

Original article

Prevalence of histologically proven acute appendicitis and incidental carcinoid tumour in the practice of surgical pathology at BPKIHS

P Upadhyaya¹, CS Agarwal², AK Karak¹, S Karki¹, A Pradhan¹, TN Subba¹

¹Departments of Pathology, ²Department of Surgery, B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

Abstract

Background: Appendicitis is the most common cause of acute abdominal pain requiring surgical intervention. **Objective:** To determine the relative prevalence of histologically proven acute appendicitis in surgically respected specimens with clinical diagnosis of acute appendicitis and also to find out the rate of occurrence of carcinoid tumour as an incidental histologic finding. **Methods:** It is a retrospective study involving all gross specimens received in the department of pathology over a period of twenty months (1.1.2006 to 31.8.2007). Histologic data on 515 appendectomy samples (clinically diagnosed as appendicitis) of the total 7295 specimens received over a period of twenty months were retrieved from the archives of department of pathology, with exclusion of appendectomy incidental to another surgical procedure. **Results:** Appendectomy specimens constituted 7.0% (n=515; M:F 1.1:1) of all surgical pathologic specimens (n=7295) at B.P.K.I.H.S. The breakups of histologic diagnoses are: acute appendicitis with or without periappendicitis and gangrenous change (93.6%, n=482), "receding appendicitis" (5.4%, n=28), and normal histology (1.0%, n= 5). Carcinoid tumours were detected incidentally in three cases (0.58%) out of all appendectomy specimens. **Conclusion:** Analysis of data revealed a prevalence of 6.99% of histologically proven acute appendicitis in this tertiary health care set up. The rate of occurrence of carcinoid tumour was 0.58%.

Keywords: appendectomy, appendicitis, appendix, Carcinoid tumor.

Introduction

Appendicitis is the most common cause of acute abdomen and can affect all age groups.¹ It is so common that a sharp onset of pain in the right lower abdomen is thought of as appendicitis even by a lay person. A clinical diagnosis is usually made by the surgeon. However, the pathologist plays an important role in confirming the diagnosis. Appendectomy is reported as one of the most frequently performed surgical procedures in the world.^{1,2} and its prevalence varies from 4.9% to 8.6%.² The pathologic

spectrum of the acutely inflamed appendix encompasses a wide range of infectious and non-infectious entities. Further, the incidental detection of a carcinoid tumour in appendectomy specimens is emphasized.

Although the peak incidence of acute appendicitis occurs in the 15–24-years age group, 5–10% of all appendicitis occurs in the elderly (i.e. those over 60 years of age) and this accounts for 5% of all acute abdominal conditions in the aged.³ The present study reviews the epidemiology, pathophysiology, the histology of cases presenting with acute appendicitis, with special reference to carcinoid tumor and the rate of negative appendectomies.

Address for correspondence

Dr. Paricha Upadhyaya

Department of pathology, BPKIHS, Dharan.

E-mail: paricha7@yahoo.com

Methods

Histologic data on all appendectomy specimens with a clinical diagnosis of acute appendicitis were retrieved from the archives of The Department of Pathology, B.P.K.I.H.S, during a period of twenty months (1.1.2006 – 31.8.2007) and analyzed retrospectively. Appendectomy done incidental to other surgical procedures were excluded.

All the appendectomy specimens were fixed in 10% formalin. Along with the histologic data clinical details and findings on gross examination were also noted.

Three sections were taken from each of the appendectomy specimen – comprising of one section from the tip, one each from proximal and mid one third. All sections were stained with haematoxylin and eosin and examined under the light microscope. Immunohistochemistry and special stains were used when required.

Data entry and analysis was done using MS Excel entry and EPI Info analysis. Chi² test was applied to test significant difference between the variables. P value less than 0.05 was considered as significant. Descriptive statistics like percentage proportion were calculated and represented diagrammatically.

Results

The total number of specimens received for histopathologic evaluation in the department of pathology over a period of twenty months was 7295, out of which 515 were appendectomy specimens which constituted 7.0% of all surgical pathologic specimens.

Out of the 515 appendectomy specimens, 294 were from males and 221 females with 1.1:1 ratio.

The highest number of patients was observed in the second to third decade that is between 11 years to 30 years of age.

Table 1: Age distribution.

Age Distribution	No of Patients
0-10	54
11-20.	147
21-30	147
31-40	73
41-50	41
>50	53
Total	515

The age ranged from 15 months to 81 years. The median age was 37 years. The mean ages of male and female patients were 30.36 and 26.98 years respectively. Ten percent (n=53) of the total cases were in the above fifty age group, out of which 3.30% (n=17) of the total patients were elderly (60 years and above) age group. The pediatric age group (upto 15 years) comprised 22.1% (n= 114) patients.

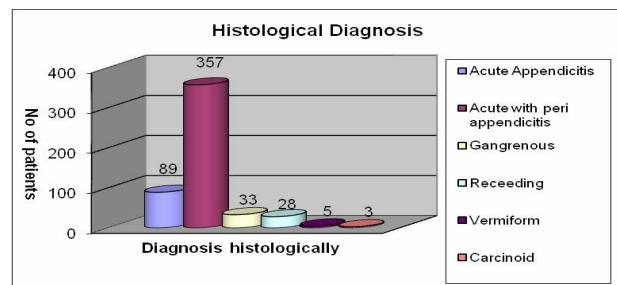


Figure 1: Histological diagnoses

Only five (5) out of the 515 appendectomy cases were cases of vermiform appendix (0.97%), the remainder 510 being appendicitis of varying severity. Therefore, the negative appendectomy rate in our hospital was around 1% (0.97%) and the average annual rate of histologically proven appendicitis was calculated to be around 6.99%.

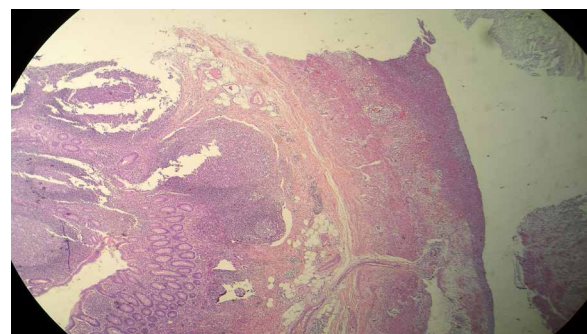


Figure 2A : Photomicrograph 1: Section from appendix shows neutrophils in the muscle layer.

Carcinoid tumors were detected incidentally in three cases (0.58%).

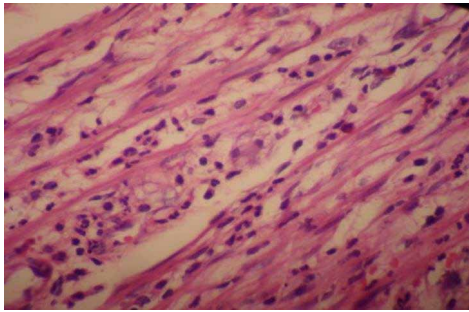


Figure 2B : Photomicrograph 2: Section from appendix shows neutrophils in the muscle and serosal layer.

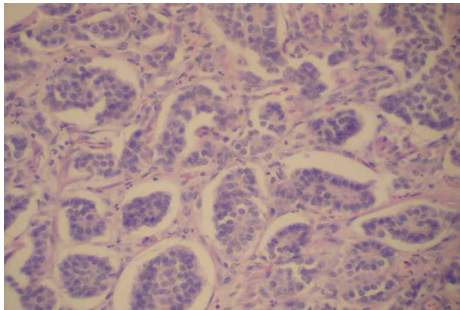


Figure 2C : Photomicrograph 3: Section from appendix shows tumor cells in nests and cords in the submucosa.

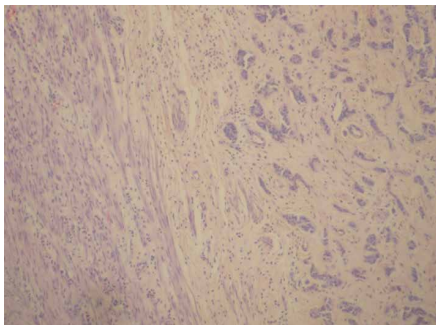


Figure 2D : Photomicrograph 4: Section examined from appendix shows uniform population of tumor cells in predominantly organoid pattern.

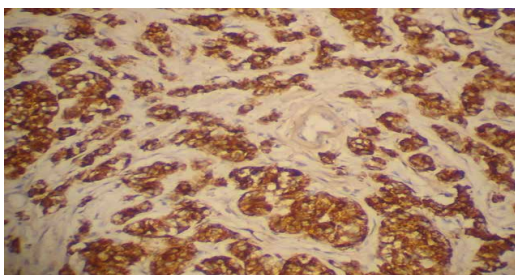


Figure 2E : Photomicrograph 5: Tumor cells

show intense cytoplasmic positivity for chromogranin.

The breakup of histologic diagnosis reveals: acute appendicitis 89 cases (17.3%), acute appendicitis with periappendicitis 357 cases (69.3%), gangrenous 33 cases (6.41%), carcinoid 3 cases (0.58%), reeeding 28 cases (5.44%) and vermiform 5 (0.97%).

Three cases of carcinoid tumour involved one female and two males, age ranging from 6 years to 38 years. In two of these specimens tumour was located in the tip while the remaining one was located in the base. The tumor was less than one cm in all specimens. Histology showed acute appendicitis with periappendicitis in two cases and gangrenous changes in one of them. The tumour was confined to the mucosa and submucosa and the resected base was free of tumour on microscopic examination.

Out of the five cases of vermiform appendix one specimen of that of a 12 year boy showed histologic features of oxyuriasis appendix.

Most of the acute appendicitis were due to non infectious obstructive cause contributed in maximum cases by the presence of fecolith (208/515), i.e. in 40% of cases. There was a single case of infectious obstructive aetiology contributed by presence of enterobius vermicularis. Tumours like carcinoid also contributed to the development of appendicitis in less than one percent (<1%) of cases.

Thirty three cases showed perforation. It showed relatively high rate of perforation in children less than ten years of age (11.1%) and in patients over 50 years (7.6%).

Table 2: Frequency of perforation in different age group

Age Group	Total no of Patients (n=515)	No of Perforation
0-10	54	6 (11.1%)
11-20	147	11 (7.5%)
21-30	147	9 (6.1%)
31-40	73	3 (4.1%)
41-50	41	0
>50	53	4 (7.6%)

When the cases were further divided into paediatric, elderly and as rest of the population, perforation peaks was identified in the paediatric and elderly age group (fig : 3).

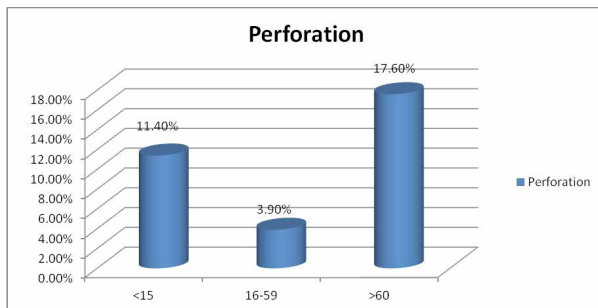


Fig 3: Perforation in paediatric, elderly and rest of the population.

When these values were compared, statistically it was observed that the perforations were significantly higher in both the paediatric ($p=0.005$) and elderly groups ($p=0.007$) as compared with rest of the population (16-60years). However, the difference in the rate of perforation between the two groups was not significant.

Demographic data

The demographic data and ethnicity of 90 patients were available. The highest number of patients had come from Sunsari (43), followed by Jhapa (18), Morang (11) Ilam (7) and Dhankutta (6). There were one patient each from Bhojpur, Saptari and Udaypur.

Most of the patients(75%) were Hindu, followed by Kirati and Buddhists. Muslim community comprised of only 1% of cases.

Most of the patients presented with pain (46.6%) followed by vomiting (19.2%) and fever (9.7%)

Discussion

Reginald Fitz, a professor of pathology first described the appendix as the source of inflammation in acute typhlitis in 1886. He coined the term appendicitis and also described the signs and symptoms of acute and perforated appendicitis and was among the first to recommend early diagnosis and operative intervention.⁴ Acute appendicitis affects all age groups. It is ranked either as the first⁵ or the

second common cause of acute abdomen in late adulthood.⁶

In the present study maximum numbers of patients were in the second to third decade and there were around 10.29% of patients in the above fifty age group.

Elderly patients who have appendicitis have a greater morbidity and mortality rate when compared with younger patients.^{3,7} It was estimated to be around 70% as compared to 1% in the general population. As compared to younger age group, elderly patients have more underlying diseases and sluggish bodily physiological reactions resulting in a higher rate of morbidity and mortality.⁸ Therefore, appendicitis in elderly patients continues to be a challenging surgical problem. In our study also the rate of perforation in appendix was 7.6% in patients over fifty years of age. This rate was second to the highest rate of 11.1% seen in the below ten age group even though the number of patients in below ten and above fifty was almost the same.

The rate of perforation in our study was highest in children below ten followed by patients in the above fifty age group. Redmond et al have also shown that the perforation rate is high in both children and elderly as in this study. However the prognosis is graver in the elderly.⁹

The perforation rate in acute appendicitis in various studies however ranged from 21% to 72%^{3,10,11,12,13}

Delay in presentation appears to be associated with risk of perforation. Some authors believe that the delay in presentation is multifactorial. Some of these elderly patients live alone and have difficulty in accessing medical care early, while others, with a higher pain threshold, would attribute the symptoms to indigestion or constipation, thus ignoring the initial symptoms until they worsen. Another major factor proposed in literature is probably the fear and anxiety associated with hospital admission in this age group.³

Considering appendicitis as one of the early

diagnostic possibilities in elderly patients with abdominal pain, followed by prompt management accordingly may improve the overall result.⁶

Contrary to the above discussion few other studies, including ours, have found that the perforation ratio is highest in younger children and then only in the elderly. Some of these studies have also shown a peak in the preschool children.^{14,15,16,17}

In our case however no such peak was observed in the preschool group and the cases were evenly distributed among all groups in children. When taken into account all patients up to fifteen years old (114 appendicectomies with 13 perforations) the perforation rate was around 11.4%, so this was also not different from patients under ten years of age, therefore still having a high perforation rate in children.

Though acute appendicitis can occur from the time of infancy to old age, the peak age of incidence is in the second and third decades of life.^{14,15,18,19,20} as also seen in our study where 294 numbers of patients were in the 2nd to 3rd decade.

History and clinical examination remains the mainstay of diagnosis in acute appendicitis. However, many surgical procedures are performed in which the appendix is subsequently found to be normal. The negative appendicectomy rate reported in the literature varies; typical figures are between 7% and 20% in men and 20% and 45% in women.¹⁴ These are high figures for a common disease.

Studies carried out around a decade back have quoted that the negative appendicectomy rate has remained largely unchanged over the last 70 years.¹⁶

In our study, however, the negative appendicectomy rate was only 1% with three males and two females. Studies done in the past show that the numbers of negative appendicectomies were larger in females than in males.^{17,18,21} The patients with negative appendicectomies, in our study, did not belong

to a particular age group and were distributed widely between 2nd to 5th decades.

The inflammation in appendicitis can vary from case to case and histology may reveal an acute appendicitis with severe periappendicitis to gangrenous changes and perforation or simply a case of receding appendicitis. Acute appendicitis with periappendicitis was the commonest histological picture in this study.

These various degrees of inflammation are said to be only due to a difference in the time of presentation i.e. patient's delay in seeking medical advice or post admission delay, and not as a result of any diagnostic dilemma,^{6,22} which stands true for our study as well as far as diagnostic dilemma is concerned as the negative appendicectomy rate in our case is very low compared to other studies. The time of presentation and delay in diagnosis, however, cannot be addressed as details pertaining to this aspect are not included in this study.

There is marked variation in the etiopathogenesis of appendicitis. Although it appears to be a result of mucosal injury, all cases of appendicitis do not show evidence of lumen obstruction by a fecolith²³.

There can therefore be a number of causes for luminal obstruction ranging from lymphoid hyperplasia due to a variety of causes, fecolith formation, foreign bodies and tumours including carcinoid, adenocarcinoma, and Burkitt's lymphoma. Luminal obstruction has been emphasized as an initiating event in the causation of acute appendicitis irrespective of the various causes. Once there is obstruction it leads to accumulation of mucosal secretion, inflammatory exudation which increases intraluminal pressure, which obstructs lymphatic drainage and thereby develops edema and mucosal ulceration, distension of appendix increases and results in venous obstruction. At the end of this process, ischemic necrosis occurs at the wall of appendix. Once there is obstruction it also causes stimulation of the visceral afferent nerve fibres and therefore

causing referred epigastric and periumbilical pain.^{4,24} Accepting these common causes and presentation, the present study also showed presence of fecolith in 40% of cases and 46% of the patients presented with pain. We would like to highlight the incidental detection of carcinoid tumour in three cases (0.58%) out of the total number of 515 appendectomy specimens.

Appendiceal tumours are uncommon and most often present as acute appendicitis.^{25,26,27} Carcinoid is reported as the most frequent tumour of appendix.^{25,27} The prevalence rate vary from 0.3 to 0.9%, 0.5 and 0.7% in appendectomy specimens.^{25,27, 28} They are found in both sexes and at any age the peak age being 30-50 years.^{27,28} Though carcinoid tumour is uncommon it can be encountered several times during the career of a surgeon (1/200-300 appendectomy).²⁹ The most common site of its occurrence in the gastrointestinal tract is in the appendix where they are single and mainly at the tip, followed by the ileum where they are frequently multiple and then the rectum.^{27, 28} Carcinoid of the appendix occurs mainly in the tip (70%), next 20% being in the mid one third and only 10% in the base.^{27, 29}

Carcinoid tumors of the appendix are usually benign. Simple appendectomy is adequate treatment for appendiceal carcinoids less than 1 cm in diameter. Tumours over 2 cm in diameter may exhibit malignant behaviour and right hemicolectomy is the choice of treatment in such cases. However, controversy exists concerning the clinical value of microscopic invasion of serosal surface, subserosal lymphatics, and/or mesoappendix for tumors smaller than 2 cm. Several authors suggested that these latter features should be considered reliable parameters of aggressive clinical behavior and, thus, recommended radical surgery (hemicolectomy) in patients having at least one of these findings. These tumours are frequently discovered incidentally during an appendectomy for acute appendicitis.^{29,30}

In our study, one case of oxyuriasis appendix

was seen in a vermiform appendix specimen. The emphasis lies that such patients should be treated with antihelminthic therapy first and an immediate surgical intervention is unwarranted.

Conclusion

Histologically proven appendicitis occurs in 6.99% of all surgical pathological specimens. The rate of occurrence of carcinoid tumour is 0.58%.

References

1. Simpson J, Samaraweera AP, Sara RK, Lobo DN. Acute appendicitis--a benign disease? *Ann R Coll Surg Engl.* 2008;90(4):313–8.
2. Shamis I, Livshits G, Feldman U. Ethnicity and familial factors in the etiology of acute appendicitis. *Am J Hum Biol.* 1994;6(3):351–8.
3. Lee JFY, Leow CK, Lau WY. Appendicitis In the elderly. *ANZ J Surg.* 2000;70(8):593–6.
4. Graffeo CS, Counselman FL. Appendicitis. *Emerg Med Clin North Am.* 1996;14(4):653–71.
5. Gurbuz AT, Muckleroy SK, Davis-Merritt D. Simultaneous acute appendicitis in monozygotic twins: coincidence or genetic? *Am Surg.* 1996;62(5):407–8.
6. Kraemer M, Franke C, Ohmann C, Yang Q. Acute appendicitis in late adulthood: incidence, presentation, and outcome. Results of a prospective multicenter acute abdominal pain study and a review of the literature. *Langenbecks Arch Surg.* 2000;385(7):470–81.
7. Hui TT, Major KM, Avital I, Hiatt JR, Margulies DR. Outcome of elderly patients with appendicitis: effect of computed tomography and laparoscopy. *Arch Surg.* 2002;137(9):995–8;999–1000.
8. Omari AH, Khammash MR, Qasaimeh GR, Shammari AK, Yaseen MKB, Hammori SK. Acute appendicitis in the elderly: risk factors for perforation. *World J Emerg Surg.* 2014;9(1):6.

9. Redmond JM, Smith GW, Wilasrusmee C, Kittur DS. A new perspective in appendicitis: calculation of half time (T(1/2)) for perforation. *Am Surg.* 2002;68(7):593–7.
10. Franz MG, Norman J, Fabri PJ. Increased morbidity of appendicitis with advancing age. *Am Surg.* 1995;61(1):40–4.
11. Lau WY, Fan ST, Yiu TF, Chu KW, Lee JM. Acute appendicitis in the elderly. *Surg Gynecol Obstet.* 1985;161(2):157–60.
12. Paaajanen H, Kettunen J, Kostianen S. Emergency appendectomies in patients over 80 years. *Am Surg.* 1994;60(12):950–3.
13. Rydén CI, Grunditz T, Janzon L. Acute appendicitis in patients above and below 60 years of age. Incidence rate and clinical course. *Acta Chir Scand.* 1983;149(2):165–70.
14. Carr NJ. The pathology of acute appendicitis. *Ann Diagn Pathol.* 2000;4(1):46–58.
15. Addiss DG, Shaffer N, Fowler BS, Tauxe R V. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol.* 1990;132(5):910–25.
16. Hale DA, Molloy M, Pearl RH, Schutt DC, Jaques DP. Appendectomy: a contemporary appraisal. *Ann Surg.* 1997;225(3):252–61.
17. Lewis FR, Holcroft JW, Boey J, Dunphy E. Appendicitis. A critical review of diagnosis and treatment in 1,000 cases. *Arch Surg.* 1975;110(5):677–84.
18. Andreou P, Blain S, Du Boulay CE. A histopathological study of the appendix at autopsy and after surgical resection. *Histopathology.* 1990;17(5):427–31.
19. Chang AR. An analysis of the pathology of 3003 appendices. *Aust N Z J Surg.* 1981;51(2):169–78.
20. Ojo OS, Udeh SC, Odesanmi WO. Review of the histopathological findings in appendices removed for acute appendicitis in Nigerians. *J R Coll Surg Edinb.* 1991;36(4):245–8.
21. Singhal V, Jadhav V. Acute appendicitis: are we over diagnosing it? *Ann R Coll Surg Engl.* 2007;89(8):766–9.
22. Pittman-Waller VA, Myers JG, Stewart RM, Dent DL, Page CP, Gray GA, et al. Appendicitis: why so complicated? Analysis of 5755 consecutive appendectomies. *Am Surg.* 2000;66(6):548–54.
23. Butler C. Surgical pathology of acute appendicitis. *Hum Pathol.* 1981;12(10):870–8.
24. Yabanoglu H, Caliskan K, Ozgur Aytac H, Turk E, Karagulle E, Kayaselcuk F, et al. Unusual findings in appendectomy specimens of adults: retrospective analyses of 1466 patients and a review of literature. *Iran Red Crescent Med J.* 2014;16(2):e12931.
25. In't Hof KH, van der Wal HC, Kazemier G, Lange JF. Carcinoid tumour of the appendix: an analysis of 1,485 consecutive emergency appendectomies. *J Gastrointest Surg.* 2008;12(8):1436–8.
26. Esmer-Sánchez DD, Martínez-Ordaz JL, Román-Zepeda P, Sánchez-Fernández P, Medina-González E. Appendiceal tumors : Clinicopathologic review of 5,307 appendectomies. *Cir Cir.* 2004; 72(5):375–8.
27. Hermans JJ, Hermans AL, Risseeuw GA, Verhaar JC, Meradji M. Appendicitis caused by carcinoid tumor. *Radiology.* 1993;188(1):71–2.
28. San-Yuan Tsai, Yi-Hong Chou, Cheng-Yi Liu, Chui-Mei Tiu, Hong-Jen Chiou, See-Ying Chiou et al. Appendicitis coexisted with an incidental carcinoid tumor. *Chin J Radiol* 2003; 28: 259-62.
29. Spallitta SI, Termine G, Stella M, Calistro V, Marozzi P. Carcinoid of the appendix : A case report. *Minerva Chir.* 2000; 55(1-2):77–87.
30. Rossi G, Valli R, Bertolini F, Sighinolfi P, Losi L, Cavazza A, et al. Does mesoappendix infiltration predict a worse prognosis in incidental neuroendocrine tumors of the appendix? A clinicopathologic and immunohistochemical study of 15 cases. *Am J Clin Pathol.* 2003;120(5): 706-11.