



# Oddballs in the Histopathological Study of Appendicular Lesions at a Tertiary Care Centre: A Retrospective Study

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**Abstract:** **Background:** Histopathological examination still remains the gold standard method for the confirmation of the appendicitis. Patients with incidental findings of tumors and parasites, do not present with the specific symptoms and hence, elective or incidental appendectomies are performed. **Aims:** To determine the various histological diagnoses of all surgically removed appendices and to find out the age and sex related incidence of appendicitis, the perforation rate and the rate of elective or incidental appendectomies. **Methods:** This was a cross sectional retrospective study at a tertiary care centre of 1043 appendectomy cases over two years period. **Results:** The mean age was found to be 29.13 years. In present, males (51.7%) slightly outnumbered females (48.3%), with male to female ratio of 1.06: 1. Most common non-neoplastic lesion was acute appendicitis (51.8%), followed by chronic/ recurrent appendicitis (31.6%). Neoplastic lesions included eight metastatic Adenocarcinoma – six from colon (0.6%) and two from ovary (0.2%). Carcinoid tumor was found in 0.2% cases and Primary Mucinous Adenocarcinoma was seen in 0.1% cases. **Limitations:** This was a retrospective study hence the follow-up of patients could not be done. **Conclusions:** Present study strongly emphasizes and recommends meticulous gross as well as microscopic examination of every appendectomy specimen.

**Keywords:** Appendix, Appendectomy, Acute Appendicitis, Carcinoid, Metastatic tumors.

## INTRODUCTION

Appendicitis is one of the most common acute surgical conditions of the abdomen, and an appendectomy is one of the most frequently performed operations worldwide.<sup>1</sup> The lifetime risk for appendicitis is 7%. The incidence of acute appendicitis roughly parallels that of lymphoid development, hence, commonly occurs in adolescents and young adults. The rate of acute appendicitis varies among countries.<sup>2</sup> In developing countries like India, the incidence is increasing in most urban centers, probably due to adoption of Western diet.<sup>3</sup> Despite of advances in technology and imaging modalities, there is dilemma in the clinical diagnosis of acute appendicitis. Histopathological examination still remains the gold standard method for the confirmation of the appendicitis. Not only the pathologic diagnosis of acute inflammation, and obstructive causes like fecoliths and lymphoid hyperplasia, but some unusual factors such as incidental tumors like carcinoid, lymphoma, primary mucinous adenocarcinoma, metastatic tumors and mucoceles and parasitic infestations like enterobiasis, ascariasis, taeniasis, amoebiasis and tuberculous, noted in the appendix highlights the importance of the pathologic analyses of every single resected appendix.<sup>1,2</sup> Patients with incidental findings of tumors and parasites, do not present with the specific symptoms and hence, elective or incidental appendectomies are performed.

This study aims to determine the various histological diagnoses of all surgically removed appendices and to find out the age and sex related incidence of appendicitis, the perforation rate and the rate of elective or incidental appendectomies.

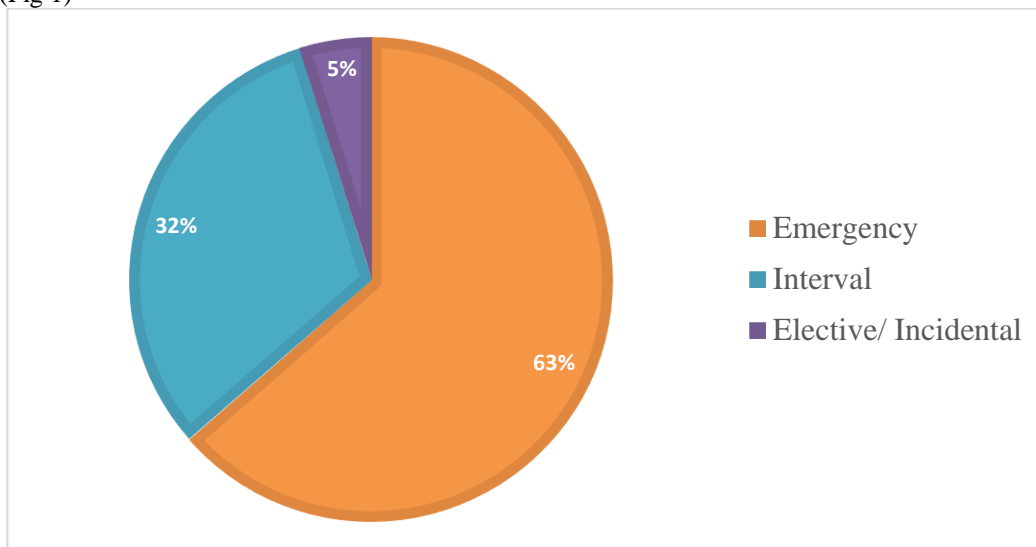
## MATERIALS AND METHODS

The present study was a retrospective cross-sectional study, carried out at Tertiary Care Teaching Hospital, in Department of Pathology, over a period of two years from August 2018 to July 2020. All emergency appendectomies and interval appendectomies performed on clinically suspected appendicitis, and incidental appendectomies which were performed during other abdominal or pelvic surgeries were included. Among 5723 histopathological specimens received, total 1043 cases were found to be of appendix. All appendectomy specimens along with their operative findings were received from Department of Surgery. Clinical history with age, presenting signs & symptoms, radiological findings were studied. Gross examination of 10% formalin fixed specimen was done and transverse and longitudinal sections were taken from the representative area. Pus pockets, perforation site and tip were carefully examined. Further histopathological processing of sections was done and slides stained with Haematoxylin and Eosin (H&E) were studied. Where ever indicated, special stains like Periodic Acid Schiff (PAS) and Masson's Trichrome were studied. Zeihl- Nelson (ZN) stain was done for Acid Fast Bacilli (AFB) in all cases of suspected tuberculous appendicitis.

## RESULTS

The incidence of Appendectomy was found to be 18.22%, out of the total Histopathological specimens received.

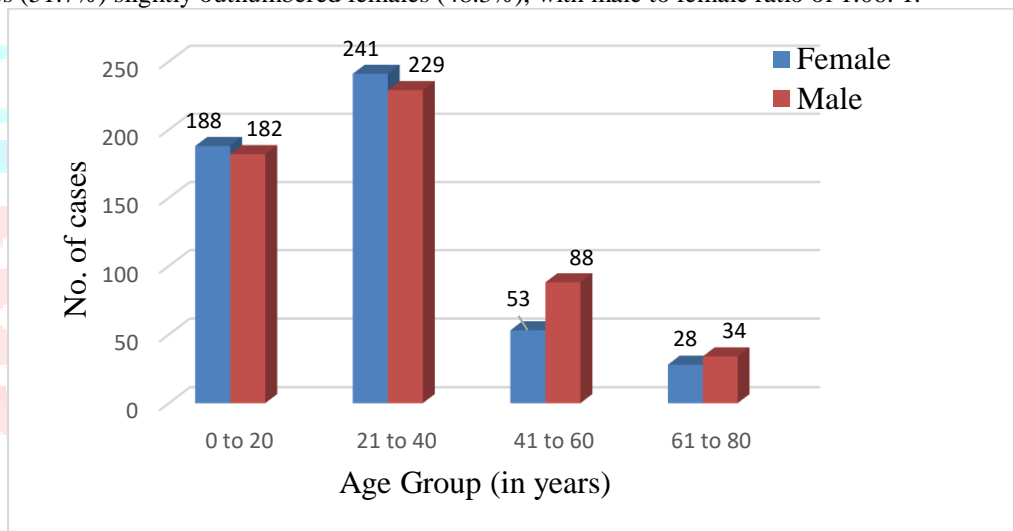
Of total 1043 appendectomies, there were 663 emergency appendectomy and 330 interval appendectomy performed for clinically suspicious appendicitis. The remaining 50 cases were elective or incidental appendectomy done for other primary abdominal or pelvic pathology, which included rare lesions like parasitic infestation in appendix, primary mucinous adenocarcinoma, metastatic adenocarcinoma and carcinoid tumors of appendix. (Fig 1)



**Figure 1: Types of Appendectomies performed (n=1043)**

Age group ranged from minimum two-years male with acute appendicitis to maximum of 79-years female with chronic appendicitis. The mean age was found to be 29.13 years.

In present study, males (51.7%) slightly outnumbered females (48.3%), with male to female ratio of 1.06: 1.



**Figure 2: Age-wise sex distribution of cases (n=1043)**

Maximum number of patients were in the age group of 21-40 years, where females were more commonly affected than males. Elderly patients, in the age group of 61-80 years, were mostly diagnosed with the neoplastic lesion of appendix, along with acute and chronic appendicitis. (Fig 2)

As shown in table 1, in the present study, non-neoplastic appendicular lesions were 1032 (98.95%) and neoplastic lesions were 11 (1.05%) out of total 1043 appendectomies.

Most common non-neoplastic lesion was acute appendicitis (51.8%), followed by chronic/ recurrent appendicitis (31.6%). Only one case (0.1%) was found to be of appendicitis with typhoid lesion. All the patients with acute appendicitis, acute necrotizing appendicitis (10.4%) and acute gangrenous appendicitis (1.4%) presented with acute symptoms of appendicitis and were operated on emergency basis. Whereas, chronic appendicitis cases were treated as interval procedure with the suspicion of appendicitis. However, granulomatous appendicitis (1.4%), mucocele (0.7%), tuberculous appendicitis (0.6%), parasitic infestations in appendix – *E. vermicularis* (0.6%), *Strongyloides* (0.2%), *Taenia* (0.1%) and *Amoeba* (0.1%) as well as typhoid lesions were all incidental findings. In these cases, operative procedure was carried out for some other pelvic or abdominal cause.

**Table 1: Distribution of Various Lesions of Appendix (n=1043)**

Diagnosis		No. of cases	Percentage (%)	
Non-Neoplastic Lesions (1032)	Acute Appendicitis	540	51.8	
	Chronic/ Recurrent Appendicitis	330	31.6	
	Acute Necrotising Appendicitis	108	10.4	
	Acute Gangrenous Appendicitis	15	1.4	
	Granulomatous Appendicitis	15	1.4	
	Parasitic	<i>E. vermicularis</i>	06	0.6
		Strongyloides	02	0.2
		Taenia	01	0.1
		<i>E. histolytica</i>	01	0.1
	Mucocele	07	0.7	
	Tuberculous Appendicitis	06	0.6	
Typhoid	01	0.1		
Neoplastic Lesions (11)	Metastatic Adenocarcinoma	Colon	06	0.6
		Ovary	02	0.2
	Carcinoid Tumor	02	0.2	
	Primary Mucinous Adenocarcinoma	01	0.1	
<b>Total</b>		<b>1043</b>	<b>100</b>	

Neoplastic lesions included eight metastatic Adenocarcinoma – six from colon (0.6%) and two from ovary (0.2%). Carcinoid tumor was found in 0.2% cases and Primary Mucinous Adenocarcinoma was seen in 0.1% cases.

## DISCUSSION

Acute appendicitis has been the most common surgical emergency for a number of decades and appendectomy is the most frequently performed abdominal operation. In the Western World, acute appendicitis accounts for about 40% of all surgical emergencies<sup>4</sup>. It is rare in Asian and African subcontinent. Present study shows the 18.22% incidence of Appendectomy, out of which maximum (63.56%) were on emergency basis. Least commonly (4.79%) were elective appendectomies. The other studies showed a variable incidence rate of appendicitis. Khan et al<sup>5</sup>, reported acute appendicitis to be the most common cause of emergency laparotomy showing incidence of 26%. However, there was a low incidence rate of acute appendicitis of only 7.46% in the study conducted by Makaju et al.<sup>6</sup>

Age incidence of appendicitis was higher in 21-40 years of age group, accounting 45.06% of the cases, in concordance with various studies.<sup>3, 7, 8</sup> Other studies<sup>3, 4, 8</sup>, showed male to female ratio ranging from 1 to 3:1, we had similar matching data with male to female ratio of 1.06:1. However, it was observed that females at adolescent age group had higher incidence than the males, in contrast to other studies. Whereas, with the advance in age, males outnumbered females.

Diagnosis of acute appendicitis requires neutrophilic infiltration of the muscularis propria. (Fig 3A) In more severe cases a prominent neutrophilic exudate generates a serosal fibrinopurulent reaction. As the process continues, focal abscesses may form within the wall (acute suppurative appendicitis). Further compromise of appendiceal vessels leads to large areas of hemorrhagic ulceration and gangrenous necrosis that extends to the serosa creating acute gangrenous appendicitis, which can be followed by rupture and suppurative peritonitis.<sup>9</sup> In present study, maximum frequency of histologic diagnoses was acute appendicitis (51.8%) followed by chronic/ recurrent appendicitis (31.6%) (Fig 3B) and acute necrotising appendicitis (10.4%) similar to other study done by Zulfikar et al.<sup>10</sup> Acute gangrenous appendicitis was diagnosed in 1.4% cases.

The incidence of granulomatous appendicitis, a rare condition that may be discovered incidentally in a patient with a clinical presentation of acute appendicitis, ranges from 0.31 to 0.95 %. Various infectious and noninfectious factors cause granulomatous appendicitis. Systemic conditions, such as Crohn's disease and Sarcoidosis, may also be associated with granulomatous inflammation of the appendix.<sup>11</sup> We found 1.4% cases of granulomatous appendicitis.

Tuberculosis (TB) may affect all tissues and organs in the body, but it most frequently involves the lungs. The GI system is ranked sixth among all extrapulmonary involvements, affecting all of the segments of the GI system, from the mouth to anus. However, the ileum and ileocecal region are the sites most commonly involved, followed by the colon and vermiform appendix. The appendix may be affected secondarily to ileocecal TB, but appendicular TB may occur in an even rarer primary form without any evidence of the disease elsewhere. The reported incidence of appendicular TB varies from 0.1% to 3.0% among all appendectomies performed. Classic histopathological analysis of an appendectomy specimen usually reveals the presence of caseating granulomas and Langhans giant cells, suggesting TB of the appendix. (Fig 3C) Although some studies have reported that treatment is not necessary for the primary disease and that appendectomy alone is sufficient, no consensus has been reached.<sup>1</sup> We reported six cases of this rare lesion undergoing an elective appendectomy with presumed appendicitis.

Chronic infections by parasites are associated with poor sanitarian conditions, ingestion of contaminated food and exposure to contaminated water.<sup>12</sup>

Parasitic infestation is thought to be one of the common causes of luminal obstruction of appendix leading to appendicitis. Several studies have found luminal parasites in the appendix associated with or without appendicitis in the range of 0.3 to 3.15%. Commonly found parasites include *Enterobius vermicularis* and *Schistosoma* species.<sup>2</sup> We reported appendicular parasitic infestations by *E. vermicularis* (six cases), *Strongyloides* (two cases) and one case each of *Taenia* and *E. histolytica*.



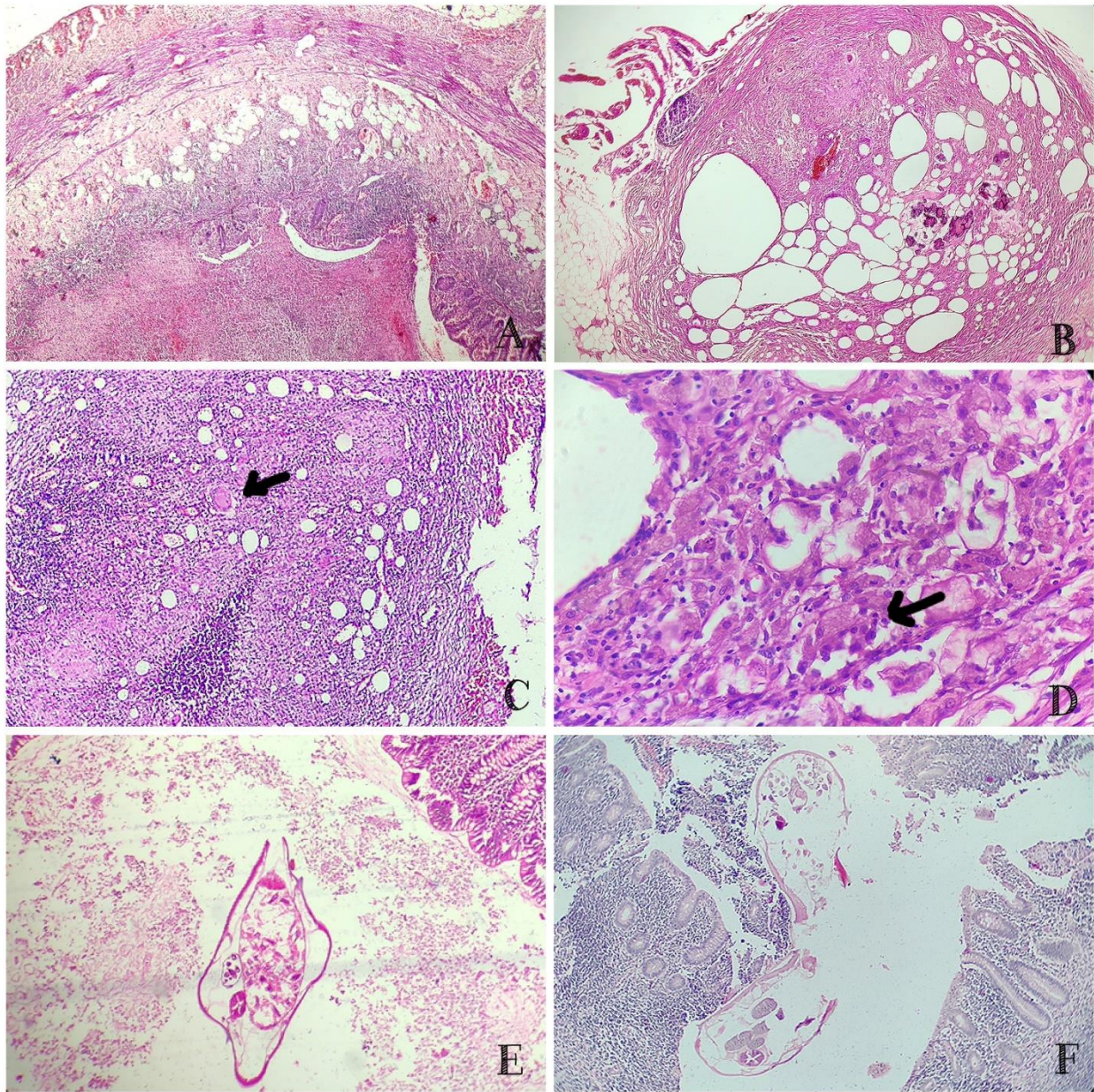


Fig A – Acute Appendicitis (H&E, 200x)

Fig B – Chronic/ Recurrent Appendicitis with fibrosis and dystrophic calcification (H&E, 200x)

Fig C – Tuberculous Appendicitis with Caseating granulomas (H&E, 400x)

Fig D – Appendicitis with Typhoid lesion with Erythro-phagocytosis (H&E, 400x)

Fig E – *Enterobias vermicularis*/ Pinworm infestation in Appendix (H&E, 400x)

Fig F – *Taenia* infestation in Appendix (H&E, 200x)

### Figure 3: Microphotographs of Non-Neoplastic lesions of Appendix

*Enterobius vermicularis*, also known as Pinworm or Oxyuris, is a widespread parasitic infection estimated to affect up to 200 million people worldwide. The association of Oxyuris and appendicitis was first made in the late 19 century, when Still initially documented this organism in the appendix lumen. While the reported incidence of Pinworm in appendectomy specimens of patients with presumed appendicitis ranged from 0.2% to 41.8%, the reported rates of inflammation in specimens from appendices infested with Pinworm ranged from 13% to 37%. (Fig 3E) Patients must receive antihelminthic treatment (oral dose of mebendazole, which is repeated in 1-2 wk) because the appendectomy treats only the consequence and not the cause of the disease.<sup>1</sup>

Strongyloidiasis is a chronic parasitic infection of humans caused by *Strongyloides stercoralis*. Ivermectin, thiabendazole and albendazole are the most effective medicines for treating the infection.<sup>13</sup> Among the infectious causes of acute appendicitis, *S stercoralis* is extremely unusual.<sup>14</sup>

Taeniasis, a well-known worm infection, is characterized by the presence of the helminth in the intestine, which is recognized by presence of a segment of the parasite in the stool. The occurrence of *Taenia spp.* in the appendix (Fig 3F) is so rare that the situation invites a case report. In cases of Taeniasis, specific species identification is not required for treatment, as patients are treated with a single dose of praziquantel.<sup>1</sup>



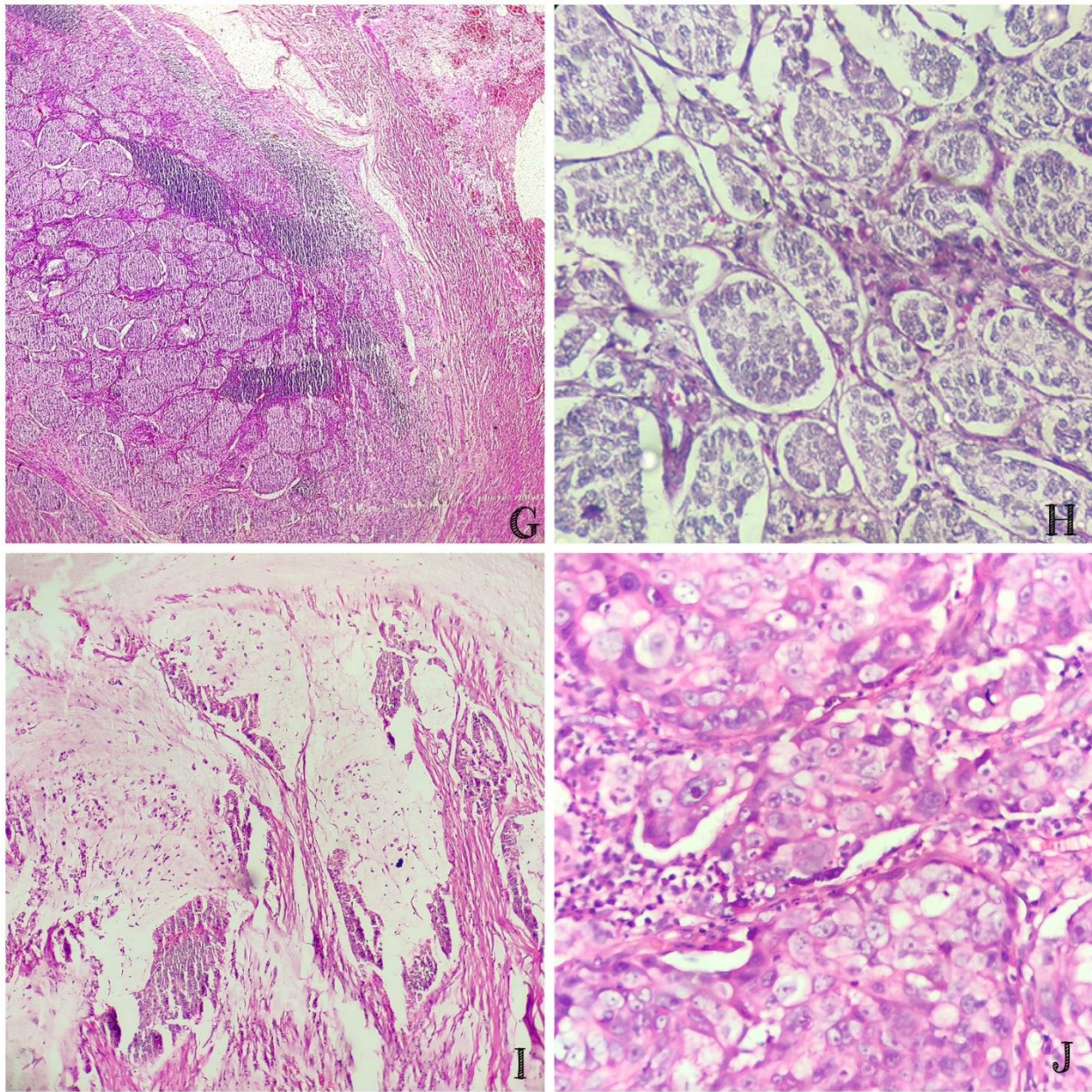


Fig G – Appendicular Carcinoid at tip of appendix (H&E, 200x)

Fig H – Appendicular Carcinoid showing salt & pepper nuclear chromatin (H&E, 400x)

Fig I – Primary Mucinous Adenocarcinoma of Appendix (H&E, 400x)

Fig J – Metastatic Colonic Carcinoma to Appendix (H&E, 400x)

#### Figure 4: Microphotographs of Neoplastic lesions of Appendix

Amoebiasis is an infection of the large intestine caused by *Entamoeba histolytica*, which affects 10% of the world population and has a worldwide distribution. This parasite is occasionally found in the appendix, usually in the lumen without accompanying inflammation, but is rarely associated with acute appendicitis. A preoperative diagnosis of amebic appendicitis is almost impossible because no clinical features or diagnostic laboratory tests distinguish amebic from bacterial appendicitis, other than a stool examination. Amoebic appendicitis has a good outcome after surgical resection and treatment with metronidazole.<sup>1</sup>

Typhoid/ enteric fever, affects upto 30 million individuals worldwide each year and is caused by *Salmonella enterica*, and its two subtypes, *typhi* and *paratyphi*. In endemic areas, children and adolescents are affected most often. Transmission occurs from person to person or via food or contaminated water. Gallbladder colonization with *S. typhi* or *S. paratyphi* may be associated with gallstones and the chronic carrier state. In the small intestine, *S. typhi* are taken up by and invade M-cells, then engulfed by mononuclear cells in the underlying lymphoid tissue. They then disseminate via lymphatic and blood vessels. This causes reactive hyperplasia of phagocytes and lymphoid tissues throughout the body. (Fig 3D) Blood cultures are positive in more than 90% of affected individuals during the febrile phase. Antibiotic treatment can prevent further disease progression. In patients who do not receive antibiotics, the initial febrile phase continues for up to 2 weeks; patients have sustained high fevers and abdominal tenderness that may mimic appendicitis.<sup>9</sup> We had one case of incidental findings of typhoid lesion with appendicitis in a 26-years male.

Malignant tumors of the appendix include carcinoids, lymphomas, primary adenocarcinomas, mucinous cystadenocarcinomas and metastatic deposits from gastro-intestinal and genito-urinary sites.

Benign tumors of the appendix consist of mucoceles, tubular adenomas, villous adenomas, leiomyomas, neuromas and lipomas.<sup>1</sup>



A mucocele of the appendix denotes an obstructive dilatation of the appendiceal lumen due to abnormal accumulation of mucus, which may be caused by a retention cyst, endometriosis, mucosal hyperplasia, cystadenoma, or a cystadenocarcinoma. The incidence of mucocele ranges from 0.2% to 0.3% of all appendectomy specimens. Mucoceles are often asymptomatic and an incidental finding at appendectomy, or during laparotomy or at histological examination of an operative specimen. However, mucoceles may be diagnosed clinically from features of acute appendicitis. Appendectomy is the standard of care for mucinous cystadenoma, whereas a cystadenocarcinoma requires a right hemicolectomy and follow-up with CT, US, and colonoscopy examinations.<sup>1</sup> Mucocele was found in 0.7% cases, in present study.

The prevalence of mucinous neoplasms is 0.2–0.4 % of appendectomies.<sup>11</sup> Mucinous tumors of the appendix are classified according to WHO 2010 as low grade or as high grade. Low-grade appendiceal neoplasms are slow growing and produce clinical picture of low-grade pseudomyxoma peritonei with unusual spread beyond the peritoneum or nodal metastasis. High-grade mucinous adenocarcinomas can also produce pseudomyxoma peritonei and is more likely to invade the underlying organs and exhibit hematogenous and lymphatic metastasis.

Present study included total of eight cases (0.8%) of metastatic deposits of Adenocarcinoma with primary site as colon (six cases) and ovary (two cases). (Fig 4J)

An appendiceal carcinoid tumor is considered the most common type of appendiceal primary malignant lesion and accounts for almost 60% of all appendiceal tumors. An appendiceal carcinoid tumor is found in 0.3%-2.27% of patients undergoing an appendectomy. Characteristics of all appendiceal carcinoids (Fig 4G,4H) predicting aggressive behavior include tumor size, histological subtype, and mesoappendiceal involvement and are smaller than 1 cm in 70%-95% of cases. An increase in metastasis risk of up to 85% occurs with a tumor of 2 cm or larger. An appendiceal carcinoid tumor larger than 2 cm should be managed with a formal right hemicolectomy.<sup>1</sup> In our study, the incidence of appendiceal carcinoid was 0.2%, which was similar to other studies. The mean age at presentation of appendiceal- Neuroendocrine Tumor (NET) is 32–43 years. Appendiceal NET are firm, grayish-white, and fairly well-circumscribed. The majority of NET are located at the tip of the appendix (75 %).<sup>11</sup>

Primary adenocarcinoma of the appendix (Fig 4I) is an extraordinarily rare tumor.<sup>1</sup> Adenocarcinoma of the appendix occurs in 0.1–0.2 % of appendectomies. The median age is in the sixth or seventh decade of life. Adenocarcinomas behave aggressively. Thus, oncologic resection with right hemicolectomy is the treatment of choice.<sup>11</sup> We reported only one case (0.1%) of primary mucinous Adenocarcinoma of appendix.

## CONCLUSION

There is high incidence of appendicitis in the second and third decades of life and slightly higher in females. Low perforation rate indicates a better prospective regarding morbidity and mortality. Appendectomy specimens removed from patients with suspected acute appendicitis often appear macroscopically normal, but histopathological analysis of these cases may reveal an underlying pathology. Findings of pelvic pathologies in females, in negative appendectomy emphasize the usefulness of the laparoscopic surgery. Present study found a higher incidence of metastatic deposits of colonic adenocarcinoma and mucinous cystadenocarcinoma of ovary to appendix, highlighting the importance of careful microscopic evaluation of incidental appendectomy. Finally, an unusual finding such as carcinoid tumor and primary Mucinous Adenocarcinoma of appendix, in the clinically suspected acute appendicitis reflects the value of histological examination of every resected appendix, the presence of which would alter the further management. The practice of incidental appendectomy in uncomplicated abdominal or pelvic surgery might decrease the rates of mortality and morbidity associated with appendicitis and appendectomy in the elderly.

Present study strongly emphasizes and recommends meticulous gross as well as microscopic examination of every appendectomy specimen.

## BIBLIOGRAPHY

- 1) Akbulut S, Tas M, Sogutcu N, et al. Unusual histopathological findings in appendectomy specimens: a retrospective analysis and literature review. *World J Gastroenterol.* 2011;17(15):1961-1970.
- 2) V Vijayasree, CSPV Sunil, Sylvester Noel, T Sesagiri Rao. Histopathological spectrum of appendicular lesions and correlation with age and sex incidence: A retrospective study. *MedPulse International Journal of Pathology.* October 2017; 4(1): 16-20.
- 3) Oguntola AS, Adeoti ML, Oyemolade TA. Appendicitis: Trends in incidence, age, sex, and seasonal variations in South-Western Nigeria. *Ann Afr Med* 2010;9:213-7.
- 4) Edino ST, Mohammed AZ, Ochicha O, Anumah M. Appendicitis in Kano, Nigeria: A 5 year review of pattern, morbidity and mortality. *Ann Afr Med* 2004;3:38-41.
- 5) Khan S, Khan IU, Aslam S, Haque A. Retrospective analysis of abdominal surgeries at Nepalgunj Medical College (NGMC), Nepalgunj, Nepal: 2 year's experience. *KUMJ* 2004;2:336-43.
- 6) Makaju R, Mohammad A, Shakya A. Acute appendicitis: Analysis of 518 histopathologically diagnosed cases at the Kathmandu University Hospital, Nepal. *KUMJ* 2010;8:227-30.
- 7) Noudeh YJ, Sadigh N, Ahmadnia AY. Epidemiologic features, seasonal variations and false positive rate of acute appendicitis in Shahr-e-Rey, Tehran. *Int J Surg* 2007;5:95-8.
- 8) Nabipour F. Histopathological feature of acute appendicitis in Kerman-Iran from 1997 to 2003. *Am J Env Sci* 2005;1:130-2. 11. Zulfikar I, Khanzada TW, Sushel C, Samad A. Review of the pathologic diagnoses of appendectomy specimens. *Ann King Edward Med Univ* 2009;15:168-70.
- 9) Kumar V, Abbas AK, Aster JC. Robbins and Cotran Pathologic Basis of Disease, South Asia Edition. Reed Elsevier: New Delhi. 2015.
- 10) Zulfikar I, Khanzada TW, Sushel C, Samad A. Review of the Pathologic Diagnoses of Appendectomy Specimens Annals. *Ann King Edward Med Univ.* 2009;15:168–178.

- 11) Limaïem F, Arfa N, Marsaoui L, Bouraoui S, Lahmar A, Mzabi S. Unexpected Histopathological Findings in Appendectomy Specimens: a Retrospective Study of 1627 Cases. *Indian J Surg.* 2015;77(Suppl 3):1285-1290.
- 12) Cruz DB, Friedrisch BK, Fontanive Junior V, da Rocha VW. Eosinophilic acute appendicitis caused by *Strongyloides stercoralis* and *Enterobius vermicularis* in an HIV-positive patient. *BMJ Case Rep.* 2012;2012:bcr0120125670.
- 13) [https://www.who.int/intestinal\\_worms/epidemiology/strongyloidiasis/en/](https://www.who.int/intestinal_worms/epidemiology/strongyloidiasis/en/)
- 14) Lamps LW. Appendicitis and infections of the appendix. *Semin Diagn Pathol* 2004;21:86–97.

