



Platelet to Lymphocyte Ratio for Prioritising Perforated or Gangrenous Appendicitis in a Triage of an Emergency Room

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AM, MMA, MAA, NTA and AKD wrote the protocol, wrote the first draft of the manuscript, managed the analyses of the study and managed the literature searches. Authors MMA, MAA, NTA and AKD did the data collection, designed the study and performed the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Some studies suggested Platelet Lymphocyte Ratio (PLR) is associated with perforated or gangrenous appendicitis. This study aimed to evaluate the effectiveness of the platelet-lymphocyte ratio in distinguishing simple acute appendicitis from perforated or gangrenous appendicitis in the clinical emergency setting

Method: This study was conducted retrospectively in academic tertiary hospital on 302 patients who had undergone appendectomy for a period of eight years from mid of 2008 to the mid of 2016. We divided them according to their histopathological results two to groups simple acute appendicitis and perforated or gangrenous appendicitis.

Results: The study demonstrated that PLR is a useful indicator in diagnosing perforated or gangrenous appendicitis with a cutoff value of 197.57 with sensitivity 63.3% and specificity 38.7% and P=0.057. The risk for developing perforated or gangrenous appendicitis in patients with high

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Platelet Lymphocyte Ratio (PLR) was 1.5 times higher than those with standard Platelet Lymphocyte Ratio odds ratio (OR): 1.58 (P=0.002).

Conclusion: PLR is a simple, cost-effective is a useful parameter that diagnoses complicated perforated appendicitis.

Keywords: Appendicitis; perforated; gangrenous; platelet-lymphocyte ratio.

1. INTRODUCTION

Abdominal pain is the most frequent cause of a visit to the emergency department (ED), estimating for 8 million (7%) of the 119 million ED visits in 2006 in the United States and acute appendicitis is one of the significant causatives of the abdominal pain [1,2] it has 0.7% occurrence chance in an individual in a lifetime [3].

Mortality rate of 0.8 per 1000 in uncomplicated stage and 5.1 per 1000 in complicated state [4] it is mainly diagnosed bases clinically on signs and symptoms and many scores have been developed to diagnose such as Alvarado score that is 90% sensitive to diagnosing acute appendicitis [5] and simple laboratory results such as white blood cell count and CRP has some role in diagnosing appendicitis [4,6].

However the status of appendicitis wither it is still in the early stages or has become complicated cannot be evaluated with accuracy by these examinations, and delay in diagnosis causes complication such as perforation or gangrenous, and according to many studies, it has a risk ranging from 14–31% [7-10].

However, the Radiological examination has shown promise in differentiating between simple acute appendicitis and perforated or gangrenous appendicitis [11], but these methods take time, expensive not readily available in all centres.

We needed for easily acquired, time-saving, cheap and available in all centers test, some studies showed that Platelet lymphocyte ratio could differentiate between simple acute appendicitis and perforated or gangrenous appendicitis [12] our aim in this study to evaluate the effectiveness of the platelet-lymphocyte ratio in distinguishing simple acute appendicitis from perforated or gangrenous appendicitis in clinical emergency setting.

2. PATIENTS AND METHODS

2.1 Ethical Considerations

We conducted this study in King Abdul Aziz University hospital affiliated to King Abdul Aziz

University and was approved accordingly from the institutional ethical committee.

2.2 Patients and Procedures

We did retrospective analysis on all the patients admitted with the initial diagnosis of appendicitis through the emergency room and subsequently underwent either open or laparoscopic appendectomy in a duration of 8 years from June 2008 to September 2016. We gathered the patient demographics, admission laboratory tests, preoperative, postoperative notes and the histopathology reports using the institution healthcare System database (Phoenix by Al Anaiyah) our inclusion criteria were any patient who had an appendectomy and had a preoperative Complete Blood Count (CBC).

At first 906 patients were identified but we excluded 604 patients due to either missing or lost records of admission CBC tests or Histopathology reports, or if they had a history of comorbidities that would affect the platelet-lymphocyte ratio like coronary artery disease, haematological or malignant disease and cerebrovascular events. Also, if they had recent blood transfusions.

302 patients remained in the study we calculated the platelet-lymphocyte ratio from the admission CBC which was analysed by an automated haematological analyser. The histopathological report was assessed to classify the patients to two groups: Group 1 simple acute appendicitis and Group 2 perforated or gangrenous appendicitis.

2.3 Statistical Analysis

Statistical Package of Social Science version 22.0 (SPSS Inc, Chicago, IL, USA) was used for the analysis of the study; we used the sample T-test to calculate the means and ranges and performed the one-way analysis of variance (ANOVA) to assess whether the means were significantly different from each other. To evaluate the significant difference of the categorical values Chi-square was used when

appropriate. And finally, Receiver Operating Characteristic analysis (ROC curve) and Youden's index were used to determine the optimal cutoff point with the optimal balanced point regarding sensitivity and specificity. Also, ROC was used to determine the Area Under the curve (AUC), CI levels of AUC. We deemed a P value of <0.05 statically significant.

3. RESULTS

The analysis of the 302 patients exhibited that the peak occurrence of acute Appendicitis is between 15 and 30 years of life, ranging from 3 to 72 years; with a mean of 23.86 years (Fig. 1).

Regarding gender nearly tow third of the patients were male 196 (64.9%), and females were 106 (35.1%) ratio of 2:1 for male and female respectively. As for the status of appendix histopathological, we found (16.2%) with perforation or gangrenous and (83.8%) simple acute appendix (Table 1).

We calculated the optimal cutoff point Using the ROC curve and Youden's index it was 197.57 with a sensitivity of 63.3% and specificity 38.7% as shown in Fig. 2 and Table 2.

From the 302 patients, 252 patients (82%) had high Platelet lymphocyte ratio level, while 50 patients (16%) had a normal level. We could attribute this to the low specificity as this marker is sensitive to the severity of the inflammation but not highly specific to complicated appendicitis itself.

We found the risk for developing perforated or gangrenous appendicitis in patients with high Platelet Lymphocyte Ratio (PLR) was 1.5 times higher than those with standard Platelet Lymphocyte Ratio odds ratio (OR): 1.58 (P=0.002). (Table 2)

Within the 49 patients with a perforated or gangrenous appendix, 38 patients (77.55%) had Platelet lymphocyte ratio level. And from the 253 patients with simple acute appendicitis (Group 1), 214 (84.58%) had a Platelet lymphocyte ratio level. (P.value = 0.225) (Tables 3).

Regarding other CBC parameter, there was no significant difference between the perforated or gangrenous appendicitis and simple acute appendix except White Blood Count (WBC) which has shown to be decreasing in the perforated or gangrenous appendicitis (Table 4).

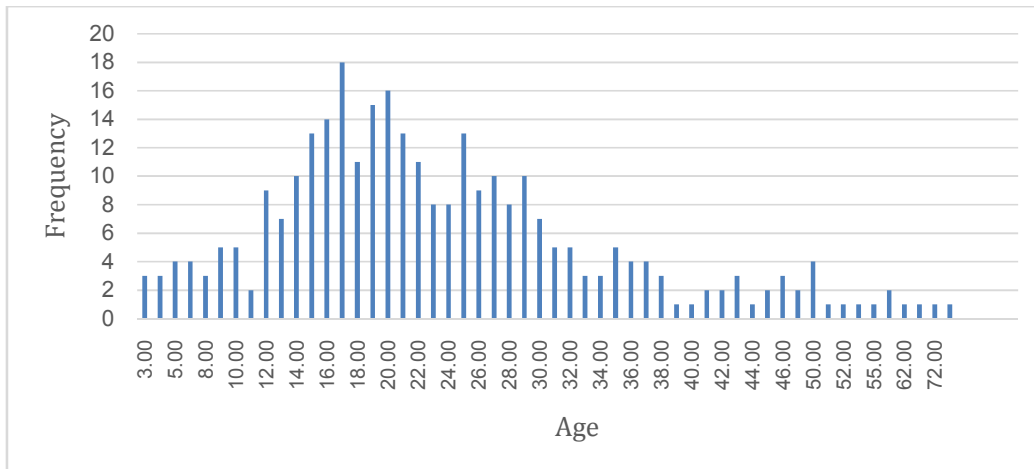


Fig. 1. Age distribution of both patients with a perforated or gangrenous appendix and acute non-perforated appendicitis

Table 1. Gender distribution of patients with a perforated or gangrenous Appendix and those with a simple acute appendix

	Perforated or gangrenous Appendix n (%)	Simple acute appendix n (%)	Total n (%)
Male	38 (77.5)	158 (62.4)	196 (64.90)
Female	11 (22.5)	95 (37.6)	106 (35.09)
Appendiceal Histology	49 (16.22)	253 (83.77)	302 (100)

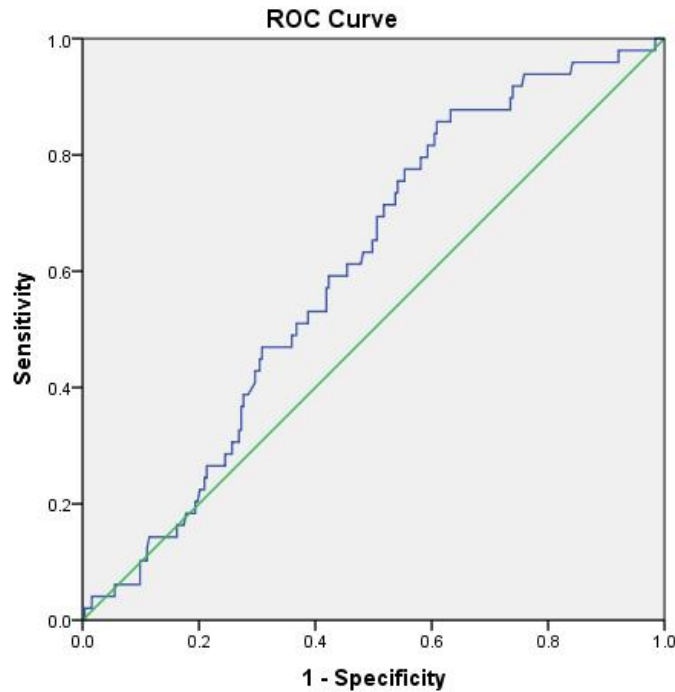


Fig. 2. PLR ROC curve

Table 2. The sensitivity and specificity of platelet lymphocyte ratio in patients with perforated or gangrenous appendicitis

Sensitivity	63.3%	
Specificity	38.7%	P=0.057
Optimal Cut off point	197.57	
Area Under the Curve (AUC)	0.586	
Area Under the Curve CI	LB: 0.502	
	UB: 0.669	
Odds Ratio	1.58	P= 0.002

Table 3. The platelet lymphocyte ratio between the two groups

	Perforated or gangrenous appendix n (%)	Simple acute appendix (%)		P.Value
Normal PLR	11 (22.5)	39 (15.4)	15.41	0.225
High PLR	38 (77.5)	214 (84.6)	84.58	

PLR: Platelet Lymphocyte Ratio

Table 4. Comparison of the mean of the other CBC parameters between the two groups

	Mean	Range	Std. Deviation	P.Value
Perforated or gangrenous appendix				
WBC	17.38	4.70-79	+/- 11.1	0.001*
Neutrophil	12.44	2.40-22.70	+/- 4.78	0.468
Lymphocyte	1.65	0.20-20.51	+/- 2.80	0.919
Acute, non-perforated appendix				
WBC	13.90	4.2-41.90	+/- 5.17	0.001*
Neutrophil	11.61	1.11-97.80	+/- 7.6	0.468
Lymphocyte	1.68	0.10-7.80	+/- 0.93	0.919

One hundred fifty-eight patients underwent open appendectomy (51.8%), while 147 (48.2%) patients underwent laparoscopic surgery.

4. DISCUSSION

The appendix is a tubular structure attached to the base of the caecum at the confluence of the taeniae coli. It is approximately 8-10 cm lengthy in adults, appendicitis is a simple inflamed appendix, and complicated appendicitis is an inflamed appendix with the presence of perforation or gangrenous [4].

A systemic review of 120 studies by Ferris et al. exhibited that appendicitis is affected by 100 in every 100,000 people in North America [13] and commonly occurs between 10 to 30 years of age and slightly more common in males than females with a ratio of 1.4:1 [4], in our study we found similar results usual age range is to between 15 to 30 years and the ratio to be 2:1 male to female.

The diagnosis of acute appendicitis is entirely based on clinical signs and symptoms and supported by laboratory and radiological investigation, majority of the patients present with periumbilical abdominal pain colicky in nature gradually becoming constant and sharp migrating to the right iliac fossa associated with nausea and vomiting, with clinical signs such as localised tenderness in the right iliac fossa specifically McBurney's point also known as rebound tenderness [4]. In complicated appendicitis, however, additionally, there is high fever and symptoms of peritonitis such as decreased appetite and chills [14].

There is no specific laboratory test to distinguish between simple acute appendicitis and perforated or gangrenous appendicitis, it is decisive to differentiate between them in an ER setting as to prioritise patients for surgical interventions many radiological investigations have shown promise such as CT and ultrasonography (USG) [11] but it is expensive, time-consuming, not readily available especially in small centres and there is the risk of radiation associated carcinoma [15] also there is 15% chance misdiagnosis [16,17].

Due to these reasons many studies proposed using simple laboratory parameters in distinguishing between the two groups as author Wilson et al. proposed white blood cell count 20.000/mm³ can be used as a cutoff value [11]

and author Chung et al. and other suggested using C-Reactive Protein (CRP) for the diagnosis of perforated or gangrenous appendicitis [18], but these tests are inconclusive alone and without the support of other radiological investigations so author Yildirim et al. proposed using of Platelet lymphocyte ratio and that it could be better than the other laboratory parameters when used alone [12].

Platelet Lymphocyte Ratio (PLR) in blood inflammatory marker used to assess severity in many clinical conditions such as non-ST elevation myocardial infarction, critical limb ischemia and End Stage Renal Disease (ESRD) [19-21]. PLR also used as a prognostic factor in many malignancies, advanced gastric carcinoma [22], colorectal carcinoma [23], and malignancies of the breast and gynecology [24-27], also studies been published for the association between PLR and periampullary carcinoma [28,29].

Recently it was proposed by Yildirim et al. that PLR could be used as a diagnostic test to distinguish between perforated or gangrenous appendicitis and simple acute appendicitis they suggested a cutoff point 169.7 with sensitivity of 74.4% and specificity of 73.5% [12], our study demonstrated an optimal cutoff point of 197.57 sensitivity of 63.3% and specificity of 38.7%, in comparison with Yildirim et al. our cut off value and sensitivity were close, but specificity deferred, we contributed our low specificity to an explanation that PLR is a marker of severe inflammation specifically but not complicated appendicitis.

We believe with our results that platelet-lymphocyte ratio could help in an ER setting to prioritise patients for emergency surgeries those with diagnosed appendicitis.

The usual therapeutic procedure for appendicitis is appendectomy [30-32] which technique is used however is based on the surgeon's expertise and OR equipment availability, in our study, we observed a near equal performing of the two-technique open 51.8% and laparoscopic 48.2%.

5. CONCLUSION

Differentiating between simple acute appendicitis and perforated or gangrenous appendicitis is challenging especially in an Emergency setting where time is crucial in prioritising patients for surgery. PLR is a simple, cost-effective that we

demonstrated in our study to be a good indicator in diagnosing perforated or gangrenous appendicitis.

6. STRENGTH AND LIMITATIONS

The limitation of this study is mostly in its nature of retrospective design, and it's been a single tertiary hospital centre-based study but based on our research we propose using PLR as a simple, cost-effective means to differentiate between simple acute appendicitis and perforated or gangrenous appendicitis with a cutoff point of 197.57 but to strengthen the study we recommend to do further studies prospective and multi-centred.

CONSENT

It is not applicable.

ETHICAL CONSIDERATIONS

We conducted this study in King Abdul Aziz University hospital affiliated to King Abdul Aziz University and was approved accordingly from the institutional ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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