

# A comparative study of mast cells in appendix

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## Abstract

**Background:** Mast cells are derived from the multipotent cells in the bone marrow and located at body sites that interface with the external environment such as the mucosa, skin, respiratory tract, and gastrointestinal mucosa.

**Objective:** (1) To compare the mast cell counts in acute appendicitis, chronic appendicitis, and appendix removed during other abdominal surgeries and (2) to investigate the role of mast cells in the pathogenesis of appendicitis.

**Materials and Methods:** One hundred fifty cases of appendix, except gangrenous appendicitis, were analyzed for mast cells counts. Qualitative data were represented in the form of frequencies and percentages. Quantitative data were represented in the form of mean and standard deviation (SD); ANOVA was the test of significance to compare the mean between the three groups.

**Result:** In this study, 150 cases of appendicitis were examined. The most common lesion that was noticed was acute appendicitis in 46 cases (30.66%), followed by chronic appendicitis in 39 cases (26%). Sixty-five (43.33%) cases were those whose appendix was incidentally removed during abdominal surgeries.

**Conclusion:** The mast cell count was the highest in chronic appendicitis when compared with acute and noninflamed appendices.

**KEY WORDS:** Appendicitis, mast cells, toluidine blue

## Introduction

A mast cell is present in different types of tissue and contains many histamine- and heparin-rich granules. They possess protective functions such as wound healing and defense against pathogens. Mast cells are derived from the multipotent stem cell in the bone marrow and are frequently located at body sites that interface with the external environment, such as the mucosa, skin, respiratory tract, and gastrointestinal (GI) mucosa.<sup>[1]</sup> They serve a function of host

defence against the invading pathogens and have a central role in the mediation of allergic response.<sup>[2,3]</sup> The mast cells play an important role in various inflammatory reactions. They also contain heparin, striptase, aryl sulphatase, beta-glucuronidase, eosinophil/neutrophilic chemotactic factor, Prostaglandin P2, platelet activating factor, and leukotrienes. Therefore, they are called as disseminated unicellular endocrine glands.<sup>[4]</sup> They are found primarily in the GI and respiratory tracts. Moreover, they are constantly seen in the appendix, the organ that is commonly removed. Although the clinical and operative protocols are well known, the pathogenesis of the acute appendicitis is poorly understood. This study was taken up with the objective to find the mast cell variation in inflamed appendix and to suggest the possible role of mast cells in the pathogenesis and outcome of acute appendicitis.

## Materials and Methods

The study was conducted in the Department of Pathology for a period of 2 years. One hundred fifty cases of appendix

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except gangrenous appendicitis were analyzed by doing the routine hematoxylin and eosin staining. Special staining of the sections was done with toluidine blue (1%) that stains the background pale blue and mast cells purple in color and examined under high-power magnification.

The number of mast cells that was present in 10 consecutive high-power fields (hotspots) was counted in all sections. All the slides were screened by two pathologists, and both of them were blindfolded for the final diagnosis.

Subjects were divided into three groups: group 1, appendix showing features of acute appendicitis; group 2, appendix showing features of chronic appendicitis; and group 3, appendix removed during other surgical procedures.

### Statistical Analysis

Data were entered using Microsoft Excel and analyzed using SPSS software, version 21. Qualitative data were represented in the form of frequencies and percentages. Quantitative data were represented in the form of mean and standard deviation (SD). ANOVA was the test of significance to compare the mean between the three groups. Post hoc Bonferroni test was done to compare the individual values between the three groups.  $P < 0.05$  was considered as statistically significant.

### Result

In this study, 150 cases of appendicitis were examined. The most common lesion that prevailed was acute appendicitis in 46 (30.66%) cases, followed by chronic appendicitis in 39 (29%) cases. Sixty-five (43.33%) cases were those whose appendix was incidentally removed during abdominal surgeries.

The mean mast cell counts in acute appendicitis, chronic appendicitis, and normal appendix were found to be  $30.23 \pm 9.48$ ,  $45.28 \pm 12.03$ , and  $26.60 \pm 8.82$ , respectively [Table 1].

It was observed that the difference in mean mast cells count between and within the groups were statistically significant [Tables 2 and 3].

Bonferroni test showed a significant difference in the mast cell count between acute appendicitis and chronic appendicitis; there was a significant difference in the mast cell count between chronic appendicitis and appendix not showing features of inflammation.

### Discussion

This study showed a significant mast cell count when compared with the normal and inflamed appendices. Moreover, the mast cell count was increased around areas of submucosa that showed fibrosis, thus suggesting that the release of the growth factors lead to a fibroblastic proliferation. In various diseases, the mast cells and fibrosis are associated with each other, and a subsequent fibrosis during its resolution results on every session of the mast cell activity.

Few studies have described a multidirectional relation between the enteric nerve system and the mast cells, but their association with nerve growth factor has not been established yet. It can be because of the possible role of mast cells in stimulating nerve growth factor (NGF) leading to nerve proliferation in acute appendicitis. Along with this, in acute appendicitis, the mast cells play a vital role in the regulation of immune events locally.

In a study done by Xiong *et al.*, the mast cells were counted, similar to our study, which showed that neuroproliferation in appendix was associated with increased mast cell density. This might occur in patients with clinical and histopathological diagnosis of acute appendicitis. These findings were significant in the GI tract, because changes in the neuronal component and the mast cell density have been reported in chronic inflammatory conditions such as Crohn's disease and ulcerative colitis.<sup>[5,6]</sup>

The study done by Di Sebastiano *et al.* showed an increase in the mast cell density and neuronal hypertrophy in some cases of negative appendectomies. This might suggest a reparative phase of a chronic inflammatory process that already existed in the appendix.<sup>[7,8]</sup> The close association of the mast cell density and the neuronal components in acute appendicitis suggested a relation between the two in this disease. There is a considerable evidence that mast cells functionally appear to nerves in the GI tract with the highest in the appendix.<sup>[9]</sup> It has been suggested that neuronal proliferation or changes in the mast cells might be associated with fibrosis and reflect a physiological ageing phenomenon. Although, in our study, all cases of acute appendicitis exhibited fibrosis that was absent or minimal, the microscopic findings of acute appendicitis with inflammatory cells in the form of neutrophils were prominent. In incidentally removed appendix during the abdominal surgeries, there was no correlation between the mast cell densities.

In acute appendicitis, NGF might be responsible for the hyperplasia of mast cells. Recent studies have shown that NGF can induce mast cells to produce prostaglandin (PG) E<sub>2</sub> that might be responsible for the modulation of mast cell and production of interleukin (IL)-6 and tumor necrosis factor (TNF) production. Under the conditions of neuronal damage and repair, the long-term mast cell PGE<sub>2</sub> response to NGF could provide a mechanism by which locally harmful responses might be limited.<sup>[10]</sup> It will be of interest to investigate the effect of NGF on PGE<sub>2</sub> production on mast cells in acute appendicitis.

#### Group 1: Acute Appendicitis

In this study, of the 150 cases, 46 (30.66%) were of acute appendicitis. Obstruction by faecolith and infection followed by inflammation were some of the common causes. The mast cell count was found to be decreased in the areas of mucosal ulceration. The type-1 hypersensitivity that causes progressive mast cell degranulation could be the trigger factor for acute appendicitis.<sup>[11]</sup>

**Table 1:** Showing the mean count of mast cells in appendicular conditions

Group	No. of cases	Mean	SD	95% confidence interval	
				Lower	Upper
Acute appendicitis	46	30.23	9.48	27.4	33
Chronic appendicitis	39	45.28	12.03	41.3	49.1
Appendix not showing features of inflammation	65	26.60	8.82	24.4	28.7
Total	150	32.57	12.53	30.5	34.5

**Table 2:** ANOVA test results comparing mean mast cell count between the three groups

Mast cells	Sum of squares	df	Mean square	f	P
Between groups	8,868.82	2	4,434.41		
Within groups	14,543.86	147	98.93	44.820	0.001***
Total	23,412.69	149			

\*\*\* means statistically significant

**Table 3:** Bonferroni test to compare the mean difference between the groups

Group (I)	Group (J)	Mean difference (I-J)	Standard error	P	95% confidence interval	
					Lower bound	Upper bound
1	2	-15.042	2.165	0.001	-20.2861	-9.799
	3	3.6391	1.916	0.179	-1.0020	8.2803
2	1	15.042	2.165	0.001	9.7997	20.286
	3	18.682	2.014	0.001	13.8031	23.561
3	1	-3.6391	1.916	0.179	-8.2803	1.0020
	2	-18.082	2.014	0.001	-23.5610	-13.803

## Group 2: Chronic Appendicitis

Of the total 150 cases, 39 (26%) were of chronic appendicitis. These cases showed an increased mast cell clustering in the vicinity of the blood vessels. There was an increase in the mast cells in the lamina propria as well.

## Group 3: Appendix Incidentally Removed During Abdominal Surgeries

In this study, of the 150 cases, 65 (43.3%) were of normal appendix that was incidentally removed during other abdominal surgeries. Histologically, the appendix that was normal showed the lowest mast cell count. These findings were supported by the study carried out by Naik et al.<sup>[12]</sup>.

## Conclusion

It can be concluded that the mast cell count was the highest in chronic appendicitis, thus indicating the growth interaction between the mast cells and fibroblasts in areas of fibrosis. The fibroblasts have an ability to make the NGF; hence, there is an abundant potential for growth interactions among the mast cells, nerves, and fibroblasts.

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