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PREDICTIVE VALUE OF LEUKOCYTIC COUNT IN ACUTE APPENDICITIS AS SEEN IN ASIR CENTRAL HOSPITAL.

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Abstract

This retrospective study was aimed to identify the level of total leukocytic count that correlates with and helps in the prediction of acute appendicitis. The total leukocytic counts (TLC) of 104 cases of appendicitis seen from June, 1994 to October, 1997 were compared with a comparative series of 125 elective cases that were admitted during the same period. Using binary tables, sensitivity, specificity, predictive values and joint probability were estimated for the different cutoff levels of TLC. The optimum cutoff point of 8,500 cells/mm^3 was obtained by plotting the positive and negative predictive values. Such cutoff point had a sensitivity = 0.78, specificity = 0.84, positive predictive value = 0.80, and negative predictive value = 0.82. The total joint probability, which is the diagnostic weight indicative of the accuracy of such cutoff point, accounted for 0.82.

These results suggest that, besides a detailed history and a thorough physical examination, TLC of 8,500 cells/mm^3 or above is worth considering in the diagnosis of acute appendicitis in Asir region. However, its use in isolation from other clinical and laboratory findings would be unjustified.

Introduction

Acute appendicitis, in its classic form, is easily diagnosed, but difficult when presenting atypically, especially in the very young, female, and elderly patients. There is a chance of perforation ranging from 5%-15% in adults and up to 59% in children (Lewis *et al.*, 1975). Death rates range from 0.17% to 7.5% (Alvarado, 1986). On the other hand, negative laparotomy has got its considerable morbidity and mortality (Lewis *et al.*, 1975 and Abu Eshy *et al.*, 1995). So, improved accuracy is desirable in order to diagnose appendicitis earlier and reduce the rate of both perforation and unnecessary appendectomy. One of the criteria that help in diagnosing acute appendicitis is the leukocyte count.

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However, in view of the different standard values of this count that had been reported in the literature and the observation of lower values in Asir General Hospital, this study was undertaken. The aim was to find out the cutoff point, which correlates with the practical usefulness of leukocytic counts in the diagnosis of acute appendicitis.

Patients and Methods

Between June, 1994 and October, 1997, the hospital records of 150 patients who underwent appendectomy on the basis of clinical diagnosis of acute appendicitis (patients group), and 150 patients who were admitted at the same period for different elective surgeries with no infection anywhere (control group) were reviewed. Data collected comprised of generic factors such as age, sex, nationality, total leukocytic counts (TLC) and the histopathological diagnosis of the removed specimens. Of these 300 cases, 71 cases were excluded for one or more of the following reasons:
-Incomplete information.
-Histologically normal appendices
-Presence of immune-suppressing, debilitating, or chronic disease(s) *e.g.* diabetes mellitus, malignancy, history of radiotherapy, chronic renal failure ..etc.

So, 104 cases of the patients group and 125 cases of the control group were considered for this study. For all patients, values of leukocytic count were cross classified according to their histologic diagnosis (appendicitis present - or absent) and by various cutoff points along the range of leukocytic counts above which subjects may be considered as having appendicitis by that leukocytic count. From these tabulations, the sensitivity, the specificity, the predictive values and joint probabilities were computed for the leukocytic counts of each cutoff point. Crossing of both curves of positive predictive value (PPV) and negative predictive value (NPV) derived the optimum cutoff level of leukocytic count for the accurate diagnosis of acute appendicitis.

Statistical analysis was conducted using the SPSS/PC+ software package. Data were analyzed using the Pearson Chi-square test to compare categorical data and Student *t-test* to compare quantitative data with 5% level of significance.

Results

The diagnostic accuracy of acute appendicitis in this series was 74%. Table-1 shows the pathological stages of the appendicitis group.

Table-1: Pathological stages of acute appendicitis.

Stage	Number	%
Simple	91	
Suppurative	5	
Gangerenous	1	
Perforated	7	
Appendix mass	1	
Total	105	

Table-2 shows the distribution of 104 patients and 125 controls according to sex, age group and total leukocytic counts. A statistically significant sex ratio was found between patients (M/F = 1.9:1) and controls (M/F= 0.9:1) with predominantly more male patients in the appendicitis group ($P<0.005$). The mean age of patients with acute appendicitis (25.6 ± 10.3 years) was significantly lower than that of their controls (38.2 ± 13.3 years)

(P<0.001). On the other hand, the mean total leukocytic count for patients (12.7±4.8 cells/mm^3) was significantly higher than that for the control group (6.3±2.0 cells/mm^3), even when adjusting for age and sex.

Table-2: Distribution of acute appendicitis cases and their controls according to some characteristics.

Characteristic	Acute Appendicitis		Control		P-Value
	No. 104		No. 125		
-Sex ratio (M:F)	69/35 (1.9: 1)		58/67 (0.9: 1)		P<0.005
Age group (year)	No.	%	No.	%	
	36	34.6	5	4.0	< 20
	56	53.8	66	52.8	20-
	10	9.6	43	34.4	40-
	2	1.9	11	8.8	60+
Mean±SD	25.6±10.3		37.9± 13.0		P<0.001
-Total leukocytic count (cells/mm)					
	8	7.7	63	50.4	3,000-
	20	19.2	45	36.0	6.000-
	23	22.1	15	12.0	9,000-
	53	51.0	2	1.6	12,000+
Mean±SD	12,7 ± 4,8		6,3 + 2,0		P<0.001

Fig.1: shows plotting of all values for positive predictive value (PPV) against the corresponding negative predictive values (NPV) to obtain the optimum cutoff level of leukocytic count. The figure shows that point corresponding to the 8,500 cells/mm^3.

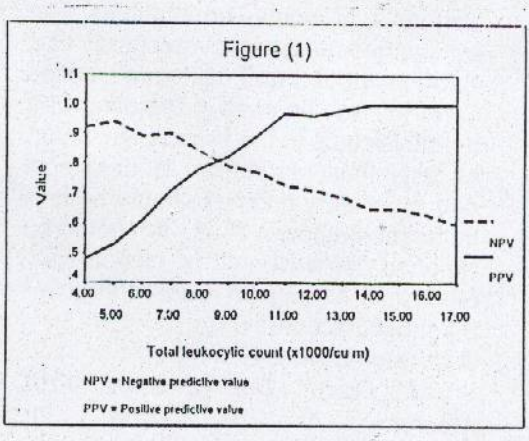

Fig.1: The cutoff point of total leukocytic count when the likelihood of appendicitis is 50%.

Table-3 shows that this cutoff level had a sensitivity = 0.78 and a specificity = 0.84. The computed positive prediction values were: PPV = 0.80 and NVP = 0.82. Thus, their cutoff level correctly diagnosed 78% of the true cases, missed 22% of these cases (false negatives) with hazards of perforation but misclassified 16% of the non-appendicitis subjects as appendicitis (false positives) with the risks of unnecessary appendectomy.

Table-3: 2 x 2 Classification of 230 subjects by histologic diagnosis of acute appendicitis as a gold standard and a cutoff point of 7,8,500 cells/mm for total leukocytic count as one diagnostic criterion.

Histologic diagnosis	Total leukocytic count (cells/mm)		Row
Total	> 8,500	<8,500	
Appendicitis - Yes	81	23	104
Appendicitis - No	20	105	125
Column Total	102	128	229

Sensitivity = 81/104 = 0.78
Specificity = 104/125 = 0.84
Positive Productive Value (PPV)=81/101 = 0.80
Negative Productive Value (NPV)=105/128= 0.82
Joint Probability of a positive test=81/229 = 0.35
Joint Probability of a negative test=105/229= 0.46
Diagnostic Weight= 0.35 ± 0.46 = 0.81.

Discussion

The diagnosis of acute appendicitis, which can represent a considerable challenge to the surgeon, remains clinical. But it can be supported by white blood cells determination as the main criteria for favoring operation over observation Nauta and Magnant, 1986 and (Wattanasirichaigoon, 1994). Leukocytosis alone was not predictive of a surgically remediable disease, which suggests that a period of observation in patients with atypical patterns of pain and no peritoneal signs is a sound treatment plan (Nauta and Magnant, 1986). Although some series showed a significant

relationship between raised white blood cell count and the neutrophils percentage in one side and the incidence of inflamed or perforated appendix on the other (Teicher *et al.*, 1983; Berry and Malt, 1984; Nauta and Magnant, 1986 and Abu Eshy *et al.*, 1995), some other studies showed this to be of no significance (Chang *et al.*, 1973; Gilmore *et al.*, 1975; Lewis *et al.*, 1975 and Deutsch *et al.*, 1983).

A considerable overlap is present between the leukocytic count of healthy persons and those with acute appendicitis (Wattanasirichaigoon *et al.*, 1994). The cutoff point will help surgeons to determine the significant value of those by statistical means. In the present study, the cutoff point of TLC is 8,500 cells/mm^3. This cutoff point, though lower than a cutoff point of 11,500 cells/mm^3 identified by Wattanasirichaigoon in Taiwan (1994), yet it has a comparable specificity (84% versus 84.2%) and slightly lower sensitivity (78% versus 84.5%). Meanwhile, the diagnostic accuracy of the cutoff point of 8,500 cells/mm^3 in the present study (0.82) is comparable with that of 10,000 cells/mm^3 (0.83) reported by Alvarado in Florida, (1986). However, this difference in the cutoff points of TLC might be partly attributed to the difference in the normal range of white cell count in these different populations.

The question is how could acute appendicitis be predicted within such cutoff point of 8,500 cells/mm^3?. For the sake of simplicity, the prior probability of appendicitis (50%) versus no appendicitis (50%) is expressed in absolute number rather than percentages (appendicitis present, No. 104: absolute, No. 125). Suppose that, based on the symptoms and signs in a given patient, the surgeon considers the likelihood of appendicitis to be about 50:50 and orders a total leukocytic count to further evaluate the patient. Table-3 shows that cross tabulation of such number of patients with TLC will result in an increase in the likelihood of appendicitis from 50 to 80 percent (PPV= 0.80) in patients when the TLC is more than 8,500 cells/mm^3, an incremental ruling-in gain of 30 percent. A normal leukocytic count, on the other hand, has reduced the likelihood of appendicitis from 50 to 18 percent (NPV = 0.82), probability of no disease is 82%, given a TLC of less than 8,500 cells/mm^3, an incremental ruling-out gain of 32 percent.

From the collective findings of this study and considering its limitations in terms of the small sample size and non-inclusion of neutrophilic count, it is concluded that the results may be considered suggestive of potential validity of the leukocytic count as a criterion for diagnosis of acute appendicitis. The satisfactory diagnostic accuracy of a cutoff point of 8,500 cells/mm^3 makes it worthy to be used in the diagnosis by physicians in the region. However, its use in isolation from other clinical and laboratory findings should be less than satisfactory. Thus, it should be weighed against other clinical and laboratory findings in order to improve diagnostic accuracy.

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