Original Article

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Histopathological Spectrum of Appendicular Lesions: A Cross-sectional Study

Pathology Section

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ABSTRACT

Introduction: Multiple pathologies, ranging from non neoplastic to neoplastic tumours that may or may not obstruct the lumen, might result in appendicitis. Uncommon neoplastic appendix lesions show diverse morphologies, resembling adenomas to colorectal carcinoma. Identifying these traits is vital to differentiate them from non neoplastic mucinous lesions, as they require varied management approaches, including follow-up and chemotherapy.

Aim: To assess the histopathological patterns in patients undergoing appendicectomy and to study the detailed morphological features of different non neoplastic and neoplastic lesions.

Materials and Methods: This cross-sectional study was conducted in western part of Maharashtra for 3 years. It involved surgically removed specimens of appendix received for histopathological evaluation of the appendix from January 2019 to December 2022. A detailed gross examination of the appendicectomy specimens was carried out. Data were analysed using Statistical Package for the Social Sciences (SPSS) software, version 22.0. Categorical data such as sex, clinical presentation, gross presentation of the appendix, and histopathological findings were presented as n (%), whereas quantitative data such as age were presented as mean±SD. A p-value <0.05 was considered statistically significant.

Results: A total of 716 patients were included in this study. The median age of the patients was 25.0 years. The majority of the population belonged to the 21-45 years age group, with 406 (56.7%) patients. The number of males were higher 236 (32.9%) than females 170 (23.4%). The number of patients with inflammatory or non neoplastic lesions was higher than those with neoplastic lesions, with 709 (99.02%) and 7 (0.98%) respectively. The highest number of patients had chronic appendicitis (284; 39.66%), followed by acute on chronic appendicitis (216; 30.16%) and acute appendicitis (188; 26.25%).

Conclusion: In cases of appendicitis, histopathological examination of the appendix should be performed as it provides crucial clinical information in addition to operative findings. Hence, it is a benchmark in diagnosing acute appendicitis.

Keywords: Acute appendicitis, *Enterobius vermicularis*, Neoplastic lesions, Non neoplastic lesions

INTRODUCTION

One of the most typical causes of sudden abdominal pain in adults and children is appendicitis, with a lifetime risk of 8.6% in men and 6.7% in women [1]. The worldwide incidence of acute appendicitis is 96.5 to 100 adults per 100,000 per year. The first line of treatment for acute appendicitis remains appendectomy; however, in some patients with uncomplicated appendicitis, antibiotics are a better option than surgery [2]. There is a significant upsurge in the incidence of appendicitis in India, mainly in urban cities, due to the increased intake of a Western diet [3]. The clinical diagnosis of acute appendicitis is challenging to establish regardless of the availability of advanced diagnostic tools, and hence histological analysis is regarded as the benchmark [4].

Multiple pathologies, ranging from non neoplastic to neoplastic tumours that may or may not obstruct the lumen, might result in appendicitis. Simple fecaliths, lymphoid hyperplasia, and worm infestation are all instances of obstructive lesions [1]. Neoplastic lesions of the appendix exhibit various morphological changes, ranging from those that resemble adenoma to those that imitate colorectal carcinoma, and they are among the uncommon lesions [5]. Identifying morphologic characteristics is necessary to distinguish between neoplastic and non neoplastic mucinous appendiceal lesions [6]. Such disparate findings require management strategies ranging from routine follow-up to extensive chemotherapy.

In light of this context, the present study aims to assess the histopathological patterns in all the patients who underwent appendectomy. Additionally, the study focuses on analysing the detailed histopathological features of non neoplastic and neoplastic lesions.

MATERIALS AND METHODS

This cross-sectional study was conducted in western part of Maharashtra for three years (January 2019 to December 2022). The Institutional Ethical Committee (IEC) approval number for this study was ICEC/01/02/2022.The written informed consent for data and images were obtained from the participants. The study included surgically removed specimens of appendix received for histopathological evaluation of the appendix.

Inclusion criteria: The study included the appendix resected along with other organs like colectomy.

Exclusion criteria: Patients with missing data (incomplete demographic information, preoperative imaging findings, surgical approach details, or histopathological reports), negative appendectomy (follicular cyst, twisted ovarian cyst, haemorrhagic endometriotic cyst), and patients in whom the appendix was removed as part of other surgical procedures, such as intestinal resection for ischaemic bowel disease and specimens from right hemicolectomies for colonic malignancies, were excluded from this study.

Data collection: Demographic details of the patients were reviewed from histopathology requisition forms, including age, gender, signs and symptoms, and significant clinical history. A detailed gross examination of the appendicectomy specimens was conducted. All tissues were stained with Haematoxylin and Eosin (H&E stain). Histopathological diagnosis were proposed based on the data, and the lesions were categorised according to the criteria stated in standard books [7].

Endpoints: The primary endpoint was to study the histopathological patterns in all patients who underwent appendicectomy. Additionally,

the secondary endpoint was to study the detailed morphological features of different non neoplastic and neoplastic lesions (benign and malignant).

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS version 22.0. Descriptive data were expressed as mean±SD (SD), as well as numbers (n) and percentages (%).

RESULTS

A total of 716 patients were included in this study. The median age was 25.0 years. The proportion of the male population (427, 59.6%) was higher than the female population (289, 40.4%). The majority of patients presented with acute appendicitis (573, 80.0%), followed by pain in the abdomen (45, 6.2%) and pain in the right iliac fossa (39, 5.4%). Approximately 469 (65.5%) of the patients had a congested gross presentation of the appendix. The demographic characteristics of the patients are summarised in [Table/Fig-1].

Age and gender-specific distribution: When the age and gender-specific distribution were considered, it was evident that the majority of the population belonged to the age group of 21-45 years (406, 56.7%). This age distribution pattern was similar in patients with inflammatory/non neoplastic lesions (400, 57.5%) and in patients with neoplastic lesions (3, 75.0%). The proportion of the male population was higher than the female population in this (21-45 years) age group of patients (236, 33% vs. 170, 23.7%). This pattern of sex distribution was consistent in patients with inflammatory/non neoplastic lesions (234, 33.6% vs. 166, 23.8%) and in patients with neoplastic lesions (3, 75.0% vs. 0). [Table/Fig-2] provides a summary of these findings.

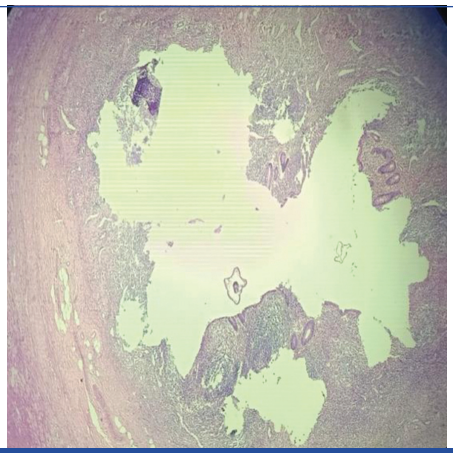
Parameter	n (%)
Age (years), median (range)	25.0 (1.5-88.0)
<20	252 (35.2)
21-45	406 (56.7)
>46	58 (8.1)
Sex	
Male	427 (59.6)
Female	289 (40.4)
Clinical presentation	
Acute appendicitis	573 (80.0)
Pain in abdomen	45 (6.3)
Pain in right iliac fossa	39 (5.5)
Appendicular perforation	14 (2.0)
Chronic appendicitis	9 (1.3)
Ruptured appendix	4 (0.5)
Subacute appendicitis	4 (0.5)
Others*	28 (3.9)
Gross presentation of appendix	
Congested	469 (65.5)
Unremarkable	181 (25.3)
Exudate present	12 (1.7)
Necrotic debris	12 (1.7)
Presence of fecalith	10 (1.4)
Pale appearance	9 (1.2)
Others**	23 (3.2)

[Table/Fig-1]: Demographic characteristics of the patients.
Data given as n (%), unless otherwise specified
Others*, acute gangrenous appendicitis with abscess, appendicular lump with abscess, appendicitis with omentum, bladder perforation with appendicitis, appendix with resected ileum, appendicitis with peritonitis, appendix with inflamed Meckel diverticulum, recurrent appendicitis, stab injury abdomen
Others**, dilated lumen, edematous appendix, lumen seen, ruptured appendix, perforated appendix, irregular congested mucoid, eroded serosa

Age (years)	Males	Females	Total (n=716)
<20	153 (21.4)	99 (13.8)	252 (35.2)
21-45	236 (33)	170 (23.7)	406 (56.7)
>46	38 (5.3)	20 (2.8)	58 (8.1)
Inflammatory/ non neoplastic (n=709)			
<20	158 (22.28)	94 (13.25)	252 (35.54%)
21-45	244 (34.41)	160 (22.56)	404 (56.98)
>46	32 (4.51)	21 (2.96)	53 (7.4)
Neoplastic (n=7)			
<20	-	-	-
21-45	4 (57.14)	-	4 (57.14)
>46	3 (42.85)	-	3 (42.85)

[Table/Fig-2]: Age and gender specific distribution in appendicitis patients.
Data given as n (%)

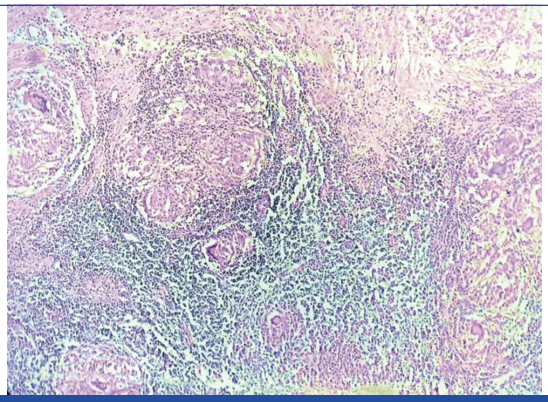
Distribution of various lesions of the appendix based on incidence: The number of patients with inflammatory or non neoplastic lesions was higher than those with neoplastic lesions (709, 99.02% vs 7, 0.98%). The inflammatory or non neoplastic lesions observed in this study included chronic appendicitis (chronic appendicitis , chronic appendicitis with RLH, chronic appendicitis with peri-appendicitis, chronic sclerosing appendicitis, chronic obliterating appendicitis, Chronic granulomatous appendicitis) in 284 patients (39.66%), acute on chronic appendicitis (acute on chronic appendicitis, acute on chronic appendicitis with peri-appendicitis, acute on chronic appendicitis with perforation) in 216 patients (30.16%), acute appendicitis (acute appendicitis, acute appendicitis with peri-appendicitis, acute phlegmonous appendicitis, acute appendicitis with perforation, acute necrotizing appendicitis, acute suppurative appendicitis, acute ulcerative appendicitis) in 188 patients (26.25%), appendicitis with parasitic infestation characterised by the presence of adult *E. vermicularis* worm in the patient's lumen [Table/Fig-3] (6, 0.83%), and tuberculous appendicitis in six patients (0.83%).



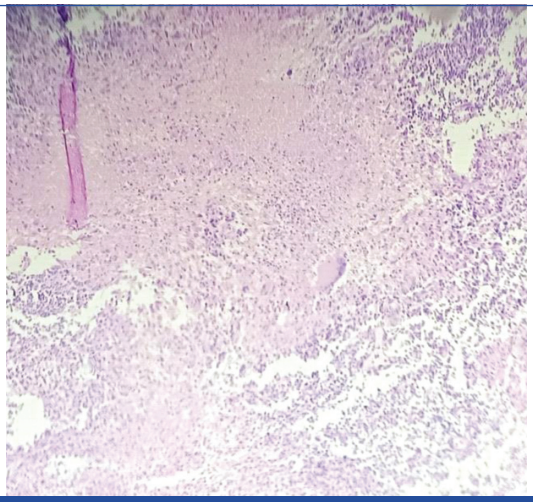
[Table/Fig-3]: Microphotograph showing worm of *E. vermicularis* in the lumen (H&E, 4x).

Upon comparing the sex distribution between non neoplastic and neoplastic lesions, it was observed that the proportion of the male population was higher than the female population in all inflammatory/non neoplastic lesions and neoplastic lesions except for chronic appendicitis (162, 57.85% vs. 118, 42.14%). In this study, granulomatous appendicitis was seen with multiple discrete epithelioid granulomas with Langhan's giant cells in the wall [Table/Fig-4], and typical presentation of granulomatous appendicitis (TB) was seen with epithelioid cell granulomas with caseation seen in the wall [Table/Fig-5]. Unexpected pathological findings such as neuroendocrine tumour, characterised by mucosal ulceration, cords, and nests of tumour cells with stippled chromatin; salt and pepper appearance in the wall (0.1%) [Table/Fig-6], Low-Grade Appendiceal Mucinous Neoplasm (LAMN) (0.1%), and mucinous adenocarcinoma (3, 0.4%), were observed in some of the neoplastic lesions of

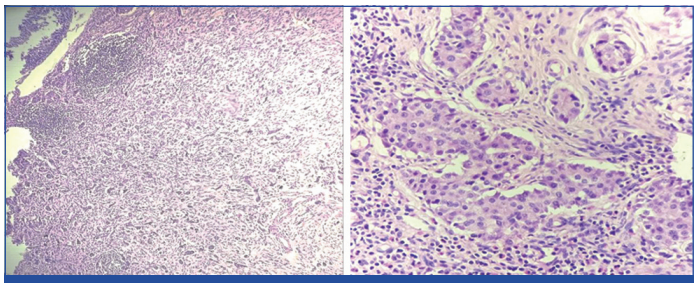
the appendix [Table/Fig-7]. Other histopathological findings of appendectomy specimens included amoebic ulcer with perforation, mucinous cystadenoma (extensively denuded mucosa, presence of mucin in the lumen, and fibrotic wall with lymphoid aggregates as seen in [Table/Fig-8]), well-differentiated adenocarcinoma with involvement of appendicular cut margin (tumour arising from mucosal epithelium involving the muscularis layer as seen in [Table/Fig-9]), acute pyogenic appendicitis with peri-appendicitis, etc.



[Table/Fig-4]: Microphotograph showing multiple epitheloid cell granulomas (H&E, 10x) (Granulomatous Appendicitis).



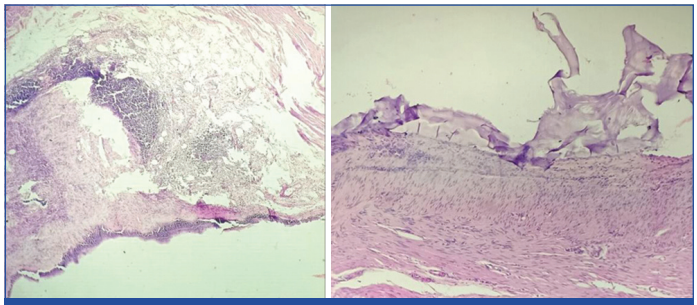
[Table/Fig-5]: Microphotograph showing epitheloid cell granulomas with caseation and langhans type of giant cell (H&E, 40x) Granulomatous appendicitis (TB).



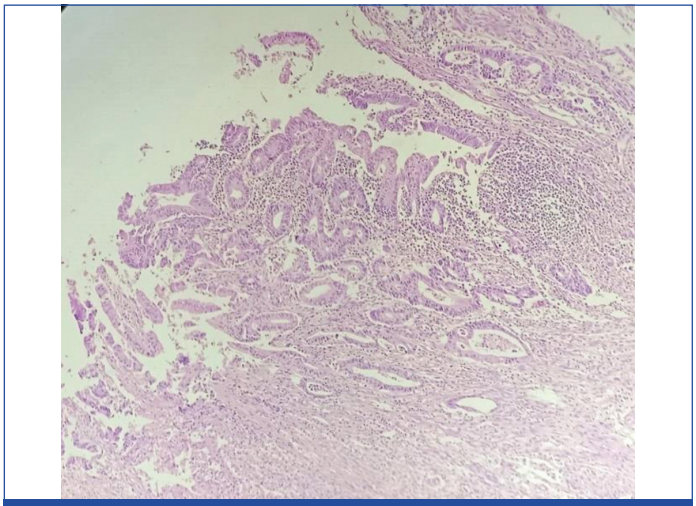
[Table/Fig-6]: Microphotograph showing nests of tumour cells with salt and pepper appearance of chromatin infiltrating the wall. Neuroendocrine tumour (H&E, 10x). Microphotograph showing salt and pepper appearance of chromatin (H&E, 40x).

Histopathological pattern	Number of patients (n=705)	Sex distribution	
		Male	Female
Inflammatory or non neoplastic lesions			
Acute appendicitis	188 (26.25)	137 (72.87)	51 (27.13)
Acute on chronic appendicitis	216 (30.16)	157 (72.69)	59 (27.31)
Chronic appendicitis	284 (39.66)	118 (41.54)	166 (58.46)
Appendicitis with parasitic infestation	6 (0.8)	3 (50.0)	3 (50.0)
Tuberculous appendicitis	6 (0.8)	3 (50.0)	3 (50.0)
Chronic gangrenous appendicitis	3 (0.41)	2 (66.67)	1 (33.33)
Appendicitis with Meckel's diverticulum	3 (0.41)	2 (66.67)	1 (33.33)
Amoebic ulcer with perforation	1 (0.13)	1 (100)	-
Acute on chronic appendicitis with Mucocele	1 (0.13)	1 (100)	-
Acute on chronic appendicitis with foreign body giant cell reaction	1 (0.13)	1 (100)	-
No appendicular tissue seen	1 (0.13)	1 (100)	-
Neoplastic lesions			
Mucinous cystadenoma	1 (0.1)	1 (100.0)	-
Mucinous adenocarcinoma	3 (0.4)	3 (100.0)	-
Neuroendocrine tumor of appendix	1 (0.1)	1 (100.0)	-
Low grade appendiceal mucinous neoplasm	1 (0.1)	1 (100.0)	-

[Table/Fig-7]: Distribution of various lesions of appendix based on incidence and sex distribution.
Data given as n (%)



[Table/Fig-8]: Microphotograph showing fibrotic, atrophic wall with lymphoplasmacytic infiltrate and mucin in lumen (H&E,10x) Mucinous Cystadenoma.



[Table/Fig-9]: Microphotograph showing tumour is seen arising from mucosal epithelium and infiltrating the wall. Well-differentiated adenocarcinoma (H&E, 10x).

Histopathological findings of appendectomy specimens: Among the cases of inflammatory appendicitis, the histopathological examination revealed that chronic appendicitis (195, 27.23%) was the most common diagnosis. In contrast, Chronic sclerosing (4, 0.55%), Chronic obliterative appendicitis (4, 0.55%), and Chronic granulomatous appendicitis were the least frequent [Table/ Fig-10]. Other histopathological findings included Acute appendicitis with Meckel's diverticulum (0.13%), Acute on Chronic appendicitis with Parasitic infestations (0.13%), etc.

Clinical diagnosis	Histopathological finding	No. of patients (n=716)
Acute appendicitis	Acute appendicitis	56 (7.82)
	Acute appendicitis with peri-appendicitis	62 (8.65)
	Acute phlegmonous appendicitis	26 (3.63)
	Acute appendicitis with perforation	27 (3.77)
	Acute necrotizing appendicitis	6 (0.83)
	Acute suppurative appendicitis	5 (0.69)
	Acute ulcerative appendicitis	6 (0.83)

Acute on chronic appendicitis	Acute on chronic appendicitis	132 (18.43)
	Acute on chronic appendicitis with peri-appendicitis	72 (10.05)
	Acute on chronic appendicitis with perforation	12 (1.67)
Chronic appendicitis	Chronic appendicitis	195 (27.23)
	Chronic appendicitis with RLH	54 (7.54)
	Chronic appendicitis with peri-appendicitis	23 (3.21)
	Chronic sclerosing appendicitis	4 (0.55)
	Chronic obliterating appendicitis	4 (0.55)
	Chronic Granulomatous appendicitis	4 (0.55)
Others	Gangrenous appendicitis	3 (0.41)
	Chronic appendicitis with parasite infestation	5 (0.69)
	Chronic appendicitis with Meckel's diverticulum	2 (0.27)
	TB appendix	6 (0.83)
	Acute appendicitis with Meckel's diverticulum	1 (0.13)
	Acute on chronic appendicitis with parasitic infestation	1 (0.13)
	Acute on chronic appendicitis with Mucocele	1 (0.13)
	Amoebic ulcer with perforation	1 (0.13)
	No appendicular tissue seen	1 (0.13)
	Mucinous cystadenoma	1 (0.13)
	Neuroendocrine tumor of appendix	1 (0.13)
	Acute on Chronic appendicitis with Foreign Body giant cell reaction to mucin Pseudomyxoma peritonei	1 (0.13)
	Low grade appendiceal mucinous neoplasm	1 (0.13)
	Well differentiated mucinous adenocarcinoma with pseudomyxoma	2 (0.27)
	Adenocarcinoma	1 (0.1)

[Table/Fig-10]: Analysis of histopathological findings of appendicectomy specimens. Data given as n (%).
RLH: Reactive lymphoid hyperplasia; TB: Tuberculosis

DISCUSSION

The diagnosis of acute appendicitis mainly relies on the evaluation of the patient's history, laboratory, and radiologic findings, in addition to the surgeon's judgment and experience [8]. There are two primary reasons for conducting a histopathological examination of the appendix: it enhances the diagnosis of pathological lesions of the appendix, and it can help identify potential additional pathologies that may not be recognisable during intraoperative procedures, which may require more aggressive management strategies [9].

However, it has been observed that excised appendix specimens are not routinely sent for histopathological examination. Some argue that this may be due to the infrequent occurrence of aberrant findings with low clinical significance or the costs associated with specimen processing [10-12]. On the contrary, a few published papers have reported that aberrant findings are more common. This highlights that the omission of histopathological examination of the appendix may result in the improper diagnosis of underlying diseases, potentially affecting the patient's treatment strategies [13].

A study by Qadir A et al., showed that appendicitis peaks in the second and third decades of life, observed in both males and females [14]. This finding was consistent with the results observed in present study, where the incidence of appendicitis was higher in the age group of 21-45 years (406, 56.7%). This was supported by other studies that have reported that almost 80% of appendicitis cases occur in individuals below 40 years of age [3,15-17].

It has been observed that males in the adolescent age group have a higher incidence of appendicitis compared to females [3,16-18]. This supports present study, which observed a higher proportion of males compared to females (427, 59.6% vs 289, 40.3%). However, a study by Vijayasree V et al., had contrasting results, showing a slightly higher female preponderance [19].

In present study, the majority of patients presented with abdominal pain (45, 6.2%), followed by pain in the right iliac fossa (39, 5.4%). This was similar to a study by Sujatha R et al., which reported the same observations [20].

In the present study, among cases of inflammatory appendicitis, the histopathological examination revealed that chronic appendicitis (195, 27.23%) was the most common diagnosis. In contrast, chronic obliterative appendicitis (4, 0.55%) and chronic sclerosing appendicitis (4, 0.55%) were the least frequent. The number of patients with inflammatory or non neoplastic lesions were higher than those with neoplastic lesions (709, 99.02% vs 7, 0.98%). This finding was consistent with the observations reported by Blair NP et al., which showed that 80.0% of appendectomy cases were non neoplastic, while only 4.0% were neoplastic [21].

This study also reported the presence of *E. vermicularis* in the appendix in 6 cases (0.83%). This finding aligns with another study by Sujatha R et al., which reported three cases (1.3%) presenting with symptoms similar to acute appendicitis [20]. Worldwide, the incidence rate of *E. vermicularis* ranges from 0.2-41.8% [22].

Upon comparing the age and sex distribution patterns between neoplastic and non neoplastic lesions, it was observed that the highest prevalence of both neoplastic and non neoplastic lesions was found in the age group of 21-45 years (non neoplastic: 404, 56.98%; neoplastic: 4, 57.14%). Additionally, the incidence of non neoplastic lesions was highest in the male population (435,61.35%) compared to the female population (274, 38.60%). Furthermore, this study found that neoplastic lesions were only observed in the male population.

Similar observations were reported by a histopathological study by Kulkarni MP et al., which concluded that the majority of patients with neoplastic and non neoplastic lesions belonged to the age group of 11-40 years and reported an overall male preponderance (241, 55.2% vs. 195, 44.7%) [23]. However, a retrospective study by Shrestha O and Baral R demonstrated contrasting results, suggesting that non neoplastic lesions were more common in younger patients with a mean age of 51.2 years [24].

The majority of carcinoids and mucinous neoplasms are accidentally diagnosed during surgery for acute appendicitis. Considering the patient's mortality and morbidity, the prompt diagnosis of cancer and initiation of appropriate treatment are highly significant. While the macroscopic features may be evident, histopathological assessment can provide valuable insights into the patient's disease and improve clinical outcomes by identifying previously unrecognised conditions [5].

The novelty of this study lies in its emphasis on the importance of histopathological examination of excised appendix specimens. It highlights the ability of histopathology to uncover additional conditions that may not be apparent during clinical assessment and surgery, which can have implications for subsequent patient care. The study also validates the diagnosis of appendicitis. While the diagnosis of acute appendicitis traditionally relies on patient history, laboratory tests, radiology, and surgeon's experience, this study underscores the importance of histopathology in improving diagnostic accuracy. It addresses the lack of routine histopathological examination of appendices, arguing that this practice can result in improper diagnosis and treatment. The findings of the study align with existing research on the age and gender distribution of appendicitis, as well as the prevalence of different pathological diagnosis. Furthermore, the study highlights the role of histopathology in early cancer diagnosis and its impact on patient outcomes, emphasising that histopathological assessment is a critical factor in the diagnosis and management of appendicitis.

Limitation(s)

The study was restricted to a single medical centre. The study employed a retrospective design, which implies its reliance on past clinical data. Retrospective studies can be susceptible to data limitations, information gaps, and the potential for recall bias.

CONCLUSION(S)

The present study concluded that males were slightly more likely than females to develop appendicitis in their second and third decades of life. In all cases of acute appendicitis, a histopathological examination of the appendix should be done as it provides crucial clinical information and operative findings. Unusual findings such as mucinous adenocarcinoma, LAMN, and neuroendocrine tumour of the appendix were reported in this study, highlighting the necessity of histological investigation for every excised appendix. Such findings can significantly impact the course of treatment. It can be concluded that histological examination is the benchmark for diagnosing acute appendicitis.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 21, 2023
- Manual Googling: Aug 16, 2023
- iThenticate Software: Oct 21, 2023 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

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- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

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