

A PROSPECTIVE STUDY TO ASSESS THE UTILITY OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF ACUTE APPENDICITIS

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ABSTRACT

Acute appendicitis is one of the most common causes of surgical emergencies in the world. It has signs and symptoms, like increased leukocyte count and right lower quadrant pain but their accuracy is questionable. Hence, it is necessary to improve the accuracy of diagnosis of acute appendicitis to prevent negative appendicectomies. In this study, we suggest that calculation of the Neutrophil to Lymphocyte ratio may provide a sensitive parameter in the preoperative prediction of acute appendicitis and may help preoperatively to differentiate complicated from non-complicated appendicitis.

METHODOLOGY

This prospective study was conducted at M.K.C.G Medical College and Hospital for a period of 2 years from August 2020 to July 2022. A total of 104 patients with complaints of right iliac fossa pain and clinically diagnosed to have acute appendicitis were considered. Clinical diagnosis was established by means of history, physical examination, laboratory, and radiological investigations. Complete blood count (includes Haemoglobin%, Total leucocyte count, Differential leucocyte count and Platelet count) was performed. The absolute neutrophil and absolute lymphocyte count was calculated and NLR derived from it.

RESULTS

In our study, the prevalence of appendicitis was higher in males (67.3%). The mean age of the patients was 36.39 +/-16.39 years. The maximum complications were seen in the age group of >55 years (81.25%). In the study, 5.8% of the patient's histopathology showed a normal appendix, 52.9% showed acute uncomplicated appendicitis and 41.3% showed acute complicated appendicitis. NLR with a cut-off value of 4.23 was estimated to differentiate normal appendix and acute appendicitis with a sensitivity of 86.8% and specificity of 60% and the NLR to differentiate between acute appendicitis and acute complicated appendicitis was taken as 5.5, with a sensitivity of 88.1% and 53.2%.

CONCLUSION

Neutrophil-to-Lymphocyte Ratio can predict both diagnosis of acute appendicitis and differentiate between complicated and uncomplicated appendicitis.

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen. The lifetime occurrence of this disease is approximately 7%, with perforation rates of 17-20%^{1,2,3,4}

The mortality risk is less than 1% in the general population, but can be around 50% in the elderly. Its diagnosis is mainly based upon clinical features with radiological investigations preserved for selected cases. Failure to diagnose acute appendicitis at an early stage may result in adverse outcomes including perforation which can be associated with significant morbidity and even mortality^{5,6}.

As severe phlegmonous or gangrenous appendiceal inflammation can perforate and cause peritonitis, emergency surgery is imperative for patients with acute appendicitis. Thus, correct evaluation of acute appendicitis helps the surgeons in stratifying the severity of acute appendicitis. Although there have been recent advances in the treatment of appendicitis, surgery is still the first choice for treatment of acute appendicitis⁷.

Despite imaging modalities and highly sensitive laboratory tests introduced into clinical use with developing technology, diagnostic difficulties are still experienced and higher perforation rates are encountered. The clinical diagnosis of appendicitis is based on clinical history and physical findings⁸.

However, in many published series, higher perforation (15-45%) and negative appendectomy (7-25%) rates demonstrate that despite evolving technological opportunities and clinical experience, a perfect diagnostic method has not yet been developed⁹. To supplement clinical diagnosis, laboratory investigations like TLC and CRP have been considered. The use of ultrasound (USG) for diagnosis has been widely accepted and studied. The Alvarado score and the Modified Alvarado score are used as diagnostic tools for acute appendicitis. While blood cells (WBC) counts are mostly elevated in patients with appendicitis¹⁰; however, an elevated WBC count has no predictive value in differentiating simple and complicated appendicitis^{11,12}. Elevated serum bilirubin has been shown to be a potential marker for perforation of appendix, but it lacks adequate sensitivity and specificity¹³⁻¹⁵. C-reactive protein (CRP) was found to be superior to bilirubin for anticipation of perforation in acute

appendicitis¹⁶. Identifying a tool or marker that can predict the diagnosis of acute appendicitis and can differentiate uncomplicated and complicated appendicitis with good sensitivity and specificity is still a subject of interest among many researchers.

However, up to date, there is no confirmatory laboratory marker for the diagnosis and prognosis of acute appendicitis.

In recent years, some researchers have reported on the predictive value of the neutrophil/lymphocyte ratio (NLR) for inflammation, which can be used as a diagnostic parameter in the perioperative diagnosis of acute appendicitis. Though there have been a few studies on NLR, all of them have reported that NLR appears to have greater diagnostic accuracy than traditional diagnostic laboratory tests (either white blood cell or C-reactive protein alone). It is also reported that NLR is an independent predictor of positive appendicitis histology.

NLR is simple to calculate and involves no additional cost, as it uses results from a standard complete blood count. The NLR is derived from the counts of circulating neutrophils and lymphocytes, both of which are major leucocyte populations. The inflammation-triggered release of arachidonic acid metabolites and platelet activating factors results in neutrophilia and cortisol-induced stress which further results in relative lymphopenia, and thus, the NLR accurately represents the underlying inflammatory process.

NLR provides information regarding two different immune and inflammatory pathways which may make it a potential marker to predict acute appendicitis and its severity. The neutrophil count highlights active and continuation of inflammation, whereas the lymphocyte count highlights the regulatory pathway.

In view of the above context, we suggest that NLR may provide a sensitive parameter in preop prediction of Acute Appendicitis and may help to differentiate complicated from noncomplicated appendicitis. Complicated appendicitis will include perforated and gangrenous appendicitis. NLR may prevent negative appendicectomies based on its predictive value.

AIMS AND OBJECTIVES: -

The objectives of the study are:

- o To evaluate the utility of NLR in pre-operative prediction of acute appendicitis
- o To differentiate between complicated and non-complicated appendicitis

MATERIALS AND METHODS

The present study was conducted at M.K.C.G. Medical College and Hospital, Berhampur during the period of August 2020 to July 2022

STUDY DESIGN

A 2-year prospective study.

STUDY PERIOD

2 year study from August 2020 to July 2022

SOURCE OF DATA

All consecutive cases coming to the emergency department and OPD of M.K.C.G. Hospital with complaints of right iliac fossa pain and diagnosed to have acute appendicitis by clinical, radiological and laboratory investigations.

SAMPLE SIZE

Sample size was calculated using the following formula: -

$$\text{Sample Size} = \frac{Z^2 \times P \times (1-P)}{d^2}$$

Where, Z = 1.96 (Standard Deviation at 95% Confidence Interval)

P = Expected Percentage from population

d = 0.05 (Expected margin of error)

Based on patient's number admitted to the Dept. of General Surgery, M.K.C.G Medical College and Hospital, Berhampur with a confirmed diagnosis of acute appendicitis fitting the inclusion criteria and underwent surgery, the time frame dictates the estimated sample size to be around 50 cases per annum. So, the sample size encountered during the study period was 100 cases. A total of 104 patients diagnosed to have acute appendicitis by clinical, radiological and laboratory investigations were selected.

SELECTION CRITERIA

Inclusion criteria

- All patients diagnosed as acute complicated or uncomplicated appendicitis clinically on admission, operated upon and confirmed by histopathological examination

Exclusion criteria

- All patients other than acute complicated or uncomplicated appendicitis were excluded.
- Presence of malignant diseases.
- Current course of chemotherapy or radiotherapy.
- Intraoperative diagnosis of intraabdominal pathologies other than appendicitis.
- Presence of known liver disease.

PROCEDURE

Ethical clearance for the study was obtained from Ethical Clearance Committee, M.K.C.G. Hospital, Berhampur. All patients who came to the Emergency Department and OPD of M.K.C.G. Hospital with complaints of right iliac fossa pain and diagnosed to have acute appendicitis were considered. The eligible patients were explained about the nature of the study and a written informed consent was taken. Thorough history was taken and clinical examination was done and was recorded on a predesigned and pretested proforma. Clinical diagnosis was done by means of history, physical examination, laboratory investigations and radiological investigations.

Complete blood count which included

- Haemoglobin%
- Total leucocyte count
- Differential leucocyte count
- Platelet count

Was measured as a part of routine lab investigations. The absolute neutrophil and absolute lymphocyte count derived from the above investigations was calculated and Neutrophil-to-Lymphocyte Ratio (NLR) was derived from it.

The diagnosis was confirmed with histopathological examination of acute appendicitis. Histopathological examinations of the appendix which showed gangrene, perforation and abscess were considered as acute complicated appendicitis.

STATISTICAL ANALYSIS OF DATA

All the quantitative parameters such as age, neutrophil-to-lymphocyte ratios (NLR), etc. were presented using descriptive statistics such as mean \pm SD, etc.

All qualitative variables like gender, types of complications, etc were presented using frequency and percentage.

ROC Curve analysis was performed to find the optimum cut-off value of NLR in predicting Acute Appendicitis.

Specificity, Sensitivity, Positive Predictive value, Negative Predictive value, and Odds Ratio also was calculated using a 2*2 table.

	UNCOMPLICATED APPENDICITIS	COMPLICATED APPENDICITIS
NLR<CUT-OFF VALUE	a	b
NLR>CUT-OFF VALUE	c	d

- SENSITIVITY= $a/a+c * 100$
- SPECIFICITY= $d/b+d * 100$
- POSITIVE PREDICTIVE VALUE= $a/a+b * 100$
- NEGATIVE PREDICTIVE VALUE= $d/b+d * 100$
- ODDS RATIO = ad/bc

OBSERVATIONS AND RESULTS

TABLE 1

SEX DISTRIBUTION

Total no. of subjects (N)=104

Sex	Frequency	Percent	Valid percent
Female	34	32.7	32.7
Male	70	67.3	67.3
Total	104	100.0	100.0

GRAPH 1: SEX DISTRIBUTION

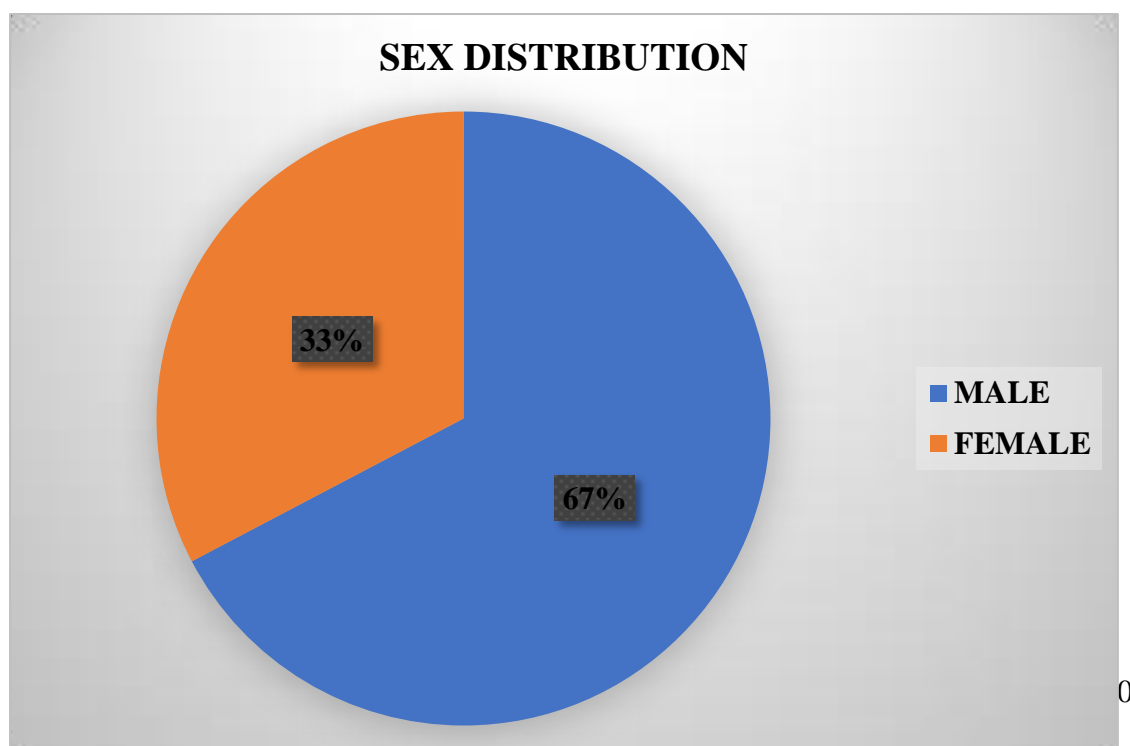
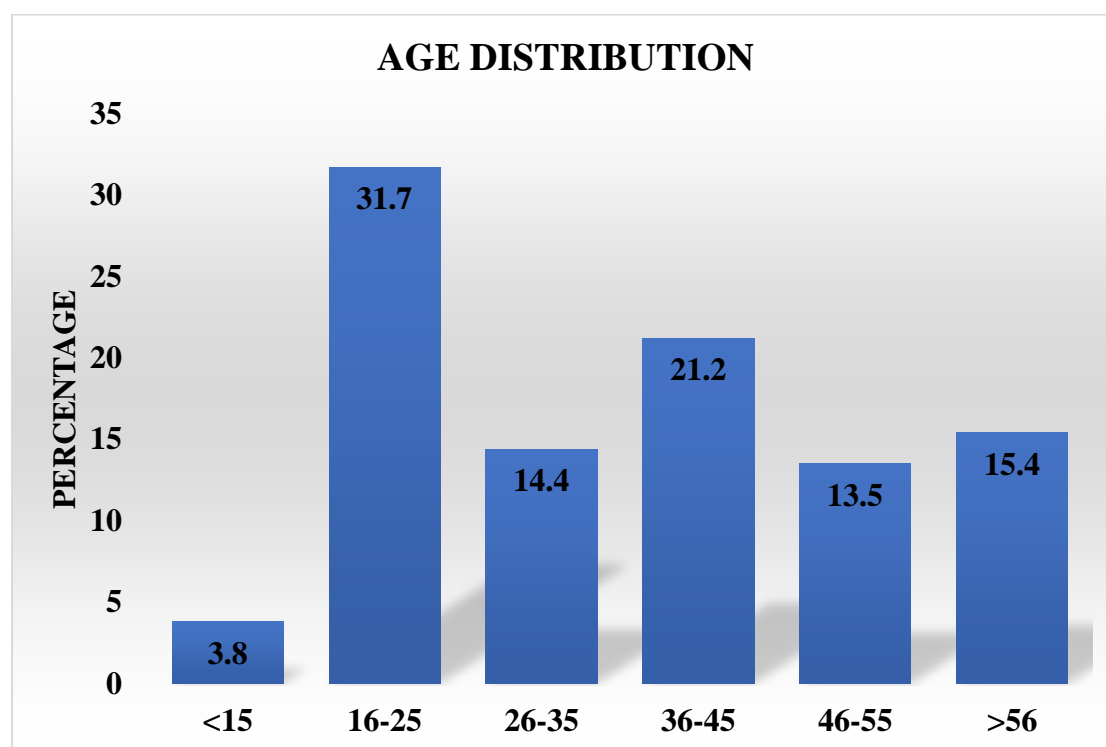


TABLE 2: AGE DISTRIBUTION

The age range for patients in our study was observed to be between 8 and 82 years, with median age of 35 years and a mean age \pm SD of 36.39 ± 16.39 years.

GRAPH 2: AGE DISTRIBUTION

The most common age group in our study was 16- 25 (31.7%) and 36- 45(21.2%) years.

TABLE 3: DISTRIBUTION OF SYMPTOMS AND SIGNS

SYMPTOMS/SIGNS	PERCENTAGE (%)
Pain abdomen	100
Rebound tenderness	46.1
Anorexia	42.3
Nausea/vomiting	69.2
Fever	38.4

GRAPH 3: SYMPTOMS AND SIGNS

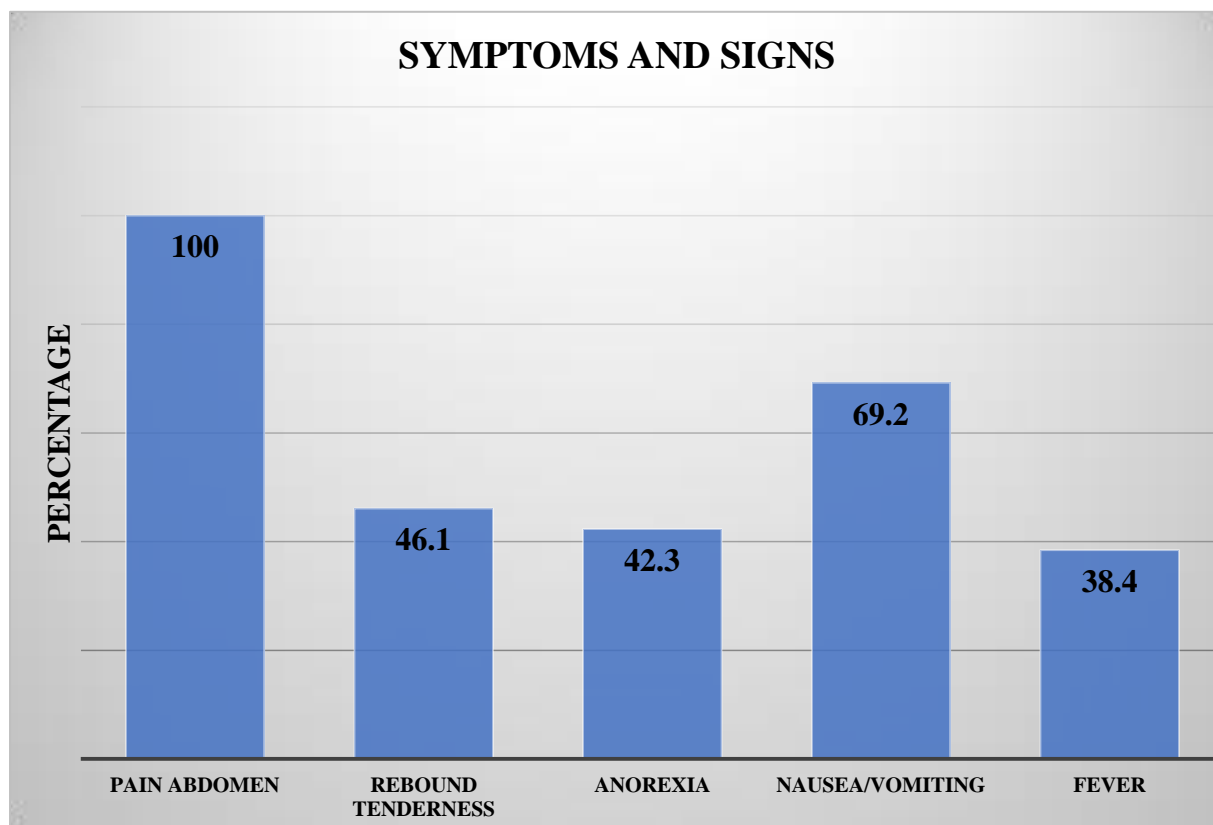
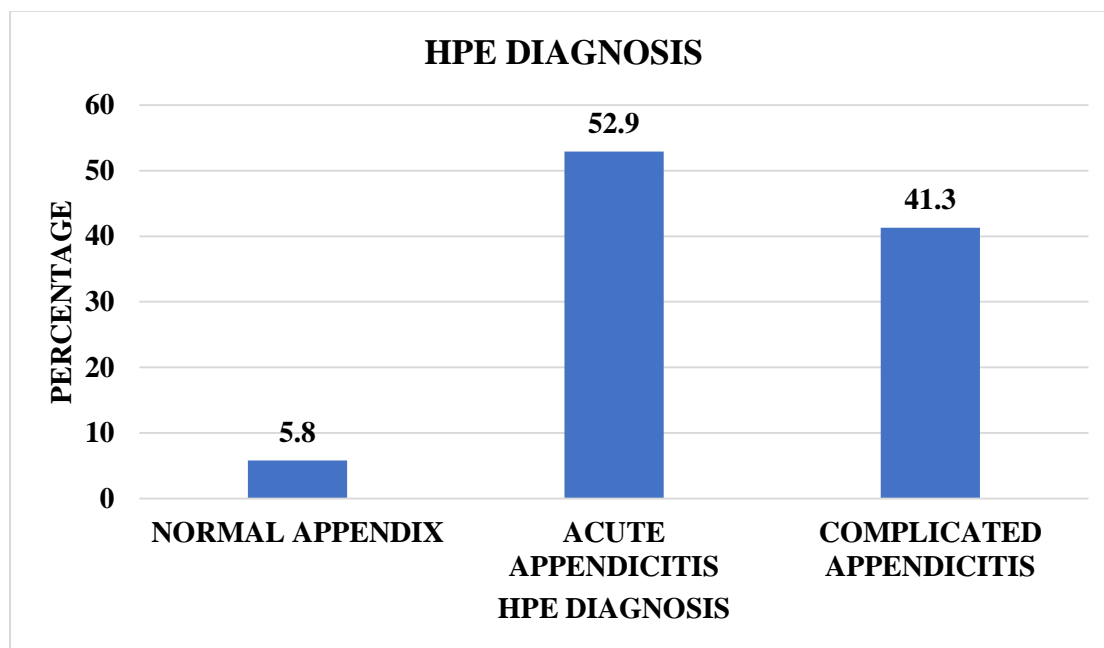


TABLE 4: DISTRIBUTION OF PATIENTS WITH RESPECT TO HISTOPATHOLOGICAL DIAGNOSIS

HPE REPORT	FREQUENCY	PERCENT
NORMAL APPENDIX	6	5.8
ACUTE APPENDICITIS	55	52.9
ACUTE APPENDICITIS(COMPLICATED)	43	41.3
TOTAL	104	100

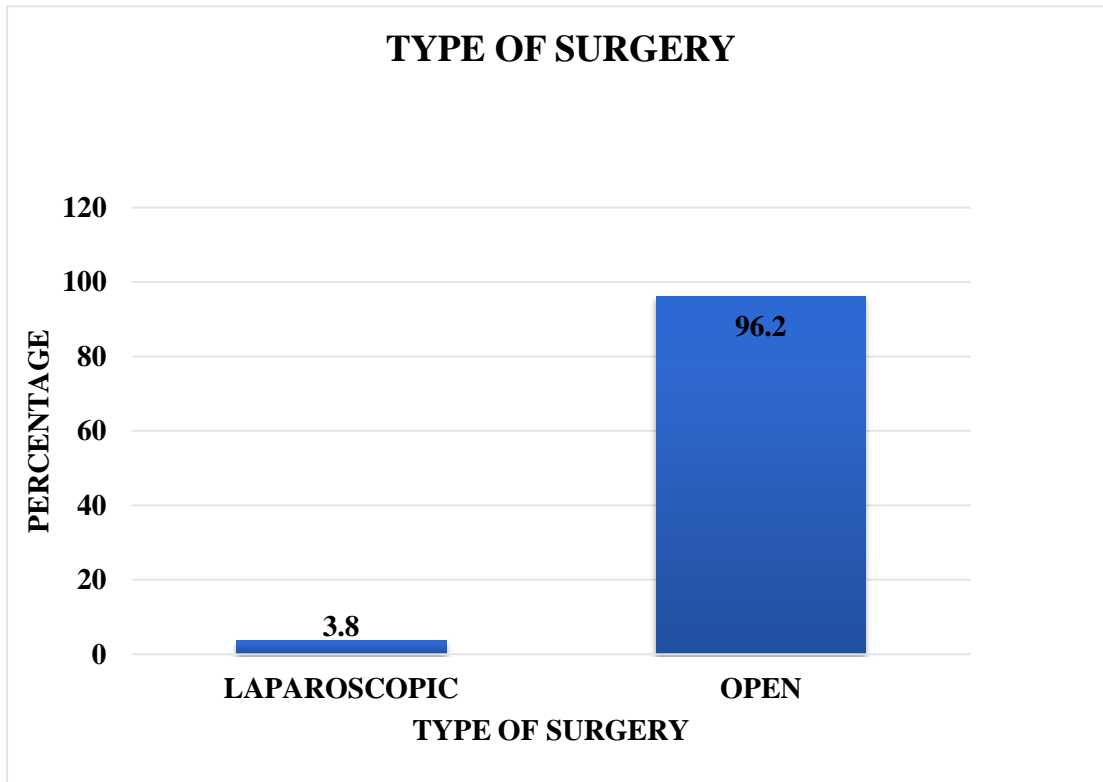
GRAPH 4: DISTRIBUTION OF PATIENTS ACCORDING TO HPE DIAGNOSIS

Of the 104 patients operated, 5.8% showed normal appendix on histopathology, 52.9% showed acute uncomplicated and 41.3% showed acute complicated appendicitis.

TABLE 5: DISTRIBUTION OF PATIENTS ACCORDING TO THE TYPE OF SURGERY

TYPE OF SURGERY	NO. OF PATIENTS	PERCENTAGE (%)
LAPAROSCOPIC	4	3.8
OPEN	100	96.2
Total	104	100

GRAPH 5: DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF SURGERY

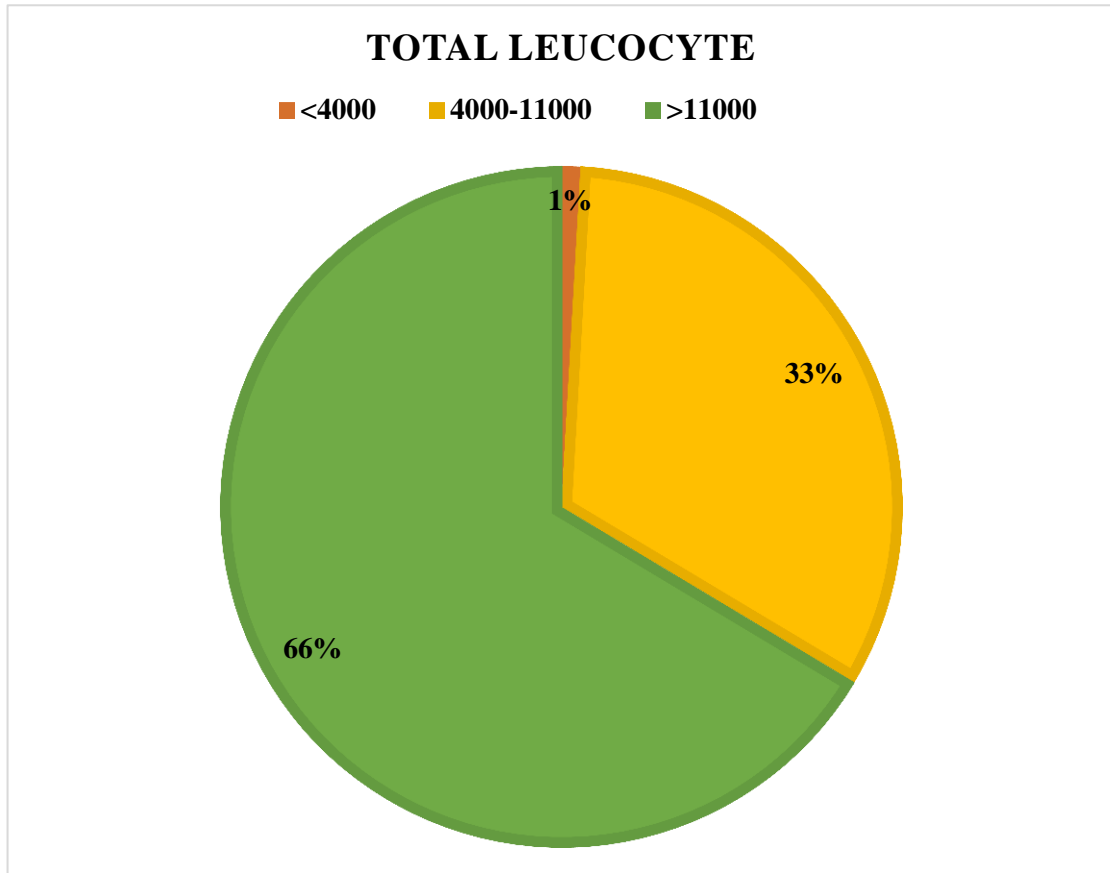


In our study, all the 104 subjects underwent appendicectomy. 4 patients (3.8%) underwent laparoscopic surgery and 100 patients (96.2%) underwent open surgery.

TABLE 6: TOTAL LEUCOCYTE COUNT DISTRIBUTION

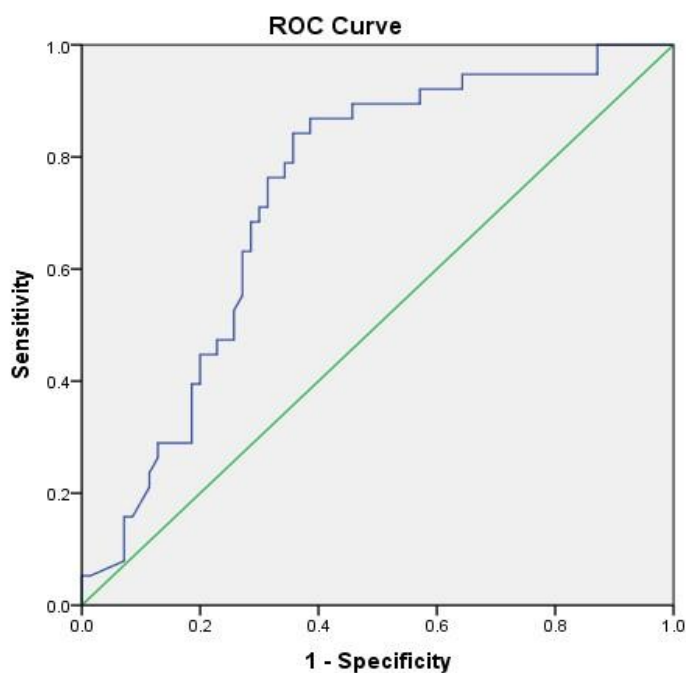
TOTAL LEUCOCYTE COUNT	NO.OF PATIENTS	PERCENTAGE(%)
<4000	1	0.961538
4000-11000	34	32.69231
>11000	69	66.34615
TOTAL	104	100

GRAPH 6: TOTAL LEUCOCYTE DISTRIBUTION



In our study, the normal range of TLC was taken as 4,000-11,000 cells/mm³ which had 32.7% of the patients. 0.96% of the patients had TLC <4,000 cells/mm³ while 66.4% of the patients had TLC >11,000 cells/mm³. The mean was 15367.43±12225 cells/mm³.

GRAPH 7: ROC CURVE FOR NLR TO DIFFERENTIATE BETWEEN NORMAL APPENDIX AND ACUTE APPENDICITIS



Diagonal segments are produced by ties.

After analyzing the co-ordinates, the best cut-off was determined as **4.23** with a sensitivity of **86.8%** and specificity of **60%** with a p value of <0.001.

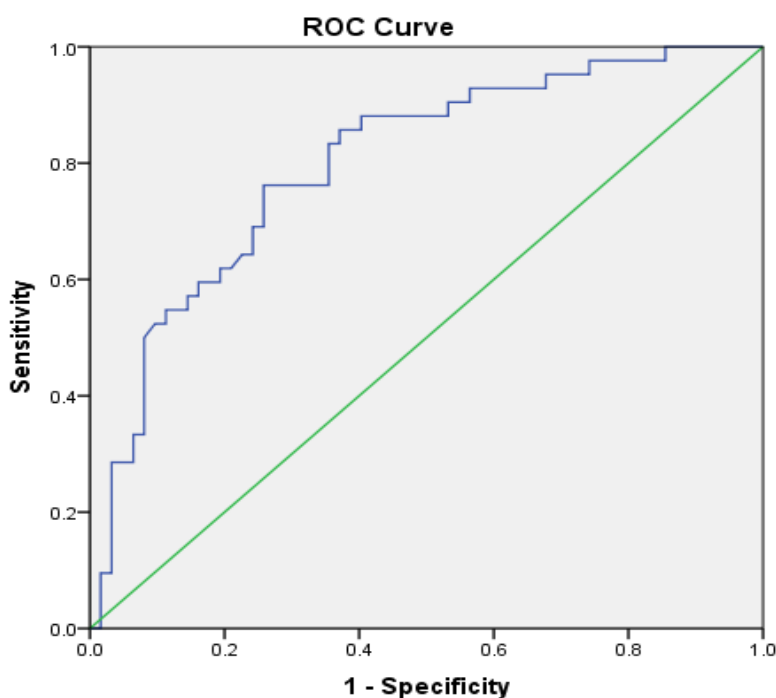
The area under the curve was **73.3%** (AUROC).

The following co-ordinate was rounded off to the closest integer value of 3 and was taken as cut-off for the NLR ratio in predicting acute appendicitis.

ROC CURVE FOR ESTIMATION OF NLR(I)

An ROC curve constructed taking neutrophil-to-lymphocyte ratio against patients suffering from acute uncomplicated and complicated appendicitis.

GRAPH 8: ROC CURVE FOR ESTIMATION OF NLR(I) TO DIFFERENTIATE BETWEEN ACUTE UNCOMPLICATED AND COMPLICATED APPENDICITIS



Diagonal segments are produced by ties.

itivity of

The area under the curve was 80% The following co-ordinate was rounded off to the closest integer value of 5.5 and was taken as cut-off for the NLR ratio in predicting the severity of acute appendicitis.

TABLE 7: AGE DISTRIBUTION AND NLR

NLR	AGE DISTRIBUTION						TOTAL
	<15	16-25	26-35	36-45	46-55	>55	
< 4	1	2	4	5	3	0	15
> 23	3	31	11	17	11	16	89
Total	4	33	15	22	14	16	104

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.536 ^a	5	.0129
Likelihood Ratio	10.698	5	.058
Linear-by-Linear Association	.050	1	.823
N of Valid Cases	104		

a. 7 cells (58.3%) have expected count less than 5. The minimum expected count is .58.

GRAPH 9: AGE DISTRIBUTION AND NLR

Acute appendicitis was commonly seen in the age group (16-25) and 36-45 years with 31 and 17 patients in each group respectively.

Age was not found to be significantly associated with NLR with a p value of 1.29.

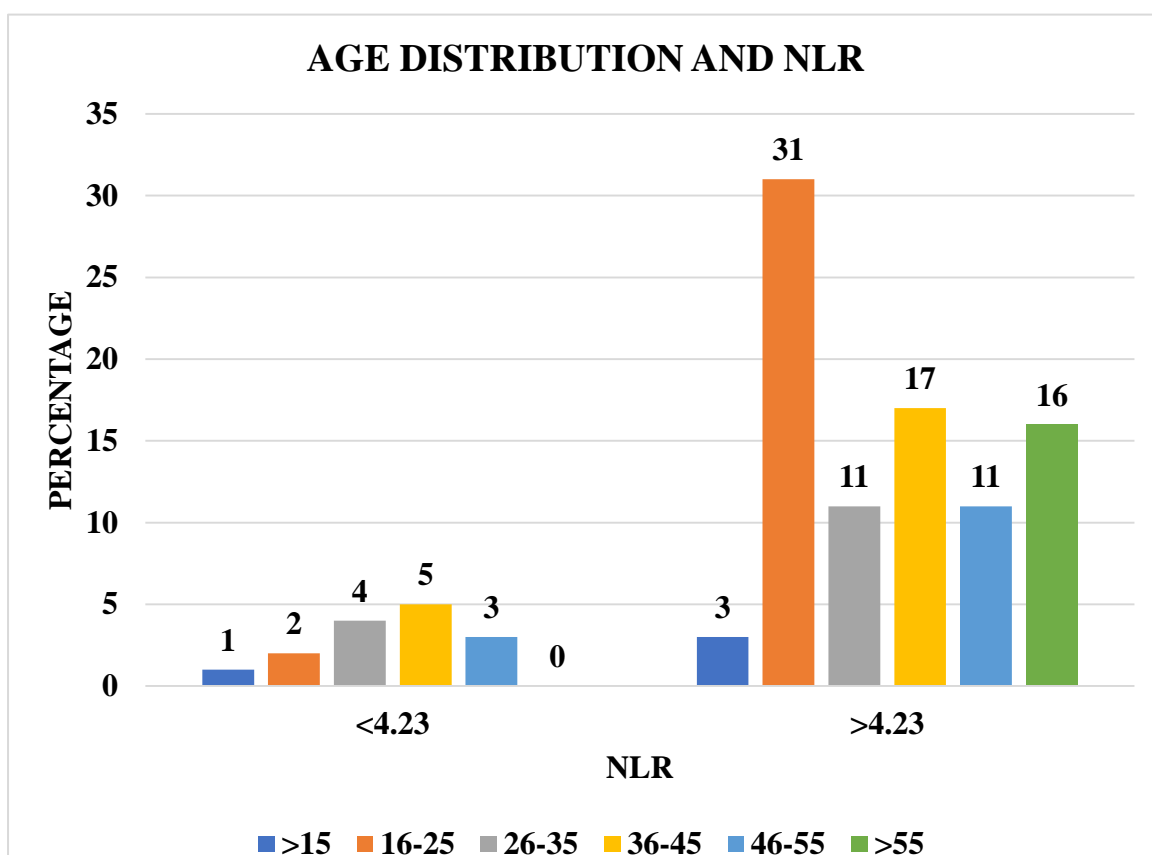


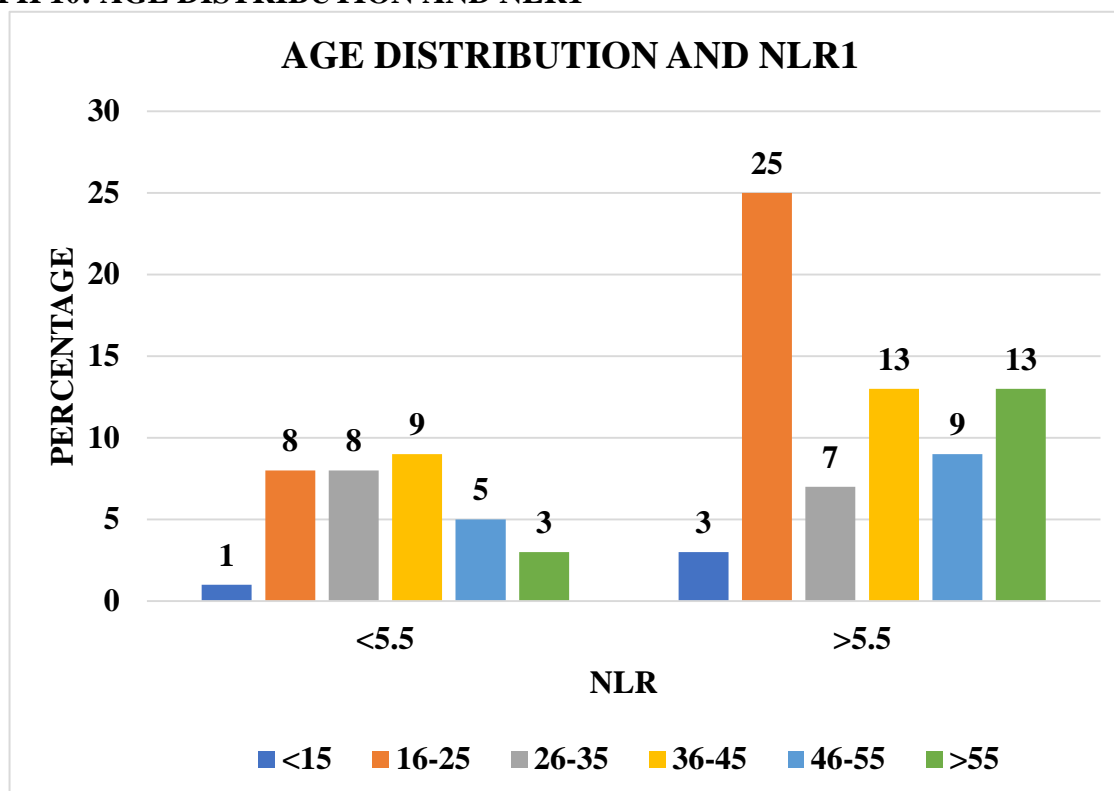
TABLE 8: AGE DISTRIBUTION AND NLR1

NLR	AGE DISTRIBUTION						TOTAL
	<15	16-25	26-35	36-45	46-55	>55	
< 5.5	1	8	8	9	5	3	34
> 5.5	3	25	7	13	9	13	70
Total	4	33	15	22	14	16	104

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.229 ^a	5	.285
Likelihood Ratio	6.212	5	.286
Linear-by-Linear Association	.008	1	.931
N of Valid Cases	104		

a. 4 cells (33.3%) have expected count <5. The minimum expected count is 1.31.

GRAPH 10: AGE DISTRIBUTION AND NLR1

The maximum patients (25 patients were seen in the age group 16-25 years) Age was not significantly associated with NLR (p value=0.285)

TABLE 9: SEX DISTRIBUTION AND NLR

SEX	NLR		Total
	≤4.23	>4.23	
Female	8	26	34
Male	7	63	70
Total	15	89	104

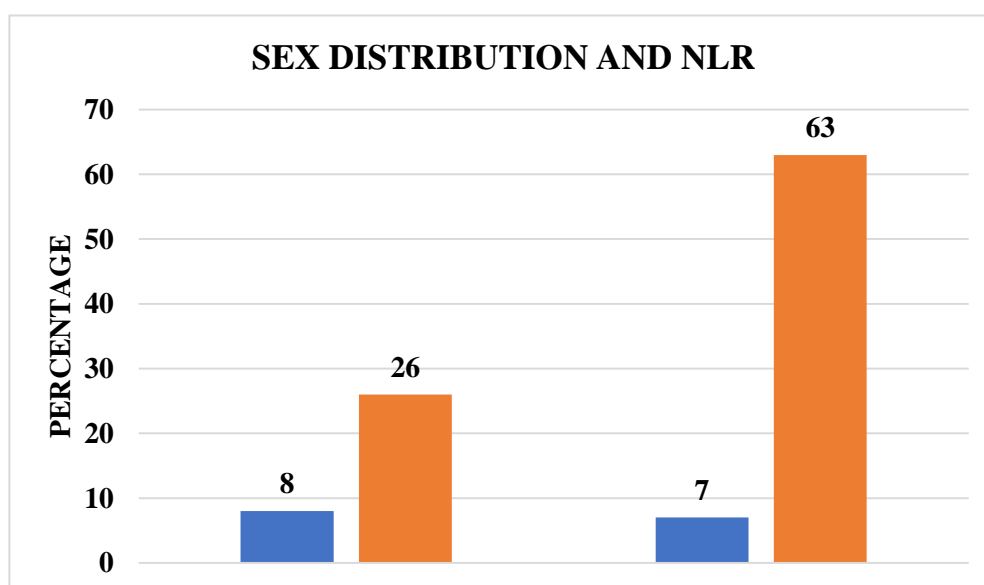
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.394 ^a	1	.065		
Continuity Correction ^b	2.386	1	.122		
Likelihood Ratio	3.202	1	.074		
Fisher's Exact Test				.079	.064
N of Valid Cases	104				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.90.

b. Computed only for a 2x2 table

GRAPH 11: SEX DISTRIBUTION AND NLR



The no. of males in acute appendicitis group (63 patients) was higher than the females (26 patients). Sex was not significant to NLR with a p value of 0.122.

TABLE 10: NLR1 AND HOSPITAL STAY(DAYS)

NLR	DAYS IN HOSPITAL		TOTAL
	<= 8	> 8	
<=5.5	28	6	34
5.5	54	16	70
Total	82	22	104

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.372 ^a	1	.542	.617	.368
Continuity Correction ^B	.126	1	.723		
Likelihood Ratio	.381	1	.537		
Fisher's Exact Test					
Linear-by-Linear Association	.369	1	.544		
N of Valid Cases	104				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.19.

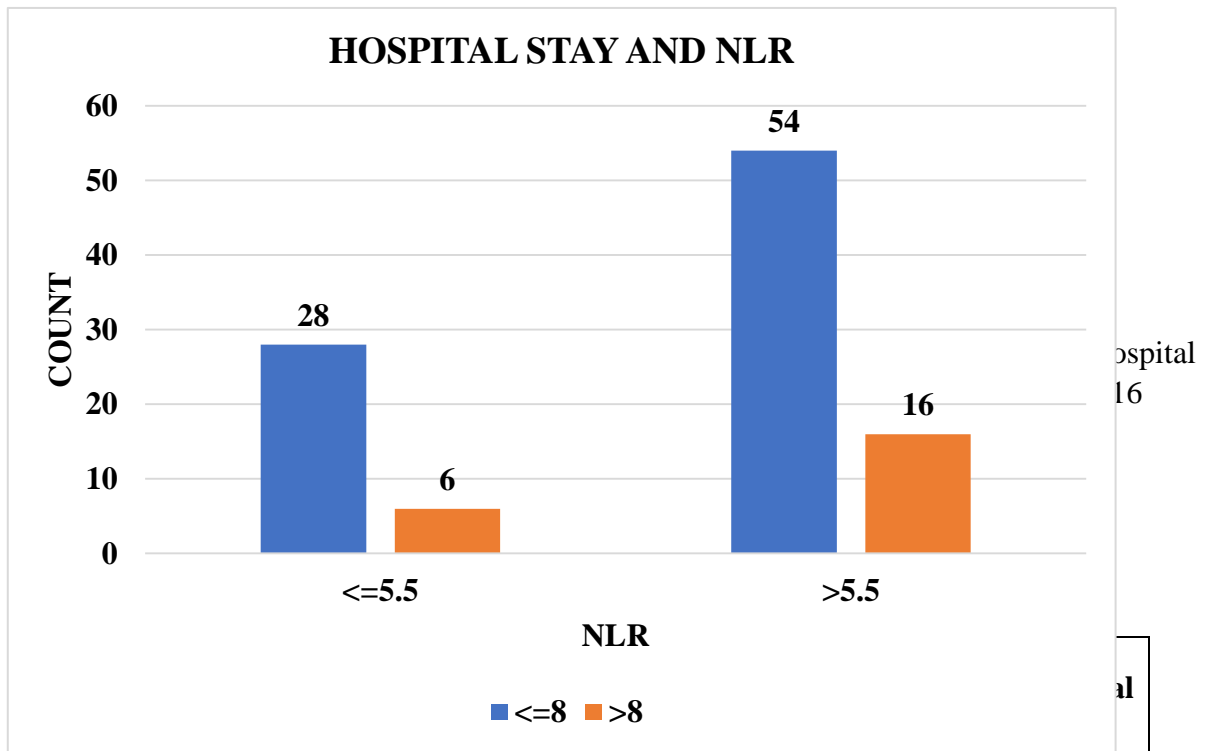
b. Computed only for a 2x2 table

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper

Odds Ratio for NLR ($\leq 5.5 / 5.5$)	1.383	.487	3.925
N of Valid Cases	104		

GRAPH 12: NLR1 AND HOSPITAL STAY



≤ 5.5	29	5	34
5.5	33	37	70
Total	62	42	104

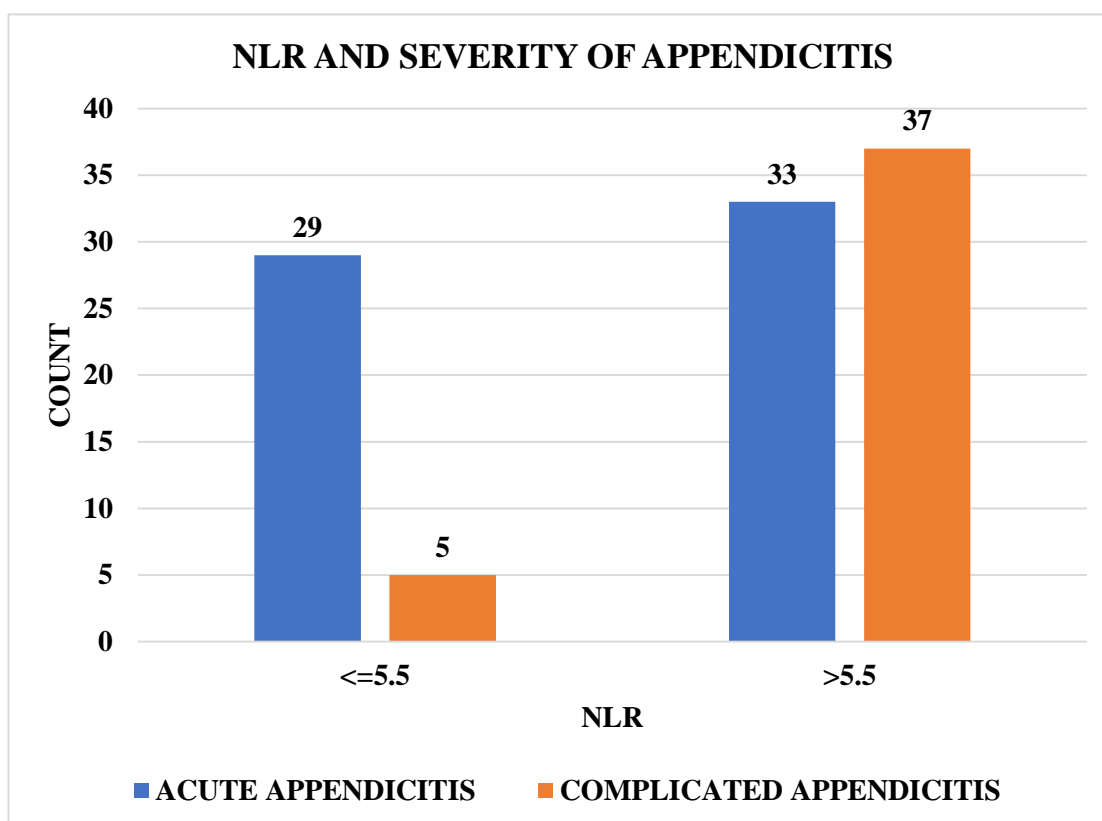
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	17.870 ³	2	.000
Likelihood Ratio	18.897	2	.000
Linear-by-Linear Association	17.542	1	.000
N of Valid Cases	104		

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 1.96.

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for NLR	9.900	3.447	28.437
N of Valid Cases	108		

GRAPH 13: NLR AND SEVERITY OF APPENDICITIS



In our study, 85.3% of patients with NLR <5.5 had acute uncomplicated appendicitis and 52.8% of the patients with NLR <5.5 had acute complicated appendicitis. NLR and severity of appendicitis was significant with p value =0.000. Odds ratio was 9.90- a patient with NLR>5.5 has 9.9 times higher the risk of developing acute complicated appendicitis than those with NLR <5.5.

TABLE 12: NLR AND TOTAL LEUCOCYTE COUNT

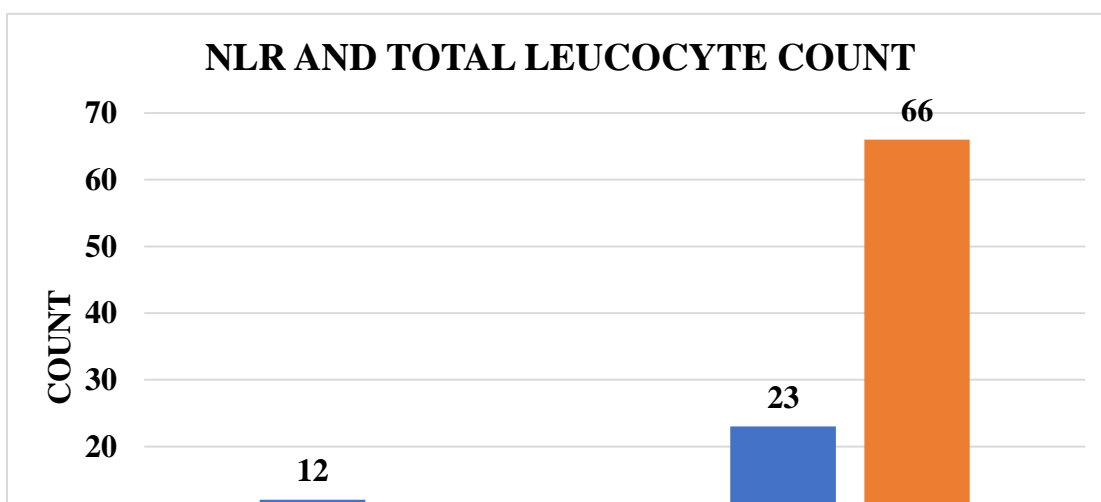
NLR	TOTAL LEUCOCYTE COUNT		Total
	<= 11000	> 11001	
<= 4.23	12	3	15
>4.23	23	66	89
Total	35	69	104

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	16.862 ^a	1	.000		
Continuity Correction ^b	14.524	1	.000		
Likelihood Ratio	16.130	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	16.700	1	.000		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.05.

b. Computed only for a 2x2 table

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for (<= 4.23 / >4.23)	11.478	2.972	44.331
N of Valid Cases	104		



In this study, 80% of the patients with NLR<4.23 had TLC <11,000 cells/mm³ and 74.1% patients with NLR>4.23 had TLC >11,000 cells/mm³. NLR and Total Leucocyte count association was found to be significant with p value <0.001.

Odds ratio was 11.48 - Patients with NLR>4.23 had 11.48 times the chances of having TLC >11,000 cells/mm³ than those with NLR<4.23.

TABLE 13 NLR AND TYPE OF SURGERY

NLR	TYPE OF SURGERY		Total
	LAPAROSCOPY	OPEN	
<=5.5	2	32	34
5.5	1	69	70
Total	3	101	104

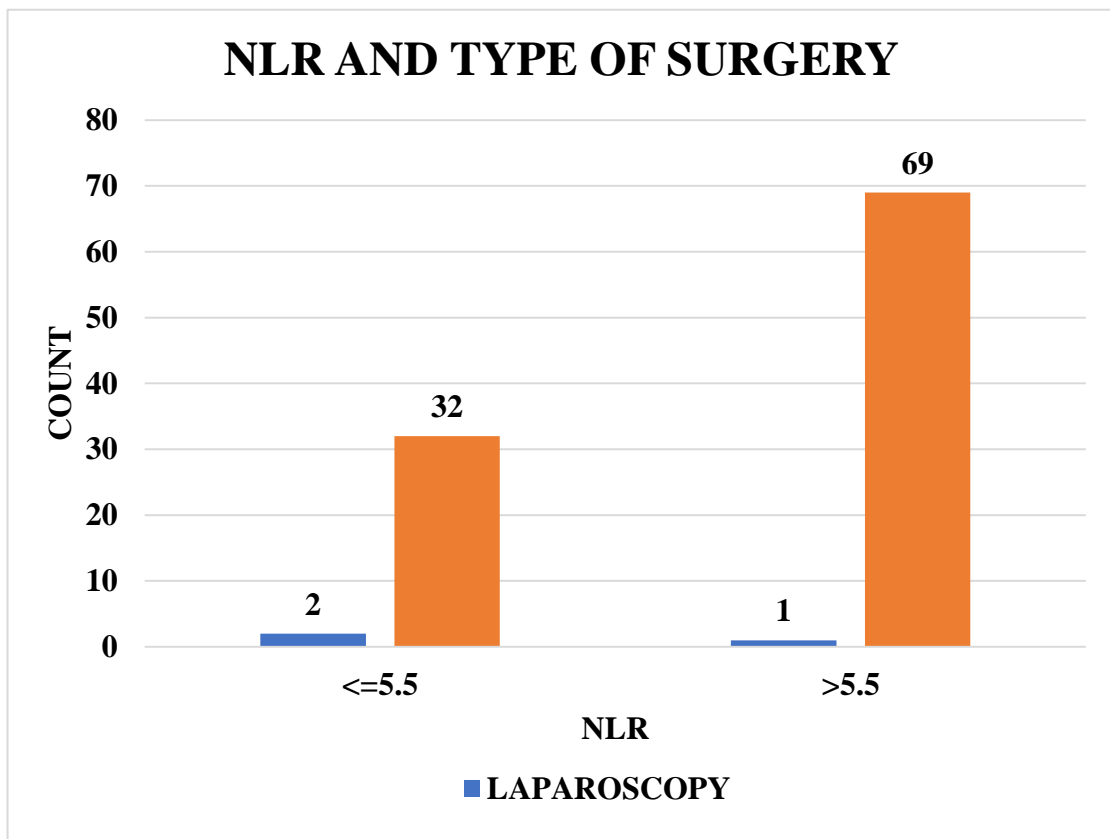
Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.620 ^a	1	.203		
Continuity Correction ^b	.421	1	.517		
Likelihood Ratio	1.492	1	.222		
Fisher's Exact Test				.249	.249
Linear-by-Linear Association	1.605	1	.205		
N of Valid Cases	104				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .98.

b. Computed only for a 2x2 table

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for NLR ($\leq 5.5 / 5.5$)	4.313	.377	49.319
N of Valid Cases	104		

GRAPH 15: NLR AND TYPE OF SURGERY



In our study, 5.8% of the patients with NLR <5.5 underwent laparoscopic appendicectomy whereas 98.5% of the patients with NLR >5.5 underwent open appendicectomy. NLR was not significantly associated with the type of surgery with a p value of 0.203.

DISCUSSION

In our present study, a total of 104 subjects were studied. It was noted that the prevalence of appendicitis was higher in males (67.3%) as compared to females (32.7%) and the male:female ratio was 2.05:1. These findings were consistent with a recent study by Ishizuka et al.⁷ which reported a higher incidence of appendicitis in males (53.6%) than females (46.3%). In the study by Ishizuka et al.,⁷ 86.5% of the males and 73.7% of the females had complicated appendicitis and gender was found to be a significant factor. In our study, though complicated appendicitis was seen in 71.42% of the males and 58.8% of the females, gender was an insignificant factor.

In this study, the range of age distribution of the patients was from 8 to 82 years with a median of 35 years and a mean age of 36.39 +/-16.39 years. The maximum no. of subjects was seen in the age group of 16-25 years and 36-45 years with 31.7% and 21.2% patients in each group respectively. The maximum complications were seen in the age group of 16-25 years with a 75.75%, 59% in the age group 36-45 and 81.25% in the age group >55. In a study by Kahramanca et al.,⁴ the mean age of the analysed group was 31.22±11.9 years. In a study by Ishizuka et al.,⁷ acute appendicitis tends to occur in relatively young individuals. It is well known that diagnosis of acute appendicitis in older patients is more difficult than in younger patients. Several previous studies have demonstrated that older patients sometimes lack not only the typical symptoms of acute appendicitis but also the characteristic laboratory data abnormalities.

In this study, all the 104 patients underwent appendectomy and the appendix was sent for histopathological examination. 5.8% of the patient's histopathology showed a normal appendix, 52.9% showed acute uncomplicated appendicitis and 41.3% showed acute complicated appendicitis. In the index study by Kahramanca et al.,⁴ a normal appendix was seen in 15.9% patients, while acute uncomplicated and complicated appendicitis was seen in 70.6 and 13.4% patients respectively. In a study by Kelly et al., the negative appendectomy rate was 12.9%. The percentage of negative appendectomies performed at our institution was 5.8%. In a study by Kum et al.,¹⁹ the authors found that appendectomies were performed on patients with normal (14%), inflammatory (70%) and perforated (16%) appendices.

38% and 96.2% patients underwent laparoscopic and open appendectomies respectively. There was no incidence of conversion of laparoscopic surgery to open surgery.

For all the 104 patients who were clinically diagnosed to have appendicitis, blood samples were sent for the measurement of TLC. 4,000cells/mm³ - 11,000 cells/mm³ was taken as the normal range. 32.7% patients had a TLC within the normal range, 66.4% of the patients had TLC >11,000cells/mm³ whereas 0.9% had a TLC>4,000 cells/mm³ showing that majority of the patients with appendicitis had a TLC within the normal range. In a study by Dnyanmote et al.,²⁰ the highest cut-off for TLC was 11,000cells/mm³.

In a study by Yazici et al.,¹⁸ an NLR >3.5 has maximum sensitivity. They also indicated that higher N/L ratios have increased specificity and positive predictive value, while the most valuable results were obtained at NLR >5. In 2014, Kahramanca et al.,⁴ published a study estimated the cut-off value of NLR as 4.68 to differentiate between normal appendix and inflamed appendix. The acute appendicitis group was divided into complicated and non-complicated appendicitis, the cut-off value for NLR was estimated as 5.74, with a 70.8%

sensitivity and 48.5% specificity. In limited number of published studies, a higher diagnostic value of NLR relative to conventional laboratory evaluations (leukocyte counts, C-reactive protein) has been indicated.

In a study by Kahramanca et al.,⁴ the researchers detected a diagnostic significance of NLR >4.68 for acute and NLR >5.74 for uncomplicated AA. However, normal ranges of NLR do not rule out a potential diagnosis of AA. Though in some publications higher cut-off values have been indicated, Ishizuka et al.,⁷ detected a lower cut-off value for NLR. Ishizuka et al.,⁷ reported cut-off value for NLR of 8 in the differential diagnosis of gangrenous appendicitis. In a study by Erkan et al.,¹⁷ 3.93 was taken as the cut off for NLR to differentiate between acute appendicitis and normal appendix. As it is seen when cut-off value gets smaller it is more efficient to diagnose AA, when cut-off value gets bigger it is more efficient to diagnose non sick patients.

In our study, NLR with a cut-off value of 4.23 was estimated to differentiate normal appendix and acute appendicitis. This NLR had a sensitivity of 86.8% which means that 60% of the patients whose diagnosis of acute appendicitis was confirmed by histopathology, have an elevated NLR. The specificity of this NLR was 60% which means it can detect 60% of the false negatives.

The cut-off value for NLR to differentiate between acute appendicitis and acute complicated appendicitis was taken as 5.5, with a sensitivity of 88.1% and 53.2%. The cut off value for complicated appendicitis was slightly higher than the NLR to predict acute appendicitis but the sensitivity and the specificity were almost similar (86.8% and 88.1%; 60% and 53.2%).

This data could have been so because of the low incidence of normal appendix in our study in comparison to the inflamed appendices. In the study by Ishizuka et al, the cut-off value for gangrenous appendicitis was considered to be 8 and the values in our study were found to be much lower than that. In the study of Yazici et al.,¹⁸ it was reported that the sensitivity is maximum when NLR is >3.5 , but specificity and PPV increase steadily when NLR increases, and the most prominent values are reached when NLR is >5 .

On comparing NLR to age distribution, it was not found to be significant (p value=0.285). In the study by Ishizuka et al, age >40 was found significant (p >0.001). On analysis of gender and NLR, gender was not found to be significant (p=0.122) which is in consistent with the study by Ishizuka et al.,⁷ There was no significant relation with the NLR and the length of the hospital stay in our study. The hospital stay in the patients could have been prolonged due to related co-morbidities and complications in the post op period.

In our study, on analysing the NLR against the TLC, it was found to be significant (p=0.00) where 74.1% of the patients in with complicated appendicitis had a TLC $>11,000$ cells/mm³. In a study by Erkan et al.,¹⁷ TLC was found to be significant (p <0.001).

SUMMARY

Acute appendicitis is one of the most common causes of surgical emergencies in the world. The diagnosis of acute appendicitis still remains a dilemma in spite of various advances in laboratory and radiological investigations. It is necessary to improve the accuracy of

diagnosis of acute appendicitis to prevent negative appendicectomies. Though there have been a few studies on NLR, all of them have reported that NLR appears to have greater diagnostic accuracy than traditional diagnostic laboratory tests. NLR is simple to calculate and involves no additional cost, as it uses results from a standard complete blood count.

In this study, we suggest that calculation of the NLR may provide a sensitive parameter in the preoperative prediction of acute appendicitis and may help preoperatively to differentiate complicated from non-complicated appendicitis.

The present study with a design of a prospective study was conducted for a period of 2 years at M.K.C.G. Medical College and Hospital from August 2020 to July 2022. A total of 104 patients were studied who were diagnosed to have acute appendicitis and underwent emergency appendicectomy.

In our study, it was noted that the prevalence of appendicitis was higher in males (67.3%) as compared to females (32.7%) and the male: female ratio was 2.05:1. The range of age distribution of the patients was from 8 to 82 years with a median of 35 years and a mean age of 36.39 +/-16.39 years. The maximum no. of subjects was seen in the age group of 16-25 years and 36-55 years with 31.7% and 21.2% patients in each group respectively. The maximum complications were seen in the age group of 26-35 years with a 75.75%, 59% in the age group 36-45 and 81.25% in the age group >55. Of all the patients who underwent appendicectomy, 5.8% of the patient's histopathology showed a normal appendix, 52.9% showed acute uncomplicated appendicitis and 41.3% showed acute complicated appendicitis.

4,000cells/mm³ - 11,000 cells/mm³ was taken as the normal range of the Total Leucocyte Count sent for all patients clinically diagnosed to have acute appendicitis. 32.7% patients had a TLC within the normal range, 66.4% of the patients had TLC >11,000cells/mm³ whereas 0.9% had a TLC <4,000 cells/mm³ showing that majority of the patients with appendicitis had a TLC more than the normal range.

In recent years, some authors reported that the neutrophil-to-lymphocyte ratio (NLR) is a predictor of inflammation and useful in the preoperative diagnosis of Acute Appendicitis.

In our study, we estimated the cut-off value for NLR to diagnose acute appendicitis was 4.23 with a sensitivity of 86.8% and a specificity of 60%. The cut-off value for NLR to differentiate between acute complicated and acute uncomplicated appendicitis was 5.5 with a sensitivity of 88.1% and 52.3%. Age distribution and sex was not considered to be significant in comparison to NLR with p values of 0.285 and 0.122. NLR was significantly associated with the histopathology report of acute complicated and uncomplicated appendicitis with p value <0.001.

Thus, in our study, we conclude that, preoperatively estimated NLR can be accepted as an easily available, affordable, adjunctive data as a factor in the diagnosis of acute appendicitis and also in predicting the severity of acute appendicitis.

An NLR with a cut-off value of 4.23 can be used in the diagnosis of acute appendicitis and an NLR of 5.5 can be used to differentiate between acute uncomplicated and complicated appendicitis.

CONCLUSION

In the present study, we conclude that

- Preoperatively estimated NLR can be accepted as an easily available, affordable, adjunctive data as a factor in the diagnosis of acute appendicitis and also in predicting the severity of acute appendicitis.
- An NLR with a cut-off value of 4.23 can be used in the diagnosis of acute appendicitis and an NLR of 5.5 can be used to differentiate between acute uncomplicated and complicated appendicitis.

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