

## Original Research Article

# Frequency of gall bladder metaplasia and its distribution in different regions of gall bladder in routine cholecystectomy specimens

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### ABSTRACT

**Background:** In India, gall stone disease is more common in women in the north, north east and east as compared to other zones in the country. Gall bladder metaplasia has been documented as the precursor lesion of dysplasia and therefore carcinoma. Present study was conducted to ascertain the frequency and type of metaplasia along with distribution in different regions of gall bladder.

**Methods:** All the post cholecystectomy gallbladder samples submitted for histopathology comprised the study material. Three sections were from body, fundus, and neck each. The five microns thick paraffin sections were cut with microtome and stained with Hemotoxylin and Eosin (H and E).

**Results:** The present study was conducted on 119 cholecystectomy specimens submitted for histopathological examination. Amongst premalignant lesions, cholecystitis with metaplasia was seen in 55 (46.2%) cases. Pyloric metaplasia without intestinal metaplasia was most common metaplasia (30.2%) followed by combined metaplasia (12.60%) and only intestinal metaplasia (3.36%). Out of 55 cases, fundus showed metaplasia in 47 followed by body (44) and neck (36).

**Conclusions:** Very high frequency of metaplasias was observed (46.2%) in routine cholecystectomy specimen with pyloric metaplasia as the predominant type and intestinal metaplasia was accompanied with pyloric metaplasia in most of the cases. Metaplasia was found to be more or less equally distributed in different regions of gall bladder.

**Keywords:** Gall bladder metaplasia, Intestinal metaplasia, Pyloric metaplasia

### INTRODUCTION

Metaplasia is change of one type of tissue to another type under chronic injury. The new tissue is much more resistant to injurious stimulus compared to the original one.<sup>1</sup> The most common examples of metaplasia are replacement of pseudo-stratified columnar epithelium of respiratory tract by stratified squamous epithelium which is very frequently seen in chronic smokers and replacement of endocervical columnar epithelium by

stratified squamous epithelium in female genital tract. Although, the metaplastic tissue may be resistant to injury but in the continued presence of injurious stimuli, it is prone to undergo dysplasia and finally carcinoma.<sup>2</sup> Gall bladder is one of the organs where metaplasia is seen rather frequently particularly in association with gall stones. Similar to the other sites in the body, gall bladder metaplasia is prone to undergo dysplastic changes and further into carcinoma.<sup>1</sup> These metaplastic changes are reversible and asymptomatic per se and only are

diagnosed when patient undergoes cholecystectomy for cholelithiasis.

Although numerous studies have been carried out, there is a paucity of literature on post cholecystectomy gall bladder histopathology data from this region of the country where cholelithiasis is extremely common. The present study was conducted in the Department of Pathology to profile histopathological changes in gall bladder samples submitted for pathologic examination after cholecystectomy over a period of six months. We intended not only to document and semi-quantify most of the histopathological changes seen in the specimens but also take into account different regions of the gall bladder being affected. The last two aspects of the present study have not been addressed in the published literature.

**METHODS**

The present study was conducted on 119 cholecystectomy specimens submitted for histopathological examination in the Department of Pathology at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, India over a period of six months after due approval from Institutional Scientific and Protocol Review Committee and Institutional Ethics Committee. All the post cholecystectomy gallbladder samples submitted for histopathology comprised the study material. Three sections were from body, fundus, and neck each. The five microns thick paraffin sections

were cut with microtome and stained with Hemotoxylin and Eosin (H and E). Careful assessment of metaplastic changes was made like cells having abundant pale, apical mucin that compresses nuclei at the base (Gastric metaplasia) and mucin containing goblet cells (Intestinal metaplasia).

**RESULTS**

There were total of 119 cholecystectomy specimens. Out of these 11 were males and 108 were females. The mean age was 42.11+-22.62years. The mean age of cases of metaplasia (n=55) was 42.15+-4.95yrs. All cholecystectomy specimens had stones.

**Table 1: The distribution of cases with metaplasia.**

	Only pyloric metaplasia	Only intestinal Metaplasia	Both pyloric and Intestinal metaplasia
No. of cases	36(30.3%)	04(3.7%)	15(12.6%)
Mean age(yrs)	42.5	43	46.2

Total cases of metaplasia were 55 (46.2%) of which 51 (42.86%) were pyloric metaplasia and 19 (15.97%) cases were intestinal metaplasia. Out of these 55 cases 15 (12.60%) were showing both types of metaplasia. Thus, pyloric metaplasia was the predominant metaplasia encountered.

**Table 2: Distribution of types of metaplasias in different regions of gall bladder.**

	No. of cases	Fundus	Body	Neck	Only in Fundus	Only in Body	Only in Neck
Pyloric(%)	51(42.9)	36 (30.3)	34 (28.6)	27 (22.7)	07 (05.9)	02 (01.7)	06 (05)
Intestinal(%)	19 (16)	11 (09.2)	10 (0.9)	09 (7.6)	04 (03.7)	03 (02.5)	04 (03.4)

We also tried to classify metaplasias’ in three degrees

*Pyloric metaplasia*

- Degree 1: pyloric metaplasia with occasional gland,
- Degree 2: pyloric metaplasia with groups of glands,
- Degree 3: pyloric metaplasia with sheets or larges bunches of glands.

*Intestinal metaplasia*

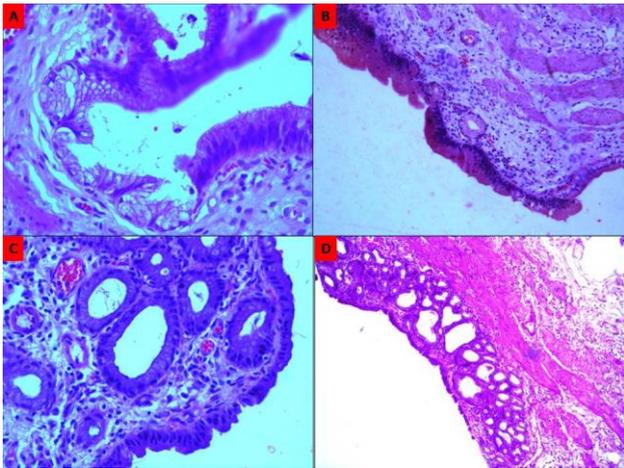
- Degree 1: Intestinal metaplasia with occasional goblet cells,
- Degree 2: Intestinal metaplasia with frequent goblet cells,
- Degree 3: Intestinal metaplasia with continuous array of goblet cells.

**Table 3: Frequency of degrees of pyloric metaplasia and their mean age.**

Pyloric metaplasia	No. of cases	Mean age (yrs)
Degree 1	24 (20%)	42.28 +- 3.53
Degree 2	16 (13.4%)	41.99 +- 25.45
Degree 3	11 (09.2%)	42.22 +- 14.14

**Table 4: Frequency of degrees of intestinal metaplasia and their mean age.**

Intestinal metaplasia	No. of cases	Average age (yrs)
Degree 1	10(08.4%)	49.5 +- 5.65
Degree 2	03(02.5%)	35.3 +- 14.14
Degree 3	06(05%)	50.3 +- 31.82



**Figure 1: A) Transition from normal gall bladder lining to pyloric metaplasia; B) Grade 1 pyloric metaplasia with occasional gland; C) Grade 2 pyloric metaplasia with groups of glands; D) Grade 3 pyloric metaplasia with sheets or large bunches of glands (H and E stain).**

**DISCUSSION**

Understandably, almost all the studies cited in the review of literature yields different outcomes which may be dictated by the ethnic-geographical, genetic and assorted other factors and not to mention the rigor with which a particular study was undertaken. The probability of finding focal changes increases with increased number of sections taken from the gallbladder.

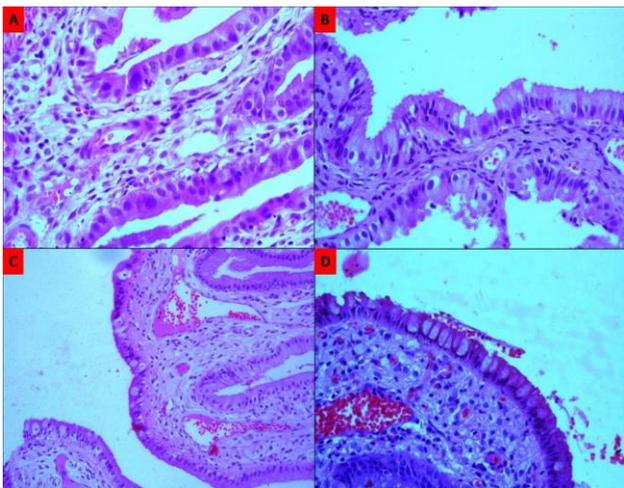
Three sections were taken from each part of the gall bladder in the present study precisely to increase the probability of finding the lesions. Also in literature, so far published there is a dearth of semi quantitative or quantitative data, for instance the extent of the lesion or the grade.

Right at the outset it would be convenient to view the following table comparing the published literature and our findings. The purpose is to make it convenient the comparison at a glance of the results published in the literature and the present study.

**Table 5: Comparison of present study with previous similar studies.**

References	No. Cases	Meta %	Pyloric %	INTES %
Mukhopadhyaya et al in 2005 <sup>3</sup>	400	NA	59.5	9.8
Yamagiva et al in 1986 <sup>4</sup>	1000	NA	NA	30.6
Duarte et al in 1993 <sup>5</sup>	162	NA	95.1	58.1
Martinez- guzman et al in 1998 <sup>6</sup>	1367	NA	50	16
Khanna et al <sup>7</sup>	140	NA	16.5	15.5
Stancu et al 2007 <sup>8</sup>	3901	5	NA	NA
Present study	119	46.2	42.5	16

Meta: Metaplasia; Pyloric: Pyloric metaplasia; Intes: Intestinal metaplasia



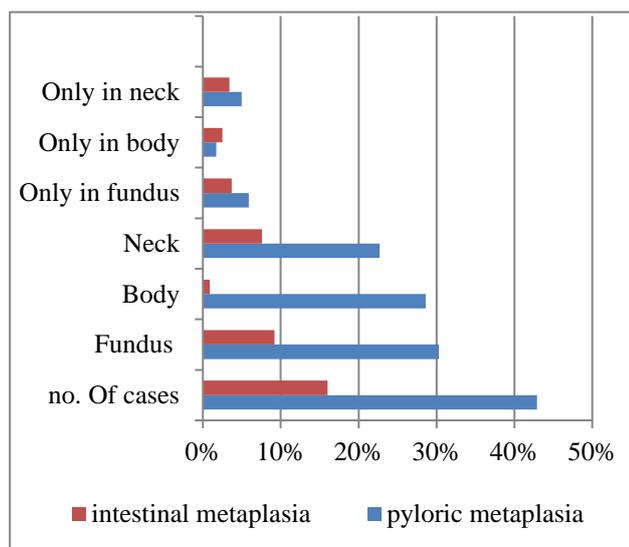
**Figure 2: A) Atypia/dysplasia; B) Grade 1 Intestinal metaplasia with an occasional goblet cells C) Grade 2 Intestinal metaplasia with frequent goblet cells; D) Grade 3 Intestinal metaplasia with continuous array of goblet cells.**

In our study there were total of 119 cholecystectomy specimens out of which only 11 were males and the rest 108 were females. The mean age at the time of operation was 42.11 +- 22.62years. The mean age in our study at the time of cholecystectomy is close to the figure by Tyagi et al which was 43.6years.<sup>1</sup> In our study female to male ratio was 9.8:1 which was in disagreement with studies by Tyagi et al and Mohan et al who reported the female to male ratio as 6.5:1, and 6.4:1 respectively.<sup>2</sup> Therefore it would be reasonable to conclude that the female population in this particular region of India have significantly more chances of having gallstones compared to other regions.

Our study revealed presence of metaplasia in 46.2% of cases. Khanna et al reported an incidence of 16.5% of pyloric metaplasia and 15.5% intestinal metaplasia.<sup>7</sup> Present study yielded 42.5% of the cases with pyloric and 16% with intestinal metaplasia which was comparable to Martinez-Guzman et al of 50% pyloric and 16% intestinal metaplasia.<sup>6</sup> Highest incidence observed by Duarte et al was 95.1% pyloric and 58.1% intestinal metaplasia.<sup>5</sup>

The mean age of the patients with pyloric and intestinal metaplasia was 42.5 and 43years respectively whereas the individuals showing both type of had mean age of 46 years. Therefore, would be reasonable to conclude that age appear to have to a limited role in metaplasia. However, a study conducted by Kozuka S et al in 1984 showed that intestinal metaplastic changes increased with age.<sup>9</sup> Only pyloric metaplasia was noted in 36 cases (30.2%) whereas only intestinal metaplasia was seen in just 4 (3.36%) of the cases. Both pyloric and intestinal metaplasia was noted in 15 (12.6%) cases. Hence, we may conclude that intestinal metaplasia is accompanied by pyloric metaplasia in most of the cases however vice versa is not true. The number of cases showing pyloric metaplasia in fundus, body or neck were 36 (30.3%), 34 (28.6%) and 27 (22.7%) where as it was 11 (09.2%), 10 (0.9%) and 09 (7.6%) respectively in case of intestinal metaplasia.

We can see that there is marginal difference between frequency of metaplasia in the fundus, body and the neck region although the chances of discovering pyloric metaplasia are more than the three times than that of intestinal metaplasia.



**Figure 3: Distribution of Metaplasias in different regions of gall bladder.**

This graph shows an interesting and important finding that metaplasias are distributed with more or less equal frequency throughout the different regions of gall bladder. Cases of metaplasia in only fundus/body/neck are very few. This may be because it is not the presence or absence or type of gall stone which determines place and type of metaplasia rather it may be chemical composition of bile (which is uniform throughout the different regions of gall bladder) which decides the type of metaplasia.

The pyloric and intestinal metaplasia in terms of degrees 1, 2, 3 and the corresponding age reveals the unexpected

pattern. One would expect that the degree of metaplasia should bear direct relationship with age. In other words, older individuals are likely to have more severe lesions. In case of metaplasia aforementioned relationship with age is absent, for instance the mean age for pyloric metaplasia degree 1, 2 and 3 are 42.28 +-3.53, 41.99 +-25.45 and 42.22 +-14.14 years respectively and for intestinal metaplasia these are 49.5 +-5.65, 35.3 +-14.14 and 42.22 +-31.82 years respectively.

One explanation would be that our system of assigning degree to lesions is not valid at the face of it. A large number of specimen examinations would have ended up finding different results. There may be other factors in terms of types, size and number of gallstones and the genetic predisposition if any for metaplasia. The results of our study appear to be at odds with that of Fernandes JE et al 2008 who concluded that intestinal metaplasia is extremely frequent in gallbladders with inflammation and lithiasis, especially in younger patients.<sup>10</sup>

**CONCLUSION**

Very high frequency of metaplasias was observed (46.2%) in routine cholecystectomy specimen. Pyloric metaplasia was the predominant metaplasia observed and intestinal metaplasia was accompanied with pyloric metaplasia in most of the cases. Metaplasia was found to be more or less equally distributed in different regions of gall bladder. More comprehensive study is required to understand natural history of metaplastic changes in gall bladder by taking into account type of gall stones, and chemical composition of bile.

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