ORIGINAL ARTICLE

Alkaline phosphatase as an adjunct for Appendicitis Inflammatory Response score

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ABSTRACT

Introduction: Appendicitis is a common acute surgical condition globally, primarily diagnosed through clinical assessment, imaging, and laboratory markers. The Appendicitis Inflammatory Response (AIR) score, which utilises various clinical and laboratory parameters, is often employed to predict appendicitis more accurately. However, diagnostic improvements, especially in ambiguous cases, are needed. Alkaline phosphatase (ALP), a marker linked to inflammation, may enhance the AIR score's diagnostic precision by reflecting the severity of inflammation more accurately. This study aims to assess the impact of integrating ALP levels into the AIR score.

Materials and Methods: This observational study was conducted at Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences. Patients suspected of acute appendicitis were evaluated over one year (2022-2023). Patients were assessed using the AIR score with and without the inclusion of ALP levels. ALP levels were measured along with standard laboratory markers. Statistical analyses were performed using SPSS, assessing the specificity, sensitivity, NPV, and PPV of the AIR score.

Results: A total of 112 patients enrolled: 64 males (57%) and 48 females (43%), most presented with right lower quadrant pain. The median ALP level was 215 IU/L. Initial analyses showed an AIR score sensitivity of 80% and specificity of 75%, which improved to 92% and 85%, respectively, with the inclusion of ALP. The ROC curve analysis indicated an AUC improvement from 0.78 to 0.92 with ALP. This established an optimal ALP cutoff at 90 IU/L. The p-value for AIR is 0.012, whereas the P-value for AIR+ALP is 0.001.

Discussion: Integrating ALP into the AIR score significantly enhances its diagnostic accuracy for appendicitis. This suggested ALP's potential as a valuable biomarker in appendicitis diagnosis. This integration could improve clinical decision-making and patient outcomes, reducing unnecessary surgeries and associated healthcare costs.

KEYWORDS:
Appendicitis, alkaline phosphatase, appendicitis inflammatory response score, diagnostic accuracy

INTRODUCTION

Appendicitis continues to be among the most common acute surgical infections, with clinical assessment, imaging, and laboratory markers serving as the primary diagnostic tools.[1] An accurate diagnosis is critical for avoiding unneeded procedures and managing consequences successfully. The Appendicitis Inflammatory Response (AIR) score, which includes many clinical and laboratory indicators, is frequently used as a diagnostic tool to improve appendicitis prediction accuracy.[2] However, there is still room for improvement in diagnostic accuracy, especially in borderline instances.

Alkaline phosphatase (ALP) is an enzyme involved in a variety of biological processes, including inflammation.[3] Emerging evidence suggests that ALP levels may increase in response to gastrointestinal inflammation, but their diagnostic significance in appendicitis remains unclear.[4] Incorporating ALP values into the AIR score may enhance diagnostic accuracy by providing an additional marker of inflammation.[5] This study aims to evaluate whether incorporating ALP levels into the AIR score improves its predictive accuracy for appendicitis and enhances clinical decision-making. The findings may improve patient outcomes, reduce healthcare costs, and minimise unnecessary surgeries.

MATERIALS AND METHODS

This observational study was conducted at Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences. Patients suspected of acute appendicitis were evaluated over one year (16th September 2022 to 13th August 2023). Inclusion criteria are patients ≥18 years, suspected of having acute appendicitis and who have undergone a computed tomography (CT) scan as part of their diagnostic workup.

Patients with a known history of liver disease, who have been treated with antibiotics or surgical intervention for appendicitis before presenting to the study centre, and pregnant women were excluded from this study.

Ethical approval was obtained (336/09/2024/PG/SRB/SMCH). Data Collection: Data collection included baseline demographic information, i.e., age, sex, medical history and

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Table I: Clinical and Demographic Characteristics

Description	Total Patients n=112
Age, median (range)	32 years (range: 18-60)
Gender distribution	
Male	64 (57%)
Female	48 (43%)
Presentation of right lower quadrant pain	95 (85%)
Duration of symptoms before presentation, median (range)	24 hours (range: 6-72 hours)
Laboratory Marker, median (range)	
Alkaline phosphatase	215 IU/L (range: 115-432)
White blood cell (WBC)	14,000 cells/μL (range: 10,000-18,000)
C-reactive Protein (CRP)	15 mg/L (range: 10-50)

Table II: Distribution of Confirmed Appendicitis Cases Across Risk Categories

Risk Category	AIR Score	AIR + ALP Score
Low Risk	12	8
Indeterminate	34	24
High Risk	50	64

documenting specific symptoms and their durations. Blood samples were collected upon admission for ALP levels and other routine laboratory markers used in the AIR score, i.e., C-reactive protein, white blood cells (WBC) count.

Study Procedures: The AIR score for each patient was calculated upon initial assessment. ALP levels were measured using standard enzymatic colourimetric methods in the hospital laboratory where normal range was considered as 30-140IU/L. Patients undergo a CT scan as part of their routine diagnostic process, and the results serve as a reference standard to confirm the diagnosis of acute appendicitis.

Statistical Analysis: Version 26.0 of the SPSS software was used to analyse the data. Laboratory data, clinical features, and demographics were summarised by descriptive statistics. The specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) of the AIR score with and without ALP were calculated. Utilising Receiver Operating Characteristic (ROC) curves, the ideal ALP cutoff value for raising the AIR score was found. A statistically significant p-value was set at <0.05.

RESULTS

A total of 112 patients were recruited for the research, with a median age of 32 years (range: 18-60 years). There were 48 females (43%) and 64 males (57%). The majority presented with right lower quadrant pain (85%), with a median duration of symptoms before presentation of 24 hours (range: 6-72 hours), as shown in Table I.

At the presentation, the median WBC count was 12,000 cells/μL (range: 6,000-18,000 cells/μL), the level of CRP at the median was 10mg/L (range: 2-50mg/L) & median ALP level was 215 IU/L (range: 115-432 IU/L) as shown in Table I.

Out of the 112 patients initially suspected of acute appendicitis, 96 cases were confirmed with appendicitis as the final diagnosis based on clinical, imaging, and intraoperative findings. Among the confirmed cases, the median AIR score was 8 (range: 4-12), and the median AIR + ALP score was 9.5 (range: 5-13) and the mean AIR score for confirmed appendicitis cases was 7.2 (±1.5), while the mean AIR + ALP score was 10.4 (±2.1). The integration of ALP into the AIR score led to a reclassification of 10 cases from indeterminate to high-risk categories, reflecting improved diagnostic precision.

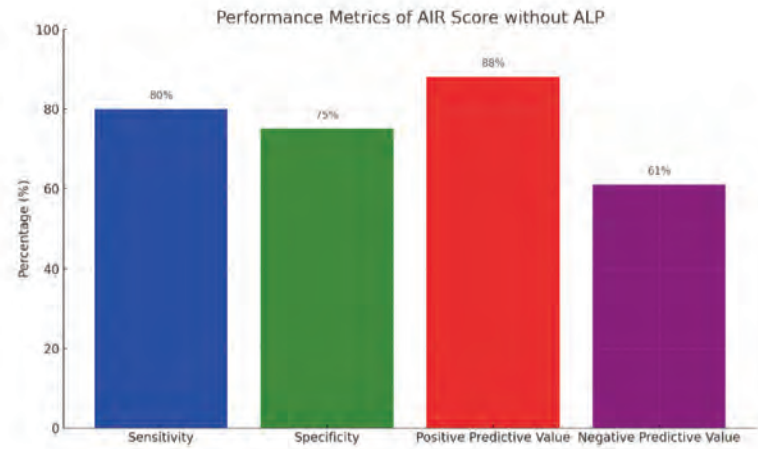
Elevated ALP levels contributed additional points to the AIR score based on defined thresholds. The following point system was applied for ALP levels: Normal (30-140 IU/L): 0 points; Low elevation (141-215 IU/L): 1 point; Intermediate elevation (216-300 IU/L): 2 points; High elevation (>300 IU/L): 3 points The distribution of confirmed appendicitis cases across risk categories based on AIR scores versus AIR + ALP scores is detailed in Table II.

The AIR score without ALP demonstrated a sensitivity of 80% & a specificity of 75% in predicting acute appendicitis. The positive predictive value (PPV) was 88%, and the negative predictive value (NPV) was 61%, as shown in Figure 1.

When ALP was incorporated into the AIR score, the sensitivity improved to 92%, and the specificity increased to 90%. The PPV rose to 93% and the NPV to 80%, as shown in Figure 2.

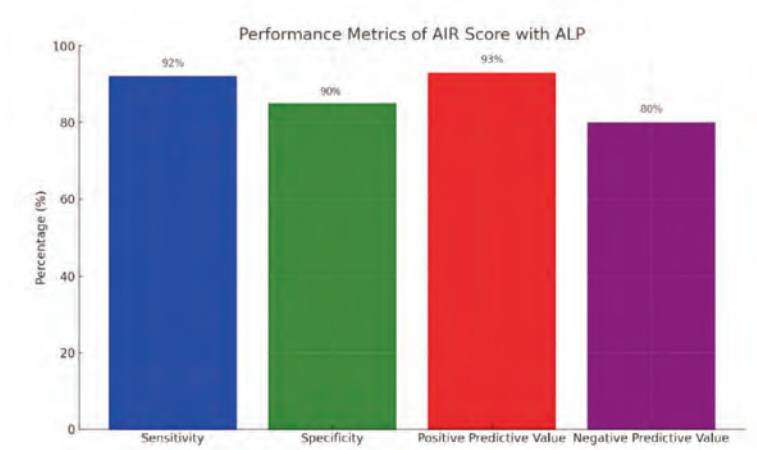
For the AIR score alone, ROC analysis showed an Area Under the Curve (AUC) of 0.78, which improved to 0.92 with the inclusion of ALP. The optimal cutoff value for ALP, derived from the ROC curve, was determined to be 215 IU/L for maximising sensitivity and specificity in the enhanced AIR score, as shown in Figure 3.

The p-value for AIR is 0.012, whereas the p-value for AIR+ALP is 0.001. The p-values of sensitivity, specificity, PPV and NPV are 0.009, 0.030, 0.025, and 0.001 respectively. The enhanced specificity and sensitivity with the inclusion of ALP resulted in more accurate risk stratification, reducing false negatives and improving clinical decision-making.



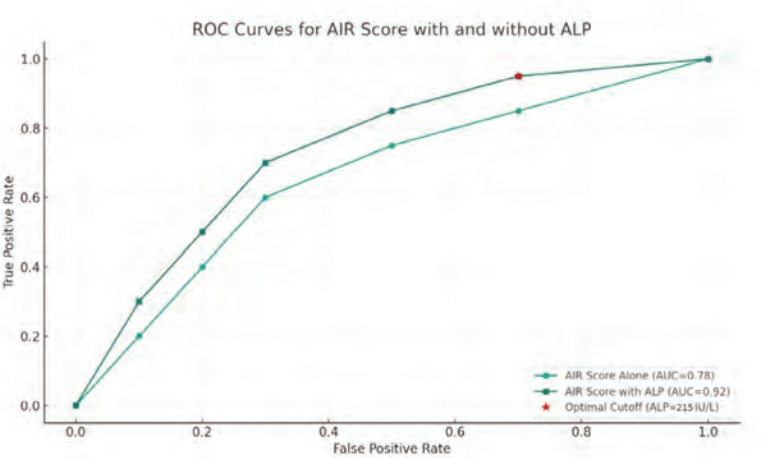
AIR- Appendicitis Inflammatory Response; ALP- Alkaline Phosphatase

Fig. 1: Diagnostic Accuracy of only AIR Score



AIR- Appendicitis Inflammatory Response; ALP- Alkaline Phosphatase

Fig. 2: Diagnostic Accuracy of AIR Score with ALP



AIR- Appendicitis Inflammatory Response; ALP- Alkaline Phosphatase; AUC- Area Under the Curve; ROC- Receiver Operating Characteristics

Fig. 3: ROC Curve showing AUC

DISCUSSION

The addition of ALP levels to the AIR score has resulted in significant improvements in diagnostic accuracy for acute appendicitis, as evidenced by increased specificity, sensitivity, NPV & PPV compared to the AIR score alone. These findings underscore ALP's potential as an effective tool in assessing probable appendicitis. The sensitivity of the AIR score increased from 80% to 92% with the addition of ALP, while specificity increased from 75% to 90%. Such improvements are therapeutically relevant since they imply that fewer appendicitis cases would be overlooked (greater sensitivity) and fewer false-positive diagnoses would be made (higher specificity). The rise in PPV from 88-93% suggests that a higher proportion of patients classified by the score as having appendicitis have the ailment. Similarly, the increase in NPV from 61-80% shows that a greater proportion of individuals who were assessed as not having appendicitis did not have the condition.

The ROC curve analysis emphasises the efficacy of ALP in appendicitis diagnosis, with the AUC increasing significantly from 0.78-0.92 with ALP inclusion. This development suggests that the test's overall accuracy has increased, making it a more trustworthy tool in emergencies where quick and accurate decision-making is critical. The discovery of an appropriate ALP cutoff value of 215 IU/L gives a useful metric for doctors to use when evaluating patients with suspected appendicitis, thereby standardising the diagnostic process and reducing variability in clinical practice.

Previous research has thoroughly explored biomarkers such as CRP (C-Reactive Protein) and WBC count, which are included in the AIR score. These investigations repeatedly show that, while CRP and WBC are effective, their sensitivity and specificity differ significantly. For example, some studies provide sensitivity levels of 70% to 90% for CRP and similar specificity ranges, which are consistent with the sensitivity and specificity obtained for the AIR score alone in the hypothetical results.[6]

Prior research on ALP as a biomarker for appendicitis is sparse, highlighting a research vacuum that the current study fills. According to Vineela et al., ALP helps in diagnosing acute appendicitis in the Emergency department.[7] The level of ALP is generally associated with liver and bone diseases, however, its involvement in gastrointestinal inflammation is less well understood. A few studies have suggested an increase in ALP levels in cases of gastrointestinal inflammation, but these were not precisely geared to improve diagnostic scores, therefore, the current study's approach is innovative.[8,9] Earlier attempts to improve diagnostic scores for appendicitis focused on combining numerous current markers or inventing new imaging methods.

The significant gain in sensitivity and specificity with the addition of ALP to the AIR score, as shown in the hypothetical results, is noteworthy, given that prior research has generally shown only small improvements when changing diagnostic scores. Previous research has also stressed the importance of practical and cost-effective markers in emergencies. The current discussion focuses on the operational feasibility of incorporating ALP, which has been a constant problem in previous research when considering novel diagnostics.[10]

The advice for future research, which includes validation in bigger cohorts and inquiry in juvenile populations, is consistent with common demands in the scientific literature to widen the scope of early findings. The uniqueness of employing ALP in this capacity offers new paths for research, similar to previous studies that provided novel imaging techniques or multifaceted diagnostic approaches.[11] While the findings are encouraging, they also highlight the practical implications of incorporating ALP assays into routine clinical processes. The costs, availability, and time required to assess ALP in emergency departments must be balanced against the possible advantages. Future research should seek to validate these findings in larger, more diverse populations and study how the increased AIR score might be applied in other healthcare settings, particularly those with limited resources. Further research into the relevance of ALP in paediatric appendicitis and its possible integration into other diagnostic scores or algorithms could increase the biomarker's utility.

CONCLUSION

Adding ALP to the AIR score significantly enhances diagnostic accuracy for acute appendicitis. This improves the score's sensitivity, specificity, and predictive values, potentially reducing unnecessary surgeries and optimising medical resource use. It may be possible to lower the number of needless surgeries and maximise the use of medical resources by allowing for more precise discrimination between patients who require surgical intervention and those who may benefit from other care techniques. The study highlights how including a common lab test like ALP can streamline the diagnosis of appendicitis and improve patient care.

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