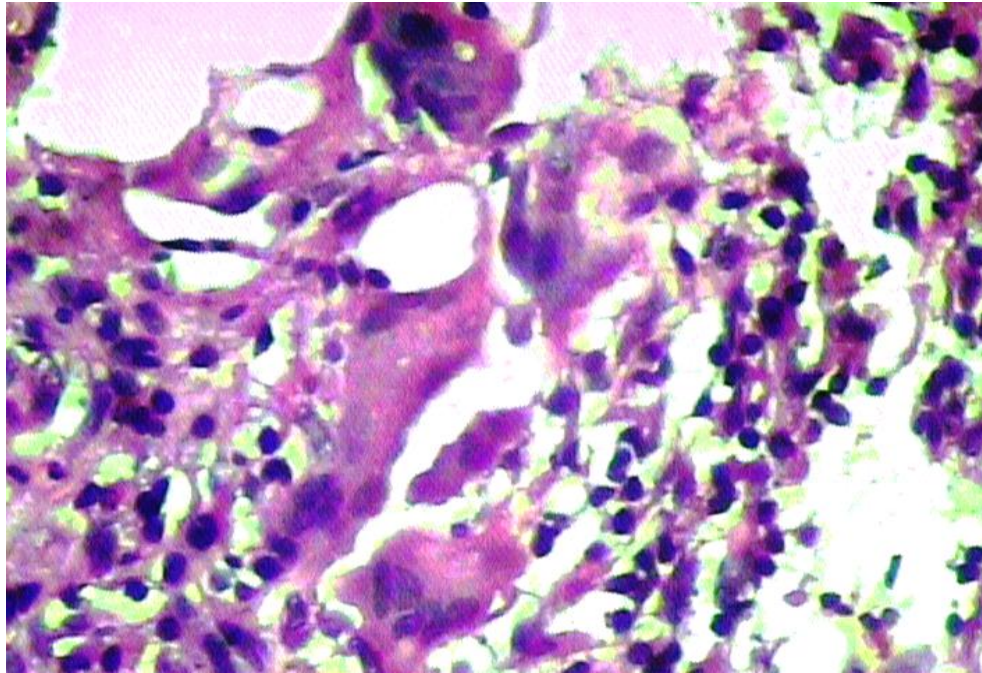


Image 6:- Chronic cholecystitis with foreign body granuloma

Chronic granumatoscholecystitis in 8 cases (image.7, image.8). Gallbladder wall is has multinucleated cells with granulomatous changes. There is rupture of Rokitansky-Aschoff sinuses with extravasation of bile, foamy macrophages with bile or iron, cholesterol clefts and multinucleated giant cell.

Discussion:-

Over ninety one per cent patients presented with pain upper abdomen, a number significantly lower than that reported by Laghari et al where all patients had upper abdominal pain.⁶ None of the patients in our study had any evidence of malignancy either clinically or on ultrasound examination.

The present study was carried out on 118 cholecystectomy specimens to determine the histopathological spectrum of gallbladder diseases. Histopathology not only establishes a tissue diagnosis in gallstone disease, but also contributes towards understanding its etiopathogenesis and can help in planning future treatment modality.

The most common histopathological finding in our study was chronic cholecystitis; 82 specimens were reported as chronic inflammation with mucosal ulceration, denudation, metaplasia to dysplasia and wall infiltration by chronic inflammatory cells like neutrophils, macrophages, plasma cells and varying degrees of fibrosis. A similar study by Memon⁷ also reports chronic cholecystitis as major histopathological finding, identified in 64.8% cases. In both the groups, majority of subjects were diagnosed as chronic cholecystitis on histopathology. Statistically, the difference between two groups was not significant ($p=0.181$) which suggests that there is no role of iron levels in histopathology of gall bladder.

Gallbladder polyps have an incidence ranging from 4.6 to 6.9 per cent⁸. In our study, no case of gallbladder polyp was identified. This low incidence can be attributed to small number of cases in our series. The prevalence of this pathology is much higher amongst males⁹.

Although there are myriad of premalignant conditions, carcinoma gallbladder has a strong association with gallstones¹⁰. The strong association between the two warrants attention paid to histopathology of specimen in all cases undergoing cholecystectomy for cholelithiasis, irrespective of presence or otherwise of any gross abnormalities. It is widely reported that long standing mucosal irritation by the stones cause atypical cellular changes and increased cellular proliferation. It has been hypothesized that in long standing cases, these areas of hyperplasia progress to metaplasia and carcinoma-in- situ¹¹. Studies confirm presence of such changes in the vicinity of gallbladder carcinoma¹².

There is one interesting finding in our study that acute cholecystitis was more prevalent in iron deficient cases which can be studied with large sample size.

Conclusion:-

The histopathological spectrum of gallbladder disease after cholecystectomy was found to be quite diverse. The most common histopathological diagnosis in gallstone disease was chronic cholecystitis, which was associated with a variety of mucosal alterations and lesions like cholestasis, metaplasia, empyema and adenomyoma. A finding suggesting higher prevalence of acute cholecystitis in iron deficient case might indicate if acute cholecystitis may be prevented using iron supplements. To establish this correlation a study with large sample size may be done.

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