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RESEARCH ARTICLE

HISTOPATHOLOGY OF ROUTINE APPENDECTOMIES IS JUSTIFIABLE

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ABSTRACT

Background: A appendix removed for acute appendicitis has been sent for histopathological examination, but this practice has been the subject of controversy. This study was conducted to assess the feasibility or otherwise of performing histopathological examination in every specimen of appendix. **Methods:** we analyzed, retrospectivelyhisto pathological reports of all appendix specimens after appendectomy in last one year. **Results: -** A total of 952 appendix specimens were sent for HPE, out of which347(36.5%) showed evidence of acute suppurative appendicitis, 219(23%) showed evidence of acute appendicitis,,174(18%) showed evidence of acute transmural appendicitis,168(17.6%) showed evidence of lymphoid follicular hyperplasia,3(0.3%) showed evidence of chronic appendicitis,4(0.4%) showed evidence of benign mucinous cyst adenoma,3(0.3%) showed evidence of carcinoid tumour,32(3.3%) were unremarkable,1(0.1%) case of xanthogranolomatous appendicitis and one poorly preserved specimen. **Conclusion:** Incidental diagnosis of carcinoma appendix is not rare,if the protocol of routine histopathology of appendix specimen is not followed, subclinical malignancies would fail to be identified with disastrous results. we strongly recommend routine histopathology of all appendix specimens.

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INTRODUCTION

Appendicitis is a common acute surgical emergency with over 40,000 cases in the UK every year (http://www.hscic.gov.uk/ catalogue /PUB12566/hosp-epis-stat-admi-proc-2012-13-tab.xlsx) and the estimated life time risk of appendicitis in the USA is 8.6% and 6.7% for males and females respectively (Addiss, 1990). The diagnosis of appendicitis is largely clinical and appendectomy is the treatment of choice. Delayed diagnosis of appendicitis could lead to complications like perforated appendix, peritonitis, sepsis, increased morbidity and mortality (Hale, 1997; Zoarets, 2014). Right iliac fossa pain can be a presenting complaint of different pathologies that may mimic appendicitis especially in the female population causing diagnostic difficulties and often leads to negative appendectomies. There is variation between institutions in the practice of routine histopathological examination of appendectomy specimens. Arguments against the practice include the rarity of incidental pathologies that may impact on treatment and also the financial implications of routine histopathological assessments (Matthyssens, 2006; Jones, 2007). Histological examination of appendix specimens is routinely done in our institution hence the need to correlate the histopathological findings with the clinical diagnosis of appendicitis Primary adenocarcinoma of the appendix is a rarity after one eliminates the mucinous cystadenocarcinoma and the carcinoid tumors associated with the production of glands and mucin (adenocarcinoids) (Carr, 1995). It can be located in any part of the appendix. The symptoms resemble acute appendicitis; actually, inflammation is often found in addition to the carcinoma (Wolff, 1976). The microscopic appearance is essentially the same as that of colorectal adenocarcinoma and is indeed referred to as colonic type (McCusker, 1973; Qizilbash, 1975). Right hemicolectomy is the treatment of choice except for very superficial tumors of well-differentiated nature that can be cured by simple appendectomy (Steinberg, 1967). Dukes staging system correlates with prognosis as well, as it does in the colorectum. (Carr, 1995). Tumors of the appendix composed entirely or partially of neuroendocrine cells are divided into two distinct categories: classic carcinoid tumor (with a minor variant), and goblet cell carcinoid tumor and its variants.

Classic (insular) carcinoid tumors are found in about 1 of every 300 routine appendectomies (Moertel, 1968) and represent the most common tumor of the appendix (Modlin, 2003). The peak incidence is in the third and fourth decades of life, but they can occur in any age group, including children (Ryden, 1975) .In most of the cases they are incidental findings in the tip of obliterated appendices, but they may be found associated with acute appendicitis as a result of obstruction of the lumen. Exceptionally, they have been found to secrete ACTH and result in a clinical picture of Cushing syndrome (Johnston,

1971). Five (4.2%) of the patients with carcinoid tumor in the series reported by Moertel et al. (1968) had an associated carcinoid of the ileum, and 19 (13%) had a second primary cancer. Carcinoid syndrome secondary to appendiceal carcinoid tumor is extremely rare and is almost always related to the presence of liver metastases (Markgraf, 1964). In terms of location within the appendix, of the 144 cases of appendiceal carcinoid tumor reported by Moertel et al. (1968). 71% were located in the tip, 22% in the body, and 7% in the base; 70% of the lesions were less than 1 cm in diameter, and only two measured 2 cm or more. Grossly, the tumors are firm, grayish white, and fairly well circumscribed but not encapsulated. They acquire a characteristic yellow color after formalin fixation. When sufficiently large, those located at the tip often result in a typical 'bell clapper' configuration of the appendix. Many examples are of microscopic size, as to make one wonder whether it is correct to regard all of them as neoplasms, as opposed to nodular hyperplasias of neuroendocrine cells, analogous to the 'tumorlets' seen in bronchiectatic lungs and the islet cell hyperplasia found in chronically inflamed pancreases.

Goblet cell carcinoid: Is the other major type of appendiceal tumor traditionally. It is also called *goblet cell type adenocarcinoid*, *mucinous carcinoid tumor*, and *microglandular* carcinoma,as well as *crypt cell carcinoma*. Grossly, it may be found in any portion of the appendix and appears as an area of whitish, sometimes mucoid induration without dilation of the lumen; acute appendicitis is a common complication. Most carcinoid tumors of the appendix are asymptomatic. The average time for a carcinoid tumor to become symptomatic is 9 years (Robertson, 2006). When the tumor is located in the tip of the appendix, which it is in approximately 75% of the cases, it generally does not present with symptoms until it becomes metastatic. When the tumor is located at the base of the appendix, it can occlude the lumen and give the patient similar signs and symptoms of appendicitis (Carr, 1995). In these patients, the diagnosis of carcinoid cancer is typically made by pathology after an appendectomy has been performed. In rare cases, the patient can present with signs and symptoms related to a carcinoid syndrome. As stated before, diagnosis of carcinoid tumor of the appendix is usually made after an appendectomy. The extent of surgery is based upon the size of the tumor, but since the majority of carcinoid tumors are found incidentally on simple appendectomies, a second surgery is sometimes needed. The National Comprehensive Cancer Network (NCCN) guidelines for treatment of carcinoid tumors state that tumors <2 cm confined to the appendix can be treated with simple appendectomy with no followup required. For tumors >2 cm, or those with extra-appendigeal invasion, an appendectomy with right hemicolectomy and cytoreductive surgery is necessary. Post-operatively, a 3 month followup which includes a history and physical (H&P), CT of the abdomen, and tests for markers (5-HIAA and chromogranin A) should be completed (Wolff, 1976). For patients with metastatic disease, somatostatin analogs can be beneficial in relieving the symptoms of carcinoid syndrome. Somatostatin, an 18 amino-acid peptide, binds to somatostatin receptors to block the secretion of hormones such as growth hormones, gastrin, insulin, and glucagon. These receptors are found on over 80% of carcinoid tumors (Akbulut, 2011). Octreotide, an eight-amino-acid, long-acting somatostatin analogue, works through G-protein activation on somatostatin receptor subtypes 2, 3, and 5 (Khairy, 2009).

Octreotide was effective in decreasing symptoms in 88% of patients and decreasing the urinary 5-HIAA in 72% of patients (Moertel, 1968). In patients who do not respond to octreotide, interferon-alpha has been added with some positive results; however, as stated by Mayer, this therapy comes at a cost of side effects which may include fever, fatigue, anorexia, and weight loss. Malignant lymphoma can also involve the appendix and cases of *Burkitt lymphoma*, *large cell lymphoma*, *low-grade B-cell lymphoma* and *myeloid sarcoma* have been seen, some of them presenting with the clinical picture of appendicitis. Kaposi sarcoma involving the appendix of HIV-infected individuals and resulting in acute appendicitis has been reported. So disregarding appendix specimen without histopathological examination is best avoided. elective approach for sending these specimens to the laboratory results in missing discrete pathologies like benign mucinous cyst adenoma. This practice of disregarding appendix specimen is standard in most hospitals on the pretext that surgeon knows best which appendix is to be sent to laboratory. Histopathology is restricted to only those specimens, which show gross abnormality. At the same time, this approach is justified by claiming that it reduces patient's financial liabilities and pathologists work load. This contradicts to the worldwide practice where appendix specimen is invariably sent to histopathological examination for the sole purpose of identifying discrete carcinoma. This study was conducted to assess feasibility or otherwise of performing histopathology in every specimen of appendix. This would ensure picking of discrete carcinoma of appendix, hidden to both eyes and touch, which in turn will assist in decreasing mortality rate.

MATERIALS AND METHODS

This study was carried out in the department of pathology, Government Medical collage Srinagar over a period of one year from may 2016 to may 2017. We analyzed retrospectively, histological reports of all appendix specimens after appendectomy in last one year. Patients with evidence of carcinoma appendix, on clinical grounds and confirmed on radiology were excluded. Demographic data such as age and sex were noted.

RESULTS

Over a periodof one year 952 appendix specimens were subjected to histopathological examination.

There were 558 males and394 females with a male to female ratio of 1.4:1.

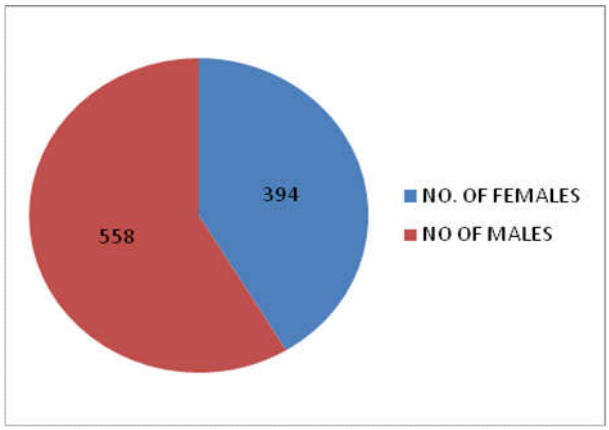


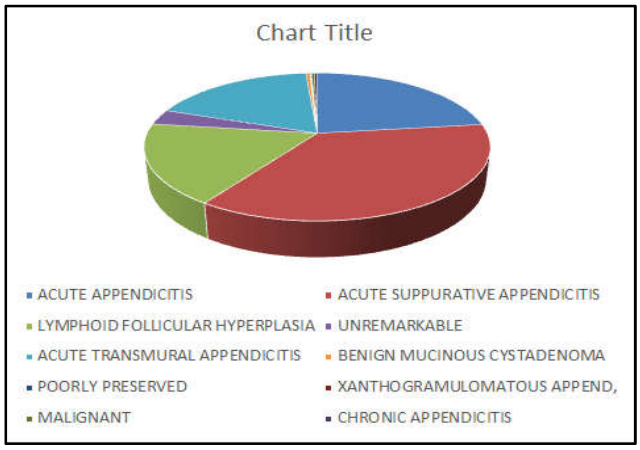
Fig. 1. Showimg sex distribution

The age of patients ranged from 1 year to >70 years.

Table 1. Showing age distribution

Age in yrs	number
1 TO 9	92
10 TO 19	288
20 TO 29	212
30 TO 39	154
40 TO 49	106
50 TO 59	49
60 TO 69	34
70 AND ABOVE	17
Total	952

Diagnosis	Percentage
Acute appendicitis	23.0042%
Acute suppurative appendicitis	36.4496%
Lymphoid follicular hyperplasia	17.6471%
Unremarkable	3.3613%
Acute transmural appendicitis	18.2773%
Benign mucinous cystadenoma	0.4202%
Poorly preserved	0.1050%
Xanthogramulomatous append,	0.1050%
Malignant	0.3151%
Chronic appendicitis	0.3151%



From the total of 952 specimens, acute suppurative appendicitis cases were 347 (36.44%), acute appendicitis were 219 (23.00%), acute transmural were 174(18.27%), acute lymphoidfollicular hyperplasia were 168 (17.68%), unremarkable were 32 (3.36%), benign mucinous cystadenoma were 4 (0.42%), malignant were 3(0.31%), chronic appendicitis were 3(0.31%),xanthogranolomatous was 1(0.10%) and poorly preserved was 1(0.10%).

Acute appendicitis and other acute conditions of appendix

AGE GROUP	MALE	FEMALE
1 TO 9	65	25
10 TO 19	155	124
20 TO 29	107	91
30 TO 39	87	61
40 TO 49	63	36
50 TO 59	28	18
60 TO 69	24	8
70 TO 79	10	4
>=80	2	0
TOTAL	541	367

Acute appendicitis and other acute conditions of appendix

MALE	FEMALE
22.2222%	24.6753%

DISCUSSION

Acute appendicitis is one of most frequent indicators of acute abdominal surgical intervention, and appendectomy is one of the most common surgical procedures performed worldwide(18).The incidence of acute appendicitis roughly parallels that of lymphoid development, with peak incidence occurring between the ages of 10 and 30 years. Although there is sex ratio equality in acute appendicitis cases occurring before puberty, the frequency in males begins to increase gradually at puberty; by the age of 15 to 25 years old, the sex ratio has shifted to 2:1 in favor of men. This bias decreases with age, and the related incidence again *becomes equal. The lifetime incidence of acute appendicitis* is estimated to be 7.0% overall, with 8.6% for men and 6.7% for women; however, the lifetime incidence of appendectomy is much lower for males than for females (12% versus 23%, respectively) (Khairy, 2009; Seetahal et al., 2011). The diagnosis of acute appendicitis relies on an evaluation of the patient's history, laboratory and radiologic findings, as well as the surgeon's subjective judgment based on experience. However, the reported rates of histology-proven negative cases following appendectomy have ranged between 9.2% and 35.0% (Khairy, 2009; Seetahal et al., 2011). Intriguingly, the rates of negative cases are particularly high for women during child-bearing years (Qizilbash, 1975). Development of luminal obstruction, regardless of etiology, has been proposed as the most significant factor in the etiopathogenesis of acute appendicitis. While the most commonly encountered underlying condition of acute appendicitis in the first two decades of life is lymphoid hyperplasia, in elderly patients it is fecal obstruction. In the current study, apart from these common factors, several unusual factors were also determined as the causes of clinical symptoms of acute appendicitis as well as the symptoms that mimicked the condition.

Carcinoid tumor, which is considered to be the most common type of appendiceal primary malignant lesion and accounts for ~60% of all appendiceal tumors, is found in 0.3% to 2.3% of patients undergoing an appendectomy. It is rare for carcinoids to be diagnosed preoperatively, and they are usually found incidentally during appendectomy (Shapiro, 2011; In't Hof, 2008). In 70% to 95% of cases, the carcinoid tumors are <1 cm and are located at the tip of the appendix (Carr, 1995). The majority of appendiceal carcinoids are benign, and metastases are rare. A near zero rate of calculated risk of metastasis from tumors <1 cm allows for management by simple appendectomy. However, increased tumor size (≥2 cm) is associated with a remarkably increased (up to 85%) risk of metastasis. Therefore, appendiceal carcinoid tumor >2 cm is usually managed by formal right hemicolectomy (Shapiro et al., 2011; In't Hof, 2008). The incidence of appendiceal carcinoid in the patient series presented herein (0.3%) was similar to that of other published studies in the collective literature. Although in majority of cases acute appendicitis is caused by fecoliths and lymphoid hyperplasia but some unusual findings observed in appendectomy specimen operated for acute appendicitis like parasitic, chronic inflammatory conditions, benign and malignant tumors which if not diagnosed and treated at right time can create lot of problems to the patient. So we emphasize and strongly recommend that all appendectomy specimens removed for acute appendicitis must be examined his to pathologically regardless whether the specimen are normal macroscopically.

CHRONIC APPENDICITIS

AGE GROUP	MALE	FEMALE
1 TO 9	0	0
10 TO 19	0	1
20 TO 29	0	1
30 TO 39	0	0
40 TO 49	0	0
50 TO 59	1	0
60 TO 69	0	0
70 TO 79	0	0
>= 80	0	0
TOTAL	1	2

CHRONIC APPENDICITIS	
MALE	FEMALE
0.1792%	0.5076%

TOTAL	0.3151%

3

BENIGN

AGE GROUP	MALE	FEMALE
1 TO 9	0	0
10 TO 19	0	0
20 TO 29	0	1
30 TO 39	0	1
40 TO 49	1	0
50 TO 59	0	0
60 TO 69	0	0
70 TO 79	1	0
>= 80	0	0
TOTAL	2	2

BENIGN	
MALE	FEMALE
0.3584%	0.5076%

TOTAL	0.4202%

4

MALIGINANT

AGE GROUP	MALE	FEMALE
1 TO 9	0	0
10 TO 19	0	0
20 TO 29	0	1
30 TO 39	1	0
40 TO 49	0	0
50 TO 59	0	1
60 TO 69	0	0
70 TO 79	0	0
> =80	0	0
TOTAL	1	2

MALIGINANT	
MALE	**FEMALE**
0.1792%	0.5076%

TOTAL	0.3151%

3

UNREMARKABLE

AGE GROUP	MALE	FEMALE
1 TO 9	2	0
10 TO 19	2	6
20 TO 29	4	5
30 TO 39	1	3
40 TO 49	3	3
50 TO 59	0	1
60 TO 69	1	1
70 TO 79	0	0
>= 80	0	0
TOTAL	13	19

UNREMARKABLE	
MALE	**FEMALE**
2.3297%	4.8223%

TOTAL	3.3613%

32

XANTHOGRANLOMATOUS APPENDICITIS	27/F	1

XANTHOGRANLOMATOUS APPENDICITIS	
MALE	**FEMALE**
0.0000%	0.2538%

TOTAL	0.1050%

POORLY PRESERVED				1

TOTAL	0.1050%

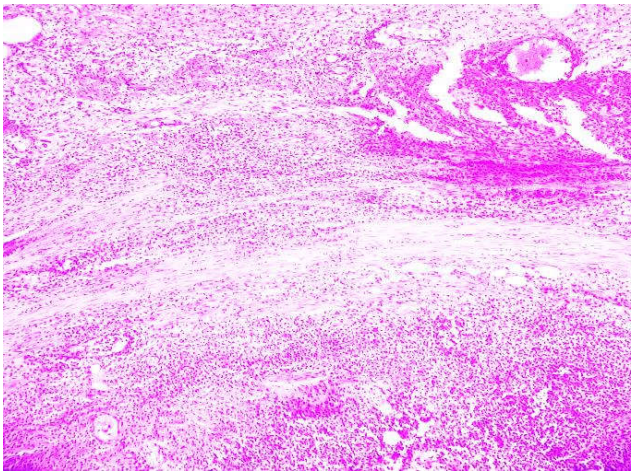


Fig 2. Showing acute suppurative appendicitis

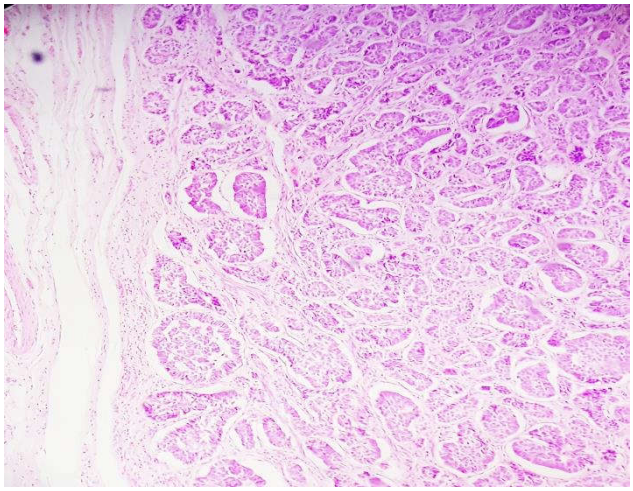


Fig 3 showing carcinoid tumor

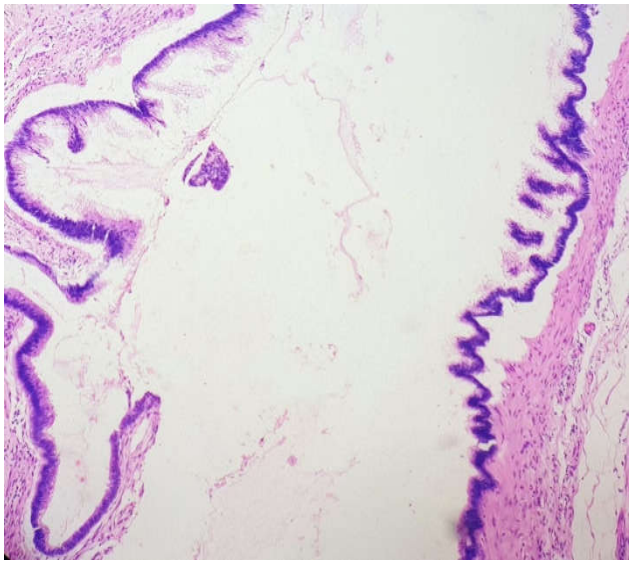


Fig 4. Showing mucinouscystadenoma

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