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Cross-sectional Study

Histopathological examination of cases with acute appendicitis, A retrospective study at King Abdulaziz University Hospital, Jeddah, Saudi Arabia

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ABSTRACT

Introduction: Appendicitis is one of the most prevalent abdominal emergencies globally. Despite the fact that acute appendicitis is a clinical diagnosis, preoperative imaging investigations are often conducted. Other disorders that might mimic acute appendicitis can occur in the appendix. The aim of this paper is to describe the histopathological findings of all appendectomy specimens.

Methods: A retrospective study of 940 cases of appendectomy that were performed between 2010 and 2017 at King Abdulaziz University Hospital, Jeddah, Saudi Arabia were reviewed. The main outcome measured in this study is to describe the histopathological findings of all appendectomy specimens. The secondary outcomes measured in this study were the disease incidence in relation to age, and gender. Moreover, the accuracy of imaging diagnostic tools were also evaluated.

Results: This study included 940 participants who underwent an appendectomy procedure. The patients' mean age was 23.4 years (±12.2), with a 3:2 male to female proportion. The incidence in males and females were 59.4% and 40.6%, respectively. Being male ($p < 0.001$), undergoing preoperative ultrasound ($p < 0.001$), having elevated white blood cells count ($p < 0.001$) was significantly associated with accurate diagnosis of acute appendicitis confirmed by histopathology. In this study, the negative cases of appendectomy that account for 14.4% were reported primarily as normal appendix with no inflammatory changes (7.44%) followed by other unexpected findings in the appendectomy specimen (3.93%) that included faecolith, granulomas, mucocele, endometriosis, food/fecal impaction, and schistosomiasis. Our study showed CT sensitivity as a diagnostic tool of acute appendicitis is 90.2%, and its accuracy is 89.4%, while US sensitivity is 46% and its accuracy is 52.4%.

Conclusion: Histopathological evaluation after common procedures, such as appendectomy, is essential to avoid missing other pathologies in the appendix. Surgeons should be aware of the uncommon histopathology findings as some disorders call for additional management beyond appendectomy. The clinical details, radiological investigations including CT scan and histopathological diagnoses are required for better management in cases of appendicular lesions.

1. Introduction

One of the most frequent abdominal emergencies globally is acute appendicitis [1]. It is less frequent at both extremes of age, but more common in the twenties and thirties [2] with a 6.7% lifetime risk in women and 8.6% in men [3].

Adoption of a low-fiber diet in developing nations has resulted in a rise in the incidence of acute appendicitis [4]. It is characterized by an

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inflammation of the vermiform inner layer of the appendix [5]. The most prevalent pathophysiological mechanisms of acute appendicitis are lymphoid hyperplasia and fecolith. Other conditions have shared a similar clinical presentation of acute appendicitis, such as endometriosis, infectious diseases, granulomatous diseases, neurofibroma, diverticulitis, and appendiceal malignancies [6–8].

The ability of clinical evaluation to accurately diagnose appendicitis is limited [9]. As a result, several imaging modalities such as magnetic resonance imaging (MRI), ultrasonography (US), and computed tomography (CT) are commonly employed to further investigate individuals suspected of having acute appendicitis [9]. The incidence of negative appendectomy has been reduced with the use of preoperative CT scan, especially in women, where it is frequently misdiagnosed as other gynecological emergency disorders [10].

Histopathological examination of appendectomy specimens provides the definitive diagnosis for all resected specimens [11]. The pathology report is crucial not just in situations of acute appendicitis, but also in cases with unexpected findings [12]. Our aims are three folds. First, is to describe the histopathological findings of all appendectomy specimens. And second, is to estimate the disease incidence in relation to age, and gender. Third, the accuracy of imaging tools (CT scan and US) in the preoperative diagnosis of appendicitis will be evaluated.

2. Methods

The STROCSS requirements were followed when reporting our paper [13].

2.1. Registration

The study was registered at ClinicalTrials.gov with a unique identifying number (NCT05391269) [14].

2.2. Patient and public involvement in research

Not involved.

2.3. Study design and settings

A retrospective cohort review was conducted in which 940 appendectomy were analyzed over a period of 8 years (2010–2017) at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. All patient electronic files underwent appendectomy were retrieved using the codes of “open appendectomy”, “laparoscopic appendectomy” and “other appendectomy".

2.4. Data collection

For each patient, we obtained demographics data, findings of preoperative imaging, the surgical approach and the histopathological reports of all resected specimens.

2.5. Histopathological examination

All specimens were submitted for routine histopathological evaluation. The fixation of the samples was done in 10% buffered formalin and the standard protocols were followed for tissue processing and paraffin embedding. Sections with 3-μm thickness were cut and stained with hematoxylin and eosin stain. The use of special stains, such as periodic acid Schiff and Ziehl Neelsen, was done wherever necessary.

2.6. Outcomes

Our primary outcome is to describe the histopathological findings of all appendectomy specimens. Our secondary outcomes are to estimate the disease incidence in relation to age, and gender as well as to evaluate the accuracy of imaging tools (CT scan and US) in the preoperative diagnosis of appendicitis.

2.7. Statistical analysis

Descriptive statistics were applied using counts, proportions (%) for categorical variables, mean, and standard deviation for continuous variables. For comparisons, the Mann Whitney *U* test and Chi-square test for non-parametric variables were performed. Data deviates from the normal distribution using the Shapiro-Wilk test ($p < 0.05$). To demonstrate statistical significance, a p-value of 0.05 (two-sided) was utilized. All data analyses were conducted with the aid of the statistical package for social sciences, version 21. (SPSS, Chicago, IL, USA).

3. Results

3.1. Descriptive analysis

A total of 940 patients who underwent appendectomy were enrolled in this study. Demographic data for the patients are shown in Table 1. The patients' mean age was 23.4 years (±12.2), with a 3:2 male to female proportion. The percentage of patients who had US was 30.9%, and 41.3% of them had acute appendicitis. The percentage of patients who got CT scans, on the other hand, was 29%, with an acute appendicitis detection rate of up to 85.7% (Table 2).

The majority of appendectomies were performed laparoscopically 71.4%. Of all the appendectomy specimens, 85.6% were consistent with acute appendicitis. The mean white blood cell count preoperatively was 13.5×10^9 per L (±5.28).

3.2. Histopathological findings

The histopathological findings of the appendectomy specimens of our cohort are demonstrated in Fig. 1. Our data showed that most of the positive appendicitis cases 85.6% were reported as acute suppurative

Table 1
Baseline characteristics of patients who underwent appendectomy from 2010 to 2017, King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia (n = 940).

Study variables	N (%)
Age, years (mean ± SD)	23.4 ± 12.2
Gender	
● Male	558 (59.4%)
● Female	382 (40.6%)
Ultrasound	
● Yes	288 (30.9%)
● No	652 (69.4%)
Ultrasound findings (n = 288)[a]	
● The appendix is not visualized	103 (35.8%)
● Acute appendicitis	119 (41.3%)
● Others	24 (08.3%)
● No appendicitis	42 (14.6%)
CT Scan (n = 940)	
● Yes	273 (29.0%)
● No	667 (71.0%)
CT scan findings (n = 273)[a]	
● No evidence of appendicitis	14 (5.1%)
● Acute appendicitis	234 (85.7%)
● Other	25 (9.2%)
Approach	
● Laparoscopic appendectomy	671 (71.4%)
● Open appendectomy	269 (28.6%)
Histopathology Results	
● Acute appendicitis	805 (85.6%)
● Negative appendicitis	135 (14.4%)
White blood cells, 10^9 per L (mean ± SD)	13.5 ± 5.28

[a] The number of patients who received diagnostic imaging differs from the total number included in the analysis.

Table 2
Relationship between acute appendicitis and baseline characteristics of the patients (n = 940).

Variable	Acute Appendicitis		P-value
	Positive N (%) (n = 805)	Negative N (%) (n = 135)	
Gender			
● Male	506 (62.9%)	52 (38.5%)	< **0.001**
● Female	299 (37.1%)	83 (61.5%)	
Ultrasound			
● Yes	227 (28.2%)	61 (45.2%)	< **0.00**
● No	578 (71.8%)	74 (54.8%)	
CT Scan			
● Yes	238 (29.6%)	35 (25.9%)	0.389
● No	567 (70.4%)	100 (74.1%)	
Approach			
● Laparoscopic appendectomy	574 (71.3%)	97 (71.9%)	< **0.001**
● Open appendectomy	231 (28.7%)	38 (28.1%)	
Age, years mean ± SD	23.2 ± 12.4	24.2 ± 10.9	0.119
White blood cells 10^9 per L mean ± SD	13.9 ± 5.11	10.5 ± 5.29	< **0.001**

appendicitis in the final histopathology report 62%, followed by perforated appendicitis 16.2% and acute hemorrhagic appendicitis 0.53%. In this cohort, the normal appendectomy rate was 14.4%. Other unexpected findings in the appendectomy specimen 3.93% included fecolith, granulomas, mucocele, endometriosis, food/fecal impaction, and schistosomiasis.

The Chi-square test was used to determine the relationship between the diagnosis of acute appendicitis and the baseline characteristics of the patients, as shown in Table 3. Being male ($p < 0.001$), undergoing preoperative ultrasound ($p < 0.001$), having elevated white blood cells count ($p < 0.001$) was significantly associated with accurate diagnosis of acute appendicitis confirmed by histopathology.

3.3. Imaging modalities' sensitivity and accuracy in detecting acute appendicitis

In our study, 288 patients received ultrasound and 273 had CT scan before having an appendectomy. CT sensitivity as a technique to diagnose acute appendicitis is 90.2%, and its accuracy is 89.4%, while the US sensitivity is 46% and its accuracy is 52.4% (Table 3).

4. Discussion

Acute appendicitis is by far the most prevalent surgical emergency for several decades [6]. Although doctors regard this as a simple diagnosis, a significant proportion of misdiagnosis frequently results in a negative appendectomy [15]. As a result, it continues to be a clinical entity and a diagnostic dilemma [16].

The incidence of appendicitis is more common in men than females [17–20]. In the current study, the incidence in males and females was 59.4% and 40.6%, respectively.

Table 3
Histopathological findings of patients who received radiographic diagnostic imaging.

US (N = 288)	Appendicitis positive histopathology (n = 230)	Appendicitis negative histopathology (n = 58)
+ve appendicitis (n = 119)	106	13
-ve appendicitis (n = 169)	124	45
CT (N = 273)	**Appendicitis positive histopathology (n = 255)**	**Appendicitis negative histopathology (n = 18)**
+ ve appendicitis (n = 234)	230	4
-ve appendicitis (n = 39)	25	14

CT: Computed tomography
US: Ultrasonography

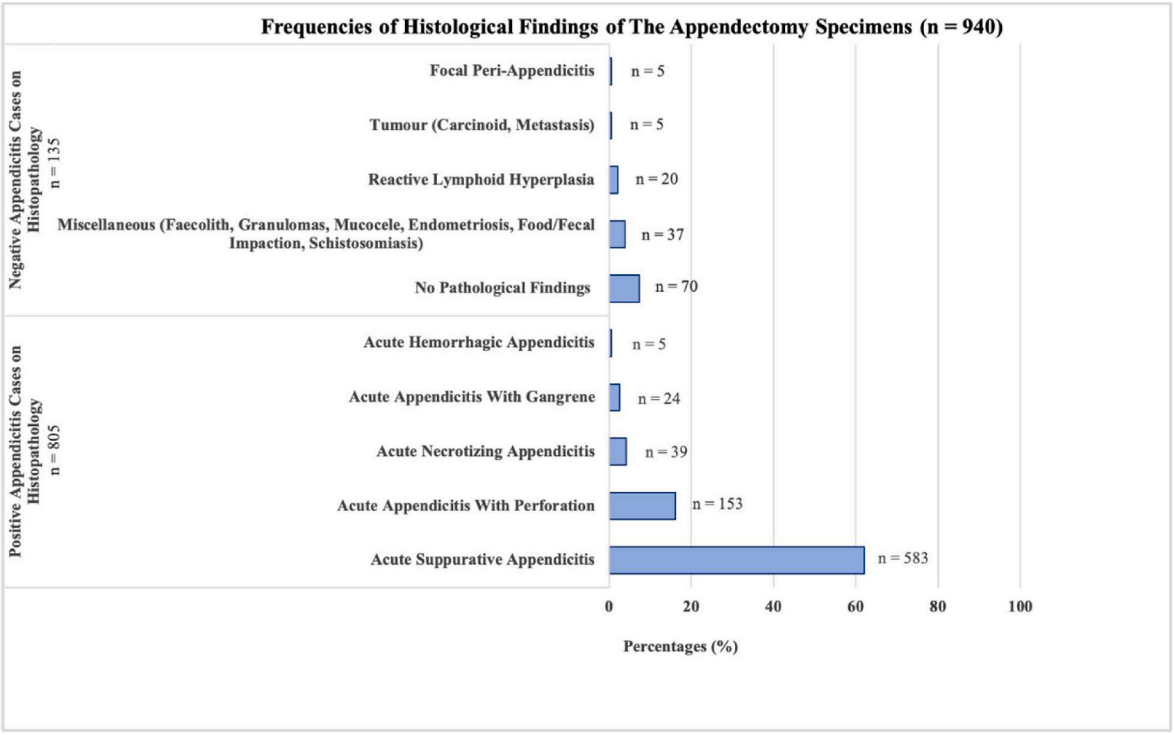

Fig. 1. Frequencies of histological findings of the appendectomy specimens (n = 940).

Our study emphasizes the need of doing basic laboratory tests and using imaging modalities to diagnose acute appendicitis. An elevated total leukocyte count with a left shift has been linked to the diagnosis of acute appendicitis [21,22]. Leukocytosis was found in both positive and negative appendicitis patients in our population. However, positive acute appendicitis patients had a considerably higher mean leukocytic count.

In the previous literature, CT scan showed specificity ranges from 89% to 98%, sensitivity ranges of 96%–97%, with a negative predicted value of 95%–98.8%, a positive predicted value of 90%–96% and accuracy of 94%–97.6% [23,24] and these estimated diagnostic values are concordant with our study. In contrast, the previous studies showed that ultrasonography has a specificity of 91%–97%, sensitivity of 74.2%–76%, negative predicted value of 76%–93%, positive predicted value of 88%–95% and accuracy of 83%–92% [23,25] and these values are non-concordant with our findings, which is likely to be related to the US limitations and the fact that it is operator dependent.

It has been noted that even when acute appendicitis was not proven by histopathology, patients' symptoms typically improve after surgery [26]. In this case, the underlying reason could be an early subclinical appendicitis at the microcellular level. As a result, macroscopic examination cannot provide an appropriate diagnosis of appendiceal inflammation, highlighting the importance of histological investigation [27].

The majority of patients in our analysis had an appendicitis histological diagnosis verified, 85.6%, and the remaining 14.4% were negative for appendicitis. This finding was consistent with many studies [28–30]. The negative appendectomy rate in our population was 14.4%, which is higher than in the literature, where it is reported to be around 6%. This could be attributed to the less frequent use of diagnostic imaging modalities at our institute [5,31,32].

Delays in identifying appendicitis can result in consequences including perforation, gangrene, and septic shock. The incidence of perforation in appendicitis was noted to be 12.6% in our study, as shown in (Fig. 1). Korner H. et al. [33] observed that perforated appendicitis occurred in 12%, with higher rates in children and the elderly, regardless of gender [33]. Gofrit O. et al. reported that the incidence of perforation in appendicitis was 8.7% [34]. The rate of gangrenous appendicitis was 2.55% in our study. A study by Kulkarni M. et al. [35] and Nabipour [36] reported the incidence of gangrenous appendicitis are 1.53% and 8% of all cases of appendicitis, respectively.

Previous studies have shown that most positive appendicitis cases were reported as acute suppurative appendicitis, gangrenous appendicitis, and perforated appendicitis, confirmed by the final histopathology [5,31,32]. These findings are consistent with our data which showed that most of the positive appendicitis cases 85.6% were reported as acute suppurative appendicitis in the final histopathology report 62%, followed by perforated appendicitis 16.2% and the lowest percentage for the acute hemorrhagic appendicitis 0.53%.

In contrast the negative appendicitis has a wide range of unusual histopathological findings including carcinoid tumor, mucocele, mucinous neoplasms, adenocarcinoma, tuberculosis, actinomycosis, *Enterobius vermicularis* parasite infection, granulomatous inflammation, appendiceal endometriosis, eosinophilic infiltration, and appendicular diverticulitis [5,31,32]. In our study, negative appendicitis, which represents 14.4% of cases were reported mainly as normal appendix with no inflammatory changes 7.44%, followed by other miscellaneous (faecolith, granulomas, mucocele, endometriosis, food/stool impaction, schistosomiasis), which represented 3.93% of the negative appendicitis cases.

Numerous studies have found that females experience more negative appendectomies than males [6,16,18,35–40]. Seetahal et al. [41] reported that 11.83% of 475,651 appendectomy cases were negative appendectomies, with women accounting for 71.6% of negative appendectomies. Gynecological disorders affecting the ovary are the most frequently mistaken for appendicitis [41]. This is consistent with the observations of this study, in which women represented about 61.5% of the negative appendectomies. This observation might be due to gynecological illnesses that resemble the clinical appearance of acute appendicitis. Benign and malignant ovarian neoplasms, ovarian cysts, leiomyomas, endometriosis and pelvic adhesions have purportedly been misinterpreted in women as acute appendicitis [41].

It is obvious from the preceding discussion that sending all appendectomy specimens for histological evaluation is both obligatory and beneficial. When the expense of the operation is weighed against the potential advantages, it is discovered that the benefit much surpasses the cost in this instance. Early detection and management of an appendicular lesion might save the patient from incurring further fees if the disease progresses to other organs.

4.1. Strength and limitations

Our main strengths of this study were the large number of patients included in the study. Moreover, this topic is understudied in our geographical region (Gulf countries).

Our major limitation of this study was that it is done in single tertiary center. As the study is in a retrospective design, the possibility of unintentional patient selection bias cannot be excluded. Hence, results should be interpreted with caution.

5. Conclusion

Routine review of all histopathological specimen after appendectomy is essential to avoid missing uncommon pathology in the appendix. Surgeons should be aware of the uncommon histopathology findings as some disorders call for additional management beyond appendectomy. The clinical details, radiological investigations including CT scan and histopathological diagnoses are required for better management in cases of appendicular lesions.

Ethical approval

The Research Committee at the Unit of Biomedical Ethics at King Abdulaziz University hospital (HA-02-J-008) approved this study with reference number (250-22).

Sources of funding

No funding was obtained for this study.

Author contribution

Conception and design of the study, Mai Kadi, Abdulaziz Saleem; Data acquisition, Rothana Alnahari, Afnan Alhawi, Romaysaa Alyamani; Analysis and interpretation of the data, Mai Kadi; Drafting of the manuscript, Mai Kadi, Ali Nasr, Alaa Shabkah, Abdulaziz Saleem.

Trail registry number

1. Name of the registry: ClinicalTrials.gov.
2. Unique Identifying number or registration ID: NCT05391269.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.clinicaltrials.gov/ct2/show/NCT05391269?term=NCT05391269&draw=2&rank=1.

Guarantor

The Guarantor are Mai Kadi and Abdulaziz Saleem.

Consent

The need for informed consent from all patients included in this study was waived because of the retrospective design. The Research

Committee at the Unit of Biomedical Ethics at King Abdulaziz University hospital (HA-02-J-008) approved this study with reference number (250-22).

Provenance and peer review

Not commissioned, externally peer reviewed.

Declaration of competing interest

The authors declare that there are no conflicts of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104401.

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