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Spectrum of Mucinous Appendiceal Neoplasms in a Tertiary Health Care Centre - A Retrospective Study

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Abstract

Background: Appendiceal mucinous neoplasms (AMNs) constitute a rare group of appendiceal epithelial tumours that carry a risk of progression to Pseudomyxoma peritonei (PMP), a severe clinical condition associated with significant morbidity and mortality. The updated 2019 World Health Organisation classification recognises three principal categories—Low-grade Appendiceal Mucinous Neoplasm (LAMN), High-grade Appendiceal Mucinous Neoplasm (HAMN), and mucinous adenocarcinoma emphasising the critical role of accurate histopathological assessment in diagnosis, prognosis, and treatment planning.

Aims: To evaluate the incidence, histopathological spectrum, and clinicopathological correlation of mucinous appendiceal neoplasms at a tertiary care centre.

Materials and Methods: A retrospective analysis of 948 appendectomy specimens received over 1.5 years in the Department of Pathology, Shimoga Institute of Medical Sciences, was conducted. All specimens were processed by standard tissue processing protocol. Histopathological examination was performed on hematoxylin and eosin (H&E)-stained sections.

Results: Sixteen cases (1.68%) were identified as mucinous neoplasms. LAMN constituted the majority at 87.5% (14/16), HAMN accounted for 6.25% (1/16), and mucinous adenocarcinoma for 6.25% (1/16). The male-to-female ratio was 1:1, with an age range of 23–73 years. The majority of cases presented clinically as acute appendicitis (75%), highlighting the diagnostic challenge.

Conclusion: Mucinous appendiceal neoplasms are underdiagnosed due to non-specific clinical presentation.

Systematic histopathological examination is indispensable for accurate classification, risk stratification, and guiding oncological management. Awareness of the risk of PMP in LAMN, even without frank invasion, is critical.

Keywords: LAMN, HAMN, appendiceal mucinous neoplasm, mucinous adenocarcinoma, pseudomyxoma peritonei, appendectomy, histopathology.

Introduction

Appendiceal mucinous neoplasms represent a rare and heterogeneous category of lesions, commonly presenting with symptoms suggestive of acute appendicitis. Primary appendiceal neoplasms are encountered in fewer than 2% of appendectomy specimens.[1] Appendiceal mucinous neoplasms constitute a rare subset of appendiceal tumors, occurring in approximately 0.5%–2% of appendectomy specimens. Their clinical relevance extends beyond their low incidence, as they exhibit a spectrum of biological behavior and may lead to significant complications.[2]

Appendiceal mucinous neoplasms in their early stages are frequently identified incidentally following appendectomy for presumed appendicitis. Advanced disease commonly presents with progressive abdominal distension secondary to the buildup of mucin within the peritoneal space.[3]

Mucinous neoplasms of the appendix are a distinct category of tumours characterised by mucin secretion and a predilection for peritoneal dissemination. Their progression can lead to pseudomyxoma peritonei (PMP), a serious condition characterised by progressive accumulation of mucinous ascites in the peritoneal cavity following rupture of a mucinous appendiceal lesion, with significant morbidity and mortality.[4,5] Early detection and precise histopathological classification play a pivotal role in the management and prognostication of appendiceal neoplasms. The 2019 World Health Organisation classification system categorises these tumours into epithelial and non-epithelial groups, including serrated lesions, mucinous neoplasms such as LAMN and HAMN, and adenocarcinomas.[6] The designation of HAMN as a distinct pathological entity highlights the evolving insights into the biological behavior of appendiceal mucinous neoplasms and reinforces the importance of tumor grading in prognostic assessment. Owing to their tendency to mimic acute appendicitis, appendiceal neoplasms are rarely diagnosed before surgery. The limited diagnostic accuracy of imaging studies further contributes to this challenge, with confirmation generally relying on histopathological evaluation. This underscores the importance of routine examination of all appendectomy specimens.[7]

Although awareness of appendiceal neoplasms has increased, data regarding their incidence and histopathological spectrum in Indian populations remain limited. Most published studies are retrospective and single-center in nature, leading to considerable variation in the reported incidence rates and distribution of tumor subtypes. This highlights the importance of generating region-specific evidence to improve understanding of disease patterns and support informed clinical decision-making. Furthermore, the optimal management of appendiceal mucinous neoplasms (AMNs) remains uncertain, with ongoing debate surrounding the appropriate extent of surgical resection and the role of adjuvant therapies such as early postoperative intraperitoneal chemotherapy (EPIC) and hyperthermic intraperitoneal chemotherapy (HIPEC).[3]

The present study aimed to determine the incidence and histopathological profile of appendiceal neoplasms in a tertiary care setting and to correlate these findings with clinical manifestations and treatment outcomes.

Materials and Methods

Study Design and Setting

This was a retrospective observational study conducted in the Department of Pathology, Shimoga Institute of Medical Sciences, Shivamogga, India, over a period of 1.5 years.

Inclusion and Exclusion Criteria

All appendectomy specimens received during the study period were included. Autolysed specimens, repeat biopsies from previously diagnosed cases, and non-mucinous tumours were excluded from the study.

Specimen Processing

All specimens were fixed in 10% neutral buffered formalin. The external surface, mesoappendix, and cut sections of the appendix were examined grossly. Representative sections were processed using standard paraffin embedding. Sections of 4-µm thickness were cut and stained with hematoxylin and eosin (H&E).

Histopathological Classification

Mucinous neoplasms were classified according to the 2019 World Health Organisation Classification of Tumours of the Digestive System. The defining histopathological features included LAMN, which exhibits a pushing border, loss of muscularis mucosae, low-grade mucinous epithelium, and no destructive invasion; HAMN, characterised by high-grade cytologic atypia with a pushing growth pattern and absence of invasion; and mucinous adenocarcinoma, which demonstrates invasive growth with extracellular mucin deposition.

Ethics Statement

All procedures performed in the current study were approved by IEC (reference number: SIMS/IEC/995/2022-23 and date: 11/11/2024) in accordance with the 1964 Helsinki declaration and its later amendments.

Informed consent was obtained from all individual participants included in the study. Formal written informed consent was not required with a waiver by the IEC.

Results

Incidence

A total of 948 appendectomy specimens were examined during the study period of 1.5 years. Sixteen cases (1.68%) were identified as mucinous appendiceal neoplasms (Table.1).

Histopathological Spectrum

LAMN was the most common diagnosis, accounting for 14 of 16 cases (87.5%). One case each of HAMN (6.25%) and mucinous adenocarcinoma (6.25%) was identified (Table.2).

Clinicopathological Features

The age of patients ranged from 23 to 73 years with an equal male-to-female ratio (1:1). Abdominal pain was the most common presenting symptom (87.5%). The most frequent pre-operative clinical diagnosis was acute appendicitis (75%), followed by intestinal obstruction, mucocele, and malignant ovarian tumour (Table.3).

Among the LAMN cases, gross examination revealed a thinned wall with a mucin-filled lumen in 2 cases (Fig.1), an unremarkable appearance in 7 cases, an appendix with an attached cystic pouch in 2 cases, 1 case with mucin deposits on the appendix, 1 case with a cystic mass and congested and distorted in 1 case. Microscopically, mucin deposits in the serosal layer

were noted in several cases, with mucin extravasation in 2 cases, raising concern for early peritoneal spread (Fig.2). One notable case showed concurrent mucin deposits in the fallopian tube, underscoring the risk of regional dissemination even in LAMN. The single HAMN case was a 55-year-old female presenting as acute appendicitis, with gross findings of a thinned wall and mucin-filled appendix. Histopathology revealed high-grade nuclear atypia and complex glandular architecture (Fig. 3). The mucinous adenocarcinoma case was a 40-year-old male presenting with a perforated appendix, in whom histopathology confirmed invasive mucinous adenocarcinoma (Fig. 4). This case highlights the critical importance of examining perforation specimens thoroughly for underlying malignancy.

Discussion

Appendiceal neoplasms are rare entities, often presenting a significant clinical challenge due to their deceptive presentation mimicking acute appendicitis. The incidence of mucinous appendiceal neoplasms in the present study was 1.68%, representing 16 out of 948 cases. This incidence is slightly higher than historical international data from the USA by Skendelas *et al*, who reported an incidence of 0.53% in 154,596 appendectomies.[8] It also contrasts with findings from Kunduz et al., who reported a lower appendiceal neoplasm incidence of 0.78% (28 out of 3554 cases).[7] However, our findings align closely with domestic data. A tertiary care centre study in Karnataka by Myageri et al. reported a comparable overall appendiceal neoplasm incidence of 1.7% in 472 cases.[10] (Table-4)

Demographics and Clinical Presentation: Our study observed an equal gender distribution with a male-to-female ratio of 50:50. This differs from other regional Indian studies; for instance, Pratheep et al. noted a slight male predominance with a ratio of 1.07:1, while Priyadharshini et al. reported a strong female predilection, with females accounting for 75% of their cases. [9,11]

Clinically, the vast majority of our patients (87.5%) presented with abdominal pain, and 75% received a preoperative diagnosis of acute appendicitis. This masking of neoplasms behind acute inflammatory symptoms is a universally documented hurdle. Priyadharshini et al. similarly found that acute appendicitis was the most frequent preoperative diagnosis in their cohort.[11] Likewise, Pratheep et al. noted right lower quadrant pain as the primary symptom in 69% of cases, and Myageri et al. reported right iliac fossa pain in an overwhelming 98.52% of their patients.[9,10]

Histopathological Spectrum: According to the 2019 WHO classification, accurate histological subtyping is fundamental. In the current cohort, Low-Grade Appendiceal Mucinous Neoplasm (LAMN) was by far the most common histological subtype, representing 87.5% of the mucinous neoplasms. High-Grade Appendiceal Mucinous Neoplasm (HAMN) and Mucinous Adenocarcinoma each accounted for 6.25% of the cases.

The predominance of LAMN is heavily corroborated by the comparative literature, though proportions vary. Pratheep et al. reported LAMN in 69.23% of their mucinous neoplasm cases, and Priyadharshini et al. found LAMN to be the most common type, representing 58.4% of appendiceal neoplasms.[9,11] Myageri et al. also found that LAMN accounted for a significant 50% of all appendiceal neoplasms.[10] In contrast, Pradhan et al. documented a slightly lower proportion of LAMN (42.85%), but a higher incidence of Mucinous

Adenocarcinoma (28.57%) and HAMN (14.28%) than observed in our study.[1]

Management and Prognosis: Because most appendiceal neoplasms are found incidentally during pathological examination, clinical management is highly dependent on the tumor type, histological grade, and pathological stage. For slow-growing and early-stage tumors like LAMN, total resection of the appendix is usually a sufficient primary treatment, provided no mucin has extruded. However, long-term follow-up is absolutely crucial to monitor for the development of Pseudomyxoma Peritonei (PMP) at an early stage. Conversely, in cases complicated by perforation, or for high-grade lesions (HAMN/Adenocarcinoma), a simple appendectomy is inadequate; these patients require aggressive surgical intervention, including right hemicolectomy and cytoreductive surgery combined with Hyperthermic Intraperitoneal Chemotherapy (HIPEC).

In conclusion, to avoid overtreatment or undertreatment, thorough histopathological classification of all resected appendices remains a fundamental prerequisite with multiple sections and/or submission of entire specimen may be needed.

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Legend Figures and Tables

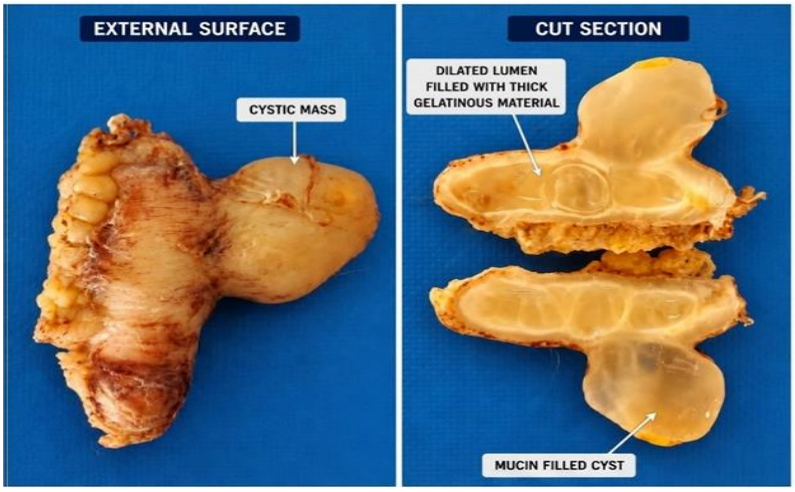

Figure 1: Gross pathology of appendiceal mucinous neoplasia. (Left)Gross specimen of vermiform appendix with attached mesoappendix and cystic mass. (Right) Cut section reveals a dilated lumen filled with glistening gelatinous mucinous material, attenuated wall and cystic mass filled with mucin

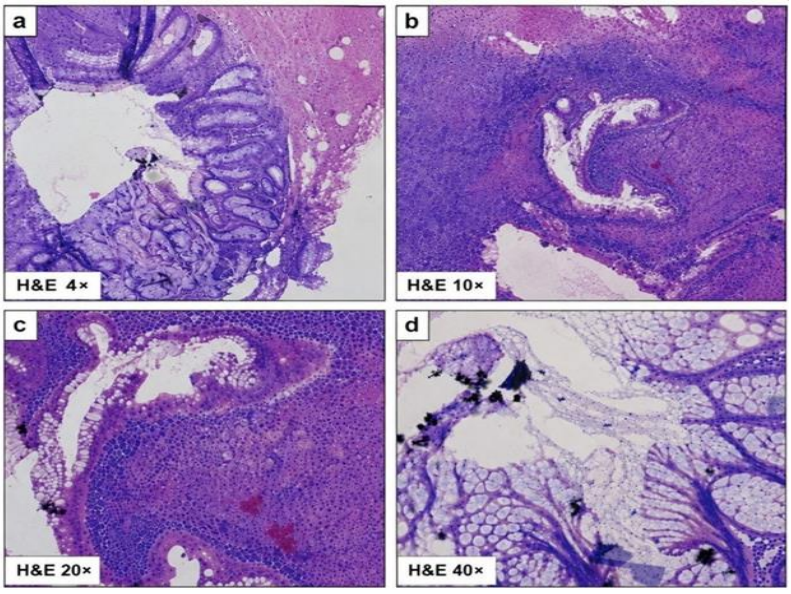

Figure 2: Low-grade appendiceal mucinous neoplasm (LAMN).

(a) H&E 4×: Dilated appendiceal lumen filled with abundant mucin and lined by villiform mucinous epithelium showing low-grade dysplasia and pushing margins.

(b) H&E 10×: Undulating mucinous epithelium with mild cytologic atypia and mucin pools dissecting the appendiceal wall without infiltrative invasion.

(c) H&E 20×: Mucin-secreting columnar epithelium with nuclear stratification, low-grade atypia, and associated chronic inflammatory infiltrate.

(d) H&E 40×: Goblet-type cells with abundant intracellular mucin and minimal atypia, with extracellular acellular mucin and no evidence of high-grade dysplasia or invasion.

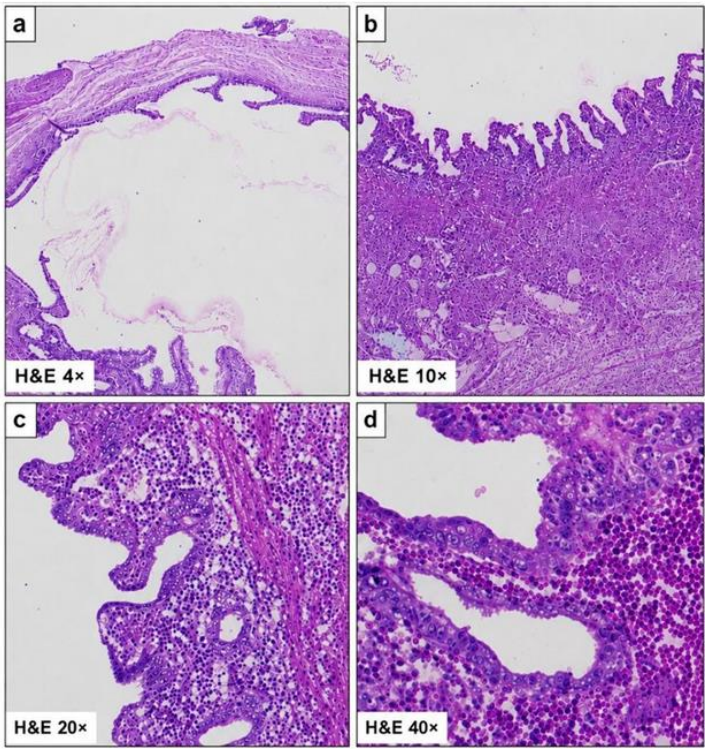

Figure 3: High-grade appendiceal mucinous neoplasm (HAMN).

(a) **H&E 4×:** Dilated appendiceal lumen filled with abundant mucin and thinning of the wall with distorted overall architecture.

(b) **H&E 10×:** Complex, crowded, and irregular glandular architecture with epithelial tufting and stratification indicating dysplasia.

(c) **H&E 20×:** Marked epithelial atypia with papillary patterns; nuclear enlargement, hyperchromasia, and loss of polarity are evident.

(d) **H&E 40×:** High-grade cytological atypia with pleomorphic nuclei, prominent nucleoli, and mitotic figures; dysplastic epithelium.

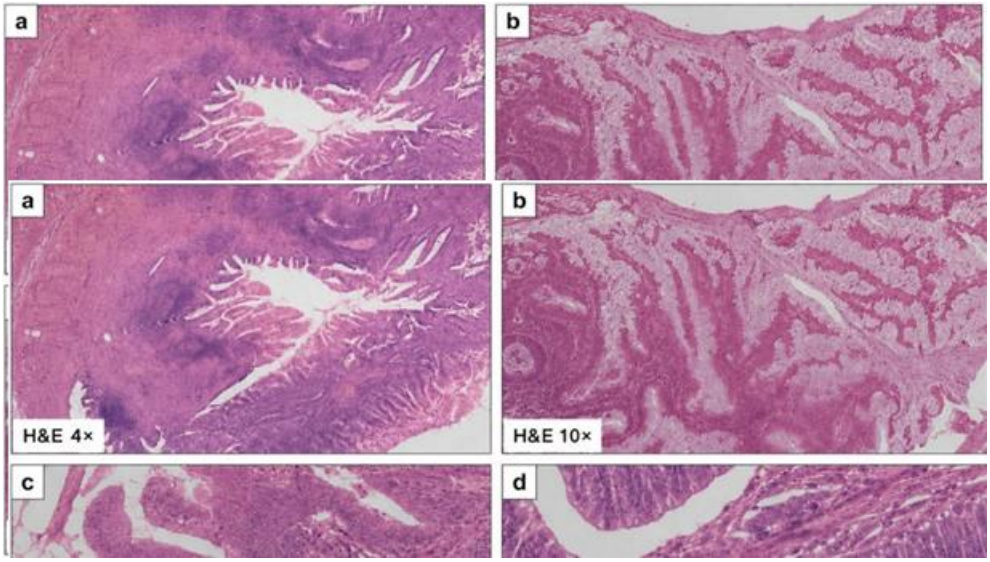

Figure 4: Mucinous adenocarcinoma of appendix.

(a) **H&E 4×:** Infiltrative mucinous adenocarcinoma showing irregular glands and mucin pools dissecting through the appendiceal wall with desmoplastic stroma.

(b) **H&E 10×:** Complex, irregular, and crowded glandular architecture with back-to-back arrangement and cribriform/papillary patterns.

(c) **H&E 20×:** Neoplastic cells with nuclear enlargement, hyperchromasia, stratification, and loss of polarity; intraluminal mucin is present.

(d) **H&E 40×:** High-grade cytologic atypia with pleomorphic nuclei, prominent nucleoli, and frequent mitotic figures;

Table 1: Clinicopathological Profile – Summary Statistics

Parameter	Value
Total appendectomy specimens	948
Mucinous neoplasms identified	16 (1.68%)
Age range	23–73 years
Male : Female ratio	1 : 1 (8M : 8F)
Most common symptom: Abdominal pain	87.5% (14/16)
Pre-operative diagnosis: Acute Appendicitis	75% (12/16)
Study duration	1.5 years

Table 2: Histopathological Spectrum of Mucinous Appendiceal Neoplasms

Diagnosis	Number of Cases	Percentage (%)
Low-Grade Appendiceal Mucinous Neoplasm (LAMN)	14	87.5%
High-Grade Appendiceal Mucinous Neoplasm (HAMN)	1	6.25%
Mucinous Adenocarcinoma	1	6.25%
Total	16	100%

Table 3: Detailed Case-wise Distribution of All 16 Cases

Sn.	Age	Sex	Clinical presentation	Clinical Diagnosis	Gross Findings	Microscopy	Diagnosis	Other Findings
1	23	F	Abdominal pain	AA	Wall thinned & mucin filled	Confined to mucosa	LAMN	–
2	73	F	Abdominal pain	Intestinal Obstruction	Unremarkable	Mucin deposits in serosal layer	LAMN	Non-specific inflammation of SI
3	35	M	Abdominal pain	AA	Wall thinned & mucin filled	Mucin deposits +	LAMN	–
4	48	F	Abdominal pain	Mucocele	Cystic mass	Mucin deposits	LAMN	–
5	61	M	Abdominal pain	AA	Unremarkable	Mucin deposits in serosal layer	LAMN	–
6	26	M	Abdominal pain	AA	Unremarkable	Mucin deposits in serosal layer	LAMN	–

7	46	M	Abdominal pain	AA	Appendix with attached cystic pouch	Mucin extravasation	LAMN	–
8	48	M	Abdominal pain	AA	Appendix with attached cystic pouch	Mucin deposits	LAMN	–
9	55	F	Ovarian mass	Malignant ovarian tumor	Mucin deposits in appendix	Mucin deposits in serosal layer	LAMN	Mucin deposits in fallopian tube
10	40	F	Abdominal pain	AA	Unremarkable	Mucin deposits +	LAMN	–
11	26	F	Abdominal distension	?TB / ?Carcinoid	Unremarkable	Mucin deposits +	LAMN	–
12	35	M	Abdominal pain	AA with adhesion	Congested & distorted	Mucin extravasation	LAMN	–
13	37	M	Abdominal pain	AA	Unremarkable	Mucin deposits +	LAMN	–
14	60	M	Abdominal pain	AA	Unremarkable	Mucin deposits +	LAMN	–
15	55	F	Abdominal pain	AA	Wall thinned & mucin filled	Mucin deposits & cellular atypia	HAMN	–
16	40	M	Abdominal pain	Perforated Appendix	–	–	Mucinous Adenocarcinoma	–

Table 4: Comparative analysis of the present study and previous studies.

Study (Region)	Total Cases & Incidence	Gender Ratio (M:F)	Primary Clinical Presentation	Key Histological Subtypes
Present Study (India)	948 cases (1.68% incidence)	1:1 (Equal distribution)	Abdominal pain (87.5%) Pre-op dx: Acute appendicitis (75%)	LAMN (87.5%), HAMN (6.25%), Adenocarcinoma (6.25%)

Skendel et al. (USA)	154,596 cases (0.53% incidence) 2124 cases (1.4% incidence)	Not specified 2:1	Not specified Pre op dx: Acute appendicitis(52%)	Adenocarcinoma (83%), Neuroendocrine (48.1%), LAMN (29.6%), Adenocarcinoma (22.2%)
Kunduz et al. (Turkey)	3,554 cases (0.78% incidence)	Not specified	Not specified	NET (60.8%), LAMN (28.5%), Adenocarcinoma (10.7%)
Myageri et al. (India)	472 cases (1.7% incidence)	1.5:1 (Male dominant)	Right iliac fossa pain (98.5%)	LAMN (50%), Carcinoid (37.5%), Goblet cell carcinoid (12.5%)