

Unraveling the Unusual Pathological Findings of Appendiceal Lesions: A Cross-sectional Study from Tertiary Care Centre in Chengalpattu, Tamil Nadu, India

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ABSTRACT

Introduction: The appendix, once considered a vestigial structure, is now recognised as a site of diverse pathologies beyond simple appendicitis through a systematic analysis of published literature and case studies. The diagnosis of appendiceal lesions is still a clinical phenomenon and a constant struggle. The gold standard for diagnosing appendiceal lesions, however, is meticulous histopathological examination.

Aim: To determine the histopathological distribution of all the appendiceal lesions and to identify the rare and unusual histopathological findings in appendectomy specimens received at a tertiary care Centre.

Materials and Methods: A cross-sectional study was conducted in the Department of Pathology at Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Chengalpattu, Tamil Nadu, India for a duration of 10 years, from August 2013 to August 2023. From the histopathological records of 832 appendectomies, 40 specimens with unusual histopathological findings were identified and analysed in this study. Relevant recorded data from all the appendiceal specimens reported during the study period, with special reference to age, sex, and histopathological findings, were retrieved and evaluated retrospectively. Corresponding slides and specimens were

reviewed. The data were presented in the form of frequency tables and percentages. The analysis was done using Statistical Package for Social Sciences (SPSS) software version 20.0.

Results: Out of 832 appendectomy specimens, there were 485 (58.29%) cases of acute appendicitis, 244 (29.33%) cases of chronic appendicitis, 59 (7.09%) cases of subacute appendicitis, and 4 (0.48%) cases of gangrenous appendicitis. Unusual histopathology findings were noted in 40 cases (4.81%). These include 17 cases of appendiceal neuroma, eight cases of Xanthogranulomatous appendicitis, seven cases of *Enterobius vermicularis*, three cases of Low-grade Appendiceal Mucinous Neoplasm (LAMN), one case of appendiceal Neuroendocrine Tumour (NET), one case of Goblet Cell Adenocarcinoma (GCA), one case of metastatic squamous cell carcinomatous deposit in the appendix, one case of urothelial rests in the appendix, and one case of appendiceal lipoma.

Conclusion: In this study, 4.81% of patients had atypical appendiceal lesions. A complete histopathological examination of appendectomy specimens increases the chances of discovering unusual lesions of the appendix. Ultimately, this comprehensive analysis will contribute to future improvements in clinical management and prognostication, fostering better patient outcomes.

Keywords: Appendiceal neuroma, Appendiceal neuroendocrine tumour, Xanthogranulomatous appendicitis, *Enterobius vermicularis*, Low-grade appendiceal mucinous neoplasm, Appendiceal lipoma

INTRODUCTION

Acute appendicitis is one of the most frequent surgical emergencies worldwide, and appendectomy specimens are among the common surgically resected specimens received by pathology laboratories. The primary cause of acute appendicitis is the obstruction of the appendix lumen. Fecoliths and lymphoid hyperplasia are the main causes of obstruction; however, uncommon circumstances can occasionally result in acute appendicitis [1,2]. Even when the macroscopic examination of the appendix appears unremarkable, careful microscopic analysis may reveal some unexpected lesions. These lesions could be benign or malignant neoplasms, as well as inflammatory processes with a specific aetiology [3]. The crucial pathology findings could be grossly missed, which could impact the treatment of patients. More than 50% of appendiceal tumours are diagnosed only by thorough histopathological examination of the appendectomy specimens [4-6]. Despite technological and imaging advancements, the clinical diagnosis and establishing the underlying aetiology of acute appendicitis remain problematic. Therefore, histopathological investigation remains the best standard method for confirming appendicitis and ruling out any other co-existing appendiceal pathological lesions [7].

The majority of research in this discipline is carried out in Western developed countries [2,4,8,9]. There is not enough data available for developing countries like India. Despite several case reports in medical literature [10-13], only a few publications provide a meticulous analysis of the various appendiceal lesions encountered in a single centre [4,8,9,14]. The present study focuses on a number of incidentally detected appendiceal lesions over the course of a decade at Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Chengalpattu, Tamil Nadu, India. With the hope that pathologists and surgeons will be reminded of the variety of lesions that can arise in the appendix through this compilation of noteworthy cases, these cases should serve as additional proof that, at times, if not always, a patient may be in danger when an organ on the operating or grossing table is ignored [15,16]. This study highlights how crucial it is to perform routine histopathological examinations following an appendectomy. It will further assist in identifying novel research possibilities specifically related to this topic.

MATERIALS AND METHODS

The current study was a cross-sectional study conducted in the Department of Pathology, Karpaga Vinayaga Institute of Medical

Sciences and Research Centre, Chengalpattu, Tamil Nadu, India, over the course of 10 years, from August 2013 to August 2023. The study analysis was carried out from September 2023 to December 2023, following approval by the Institutional Ethics Committee (ECR/1425/Inst/TN/2023).

Inclusion criteria: The study included records of appendectomy specimens from all age groups and genders during the 10 year study period.

Exclusion criteria: Autolysed and inadequate samples were excluded from the study.

Sample size: A total of 832 samples were collected based on the inclusion criteria.

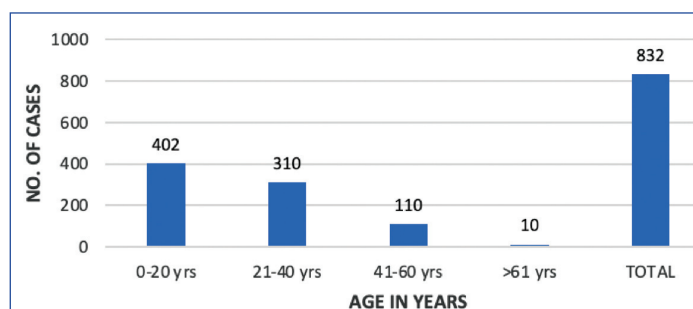
Appendectomy specimens received during the study period were retrospectively analysed, with particular attention paid to age, gender, and histopathological reports. Data from histopathological reports were retrieved, corresponding histopathology slides were reviewed, and unusual findings were recorded maintaining patient's confidentiality. The appendix samples were based on the gross appearance of the organ to the unaided eye. For an appendix that appeared normal, one random cross-section was obtained from the body, often close to the resected base, and one half of the tip (approximately 1 cm in length) was sampled as a longitudinal section. For microscopic analysis, both of these sections were processed in a single block. In cases of any unusual pathology noted, sampling was appropriately adjusted to include those unusual lesions. Additional sections for appendiceal tumours, such as sampling the resected margin, serial cross-sections of the entire appendix at intervals of 3-5 mm, and transverse sections at the site of perforation, were a few examples.

STATISTICAL ANALYSIS

The data were entered into a Microsoft Excel sheet. The results were expressed in terms of frequency and percentages. Statistical analysis was conducted using SPSS software version 20.0.

RESULTS

A total of 832 appendix specimens were received by the Histopathology Department. Unusual histopathological findings were found in 40 cases (4.81%) out of the 832 appendicitis cases that were clinically identified. The age range of 0-20 years had the highest rate of appendiceal lesions, accounting for 402 cases [Table/Fig-1].



[Table/Fig-1]: Distribution of appendiceal lesions by age group.

Among the 832 cases of appendiceal lesions, there were 549 (65.99%) males and 283 (34.01%) females, with a male-to-female ratio of 1.9:1. After the final histological examination of the 832 appendiceal lesions, 40 (4.80%) cases were found to have atypical features, with acute appendicitis accounting for the majority of cases at 485 (58.29%) [Table/Fig-2].

The histopathological distribution of unusual appendiceal lesions is summarised in [Table/Fig-3]. Out of the 40 patients, 26 (65%) were male and 14 (35%) were female, with ages ranging from 15 to 70 years.

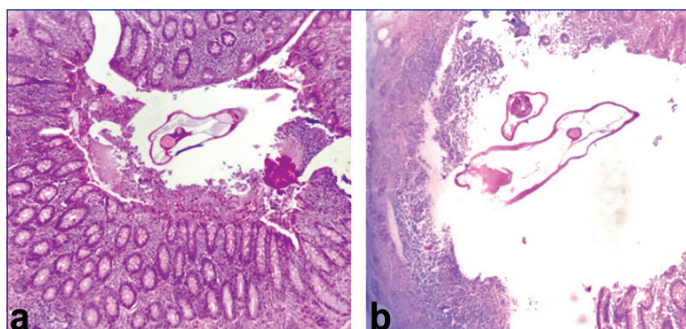
Histopathological diagnosis	n (%)
Acute appendicitis	485 (58.29)
Subacute appendicitis	59 (7.09)
Chronic appendicitis	244 (29.33)
Gangrenous appendicitis	4 (0.48)
Unusual appendiceal lesions	40 (4.81)
Total	832 (100)

[Table/Fig-2]: Histopathological diagnosis for various appendiceal lesions.

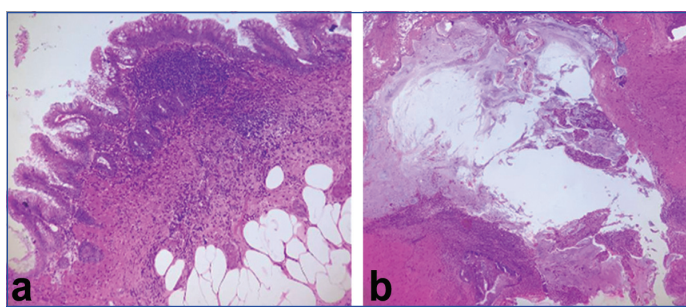
Unusual appendiceal lesions	Rate (%)
Appendiceal neuroma	17 (2.04)
Xanthogranulomatous appendicitis	8 (0.96)
<i>Enterobius vermicularis</i>	7 (0.84)
Low-grade Appendiceal Mucinous Neoplasm (LAMN)	3 (0.36)
Appendiceal Neuroendocrine Tumour (NET)	1 (0.12)
Goblet Cell Adenocarcinoma (GCA)	1 (0.12)
Metastatic squamous cell carcinomatous deposit in appendix	1 (0.12)
Urothelial rests in appendix	1 (0.12)
Appendiceal lipoma	1 (0.12)

[Table/Fig-3]: Histopathological distribution of unusual appendiceal lesions.

The unusual findings in the 40 patients, in descending frequency, were appendiceal neuroma (n=17), xanthogranulomatous appendicitis (n=8), *Enterobius vermicularis* (n=7), LAMN (n=3), appendiceal NET (n=1), GCA (n=1), metastatic squamous cell carcinomatous deposit in the appendix (n=1), urothelial rests in the appendix (n=1), and appendiceal lipoma (n=1) [Table/Fig-4-11].



[Table/Fig-4]: Appendicitis with luminal *Enterobius vermicularis*, H&E (a) 10x, (b) 40x.

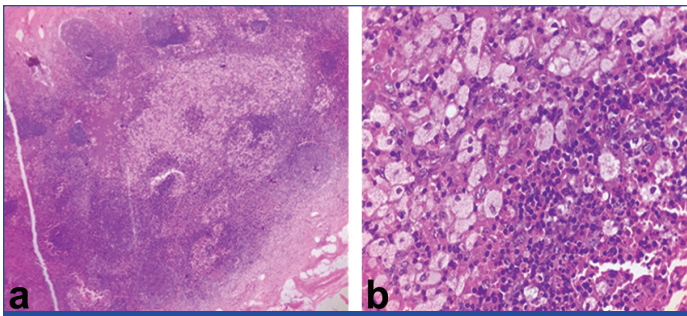


[Table/Fig-5]: a,b Appendix showing non invasive villous proliferation of mucinous epithelial cells having elongated nuclei exhibiting low grade nuclear atypia and abundant apical mucin with evidence of luminal extravasated mucin- Low-grade Appendiceal Mucinous Neoplasm (LAMN), H&E (a) 10x, (b) 40x.

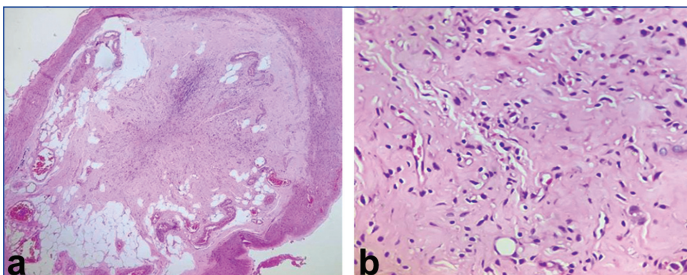
In the unusual findings, a single case each of appendiceal NET, GCA, metastatic squamous cell carcinomatous deposit in the appendix, urothelial rests in the appendix, and appendiceal lipoma (0.12%), were identified respectively. LAMN was found in three cases (0.36%) [Table/Fig-4-11].

DISCUSSION

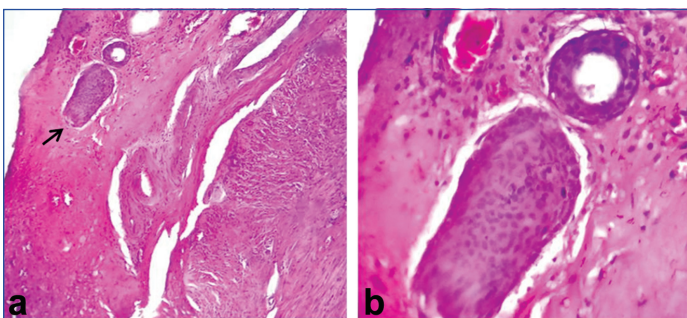
The current study found that appendiceal neuroma was the most common unusual appendiceal lesion, accounting for 17 (2.04%) cases, which was consistent with previous studies by Dincel O et



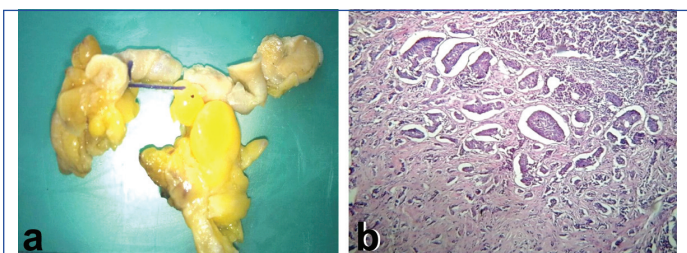
[Table/Fig-6]: Appendix showing mucosal and submucosal replacement by collections of histiocytes with abundant granular eosinophilic cytoplasm admixed by variable amounts of lymphocytes, plasma cells and eosinophils– Xanthogranulomatous Appendicitis, H&E (a) 10x, (b) 40x.



[Table/Fig-7]: Appendix showing complete luminal obliteration, replaced by proliferating bland spindle cells and adipose tissue– Appendiceal Neuroma, H&E (a) 10x, (b) 40x.

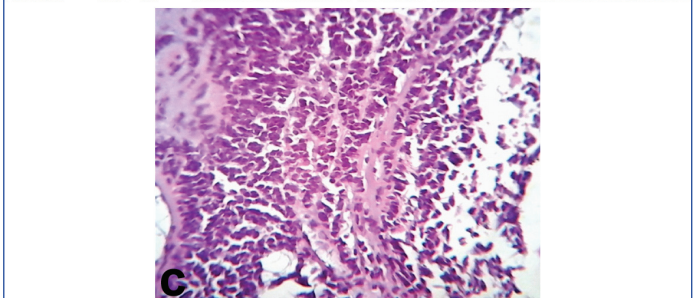
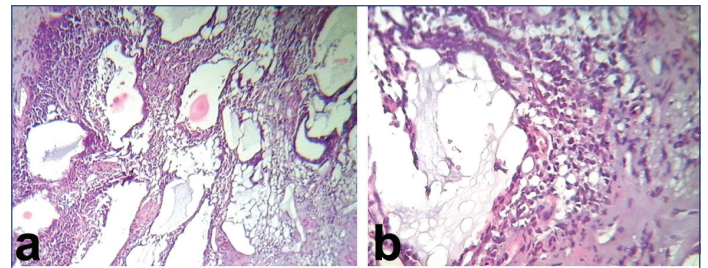


[Table/Fig-8]: Urothelial rests in appendiceal wall, H&E (a) 10x, (b) 40x.

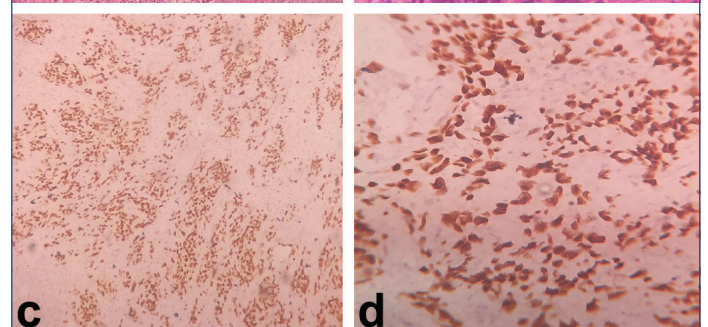
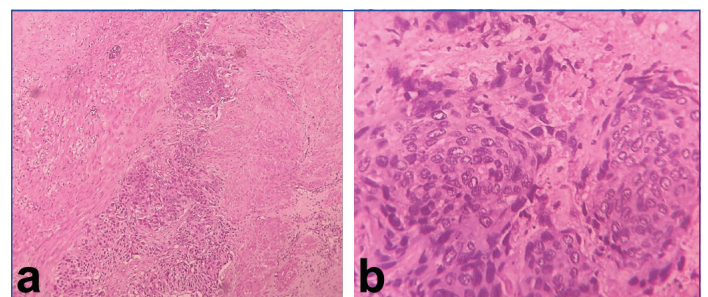


[Table/Fig-9]: (a) Gross picture showing tip of appendix with typical yellowish discoloration; (b,c) Nested growth pattern of tumour with monomorphic nuclei having salt and pepper chromatin– Appendiceal neuroendocrine tumour , H&E (b) 10x, (c) 40x.

al., and Yilmaz M et al., [4,17]. However, Akbulut S et al., Harman Kamali G et al., and Al-Balas H et al., reported lower rates of appendiceal neuromas [2,8,14]. Appendiceal neuroma, formerly known as fibrous obliteration of the appendix, is characterised by hyperplasia of S-100 positive neural components and is more frequent in advanced age groups of patients. Its mimics include neurofibroma, schwannoma, and gastrointestinal stromal tumours, although these findings are uncommon in the appendix [15].



[Table/Fig-10]: Cords and clusters of tumour cells along with few goblet cells and extracellular mucin – Goblet Cell Adenocarcinoma (GCA), H&E (a) 4x (b) 10x (c) 40x.



[Table/Fig-11]: Squamoid tumour cells in nests and islands encroaching the submucosal layer of appendix– metastatic squamous cell carcinomatous deposit appendix, H&E (a) 10x, (b) 40x; p63- Diffuse strong nuclear positivity in the tumour cells. IHC (c) 10x, (d) 40x.

Xanthogranulomatous appendicitis accounted for eight cases (0.96%) in the present study. Studies by Dincel O et al., and Memon I et al., showed the lowest rates of xanthogranulomatous appendicitis among appendiceal lesions [4,18]. Given their yellow colour grossly and reported prevalence in adults, they may mimic neuroendocrine lesions [15]. Possible causes for this condition include lymphatic blockage, infection, immunologic abnormalities, and defective lipid transport [10].

In the present study, *Enterobius vermicularis* was identified in seven patients post-appendectomy, with five of them being male patients and two being female patients. All patients received appropriate medication postsurgery. Akbulut S et al., and Memon I et al., found *Enterobius vermicularis* to be the most common cause of atypical appendiceal lesions [2,18]. *Enterobius vermicularis*, formerly known as *Oxyuris vermicularis*, is a prevalent, family-wide disease with no symptoms, high cure rates, and frequent recurrences, particularly among individuals with poor hygiene, small children, carrier parents, and homosexuals [14,19].

The present study found three cases (0.36%) of LAMN, which was consistent with other studies by Akbulut S et al., Dincel O et al., Harman Kamali G et al., Yilmaz M et al., and Memon I et al., [2,4,8,17,18].

According to the study by Yabanoglu H et al., LAMN had the highest incidence rate and was the most common lesion [9]. LAMNs are appendix tumours that are relatively uncommon, though their incidence is rising. Patients with LAMN frequently have symptoms similar to appendicitis [20]. Histologically, they are distinguished by mucinous epithelium and low-grade cytologic atypia but lack overtly aggressive characteristics like an infiltrative growth pattern or destructive invasion with an accompanying desmoplastic reaction of the stroma. Following appendectomy, patients tend to have a very low chance of disease recurrence [11].

The present study found a lower rate of appendiceal NET, with only one case (0.12%) presenting with acute appendicitis. Harman Kamali G et al., had reported the highest rate of this lesion in their study [8]. The most common type of appendix tumours are neuroendocrine neoplasms, known as carcinoids in the past. These tumours develop slowly, and it is extremely uncommon to diagnose carcinoids before surgery since they are typically discovered during an appendectomy [21].

The present study showed one case of GCA (0.12%), which was similar to the study by Akbulut S et al., [2]. GCA is an unusual primary amphoteric tumour of the appendix distinguished by dual endocrine cells and goblet-like mucinous cells arranged in tubules. The World Health Organisation (WHO) officially adopted the term GCA in their 2019 Classification of Tumours of the Digestive System, stating that using the old term Goblet Cell Carcinoid (GCC) is not recommended [22]. Recent research indicates that GCCs have immunohistochemical and biological profiles more similar to adenocarcinomas than traditional carcinoids, potentially resulting in their aggressive behaviour and necessitating more comprehensive treatment [23].

Metastatic squamous cell carcinomatous deposits in the appendix are rare, primarily spreading from epithelial, ovarian, and colorectal cancers. Cervical squamous cell carcinoma primarily metastasises to pelvic, inguinal, and supraclavicular lymph nodes, following the rectum, vagina, endometrium, bladder, and paracervical tissue [24]. In this study, a single case was reported that was staged as carcinoma cervix IVB (advanced stage). The immunohistochemical findings showed diffuse strong cytoplasmic positivity for pan-cytokeratin (CK) and diffuse strong nuclear positivity for p63, which further confirmed the squamous origin. The prognosis is dire when appendicular metastases are present, as they signify advanced illness.

Urothelial rests, or Walther rests, are benign nests of epithelial cells most commonly found in the female gynaecological tract. There are only four documented cases in the appendix, and no additional treatment is needed for these lesions [12]. In this study, a single case of urothelial rest in the appendix of a male patient was

reported. Urothelial rests are rather infrequent in the appendix of male patients. To distinguish this entity from other morphologically comparable lesions, such as reactive mesothelial hyperplasia or carcinoid tumours, knowledge of this entity is crucial.

The rare occurrence of appendiceal lipomas is often associated with torsion, suggesting that it may be underreported due to its perceived prevalence or that it may be an uncommon occurrence, particularly in the subserosal form, as observed in present case. It is a condition characterised by increased infiltration of differentiated fat in the submucosal layer of the bowel, with an unknown aetiology and a lack of capsule [13]. In the present study, a single case of appendiceal lipoma was reported.

In this study, there was only one instance of appendiceal lipoma, urothelial rests in the appendix, and a metastatic squamous cell carcinomatous deposit in the appendix, each representing 0.12% of the total. In comparison with earlier studies by Akbulut S et al., Dincel O et al., Harman Kamali G et al., Yabanoglu H et al., Al-Balas H et al., Yilmaz M et al., and Memon I et al., these cases were quite unusual [2,4,8,9,14,17,18]. The distribution and frequency of various unusual appendiceal lesions in the present study are compared with a few published studies, and the results are tabulated [Table/Fig-12,13] [2,4,8,9,14,17,18].

Comparing the current study to previous studies, there were no uncommon appendiceal lesions such as tuberculous appendicitis, lymphoma, hyperplastic polyps, schistosomiasis, amoebiasis, endometriosis, adenocarcinoma, or a gastrointestinal stromal tumour.

Authors	Place and publication year of study	Study period (years)	Cases (n)	Unusual appendiceal lesions	Rate (%)
Akbulut S et al., [2]	Turkey, 2011	4	5262	54	1.02
Dincel O et al., [4]	Turkey, 2018	4	1970	59	2.99
Harman Kamali G et al., [8]	Turkey, 2022	6	6785	98	1.44
Yabanoglu H et al., [9]	Turkey, 2014	14	1466	57	3.88
Al-Balas H et al., [14]	Jordan, 2021	6	1510	72	4.76
Yilmaz M et al., [17]	Turkey, 2013	12	1621	134	8.26
Memon I et al., [18]	Pakistan, 2014	7	2157	138	6.39
Present study	India, 2024	10	832	40	4.81

[Table/Fig-12]: Comparison of distribution of unusual appendiceal lesions with other studies [2,4,8,9,14,17,18].

Unusual appendiceal lesions	Present study Rate (%)	Akbulut S et al., [2] Rate (%)	Dincel O et al., [4] Rate (%)	Harman Kamali G et al., [8] Rate (%)	Yabanoglu H et al., [9] Rate (%)	Al-Balas H et al., [14] Rate (%)	Yilmaz M et al., [17] Rate (%)	Memon I et al., [18] Rate (%)
Place and publication year of study	India (2024)	Turkey (2011)	Turkey (2018)	Turkey (2022)	Turkey (2014)	Jordan (2021)	Turkey (2013)	Pakistan (2014)
Appendiceal neuroma	17 (2.04)	1 (0.01)	19 (0.86)	2 (0.02)	-	1 (0.06)	62 (3.82)	-
Xanthogranulomatous appendicitis	8 (0.96)	-	2 (0.10)	-	-	-	5 (0.30)	1 (0.04)
<i>Enterobius vermicularis</i>	7 (0.84)	37 (0.70)	11 (0.55)	10 (0.14)	15 (1.02)	12 (0.79)	31 (1.91)	67 (3.10)
Low-grade Appendiceal Mucinous Neoplasm (LAMN)	3 (0.36)	6 (0.11)	9 (0.45)	12 (0.17)	16 (1.09)	-	11 (0.67)	11 (0.50)
Appendiceal neuroendocrine tumour	1 (0.12)	5 (0.09)	8 (0.40)	38 (0.56)	7 (0.47)	4 (0.26)	6 (0.37)	13 (0.60)
Goblet Cell Adenocarcinoma (GCA)	1 (0.12)	1 (0.01)	-	-	-	-	-	-
Metastatic squamous cell carcinomatous deposit in appendix	1 (0.12)	-	-	-	-	-	-	-
Urothelial rests in appendix	1 (0.12)	-	-	-	-	-	-	-
Appendiceal lipoma	1 (0.12)	-	-	-	-	-	-	-
Other rare lesions	-	4 (0.07)	10 (0.50)	36 (0.53)	19 (1.29)	55 (3.64)	22 (1.35)	45 (2.08)

[Table/Fig-13]: Comparison of current study with few selected studies [2,4,8,9,14,17,18].

Limitation(s)

There are some limitations in the current study, the primary one being the retrospective nature of the study and, secondarily, the data from a single centre. Future research can be carried out in the epidemiology of unusual findings; this will assist in taking a better approach to the case and thereby help in finding accurate aetiologies for such conditions.

CONCLUSION(S)

The prevalence of atypical appendiceal lesions was found to be 4.81% in this study. This study emphasises the fact that even an appendix that seems normal may conceal or show signs of a variety of potentially treatable, bothersome, and/or crucial lesions, such as those important for tumour staging. Patients with unusual pathological findings require further testing, more careful clinical attention, years of follow-up, and a multidisciplinary approach. The condition may not be completely cured, if uncommon causes are missed. Thus, all appendectomy specimens should undergo meticulous histopathological examination, even when the specimens are macroscopically normal, irrespective of clinical and radiological findings. This is so that any lesions found might potentially have treatment implications or future implications. Pathologists must be vigilant while sampling and analysing appendectomy specimens, and surgeons should sensitise patients with suspected appendicitis about the necessity of this microscopic assessment.

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