



The Negative Appendectomy Rate in Different Age Groups Compared with Preoperative Investigations.

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Abstract: Introduction: Despite being one of the commonest emergency surgical procedure, about 20% of appendectomies performed world wide yields histologically normal appendix. This study compares the normal appendectomy rate (NAR) in different age groups compared with preoperative investigations aiming to reduce NAR. **Method:** This study included 458 patients who underwent appendectomies at Ain Shams University Hospitals in Cairo and Queen Elizabeth Hospital – King’s Lynn, UK. All of them had emergency appendectomy between 01/06/2016-30/06/2018. The results were divided into three groups: Appendicitis, normal appendix, or other findings. Laboratory and radiological findings including white cell count (WCC), C-reactive protein (CRP) level, abdominal ultrasound (USS) and computed tomography (CT) scan results were collected and compared with histological findings. **Results:** We had 458 appendectomies performed. The rates of inflamed, normal, and other findings were 69.2%, 16.4%, and 14.4% respectively. 96.2% of patients with appendicitis had raised WCC or CRP. Appendicitis was histological confirmed in 96.4% of patients with radiologically diagnosed appendicitis (97% and 93% for CT and USS respectively). Women of childbearing age had (30.6%) NAR compared to (9%) in men. **Conclusion:** Women in childbearing age have the highest NAR. Normal inflammatory markers and radiology support a more conservative approach in this group to reduce the overall NAR. Low-dose or reduced-range CT scans might be considered in this group.

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1. Introduction:

Despite being one of the commonest surgical emergencies, acute appendicitis remains a challenging diagnosis to make with one in every five appendectomy specimens shows normal appendix. Challenges to face the surgical team is the ability to diagnose appendicitis in early stages before complications as perforation or peritonitis occur while trying to prevent unnecessary operations for patients with a normal appendix.

Other conditions that can present with same symptoms as appendicitis include ovarian cysts, mid-cyclic symptoms in females, urinary tract pathology and non-specific abdominal pain. Most of these conditions are common in females within the childbearing age group.

In this study, we looked at the histological results of all appendectomies performed over 2 years at our department to assess and compare the normal appendectomy rate within different age groups and to correlate the results of the preoperative investigation with histological findings aiming to achieve a lower rate of normal appendectomy.

2. Patients and Method:

All 458 patients who underwent emergency appendectomy for clinically suspected acute appendicitis at Ain Shams University Hospitals in Cairo and Queen Elizabeth Hospital – King’s Lynn, UK during the period between June 2016 and July 2018 were included in this study. Patients who had appendectomy as part of other procedures were excluded. Histology reports were examined to identify the final diagnosis of acute appendicitis, removal of a normal appendix or other incidental findings. Lymphoid hyperplasia, faecolith, Fibrous obliteration of the appendix, Enterobius infestation and healing inflammation of the appendix in absence of histological features of acute appendicitis were considered as incidental findings. Preoperative laboratory and radiological results including the white cell count (WCC), C-reactive protein (CRP) level, abdominal and pelvic sonography and computed tomography scan (CT) results were collected and compared with histological findings. The results were analysed and compared in relation to patients’ gender and age. The results of female patients in the childbearing period (16-40 years old) were analysed separately.

3. Results:

There was a total of 458(260 females, 56.8%) patients, a median age of 25 (3-85 years) who had appendectomy during the study period and were all included in this study. This included 121 (26.4%) female patients in the childbearing age group (16-40 years old).

Histological findings

In 317 patients (69.2%), the postoperative histology confirmed acute appendicitis including 58 (12.6%) patients with a gangrenous or perforated appendix. Abimodal distribution of the percentage of a gangrenous appendix in relation to patients' age groups was found. Patients younger than 10 or older than 40 years old had a higher incidence of complicated appendicitis (figure 1). The rate of gangrenous appendicitis in the women in the childbearing period was 2.5% only. There were 66 (14.4%) cases with abnormal histological findings in the appendix but without evidence of acute inflammation. The normal appendectomy rate (NAR) was 16.4% (75 patients). The distribution of histological findings according to different patients' groups is summarised in Table 1.

Amongst the 66 patients with incidental abnormal findings of the appendix, there were 7 cases of appendicular neoplasms including 4 neuroendocrine tumours and 3 Low-grade appendiceal mucinous neoplasms (LAMN). One patient had a benign sessile polyp. Other incidental findings included appendicular faecolith without acute appendicitis, fibrous obliteration of appendicular tip, Enterobius vermicularis, healing inflammation of the appendix, appendicular lymphoid hyperplasia, torsion of appendiceal epiploicae, peri-appendiceal inflammation, and luminal pus without inflammation of appendix (table 2: abnormal findings).

Radiological findings

A preoperative CT scan of the abdomen and pelvis was performed in 108 (23.6%) patients, 93 (86.9%) of them were 40 years old or above. In 100 patients, the CT scans reported acute appendicitis and were histologically confirmed in 97 (97%) out of them. In the remaining 3 patients, 2 had abnormal findings and one patient had a normal appendix. There were 8 patients who underwent surgery despite normal findings on their preoperative CT scans. The histological examination of the appendix in these 8 patients showed acute appendicitis, abnormal findings (faecolith, and fibrous obliteration of tip) and 2 normal appendixes.

Abdominal and pelvic sonography was performed in 104 cases, 89 of them were females (85.6%). Scans showing normal appendix or could not

visualize the appendix were considered as a negative. Sonographic diagnosis of appendicitis was reported in 14 out of the 104 patients and this was histologically confirmed in 13 (93%) of them. Out of the 90 cases who had no abnormality diagnosed by the ultrasound scan, 35 (39%) patients had normal histology, 34 (38%) patients had features of acute appendicitis and 21 (23%) patients had other abnormal findings on their histology report. (Table 3: Radiological findings).

Inflammatory markers

Among the 317 patients with histological acute appendicitis, 305 (96.2%) patients had abnormal inflammatory markers (WCC <4 or $>10 \times 10^3/\mu\text{L}$ or CRP more than 10 mg/L) (Table 4) with a median WCC of $12.9 \times 10^3/\mu\text{L}$ (range: $2.8-33 \times 10^3/\mu\text{L}$) (Figure 2), and a median CRP of 49 mg/L (range: 4-483 mg/L) (Figure 3). In the 141 patients without acute appendicitis on histology, the inflammatory markers were normal in 72 (51.1%) patients. The median WCC was $7.9 \times 10^3/\mu\text{L}$ (range: $2.5-25.6 \times 10^3/\mu\text{L}$) (figure 2), and CRP median was 4mg/L (range: 4-286 mg/L) (Figure 3). All 58 patients with gangrenous perforated appendix showed abnormal preoperative inflammatory markers. Just above 81% of patients with abnormal preoperative inflammatory markers had inflamed appendix on histology, while 85% of those with normal preoperative markers of inflammation had a non-inflamed appendix.

Females in the childbearing age (16-40 years old) group

There was a 121-female patient in the age group between 16-40 years old. 65 (53.7%) of them had acute appendicitis while 37(30.6%) patients had a normal appendix and 19 (15.7%) patients had other abnormal findings without inflammation (table 1). Preoperative CT scan was performed in 3 patients and showed acute appendicitis in all of them, this diagnosis was also confirmed on histology. USS was performed in 56 patients, 9 of them were diagnosed as acute appendicitis by USS and this was confirmed on histology in 8 of them. There was 20 histological diagnosis of acute appendicitis among the 47 normal USS. Abnormal preoperative WCC or CRP levels were present in 60 (92%) out of the 65 patients with histological appendicitis, while 26 (46.5%) patients among the 56 with non-inflamed appendix had normal preoperative WCC and CRP levels.

Statistical analysis:

Baseline characteristics and results were calculated and compared with the use of the chi-square test for categorical variables and the Wilcoxon test and Student's t-test for continuous variables. Significance was predetermined at $p = 0.05$.

Table 1: The histological findings in different age groups presented as numbers (percentage).

	MALES	FEMALES (16-40 YEARS)	FEMALES (<16 & >40 YEARS)	
INFLAMED	154 (78%)	65 (53.7%)	98 (71%)	317 (69.2%)
ABNORMAL FINDINGS	26 (13%)	19 (15.7%)	21 (15%)	66 (14.4%)
NORMAL	18 (9%)	37 (30.6%)	20 (14%)	75 (16.4%)
TOTAL	198 (43.3%)	121 (26.4%)	139 (30.3%)	458
GANGRENOUS/PERFORATED APPENDIX	33 (17%)	3 (2.5%)	22 (16%)	58 (13%)

Table 2: Abnormal histological findings, number (percentage from total appendicectomies)

Abnormal findings	66 (14.4%)
Faecolith	16 (3.5%)
Fibrous obliteration of tip	12 (2.6%)
Enterobius infection	10 (2.2%)
Lymphoid hyperplasia	9 (2%)
Healing inflammation	8 (1.7%)
Neoplasm	7 (1.5%)
Torsion of appendices epiploicae	1 (0.22%)
Pus without inflammation	1 (0.22%)
Adenomatous polyp	1 (0.22%)
Peri-appendiceal inflammation	1 (0.22%)

Table 3: Radiological findings and correlation with histology results, numbers (percentage)

	Histological Findings		
	Appendicitis	Abnormal	Normal
Ultrasound scan (104 patients)			
Appendicitis	14	13 (93%)	1 (7%)
Normal	90	34 (38%)	21 (23%)
CT scan (108 patients)			
Appendicitis	100	97 (97%)	2 (2%)
Normal	8	3 (37.5%)	2 (25%)

Table 4: Preoperative inflammatory markers and histological results of appendicectomy

	Inflammatory markers	
	Normal (n=84)	Abnormal (n=374)
Inflamed Appendix (n=317)	12	305
Non-inflamed Appendix (n=141)	72	69

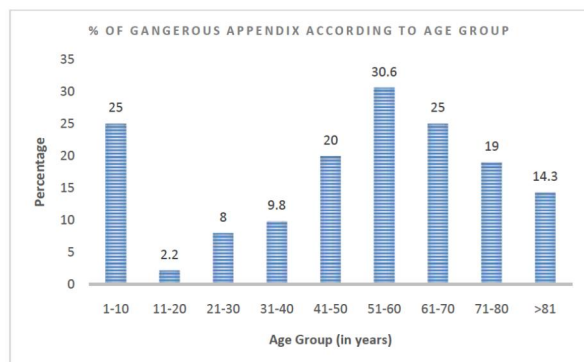


Figure 1: Gangrenous appendix percentage compared to different age groups.

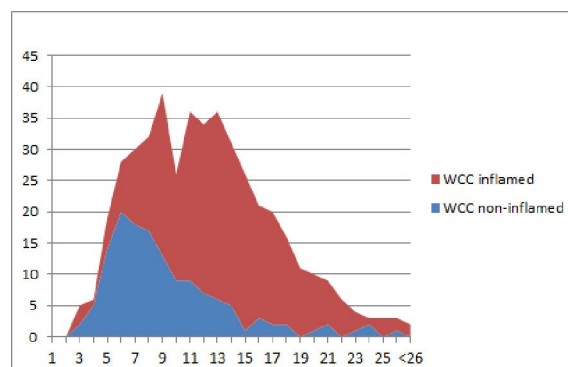


Figure 2: Comparison of WCC between histologically inflamed and non-inflamed appendix.

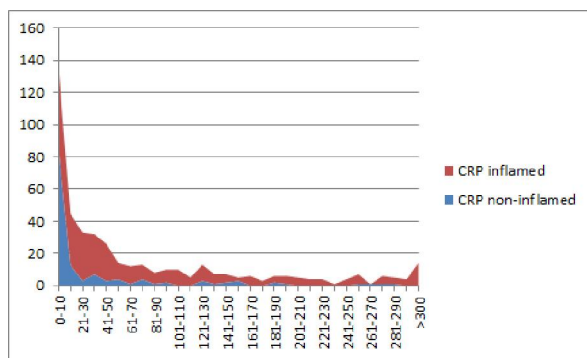


Figure 3: Comparison of CRP between histologically inflamed and non-inflamed appendix.

4. Discussion:

Between 30,000 to 40,000 emergency appendectomies are performed in the UK annually[1] with an average histologically normal appendix rate (NAR) of 20%[2]. This rate is considerably higher if compared with the reported NAR of 2.9% in USA[3] and 3.3% in the Netherlands [4]. One in 6 patients in the current study had a histologically normal appendix. This rate was significantly higher in the women aged between 16- and 40-years old group when compared to the other groups (30.6% vs 11.3%, $p < 0.0001$). The rate of negative appendicitis was also higher, although statistically non-significant, in women in the non-childbearing age group compared to male patients (14% vs 9%, $p = 0.130$). An accurate diagnosis of appendicitis is more difficult in women especially those in the childbearing age group due to a wider range of other conditions with similar clinical presentation [5,6]. Lowering the NAR in this group of patients would have significantly reduced the overall NAR in the current study. It was also found that this age group had the lowest rate of perforated or complicated appendicitis compared to other groups in our study.

Preoperative blood results and radiological investigations play an important role in the clinical diagnosis of acute appendicitis especially in patients with equivocal clinical signs. Abnormal inflammatory markers can be non-specific, however, the presence of normal inflammatory markers in patients with pain in the right iliac fossa supports the absence of complicated appendicitis. None of the 84 patients with normal preoperative inflammatory markers in the current study was found to have a perforated or gangrenous appendix, and 72 (85%) of them had a normal appendix. On the other hand, only 18.6% of the 374 patients who had an abnormal WCC and/or CRP had a histologically normal appendix.

Pelvic sonography was the first line diagnostic test in the women of childbearing age in this study.

While 93% of patients with positive USS results had appendicitis on histology, 34 (37.7%) out of the 90 patients with a negative preoperative USS were found to have inflamed appendix on histology. D'Souza and his colleagues reported the results of 573 pre-appendectomy ultrasonography. The sensitivity and specificity of ultrasonography for the diagnosis of appendicitis was 51.8% and 81.4%[7]. This concludes that ultrasound can be used as a positive marker for appendicitis while a negative or non-conclusive report cannot exclude appendicitis.

CT scan is considered the most sensitive and specific investigation for acute appendicitis with reported sensitivity and specificity of 98.5% and 98% and negative and positive predictive values of 99.5% and 93.9% respectively [8]. In the current study, 97% of CT scans reported as appendicitis were associated with histological evidence of appendicitis. CT scans, however, are uncommonly requested for patients younger than 45 years old to avoid the risk of ionizing irradiation. The majority (87%) of patients who had CT scans in this study were older than 40 years old. A meta-analysis by Yun et al comparing low- and standard-dose CT for the diagnosis of acute appendicitis reported a sensitivity of 96.25% and specificity of 93.22% for low-dose CT [9]. The authors concluded that Low-dose CT was highly effective in the diagnosis of suspected appendicitis and can be considered as an alternative first-line imaging test which reduces the potential risk of exposure to ionizing radiation[9]. Another reported alternative is the reduced range CT scan (from L1 to symphysis pubis) which was found to have a comparable diagnostic performance with a remarkable reduced total and organ radiation dose (especially breast and testicle dose) when compared to full range CT[10].

In conclusion, this study reports the outcome of appendectomies performed over 2 years period at a UK DGH. It draws attention to the high rate of negative appendectomy in women of reproductive age group and compares the results of preoperative investigations with the histological results of appendectomy. The results suggest that a more conservative approach in the females in the reproductive age group especially with normal preoperative inflammatory markers can reduce the NAR. USS scan is still considered the first line diagnostic test in this group of patients looking for radiological signs of acute appendicitis or other pathology. Patients with negative USS should have a serial examination. The utilization of low dose [9] or reduced range [10] CT scan in this age group can significantly reduce the rate of unnecessary surgery especially when surgery is deemed to be a high-risk alternative. MRI scan also represents an alternative modality in young females with diagnostic accuracy

similar to CT scan [11] and it was found to be cost effective when compared to normal appendectomy [12]. Van Rossem et al audited the nationwide effect of a new guideline in the Netherland mandating preoperative imaging in patients with suspected acute appendicitis across 62 Dutch hospitals and reported a decrease in the normal appendectomy rate from 15 to 3.3% [4]. Similar results can be achieved in the UK to reduce the high NAR.

Conclusion:

Women in childbearing age have the highest rate of normal appendectomy. Normal inflammatory markers support a more conservative approach in this group of patients and the usage of low-dose or reduced-range CT scans can reduce this normal appendectomy rate to reach the rates in other countries.

Conflict of Interest Statement

Authors declare there is no conflict of interest in this article.

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