Platelet To Lymphocyte Ratio : A Biomedical Marker For The Pre-Operative Diagnosis Of Acute Appendicitis

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Abstract

Acute appendicitis is the most common surgical pathology diagnosed in patients admitted to emergency departments with abdominal pain. Laboratory parameters such as fullblood count, Neutrophil Count, Neutrophil to Lymphocyte Ratio(NLR), Platelet Count (PLT), and Mean PlateletVolume (MPV) in the diagnosis of acuteappendicitis. The aim of this study was to determine the utility of the Platelet to Lymphocyte Ratio (PLR) value as a biomedical marker in the diagnosis as well as to predict the severity of acute appendicitis.

Materials and Methods: History, meticulous physical examination, complete haemogram test, ultrasonography of the whole abdomen done and all patients taken up for emergency open appendectomy. The resected appendix specimens were sent for HPE Examination and divided into 3 groups based on HPE (normal appendix, acute appendicitis, acute necrotizing appendicitis with perforation). The data were collected, analysed.

Results: Thestudy included 136 patients, 82 males and 54 females. TLC and Neutrophil Count values of group A were lower than those of group B and C values (p< 0.001). Platelet Count values of group C were higher than the other groups (p< 0.001). NLR and PLR values of group A were lower than the other groups (P< 0.001). The receiver operating characteristic (ROC) curve analysis demonstrated that PLR and NLR values were sensitive and specific to differentiate normal appendix, acute appendicitis and acute necrotising appendicitis with perforation.

Conclusion: This study demonstrated that Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio values could be used as new biomarkers to differentiate normal appendix from acute appendicitis and as well as perforated appendicitis.

Keywords: Appendicitis, perforated, Neutrophil, Lymphocyte, Platelet, Ratio

Introduction

The Appendix was first described by the physician, anatomist Berengario Da Carpi in 1521. Morgagni in 1719 published a detailed account of Appendix, its site and relation in his "AchersariaAnatomica". Verneys in 1710 coined the term "Vermiform Appendix".Acute Appendicitis is the most common surgical pathology diagnosed in patients admitted to emergency departments with abdominal pain. [1-3]The cause of Appendicitis is considered to be obstruction of the Appendiceal lumen and the subsequentonsetofbacterialinfection. Luminal obstruction can be produced by various mechanisms and it results in the retention ofmucus. Ifbacterial infection supervenes, the intraluminal pressure increases, leading to interruptionoflymphatic flow and the development of Appendiceal edema. This process leads to AcuteAppendicitis characterized by

distension of the Appendix and vascular congestion, which is designated as Catarrhal Appendicitis.Local circulatory dysfunction,will result in infarction opposite the junction between the Mesoappendix and Appendix, where the blood supply is inadequate. As a result, the Appendix becomes congested dark red with black necrotic areas, a condition that is designated as GangrenousAppendicitis. If perforation of the necrotic wall occurs, Appendicitis becomes complicated by perforative peritonitis.[4] In literature it has been reported that here is a lifetime incidence of this disease of approximately 7% and a perforation rate of 17%–20%. The mortality risk is less than 1% in the general population, but when it comes to elderly patients it can increase to 50 %. The urgent and accurate diagnosisof AcuteAppendicitis is essential for preventing potential complications for the patients.A raised Leucocyte Count has been reported to be a sensitive test for Acute Appendicitis by many authors, but is not diagnostic because of its low sensitivity. In order to determine the clinical severity of Acute Appendicitis, different laboratory parameters have been tested and studied. [5-8]Some laboratory parameters have been tried in recent clinical studies that can help the Surgeon to diagnose the patient more accurately, including haematological parameters such as fullblood count, Neutrophil Count, Neutrophil to Lymphocyte Ratio(NLR), Platelet Count (PC), and Mean PlateletVolume (MPV) in the diagnosis of AcuteAppendicitis and theprediction of complications.[9-12] But very few studies are found that have examined the predictability of Platelet to Lymphocyte Ratio (PLR) in the diagnosis of Acute Appendicitis and the prediction of complications. The aim of this study was to determine the utility of the Platelet to Lymphocyte Ratio (PLR) value as a biomedical marker in the diagnosis of Acute Appendicitis and to predict the severity of Appendicitis using this biomedical marker.

Materials And Methods

A cross sectional study was conducted in the Department of General Surgery, Jawaharlal Nehru Institute of Medical Sciences, Imphal. The study was conducted over a period of two years from 1st September 2019 to 31st August 2021.All cases of Acute Appendicitis more than 18 years of age who were willing to undergo emergency open Appendectomy were included in the study. Exclusion criteria were history of previous abdominal surgery, patients with appendicular tumour, patients having blood dyscrasias and immune-compromised patients and patients under 18 years of age. History, meticulous physical examination, complete haemogram test, ultrasonography of the whole abdomen were done and all patients were taken up for emergency open appendectomy. The resected appendix specimens were sent for Histopathological Examination and divided into 3 groups based on HPE (Normal Appendix, Acute Appendicitis, Acute Necrotizing Appendicitis with Perforation). The data were collected, analysed.

Surgical Procedure

Under spinal anaesthesia, open Appendectomy done. At the end of the operation, the surgical area washed using saline solution and close in layers. All collected Appendectomy specimens were sent for histopathological examination.

Biochemical Analysis

Routine haematological parameters were examined in EDTA anti-coagulated venous blood samples taken on admittance and sent to the department of pathology laboratory. The platelet Count, MPV(Mean Platelet Volume), Total Leukocyte Count (TLC), Absolute Neutrophil Count and Lymphocyte Count were determined using 5 parts automated cell counter (ABX Pentra ES 60). The histogram was analysed. A peripheral blood smear was prepared and analysed for confirmation of the automated cell counter findings. Manual Platelet Count was performed using 1% ammonium oxalate, whenever necessary.

Statistical Analysis

All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.Patients were divided into 3 groups based on HPE: Group A (Normal Appendix), Group B (Acute Appendicitis) and group C (Acute Necrotizing Appendicitis with Perforation).

The association between HPE (Group A, B & C) and MPV, TLC, NC (Neutrophil Count), LC (Lymphocyte Count), PC, NLR, PLR was assessed

by comparing the median (Inter Quartile Range). Kruskal Wallis test was used to assess statistical significance. The association between HPE (Group A, B & C) and age group, gender, Rebound tenderness, Rovsing's Sign was assessed by cross tabulation and comparison of percentages. Odds ratio along with 95% CI is presented. Chi square test was used to test statistical significance.The utility of NLR, PLR in predicting HPE was assessed by Receiver Operative curve (ROC) analysis. IBM SPSS version 21 was used for statistical analysis.

Results

A total 136 people were included in the final analysis.Among the 136 patients 20 patients (14.7%) had a Normal Appendix in Histopathology, 106 patients (77.9%) presented with Acute Appendicitis and 10 patients had Acute Necrotizing Appendicitis with perforation.All the 136 patients were divided into 3 groups based upon the HPE examination. They were categorized based upon the age groups. Among the 20 patients in Group A 7 patients (35%) were in the age group of less than 30 years. 7 patients (35%) were in 31 to 40 years of age. In Group B where 106 patients presented with Acute Appendicitis 54 patients (50.9%) were less than 30 years of age. 27 patients (25.5%) in the age group of 31 to 40. In Group C where 10 patients presented with Acute

Appendicitis with perforation 3 patients (30%) were less than 30 years old. 2 patients (20%) presented in all three groups of 31 to 40, 41 to 50 and 51 to 60. There is no statistically significant association found between age groups and the groups categorized based upon the HPE examination.Among the 20 patients in Group A 15 were males and 5 were females. In group B of 106 patients majority of 60.4% were males 39.6% were females.

In Group C of 10 patients 7 were females and 3 were males. There is no statistically significant association found between gender and the groups of HPE. 16 patients in group A, 79 patients in group B, 8 patients in group C had rebound tenderness. 15 patients in group A, 67 patients in group B, 4 patients in group c had Rovsing's sign..No statistically significant difference found between the 3 groups on considering factors like rebound tenderness, Rovsing's sign, median MPV, median LC. There is a statistically significant difference found between the 3 groups on considering the parameters like TLC, NC, PC, NLR, PLR. On considering NLR and PLR, PLR had a better sensitivity and specificity of 80% and 70% respectively. Between group A and group B. between group B and group C, PLR is a better predictor with a sensitivity of 93% and a specificity of 65%.

Table 1 Descriptive analysis of three groups in study population (N=136)

HPE	Frequency	Percentage
Group A (Normal HPE Appendix)	20	14.7%
Group B (Acute Appendicitis)	106	77.9%
Group C (Acute Necrotising Appendictis with perforation)	10	7.4%
Total	136	100%

Table 2 Comparison of median MPV across HPE (N=136)

HPE	MPV	P value	Kruskal Wallis P value
Group A	10 (10, 11)	Group A vs B=0.285	

Group B	10.50 (10, 11)	Group A vs C= 0.267	0.435
Group C	11 (10, 11.25)	Group B vs C= 0.568	

Table 3 Comparison of median TLC across HPE (N=136)

HPE	TLC	P value	Kruskal Wallis P value
Group A	6700 (5735, 7325)	Group A vs B= <0.001	<0.001
Group B	9500 (7975, 12000)	Group A vs C= <0.001	
Group C	12557.50 (8942.50, 16170)	Group B vs C= 0.073	

Table 4 Comparison of median NLR across HPE (N=136)

HPE	NLR	P value	Kruskal Wallis P value
Group A	2.17 (2.05, 2.29)	Group A vs B= <0.001	<0.001
Group B	3.70 (3.40, 4.46)	Group A vs C= <0.001	
Group C	4.65 (3.70, 5.72)	Group B vs C= 0.051	

Table 5 Comparison of median PLR across HPE (N=136)

HPE	PLR	P value	Kruskal Wallis P value
Group A	77 (71.25, 90.75)	Group A vs B= 0.001	<0.001
Group B	122 (111, 131.25)	Group A vs C= <0.001	
Group C	146 (118.50, 204)	Group B vs C= 0.003	

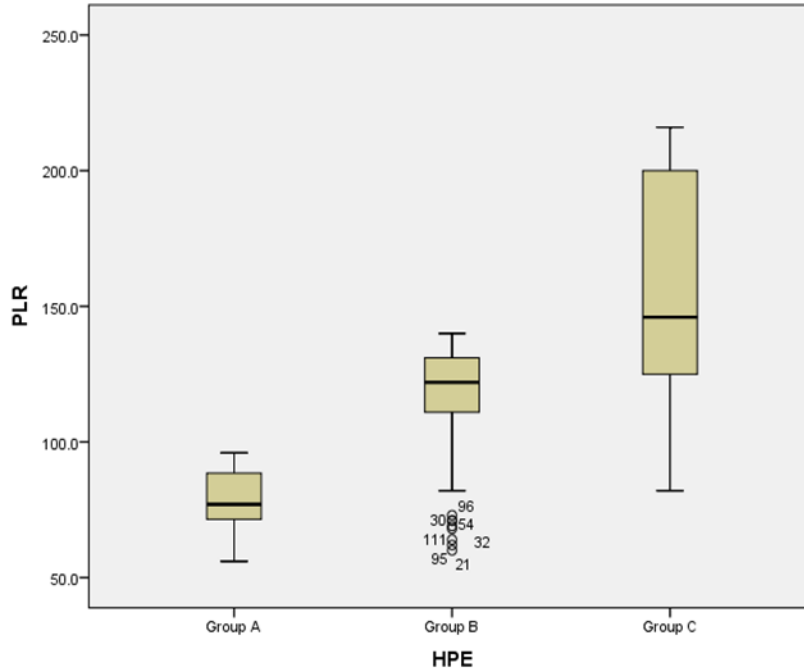**Figure 1 Box plot diagram of median PLR across HPE (N=136)**

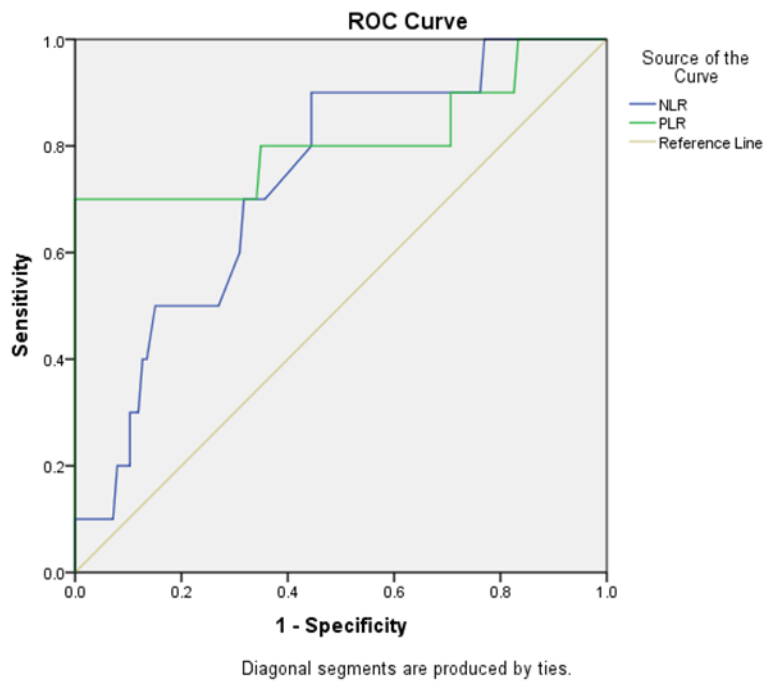**Figure 2 Predictive validity of NLR, PLR in predicting group A, B (ROC analysis)**

Figure 3 Predictive validity of NLR, PLR in predicting group A, C (ROC analysis)
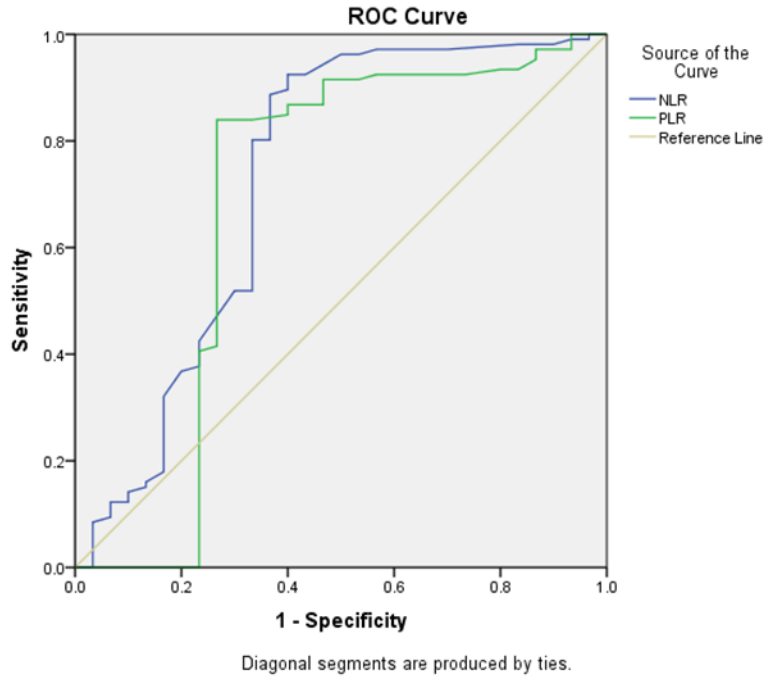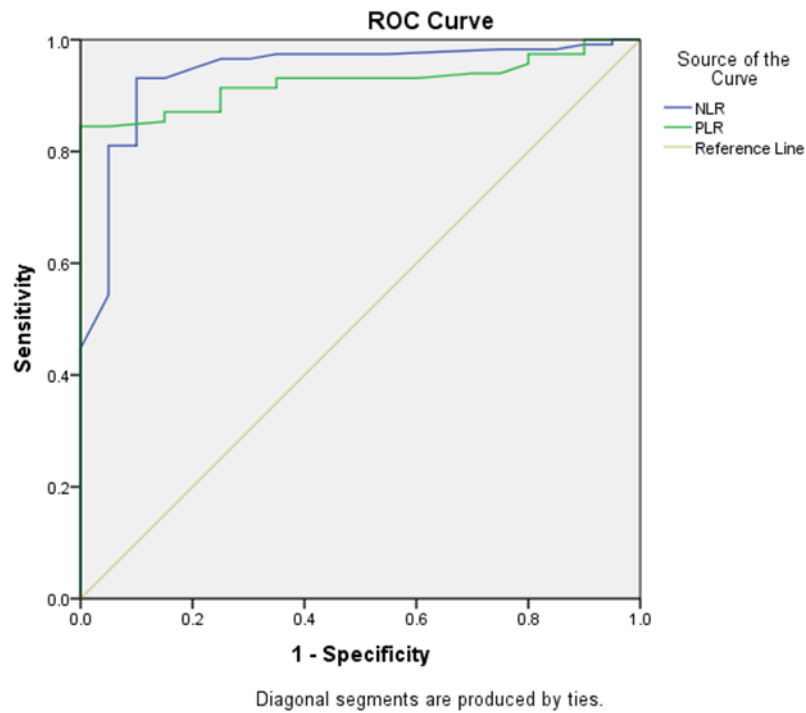

Figure 4 Predictive validity of NLR, PLR in predicting group B, C (ROC analysis)

	HEP	Area under the curve	P value	Cut off value	Sensitivity	Specificity
NLR	Group A, B	0.734	0.014	3.72	70%	65%
	Group A, C	0.729	<0.001	3.42	71%	67%
	Group B, C	0.94	<0.001	2.85	93%	85%
PLR	Group A, B	0.812	0.001	99.5	80%	70%
	Group A, C	0.686	0.002	115.50	63%	74%
	Group B, C	0.92	<0.001	82.50	93%	65%

Discussion

In our study around 64 patients out of the 136 were under the age of less than 30 years whereas 72 patients were greater than 30 years old. Males were 82 in number and females were 54 in number. Similar type of study participants in studies like FarukPehlivanli et al [9].No statistically significant difference found between the 3 groups on considering factors like rebound tenderness, Rovsing's sign, median MPV,median LC.There is a statistically significant difference found between the 3 groups on considering the parameters like TLC,NC,PC,NLR,PLR. The leucocyte count was decreased in Normal Appendix whereas comparatively it was increased in Acute Necrotizing Appendicitis with perforation and Acute Appendicitis. In a study conducted by Zuhoor K AI-Gaithy et al [10], TLC and NC were higher in patients with inflamed and complicated than Normal Appendix and in complicated than inflamed AppendixThe NC was also increased in Acute Necrotizing Appendicitis with perforation and Acute Appendicitis and decreased in Normal Appendix, whereas the LC is high in Acute Appendicitis and it is low in acute necrotizing appendicitis with perforation. PC was increased in group C and low in Group A.NLR and PLR both are higher in Acute Necrotizing Appendicitis with perforation and it is decreased in normal appendix. In a study conducted by DediPrasetya et al [11], Neutrophil to Lymphocyte Ratio has got a high accuracy for diagnosis of Acute Appendicitis and distinguishing a complicated Appendicitis from Non-complicated cases. A study by Shahab Hajibandah et al [12] had similar findings where Neutrophil to Lymphocyte Ratio predicts both diagnosis and severity of Appendicitis. In our study total LC, NC, LC, PC, NLR, PLR were used in differentiating Acute Necrotizing Appendicitis with perforation, Acute Appendicitis from Normal Appendix. Similar findings were observed in studies like Cinaret al.[13]

Based upon the ROC analysis it was observed that NLR as a better biomarker in differentiating acute appendicitis and acute necrotizing appendicitis with a sensitivity of 93% and a specificity of 85%.On considering PLR as a biomarker can differentiate acute appendicitis and acute necrotizing appendicitis with a sensitivity of 93% and a specificity of 65%. PLR is a better biomarker in differentiating normal appendix from acute appendicitis with a sensitivity of 80% and a specificity of 70%.similar findings were obtained in studies likeYazaret al.[14]

Conclusion

Acute Appendicitis continues to be the most common surgical emergency. An accurate, safe and non-invasive approach for the diagnosis of Appendicitis is essential. The results of this study demonstrated that Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio values could be used as new biomarkers that could be helpful to differentiate Normal Appendix from Acute Appendicitis and as well as Perforated Appendicitis. They are cost effective and easily accessible parameters in resource poor settings. Therefore, in addition to medical history, surgical examination and imaging

techniques, they should be considered as reasonable tools in the evaluation of Acute Appendicitis and in predicting severity of Acute Appendicitis.

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