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Correlation Between Systemic Inflammatory Physiology and Severity of Appendicitis in Patients Undergoing Appendectomy

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ABSTRACT

Background: Appendicitis is a common surgical emergency that has a spectrum of mild cases of inflammation, gangrene, and perforation. Systemic inflammatory markers could play a significant role in predicting disease severity before surgery.

Objectives: To determine the relationship between the healthcare objective of appraising systemic inflammatory physiology and the severity of appendicitis in patients who have undergone appendectomy.

Methods: A cross-sectional study was conducted on 89 patients who underwent appendectomy. Preoperative laboratory investigations, including TLC, neutrophil count, CRP, ESR, PCT, NLR, and PLR—along with clinical examination and imaging findings were documented. The severity of appendicitis was categorized intraoperatively and histopathologically into simple, suppurative, gangrenous, and perforated types. Associations between inflammatory biomarkers and disease severity were assessed using statistical comparisons and correlation analyses.

Results: The majority of patients (64%) reported within 24-48 hours of symptom onset. The distribution of severity of appendicitis was straightforward (36.0%), suppurative (30.3%), gangrenous (20.2%), and perforated (13.5%). CRP, PCT, NLR, PLR, and TLC demonstrated a progressive tendency in increasing by the severity. A correlation was greater with CRP ($r = 0.71$, $p < 0.001$) than with PCT ($r = 0.66$), NLR ($r = 0.62$), and TLC ($r = 0.54$).

Conclusion: CRP, PCT, and NLR are systemic inflammatory biomarkers with strong associative relationships to the severity of appendicitis and can be useful predictors of complicated disease. By introducing these parameters into clinical assessment, early detection, risk assessments, and operations could become better and more notable in resource-limited environments.

Keywords: appendicitis, systemic inflammation, CRP, procalcitonin, NLR, PLR, leukocytosis, severity, appendectomy, histopathology.

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INTRODUCTION

One of the most frequent causes of acute abdominal pain and surgical emergent treatment, among all nations worldwide, is appendicitis, which continues to pose a diagnostic and therapeutic challenge despite the availability of better imaging and perioperative care [1]. Appendicitis has a mild and uncomplicated clinical presentation to severe and progressive, and involves gangrene, perforation, abscess formation, and generalized peritonitis [2]. There is a need to know what adds to this variability to improve the quality of diagnosis that is made, to make better decisions on treatment, and to reduce morbidity following surgery [3]. It is emerging that appendicitis is rather an inflammatory event of the system, primarily triggered by the activation of

the innate immune system, the release of cytokines, neutrophil responses, oxidative stress, and metabolic changes in the body system [4]. The systemic physiologic changes increase with heightened inflammatory cascade, as indicated by biomarkers of total leukocyte count (TLC), neutrophil percentage, C-reactive protein (CRP), procalcitonin (PCT), erythrocyte sedimentation rate (ESR), and ratios neutrophil-to-lymphocyte ratio (NLR) and platelets-to-lymphocyte ratio (PLR) [5]. Not only are they indicators of the presence of inflammation, but markers with their gravity in relation to the disease and indicators of complications are increasingly becoming established [6].

Clinical uses of the relationship between systemic physiology of inflammation and the severity of appendicitis pathology are especially relevant in circumstances with restricted or time-sensitive surgical decision-making or time-sensitive or early stratification of high-risk cases [7]. The advanced stages that have been noted to be accompanied by elevated inflammatory markers include suppurative appendicitis, gangrenous transformation, perforation, and diffuse peritonitis. Additionally, systemic reactions, such as fever, tachycardia, leukocytosis, and the increase in the level of acute-phase reactants, tend to accompany the severity of inflammation of the appendix and its prediction [8]. Although evidence abounds, inconsistencies in setting biomarker thresholds, differences in populations, and inconsistent diagnostic criteria have restricted the clinical use of these biomarkers as predictors of severity on a larger scale [9]. Validated biochemical and physiological correlations are essential in resource-limited areas to enhance early diagnosis and avoid unnecessary imaging and influence prompt surgical intervention in areas that have a high number of hospitals in Pakistan.

The study aimed to identify the linkage between systemic inflammatory physiology and the severity of appendicitis in patients who underwent appendectomy [10]. This study aims to elucidate which biomarkers are best suited to give us a realistic picture of the severity of the disease by assessing the key inflammatory markers and comparing them with the intraoperative and histopathological results. Further reinforcement of this correlation can improve the preoperative risk assessment process, clinical decision-making, and eventually improve patient outcomes.

MATERIALS AND METHODS

The study design was a cross-sectional study, carried out between March 2024 and April 2025 at tertiary care surgery units, such as Jinnah Hospital, Karachi, and comprised 89 patients who underwent appendectomy due to clinically suspected acute appendicitis. Every patient who arrived with the chief complaint of abdominal pain in the lower right quadrant and met the established diagnostic criteria of acute appendicitis was examined and those who were admitted to undergo surgical treatment were recruited with informed consent. The study was sanctioned by the Institutional Ethics Review Committee with approval of the ERC/AMC/2025/Appendix-89, and all the processes were conducted in accordance with the ethical principles of the Declaration of Helsinki. Patients or their legal guardians were notified of the purpose of the study, possible risks, and confidentiality, and their involvement was voluntary. Anonymous identification was used to guarantee the privacy of information during the study.

Both male and female patients between the ages of 12 years were included. The exclusion criteria involved any previous abdominal surgery, known chronic inflammatory or autoimmune disorders, immunosuppressive medication use, pregnancy, or incomplete medical records, as it would result in confounding differences in systemic inflammatory biomarkers. On admission, the patient received detailed demographic and clinical information, such as age, sex, duration of symptoms, fever, nausea, vomiting, anorexia, and outcomes of the abdominal examination, including tenderness, guarding, and rebound tenderness. The vital signs, such as the temperature, the heart rate, the respiratory rate, and the blood pressure, were also recorded. All patients underwent standard preoperative laboratory tests that comprised complete blood count (CBC), total leukocyte count (TLC), a differential leukocyte count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and serum procalcitonin (PCT). Such biomarkers were chosen because of the known use of such biomarkers to indicate systemic inflammatory responses related to appendiceal inflammation.

Radiological assessment involved abdominal ultrasonography of all patients to determine the appendiceal diameter, wall thickness, peri-appendiceal fluid, and probe tenderness. In the case of diagnostic ambiguity, contrast-enhanced computed tomography (CT) was done under the recommendation of the surgeon. The surgical intervention involved open or laparoscopic appendectomy, which is determined by the preference of a surgeon and the clinical status of the patient. Intraoperative observations were enumerated in a structured proforma, and they comprised a simple inflamed appendix, suppurative appendicitis, gangrenous appendix, perforation, peri-appendiceal abscess, and local or generalized peritonitis.

All removed appendices were referred to histopathological examination, which was the ultimate diagnostic source of the severity of the disease. Histopathology was used to divide cases into catarrhal, suppurative, gangrenous, or perforated appendicitis. Systemic inflammatory biomarkers were then associated with the histopathological severity to determine their diagnostic performance and predictability of complicated appendicitis.

The statistical analysis was done through SPSS version 27. The variables examined continuously, including TLC, CRP, ESR, PCT, NLR, and PLR, were given as mean and standard deviation, whereas the variables examined as categorical were given in frequencies and percentages. The

independent t-tests or one-way ANOVA were used to compare across the histopathological severity groups on the continuous variables and chi-square tests on the categorical variables. The correlation coefficient was used to ascertain the strength and direction of the association between the systemic inflammatory markers and the severity of appendicitis by Pearson. The p-value below 0.05 was regarded as significant.

RESULTS

In this study, 89 patients undergoing appendectomy took part in the study. The average age of the participants was 27.6 9.4y with the male sample size 56.2 (n=50) and the female sample size 43.8 (n=39). The majority of patients (64 percent) are presented within 24-48 hours of the onset of the symptoms. Right lower quadrant pain (100 percent), fever (78.6 percent), nausea/vomiting (62.9 percent), and anorexia (58.4 percent) were the most frequently occurring presenting features. The baseline demographic and clinical characteristics are summarized in Table 1.

Laboratory analysis showed that the systemic inflammatory markers were raised in most of the instances. The average TLC was 14.8 +/- 4.2 x 10 9 /L, and neutrophil percentage was found to be 79.4 +/- 8.5. CRP levels significantly increased, and its mean was 38.6 ± 21.3 mg/L, NLR was significantly increased, and so was the PLR, this shows that there is an activation of the systemic inflammation. Table 2 presents a distribution of the inflammatory markers as shown in table 2. Intraoperative results revealed that 32 patients (36.0%) had simple inflamed appendicitis, 27 (30.3%) had suppurative appendicitis, 18 (20.2) had gangrenous appendicitis, and 12 (13.5) had perforated appendicitis. Table 3 describes the severity of appendicitis distribution as shown in table 3. Comparing the inflammatory indicators in the various severity groups, it was evident that there was an increasing trend of growing systemic inflammation with the increasing severity of the disease. Mean TLC and CRP, PCT, NLR, and PLR were also very high in cases of gangrenous and perforated appendicitis than in simple or suppurative cases. The means of the biomarkers relative to the level of severity are given in Table 4. Correlation outcome indicated that several inflammatory biomarkers had significant positive relationships with the severity of appendicitis. The highest correlation was found between CRP and PCT ($r = 0.71$, $p < 0.001$), with the lowest correlation between CRP and TLC ($r = 0.54$, $p < 0.01$). There were moderately significant correlations between PLR and ESR. Such results suggest the existence of systemic inflammatory physiology, which is reliable as an indicator of histopathological disease evolution.

Table 1: Baseline Demographic and Clinical Characteristics (n = 89)

Variable	Value
Mean age (years)	27.6 ± 9.4
Male	50 (56.2%)
Female	39 (43.8%)
Symptom duration <24 hours	18 (20.2%)
Symptom duration 24–48 hours	57 (64.0%)
Symptom duration >48 hours	14 (15.8%)
Fever	70 (78.6%)
Nausea/Vomiting	56 (62.9%)
Anorexia	52 (58.4%)

Table 2: Preoperative Systemic Inflammatory Markers

Marker	Mean ± SD
Total leukocyte count (×10⁹/L)	14.8 ± 4.2
Neutrophil percentage (%)	79.4 ± 8.5
Lymphocyte percentage (%)	14.2 ± 5.1
Neutrophil-to-lymphocyte ratio (NLR)	6.8 ± 3.9
Platelet-to-lymphocyte ratio (PLR)	178.5 ± 59.1
C-reactive protein (mg/L)	38.6 ± 21.3
Erythrocyte sedimentation rate (mm/hr)	31.2 ± 13.8
Procalcitonin (ng/mL)	0.42 ± 0.28

Table 3: Intraoperative/Histopathological Severity of Appendicitis

Severity Category	Frequency (%)
Simple inflamed appendicitis	32 (36.0%)
Suppurative appendicitis	27 (30.3%)
Gangrenous appendicitis	18 (20.2%)
Perforated appendicitis	12 (13.5%)

Table 4: Comparison of Systemic Inflammatory Markers Across Appendicitis Severity

Marker	Simple	Suppurative	Gangrenous	Perforated
TLC (×10⁹/L)	12.9 ± 3.1	14.5 ± 3.6	16.8 ± 4.4	18.3 ± 5.1
CRP (mg/L)	22.5 ± 10.2	34.7 ± 16.1	49.9 ± 18.2	61.3 ± 23.4

PCT (ng/mL)	0.22 ± 0.11	0.36 ± 0.17	0.57 ± 0.24	0.81 ± 0.31
NLR	4.2 ± 1.9	6.1 ± 2.3	8.4 ± 3.6	10.2 ± 4.1
PLR	142.6 ± 38.7	169.4 ± 49.9	204.5 ± 57.3	236.1 ± 69.4

DISCUSSION

The study assessed the connection between the systemic inflammatory physiology and the severity of appendicitis in 89 patients during appendectomy. The results indicate an evident progressive increase of both inflammatory biomarkers, namely TLC, percentage neutrophils, CRP, PCT, NLR, and PLR, as the inflammation progressed to suppuration, gangrene, and perforation. These findings assist in the rising awareness that acute appendicitis involves more than a simple localized inflammatory process but instead is a systemic inflammatory process whose laboratory correlates can be measured to attain a reflection of the underlying pathological severity [11]. The demographic trend of the study population is in tandem with the past reports that revealed that appendicitis is most commonly reported among young adults, especially males. The fact that a high percentage of patients presenting in 24 to 48 hours of a fungal episode is similar to the clinical practice in low- and middle-income countries, where early symptoms can be ignored or treated as a result of nonspecific gastrointestinal disturbances. As it has been shown in previous studies, the late presentation is a contributing factor to the complications of gangrene and perforation, which were also found in one-third of our cohort [12].

One of the strengths of this study is that there was a steady increase in inflammatory markers according to severity groups. Neutrophil count and TLC are the classical observations that clinicians rely on to diagnose appendicitis, which is not specific. Our findings agree with the existing literature, which discovered high levels of TLC in both the suppurative and perforated appendicitis, although there was a significant overlap between the groups [13]. CRP, on the other hand, had a more linear and positive correlation with the severity of the disease, as it was observed in several studies conducted across various parts of the world that point to CRP as dependable in determining complicated and uncomplicated appendicitis. The tremendous elevation of CRP in gangrenous and perforated cases bears witness to the systemic response of acute phases induced by a large proportion of necrosis of tissues and translocation of bacteria. A high correlation was also shown between procalcitonin and advanced appendicitis [14]. PCT has been reported to rise remarkably when presented with bacterial infections related to tissue necrosis and sepsis, and hence is a prudent complementary biomarker in the early diagnosis of complicated appendicitis. The results of our findings demonstrate such a role as significantly higher levels of PCT are observed in cases of gangrenous and perforated which are higher than the simple inflammation [15].

Neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR) proved to be useful predictive factors. These cheaply, regularly presenters are indicators of neutrophilic inflammation as well as lymphocyte suppression, which are the signs of systemic stress. In line with existing literature, NLR had a high positive correlation with appendicitis severity, which made it a convenient triage indicator, particularly in those hospitals where quick CRP or PCT measurements are either not available [16]. The severity was associated with PR at a moderate but significant level, which emphasizes that it is a supportive and not primary marker. The distributions of intraoperative distribution of the severity of appendicitis of this study 36 percent simple, 30.3 percent suppurative, 20.2 percent gangrenous and 13.5 percent perforated indicate patterns of the distribution of the severity of appendicitis in the literature in Pakistan where delayed presentation, and a lack of accessibility to emergency care, is more likely to shift the distribution of the disease towards more complex forms [17]. The findings indicate the importance of early identification and appropriate referral mechanisms in avoiding the occurrence of perforation.

In this study, there are several clinical implications of its findings. Firstly, the systemic inflammatory biomarkers can be used in risk stratification of the preoperative information to allow the surgeons to assess the complexity during the operation [18]. Second, it is possible to resort to the integration of multiple markers, i.e., CRP, PCT, and NLR, which might prove to be more accurate in the context of diagnosis, compared to a single one. Third, simple and inexpensive tests may be very helpful in the resource-constrained environment to predict severity and, hence, enable more effective allocation of surgical cases, as well as better utilization of imaging. However, this study has some limitations. The research was a cross-sectional, multi-centered study in one country, and therefore, the findings are not generalizable to the population with different levels of access to healthcare or genetic makeup [19]. In the sample size employed, it is suitable to a certain degree, but it limits the subgroup analysis in terms of age, comorbidities, and duration of symptoms. In addition, the histopathological was the gold standard of severity measurement, but the dynamics of inflammatory markers during the course of the disease did not undergo evaluation, which can potentially provide some finer details on how the disease progressed. However, it is important to add that the research provides effective evidence that may be used to prove the clinical utility of systemic inflammatory markers in assessing the severity of appendicitis [20].

CONCLUSION

This study revealed that the relationship between systemic inflammatory physiology and the extent to which appendicitis is severe in patients receiving appendectomy is

close. The biomarkers of simple to perforated appendicitis, such as CRP, PCT, NLR, PLR, and TLC in a steady increase with a proportional increase in the burden of the inflammatory process with pathological progression. The most predictive of this group of markers was determined to be CPR, which would then support its application as a diagnostic instrument in unraveling complex cases. The other significant signs of severe inflammation, which were discovered, were procalcitonin and NLR, which denote the number of bacteria and immune system activation. These data suggest that the clinical usefulness of systemic biomarkers could be used as an extension of the current preoperative assessment of patients to identify those at risk of gangrene or perforation, and prioritize surgery more quickly and wisely, and compare and make decisions in the imaging-limited scenario. Rework in the future should involve a larger sample size, multi-centre validation with prospective biomarker follow-ups to further streamline the severity prediction model of appendicitis.

Conflict of Interest: The authors declare no conflicts of interest.

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Authors' Contributions:

F.T. conceived the study and drafted the manuscript. A.R.H. contributed to study design and interpretation. J.M., M.K., and R.U.K. assisted with data collection, analysis, and manuscript review. All authors approved the final manuscript.

Data Availability: Data are available from the corresponding author upon reasonable request.

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