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## Predicting negative appendectomy by using demographic, clinical, and laboratory parameters: A cross-sectional study

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### ABSTRACT

**Introduction:** Acute appendicitis (AA) is still the most common acute surgical disease. While negative appendectomy (NA) is inevitable, one of the greatest challenges a surgeon faces when treating patients with a primary diagnosis of AA is to decrease NA without increasing the morbidity and mortality rates. This study was conducted to evaluate the frequency of symptoms, signs, laboratory data and the diagnostic values of these findings as regards avoiding NA in patients with a primary diagnosis of AA.

**Methods:** In a cross-sectional study, 1197 patients with a primary diagnosis of AA who underwent open appendectomy in two general military hospitals with a primary diagnosis of AA were evaluated over a two-year period. Data were compared between the two groups; namely those with AA and the ones with NA. Statistical analysis was performed using one-way ANOVA, Kappa and odds ratio correlation coefficients and the logistic regression model. **Results:** The mean age was  $24.1 \pm 0.25$  years. There were 911 (76.1%) males. Rate of NA was 18.2%. The regression model revealed that being younger ( $<21$  years old) ( $P = 0.049$ ), being female ( $P = 0.001$ ), having a lower percentage of polymorph nuclear (PMN) cells ( $P = 0.024$ ) and a lower heart rate ( $P = 0.021$ ) could be regarded as independent predictors of NA ( $P < 0.001$ ).

**Conclusion:** Obtained results indicate that female gender, low PMN percentage and pulse rate, and age below 21 years can provide important diagnostic information in addition to other diagnostic workups to prevent unnecessary laparotomies.

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## 1. Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen.<sup>1</sup> The decision to perform operation on a patient with suspected AA is based mainly on disease history and physical findings; however, the clinical presentation is seldom typical.<sup>2</sup> The three signs and symptoms most predictive in the diagnosis of AA are pain in the right lower quadrant

(RLQ), abdominal rigidity and the migration of pain from the periumbilical region to RLQ.<sup>3</sup> The lower duration of pain has also been shown to be an important positive predictor of AA.<sup>4</sup>

Since delayed diagnosis and treatment of AA are associated with an increased rate of morbidity and mortality, timely intervention is crucial.<sup>5–8</sup> The rate of negative laparotomy has been reported to be from 2 to 30%.<sup>2,9</sup>

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The aim of this study was to assess the predictive value of different factors including disease history, clinical presentation, physical examination findings, and laboratory examinations in patients hospitalized due to suspected appendicitis.

## 2. Patients and methods

This analytic cross-sectional study was performed by reviewing the medical records of 1197 patients who had been admitted for suspected appendicitis and undergone open appendectomy operations between July 1997 and June 1999 in two general military hospitals. A checklist which contained 48 questions was designed to collect these variables: demographic factors, clinical presentation (quality, duration, and shift of the pain and associated symptoms like nausea, vomiting, urinary symptoms, etc.), physical examination results, and laboratory factors. In the aforementioned training hospitals, the primary diagnosis, having been first suggested by the residents, is confirmed by a surgeon before surgery. In this study, AA was defined as the presence of polymorph nuclear (PMN) cells in the muscular layer of the appendix, while NA was the indicator of no significant pathologic change in the appendix according to the pathologist's reports. This study considered the presence of all types of dysuria, frequency and urgency as urinary symptoms. For data analysis, descriptive indices, such as frequency, mean, standard error (SE), statistical tests, including Chi-square and one-way ANOVA and finally correlation coefficients, such as Kappa and odds ratio were used. Wald forward logistic regression model was employed to predict NA with SPSS 11.5 software (SPSS Inc., Chicago, Illinois, USA). The study protocol was in conformity with the ethical guidelines of the 1975 Declaration of Helsinki.<sup>10</sup>

## 3. Results

There were 911 males and 286 females and their mean ( $\pm$ SE) age was 24.1 ( $\pm$ 0.25) year (range, 4–74 years). The most frequent clinical finding was tenderness in the right lower quadrant (RLQ) region (86.1%). Demographic, clinical, and laboratory characteristics of patients are presented in Table 1.

In 16 out of 1197 cases with a primary diagnosis of AA, the pathologic records were not available. The pathologic diagnosis of 966 cases (81.8%) was AA and in other 215 cases (18.2%) the pathologic diagnosis was a normal appendix (NA). The age, symptoms and signs in the patients with AA and NA are compared in Table 2.

Pain was continuous in the majority of the patients (740 cases, 62.7%). The initial location of pain was periumbilical in 364 patients (30.8%), and the RLQ was the most common site of final pain location which was reported in 975 cases (82.5%). The characteristics of pain in cases with AA and those with NA are compared in Table 3.

The frequency of NA in males and females were 149 (16.4%) and 66 (23.2%), respectively, which indicated a significant statistical difference ( $P = 0.009$ ).

The mean ( $\pm$ SE) percentage of PMN in patients with NA was significantly lower compared to AA patients ( $72.7 \pm 1.4\%$

**Table 1 – Baseline characteristics of the studied patients with primary diagnosis of acute appendicitis (n = 1197)**

Characteristics	
Age (mean $\pm$ SE), year	24.1 $\pm$ 0.25
Gender, male	911 (76.1%)
Duration of hospitalization (mean $\pm$ SE), day	3.7 $\pm$ 0.06
Chief complaint	
Abdominal pain	1185 (99%)
Vomiting	7 (0.6%)
Anorexia	3 (0.3%)
Nausea	1 (0.08%)
Urinary frequency	1 (0.08%)
Duration of pain from the onset until hospitalization (mean $\pm$ SE), hours	30.8 $\pm$ 1.4
Tachycardia	145 (12.1%)
Fever	461 (38.5%)
Leukocytosis	819 (68.4%)
PMN > 75%	737 (61.6%)
Hematuria	110 (9.2%)
Bacteriuria	315 (26.3%)

**Table 2 – Comparison of age, symptoms and signs between patients with acute appendicitis and negative appendectomy**

	Acute appendicitis (n = 966)	Negative appendectomy (n = 215)	Sig.
Age (mean $\pm$ SE), year	24.5 $\pm$ 0.3	22.5 $\pm$ 0.6	0.002
Pulse rate (mean $\pm$ SE)	84 $\pm$ 0.4	82 $\pm$ 0.8	0.017
Oral temperature (mean $\pm$ SE), °C	37.3 $\pm$ 0.02	37.2 $\pm$ 0.04	0.025
Duration of hospitalization (mean $\pm$ SE), day	3.8 $\pm$ 0.07	3.4 $\pm$ 0.09	0.038
<b>Symptoms</b>			
Anorexia	813 (84.1%)	185 (86%)	NS
Nausea	787 (81.4%)	173 (80.4%)	NS
Vomiting			NS
<3 times	440 (45.5%)	109 (50.7%)	
$\geq$ 3 times	93 (9.6%)	23 (10.7%)	
Urinary symptoms	826 (85.5%)	161 (74.9%)	0.005
Diarrhea	179 (18.5%)	36 (16.7%)	NS
Constipation	146 (15.1%)	36 (16.7%)	NS
Vaginal discharge	26 (2.7%)	6 (2.8%)	NS
<b>Signs</b>			
Maximal tenderness site			NS
RLQ	893 (92.4%)	199 (92.5%)	
Suprapubic	21 (2.2%)	6 (2.8%)	
Periumbilical	18 (1.8%)	5 (2.3%)	
LLQ	13 (1.3%)	2 (0.9%)	
Rebound tenderness	858 (88.8%)	175 (81.4%)	0.017
Cough tenderness	850 (88%)	188 (87.4%)	NS
Rowling's sign	696 (72%)	131 (61%)	NS
Psoas sign	635 (65.7%)	155 (72%)	NS
Obturator sign	590 (61%)	135 (62.8%)	NS
Guarding	186 (19.2%)	22 (10.2%)	NS
Shift of pain to the RLQ	908 (94%)	169 (78.6%)	0.007

Abbreviations: NS, not significant; RLQ, right lower quadrant; LLQ, left lower quadrant.

**Table 3 – Comparison of pain characteristics between patients with acute appendicitis and negative appendectomy**

	Acute appendicitis (n = 966)	Negative appendectomy (n = 215)	Sig.
<i>Quality of pain</i>			NS
Persistent and without change	623 (71.5%)	130 (67%)	
Intermittent and colic type	121 (13.9%)	35 (18%)	
Persistent but increasing	113 (13%)	25 (12.9%)	
Persistent but decreasing	14 (1.6%)	4 (2.1%)	
<i>Primary location of pain</i>			0.018
Periumbilical	304 (34.5%)	60 (30.9%)	
RLQ	215 (24.4%)	68 (35.1%)	
Epigastric	156 (17.7%)	24 (12.4%)	
Suprapubic	48 (5.4%)	19 (9.8%)	
Non-localized	87 (9.9%)	13 (6.7%)	
<i>Final location of pain</i>			NS
RLQ	807 (92.7%)	168 (88.9%)	
Suprapubic	16 (1.8%)	6 (3.2%)	
Periumbilical	15 (1.7%)	4 (2.1%)	
Non-localized	12 (1.4%)	4 (2.1%)	

Abbreviations: NS, not significant; RLQ, right lower quadrant.

as opposed to  $76.3 \pm 0.5\%$ ,  $P = 0.009$ ). There were 33.3% of cases with NA in patients with white blood cells (WBC)  $< 4000/\text{ml}$ . This figure was 29.4% in patients with WBC between 4000/ml and 9999/ml, and 11.7% in cases with WBC between 10,000/ml and 18,000/ml ( $P < 0.001$ ). Leukocytosis (leukocyte count equal to or higher than 10,000/ml) which was observed in 27 patients (12.5%) with NA was lower in comparison to patients with AA (284 cases, 29.4%) and this difference was statistically significant ( $P < 0.001$ ).

Preoperative and intraoperative diagnoses had a statistically significant relationship ( $P < 0.001$ , Kappa = 0.344), and so did diagnoses during surgery and final pathologic diagnoses ( $P < 0.001$ , Kappa = 0.131).

The regression model revealed that among the factors with significant difference between NA patients and AA, only being younger ( $< 21$  years old) ( $P = 0.049$ ), being female ( $P = 0.001$ ), having a lower percentage of PMN ( $P = 0.024$ ) and a lower heart rate ( $P = 0.021$ ) could be regarded as independent predictors of NA ( $P < 0.001$ ). Odds ratio (OR) and its 95% confidence interval of these independent variables are demonstrated in Table 4. It shows that being female will increase the probability of NA by 2.1 fold, whereas when we have a one-unit increase in age, pulse rate and PMN percentage, this probability will be 1.557, 1.022 and 1.016 times, respectively.

**Table 4 – Odds ratio. Its 95% confidence interval and significance level of predictors of negative appendectomy**

	Odds ratio (OR)	95% Confidence interval of OR	Sig.
Female	2.144	1.34–3.431	0.001
Age $< 21$ years	1.557	1.002–2.419	0.049
Lower heart rate	1.022	1.003–1.041	0.021
Lower PMN percentage	1.016	1.002–1.03	0.024

#### 4. Discussion

In this study, the ratio of males to females was 3, whereas in other studies it is usually about 1.3.<sup>9,14</sup> It seems that owing to the military nature of our hospitals, most of the patients were male. Excluding the conscript soldiers referring to our hospitals alters this ratio to 1.5. As a result, the findings of this study cannot be generalized in terms of sex distribution.

One important finding in our study was a higher percentage of NA in females than that in males, which tallies with the results of other studies.<sup>1,8,9,12</sup> Consequently, the authors believe that NA is more frequently seen in females because of ovary and fallopian tube diseases.<sup>1,13</sup>

Many authors have maintained that abdominal pain will finally localize in the RLQ.<sup>1,14,15</sup> Likewise, final localization of pain in the RLQ was significantly higher in cases with AA in this study when comparisons were made with that in other studies.

The chief complaint (abdominal pain) and the most common clinical sign (tenderness and/or rebound tenderness) were completely compatible with the ones reported in other studies.<sup>9,11,14,16</sup> Anorexia, nausea and vomiting have a clinical importance in AA.<sup>14</sup> However, some studies confirm that nausea and vomiting do not have a diagnostic value for differentiation between AA and NA.<sup>12</sup> Also, others have mentioned that when they are absent, AA cannot be ruled out.<sup>15</sup> This study supports this idea as well. The mean duration of hospitalization (3.7 days) is not too long for an open appendectomy.<sup>16</sup>

In this study, an increase in WBC count resulted in a significant decrease in NA. Other authors have reported the same finding,<sup>9,14,16</sup> which shows the importance of WBC in ruling in AA despite the fact that it cannot be put in the regression model. There are those, however, who believe that leukocytosis has too poor a specificity to use for the diagnosis of AA.<sup>17–21</sup> Relying upon the leukocyte count alone to make a management decision in case of suspected appendicitis may result in misdiagnosis or unnecessary surgery.<sup>22</sup> NA was 18.2% in the current study, which is relatively high. Most authors have accepted the rate of 10–15%,<sup>9,14,23</sup> although there is a study putting the percentage rather higher (20–40%).<sup>8</sup> In the past, the rate of NA was up to 20%, but now accessibility to sonography and computed tomography (CT) scan means that this value can no longer be accepted as a standard.<sup>14</sup> Indeed, 17 prospective studies on 925 appendectomies have come up with a range of 3.1–28% and a mean of 14.5% for NA.<sup>16</sup>

When AA is not clinically suspected very much, observation and repeated physical examinations, specifically in the absence of paraclinic facilities, can reduce the percentage of NA. Nonetheless, the percentage of perforation will not change significantly.<sup>14,24</sup> If the initial clinical presentation does not suggest the need for immediate surgery, the patient should be kept under observation for 6–10 h in order for the diagnosis to be clarified.<sup>25,26</sup> This precautionary measure may reduce the rate of unnecessary laparotomy without increasing the rate of appendiceal perforation.<sup>24,27,28</sup>

A meta-analysis has demonstrated that all clinical and laboratory variables are weak discriminators individually; they achieve a high discriminatory power when combined.

Laboratory examinations of the inflammatory response, clinical descriptors of peritoneal irritation and a history of the migration of pain yield the most important diagnostic information and should be included in any diagnostic assessment.<sup>29</sup>

In the present study, the regression model showed that younger female with lower PMN percentages and heart rates are the most probable cases for NA.

In conclusion, if a patient with a primary diagnosis of AA is a female below the age of 21 with PMN lower than 75%, WBC less than 10,000/ml and urinary symptoms but without prominent rebound tenderness, the surgeon should find more acceptable reasons for appendectomy because of the significantly high probability of NA in such a situation. Repeated physical examination, imaging modalities such as ultrasound, spiral CT scan, isotope scan and even laparoscopy can be performed (if indicated) for more precise decision making. Radiological evaluations can be helpful only in specific conditions and are not routinely advised.<sup>14</sup>

#### Conflict of interest

There is no conflict of interest in this study.

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#### Ethical approval

Ethical approval was given by the "Scientific Committee of the Research Department of Baqiyatallah Medical Sciences University (code no. 75/016-Un-M)".

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