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Original Research Article

Lymphocyte-to-C-reactive Protein (CRP) Ratio: A New Biomarker to Predict Perforation in Acute Appendicitis

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Abstract:

Background: In Appendicitis is a frequent cause of abdominal pain worldwide. Around 18%-34% of patients may present with perforations & risk of life. Various inflammatory markers have been evaluated in this regard one such is the Lymphocyte to C reactive protein ratio which has shown to be a promising inflammatory marker with high sensitivity & specificity in the differentiation of perforated & non-perforated appendicitis cases.

Aims & Objectives: The study aimed to assess the role of the Lymphocyte to C reactive protein ratio in predicting perforation in acute appendicitis.

Material & Methods: This prospective observational study recruited 120 patients who underwent surgery for acute appendicitis who came to our Tertiary care Hospital between January 2022 and August 2022. Patients > 18 yrs of age, diagnosed with acute appendicitis and perforated acute appendicitis were included. For all the patients, preoperative complete blood count, and C reactive protein was undertaken, and histopathological samples were sent for analysis. The patients were divided into two groups: Group A included nonperforated acute appendicitis (n=102); Group B included perforated appendicitis cases (n=18). Age, gender, preoperative WBC count, platelets count, neutrophil count, lymphocyte count, C reactive protein, postoperative length of hospital stay & Lymphocyte to C reactive protein ratio were recorded.

Results: Mean age in Group A was 38. 45±14.65 yrs while in Group B it was 49.67 ±16.43 yrs. The mean age in Group B was statistically significantly higher than Group A ($p<0.05$). Out of 120 patients with appendicitis, 58.4 % were males, and 41.6% were females. Average hospitalization days in group A were 1.52±1.21 which was statistically significantly lower than in Group B 4.72±1.01 days ($p <0.05$). The values of WBC, platelet, neutrophil & CRP values were statistically significantly higher in Group B ($p <0.05$). The lymphocyte and LCR values were statistically significantly lower in group B. LCR at a cut of 0.23, had a sensitivity & specificity of 74.8% & 84.4% at a 95% confidence interval.

Conclusion: Thus, this study concludes that Lymphocyte to C reactive protein ratio an inflammatory marker can be used as a potential tool for predicting perforation in acute appendicitis patients. It is an easily available affordable marker with high sensitivity and specificity.

Keywords: Acute Appendicitis, Lymphocyte to C reactive protein ratio (LCR), perforated Appendicitis, Inflammatory markers

Introduction

Acute Appendicitis (AA) is the most common acute gastrointestinal inflammatory disorder in adults, frequently requiring surgery & hospital stay. There is a risk of 7-8% in the lifetime of an individual to develop AA. [1] Appendicitis is most prevalent in the 11-30-year-old age group.[2]. Recently, Appendicitis cases in 31-40 yrs. of age patients have increased to 19.40%.[3] AA is grouped as simple and complicated. Simple appendicitis is a suppurative or phlegmonous appendicitis with or without intraabdominal abscess. Complex appendicitis includes gangrenous appendicitis, perforated appendicitis (PA), and/or appendicitis with abscess formation. [4] The incidence of perforation is ranged between 20% and 30% but it can be up to 50% in older age groups.[5]

The standard management is emergency appendicectomy. Previous beliefs that every AA will develop into PA with high mortality rates led to early appendicectomy without delay. Sallinen V in a meta-analysis in 2016 reported the development of complicated appendicitis in 5-28% of all appendicitis cases, with perforation at 20%.[6] Gavriilidis P et al 2019 observed a 0.3% mortality rate in simple appendicitis to 6% in PA. Thus, early diagnosis & timely intervention is essential to prevent complications.[7] Confirmation of diagnosis is done by radiological imaging techniques like ultrasonography, and computed tomography. In the recent past, various inflammatory biomarkers have been assessed as an easy, inexpensive potent tool for early diagnosis of complications like a perforation in AA cases.[8]

Ünal Y et al 2018 [9] &Yazar et al 2015[10] observed the potential role of inflammatory markers like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) for the differentiation of AA and A. Lymphocyte-to-C-reactive protein ratio (LCR) has been shown to be potential inflammatory mediator predicting prognosis in various diseases. Okugawa et al. noted a reduction in the perioperative LCR level to be a negative prognostic factor for disease-free survival in colon cancer cases. Reduction in LCR level is an independent predictive factor in short-term follow-up for complications after surgery.[11] Ugurlu et al 2021, evaluated LCR to predict perforation in AA.[12] Thus, the present prospective observational study was designed to assess the role of LCR in predicting perforation in acute appendicitis.

Material & Methods

This prospective observational study recruited 120 patients who underwent surgery for acute appendicitis who came to our Tertiary care Hospital between January 2022 and August 2022.

Patients > 18 yrs of age, diagnosed with acute appendicitis and perforated acute appendicitis were included. Exclusion criteria in our study pregnant females, patients with known rheumatological, hematological, and oncological diseases, those with acute cardiovascular disease, and patients with known kidney and liver failure were excluded.

For all the patients, preoperative complete blood count, and CRP was undertaken, and histopathological samples were sent for analysis. LCR was calculated by the ratio of lymphocyte counts to CRP.

Approval from the Hospital ethics committee was sought. Written informed consent was sought from all the patients.

The patients were divided into two groups: Group A – nonperforated acute appendicitis (n=102) and Group B – perforated appendicitis (n=18)

The following parameters were recorded age, gender, preoperative WBC, platelets, neutrophil, lymphocyte, CRP, postoperative length of stay, and LCR.

Statistical analysis:The collected data were tabulated & put into statistical analysis using the SPSS(Version 22). Demographic

variables were reported as number (n) and percentage (%). Continuous variables were reported as mean ±SD. Intergroup comparison is done using the Chi-square test. At a 95% confidence interval $p<0.05$ was taken as statistically significant.

Results

Out of 120 patients who underwent appendicectomy, Group A (n=102) included 85% of patients who had no perforation. Group B (n=18) included 15 % of patients who had perforation. The mean age of Group A patients was 38. 45±14.65 yrs while in Group B it was 49.67 ±16.43yrs. The mean age in Group B was statistically significantly higher than Group A ($p<0.05$). Out of 120 patients with appendicitis, 58.4 % were males, and 41.6% were females.

Table 1: Depicts the values of WBC, platelet, neutrophil, lymphocyte, CRP, and LCR in Group A and Group B

Blood Parameters	Group A (mean ±SD)	Group B (mean ±SD)	P value
WBC	12.6±3.51	15.55±2.49	<0.05
Platelet	220.5±58.7	265.5±116.9	<0.05
Neutrophil	7.62±3.15	12.52±3.43	<0.05
Lymphocyte	1.58±0.78	1.02±0.27	<0.05
CRP	4.82±2.28	11.81 ± 09.61	<0.05
LCR	0.42±0.54	0.08±0.13	<0.05

Average hospitalization days in group A were 1.52±1.21 which were statistically significantly lower than in Group B i.e., 4.72±1.01 days ($p <0.05$).

The values of WBC, platelet, neutrophil and CRP values were statistically significantly higher in Group B ($p<0.05$). The lymphocyte and LCR values were statistically significantly lower in Group B. (Table 1) LCR at a cut-off of 0.23, had a sensitivity & specificity of 74.8% & 84.4% at a 95% confidence interval.

Discussion

This prospective observational study compared the LCR ratio between the patients undergoing appendicectomy. Out of 120 patients who underwent appendicectomy, Group A (n=102) included 85% of patients who had no perforation. Group B (n=18) included 15 % of patients who had perforation. Similarly, Livingstone et al study stated the rate of perforation variation from 16% to 40%, with higher cases observed in younger age groups (40-57%) & in patients >50 yrs (55-70%).[13]

The mean age of Group A patients was 38. 45±14.65 yrs while in Group B it was 49.67 ±16.43yrs. The mean age in Group B was statistically significantly higher than in Group A ($p<0.05$). In Ugurlu et al 2021, the average age of the AA group was 37.79 ±15.34 & perforation group was 45.97 ±15.72 yrs with the difference being statistically significantly.12In the present study, out of 120 patients, 58.4 % were males & 41.6% were females. Similarly, in Ugurlu et al 2021 study, 41.7% of females and 197 men (59.3%) were observed, the difference between groups being statistically significant. But the study disagrees it is clinically significant.[12]

In the present study, Group A observed the average hospitalization to be 1.52±1.21 days which was statistically significantly lower than in Group B which was 4.72±1.01 days ($p<0.05$). Consistent findings were noted by Ugurlu et al 202112. Andersson RE 2013 observed the average hospital stay to be three-fold in the perforation group.[14]

In the present study, an increase of WBC, platelet, neutrophilic counts & CRP were noted in both groups with statistically significantly higher counts in Group B. Consistent with the results of our study,

Şahbaz et al 2014 observed statistically higher WBC count in patients with complicated appendicitis. The area under curve value for leucocyte count & neutrophil was 0.596 & 0.500 respectively. WBC counts were more efficient to predict acute appendicitis diagnosis.[15]

Anderson M 2008 discussed a neutrophil ratio >85% being associated with appendicular necrosis and perforation. Şahbaz et al 2014 noted no statistically significant difference in the neutrophil ratio between simple and complicated appendicitis. Thus, the neutrophil ratio was not a significant laboratory test sufficient to predict complicated appendicitis.[15] Al-Gaithy et al study in 456 patients with appendicitis stated that WBC and neutrophil counts, could not be used as single diagnostic markers as they have low sensitivity and specificity & do not show the severity of appendicular inflammation. [16]

In the present study, Lymphopenia was observed in all the patients with a greater reduction in Group B which was statistically significant (<0.05). In acute inflammation, increased severity of infection & stressful situations with the rise in cortisol production, a greater reduction in lymphocytes is observed.[17] In the present study, CRP values were higher in Group B (11.81 ± 09.61) as compared to Group A (4.82±2.28). Similarly, in Ugurlu et al 2021 study CRP in the perforation group (10.36±10.56) were statistically significantly higher than non-perforated group (4.74±2.550).[12] CRP has widely been used as an indicator of acute inflammation with a half-life of 16 hr with values reaching up to 1000 folds after acute stimulus.[18] Consistent to this, Özozan ÖV et al 2020, observed CRP > 35 mg/dl to be a significant marker of inflammation of the appendix.[19]

In the present study, at LCR cut off 0.23, sensitivity & specificity at 95% confidence intervals were 74.8% & 84.4%. Similarly, Ugurlu et al 2021 observed at an LCR cut-off of 0.223, the area under curvature was 0.742 & Sensitivity & specificity at 95% confidence intervals were 76.5% & 78.7%. When compared to NLR & PLR, LCR had a higher specificity and sensitivity.[12] Eyvaz K 2022 study in the receiver operating characteristic curve (ROC) analysis noted at a cutoff of 0.17 value LCR had 52% sensitivity and 88.2% specificity.[20]

In the present study, low LCR has been noted in Group B patients with perforated appendicitis. Similarly, Ugurlu et al 2021 study observed low lymphocyte count & low LCR in perforated appendicitis patients.[12] Lagunas-Rangel FA 2020, reported low LCR levels can predict poor prognosis in coronavirus disease patients.[21] An LCR level <0.02 with 80% sensitivity & 80.2% specificity can be useful in predicting intestinal ischemia in strangulated hernia cases.[22] Ullah et al 2020 study, observed low LCR values to be an indicator of mortality in COVID-19 patients.[23]

Conclusion

The early diagnosis of acute appendicitis is still a challenging task. The delay in treatment or other interventions can pose a risk of perforations. Thus, differentiation of patients at risk of perforations is of utmost importance to decrease mortality & duration of hospital stay. Further, LCR can be an inexpensive & easy inflammatory marker when other imaging modalities are not available. It has a high sensitivity & specificity in the identification of perforated appendicitis cases & serves as a promising tool.

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