ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 2, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

A COMPARATIVE STUDY TO EVALUATE THE POSITIVE PREDICTIVE VALUE OF BIOCHEMICAL MARKERS WITH CLINICAL RIPASA SCORE IN ACUTE APPENDICITIS: AN *IN VIVO* STUDY

HARPINDER SINGH, VISHWAS JOHRI, TEJPAL SINGH SARAN*

Department of General Surgery, Pacific Medical College and Hospital, Udaipur, Rajasthan, India.
***Corresponding author: Dr. Tejpal Singh Saran; Email: tejuchoudhary07@gmail.com**

Received: 10 May 2023, Revised and Accepted: 16 August 2023

ABSTRACT

Objective: We evaluated the positive predictive value of biochemical markers with clinical Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score and the sensitivity and diagnostic accuracy.

Methods: 75 patients who presented to the Emergency/General Surgery Department of Pacific Medical College and Hospital, Udaipur, with right iliac fossa (RIF) pain and who were suspected of acute appendicitis. A detailed history, clinical examination, and laboratory investigations were done which included a routine RIPASA score calculated.

Results: RIF pain was present in all the patients, followed by vomiting (98.67%), and fever in 92%. Twenty-one patients had raised white blood cell (WBC) counts, out of them 15 patients had both raised WBC counts and raised C-reactive protein (CRP) and 6 had normal CRP. 52 patients had raised CRP levels, out of them 15 patients had both raised WBC counts and raised CRP and 37 had normal WBC counts. 17 patients had both CRP and WBC counts in normal range, but were diagnosed to have appendicitis according to RIPASA score. Our results show that raised CRP and WBC counts had a sensitivity of 28.85% and specificity of 73.91% with a diagnostic accuracy of 42.67%.

Conclusion: When combined with WBC, CRP has good discriminatory power for appendicitis despite its inability to reliably predict acute appendicitis when used alone. However, a cutoff point for CRP that predicted perforated appendicitis could not be determined.

Keywords: C-reactive protein, White blood cell, Raja Isteri Pengiran Anak Saleha Appendicitis, Acute appendicitis, Appendectomy.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i2.48290. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

One of the most researched fields pertaining to appendicitis is the one involving diagnosis. Over the years, various types of investigations, including laboratory, scoring, and radiological, have been studied in detail with the aid of trials. These were conducted in the hope of finding the most sensitive test for diagnosing acute appendicitis [1].

Appendicitis which if caught early and managed appropriately can be the most uneventful surgery, while the other end of the spectrum is also true, that when missed appendicitis can turn into a disease with great morbidity and mortality [2]. To decrease the number of unnecessary appendicectomy, significance of laboratory investigations such as white blood cells (WBC) and C-reactive protein (CRP). have been emphasized [3]. Many scoring systems were developed to arrive at the diagnosis. These scoring systems are based on clinical features, and laboratory investigations [4].

Studies show that serum bilirubin is raised in acute appendicitis and appendicular perforations.

Hence, having understood the importance of early and right diagnosis, and having understood that clinical evaluation provides the best and most accurate diagnostic modality for appendicitis, many clinical scoring systems have been developed over the years. This has aided the clinician to a large extent in coming to the right diagnosis and providing early management [5].

What began as a single scoring system, evolved into many over the years, as people constantly made modifications to the existing scoring systems based on the local demographics or by adding more factors [6].

Due to the fact that Alvarado and Modified Alvarado were created in Western nations but did not perform as well when applied to Asian cultures, a new scoring system was required.

This brought along the next problem, of finding the single best scoring system, or the scoring system with the maximum sensitivity and diagnostic accuracy. As a result, multiple studies have been done with randomized controlled trials comparing various scoring systems in different parts of the world [7].

Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score is a fairly newer scoring system developed in 2008, where a study was done in RIPAS Hospital, Brunnei Darssalem, to find out. Appendicitis is one of the routine conditions evoking emergency surgery worldwide [8].

A. Rationale: To evaluate the positive predictive value of biochemical markers with clinical RIPASA score, to find out which is a better diagnostic tool for acute appendicitis in the Indian population [9].
B. Expected outcome and application: To check the sensitivity and diagnostic accuracy of RIPASA score from biochemical markers. To highlight the best way to approach them.

METHODS

This study was conducted after taking proper Institutional Ethical Committee. 75 Patients who presented to the Emergency/General Surgery Department of Pacific Medical College and Hospital, Udaipur for 18 months from January 2021 to June 2022 with right iliac fossa (RIF) pain and who were suspected of acute appendicitis were considered for the study.

Patients who did not give consent, RIF had a noticeable mass there, severe medical disease (psychiatric illness, cirrhosis, and coagulation

disorders) requiring intensive care, and other associated conditions (pregnancy, any malignancy, generalized peritonitis) were excluded from the stduy.

A detailed history, clinical examination, and laboratory investigations were done which included a routine RIPASA score calculated. Both RIPASA and biochemical investigations were applied to them, but management was carried out as per the RIPASA score. A specially designed proforma was filled in for each patient.

Normal reference range of WBC taken as 4000–11,000/cumm and for CRP <5 mg/L. WBC >11,000/cumm was considered as high and <4000 as low. Similarly for CRP.

RIPASA score

Parameter	Score
Age	1 pt (if<40 years) or 0.5 pt (if>40 years)
Sex	1 pt (if M) or 0.5 pt (if F)
RIF pain	0.5 pt
Migration to RIF	0.5 pt
Nausea/vomiting	1 pt
Anorexia	1 pt
Duration of symptoms	1 pt (if<48 h) or 0.5 pt (if>48 h)
RIF tenderness	2 pt
RIF guarding	2 pt
Fever	1 pt
Raised WBC count	1 pt
Negative urinalysis	1 pt
Maximum score/min score	12 pt/2 pt

RIF: Right iliac fossa, WBC: White blood cell

Management guidelines based on total score

<5 = There is a low likelihood of acute appendicitis; monitor the patient, repeat the score in 1–2 h, and discharge if the score drops. If your score rises, adjust your treatment accordingly.

Perform abdominal ultrasound investigations to rule out acute appendicitis or observe and repeat scoring in 1–2 h if the score is 5–7.0.

Patients may need admission for observations

7.5–11.0 = Probability of acute appendicitis high, admit the patient and repeat score in 1–2 h time. If remains high, prepare patients for appendicectomy procedure. In female patients, suggest performing abdominal ultrasound investigations to rule out gynecological causes of RIF pain [10].

Plan for admission and appendicectomy if your appendix is definitely acute (>12).

The final diagnosis was confirmed either by computed tomography (CT) scan, intra-operative findings, or post-operative HPE report. The final diagnosis was analyzed against both RIPASA and biochemical markers. Sensitivity, specificity, positive predictive value, negative predictive value (NPV), and diagnostic accuracy were calculated and analyzed comparatively with a Chi-square test (SPSS software).

Operative findings, post-operative course, and treatment and outcome

Post-operative complications, histopathological correlation (if any), duration of hospital stay, and follow-up.

RESULTS

During the 18-month from January 2021 to June 2022, a study on the use of RIPASA score was made on a consecutive series of 75 patients admitted to the Department of Surgery, Pacific Medical College, Udaipur, with clinical features suggestive of acute appendicitis. The results are as follows:

Maximum number of patients 67% were in the age group of <30 years of age, followed by 12% in 31–40 years, 9.33% in 41–50 years, 6.67% in 61–70 years, and 5.33% in 51–60 years. The mean age of patients was 29.97±15.07 years (Graph 1).

There were almost equal number of patients of both the genders (Graph 2).

RIF pain was present in all the patients, followed by vomiting (98.67%), and fever in 92%. Migrating pain was observed in 36% of cases (Table 1).

On per abdomen examination, RIF tenderness and rebound tenderness were seen in all of the patients. Guarding was observed in 20% of them.

Our results show that raised CRP counts have a sensitivity of 68.06% and specificity of 0% (as the present study comprised of 75 patients only) with a diagnostic accuracy of 65.33%.

Twenty-one patients had raised WBC counts, out of them 15 patients had both raised WBC counts and raised CRP and 6 had normal CRP (Table 2).

Fifty-two patients had raised CRP levels, out of them 15 patients had both raised WBC counts and raised CRP and 37 had normal WBC counts (Table 3).

Seventeen patients had both CRP and WBC counts in normal range, but were diagnosed to have appendicitis according to RIPASA score.

Our results show that raised CRP and WBC counts had a sensitivity of 28.85% and specificity of 73.91% with a diagnostic accuracy of 42.67% (Table 4).

WBC counts were normal in 96.3% of acute appendicitis cases, whereas in cases of perforated appendix, gangrenous appendicitis and acute suppurative appendicitis cases had raised WBC counts in 28.57%, 23.81%, and 33.33%, respectively (Table 5).

DISCUSSION

Numerous techniques have been researched in an effort to lessen the removal of a healthy appendix without raising the perforation rate, as appendicitis remains difficult to diagnose. Laparoscopy, CT, ultrasonography, and other radiological techniques have all been studied in the past. Numerous diagnostic scores have been recommended, but the majority are complex and challenging to use in a clinical setting.

The patient's age and gender, a thorough clinical history that includes RIF pain, migration to RIF, anorexia, nausea, and vomiting, a clinical examination that includes RIF tenderness, localized guarding, rebound tenderness, Rovsing's sign, and fever, as well as two straightforward investigations, are all that are needed to quickly diagnose acute appendicitis (raised white cell count and a negative triage urinalysis, which is defined as the absence of red and WBCs, bacteria, and nitrates, are both indicators of infection).

In the present study, maximum number of patients 67% were in the age group of <30 years of age, followed by 12% in 31–40 years, 9.33% in 41–50 years, 6.67% in 61–70 years and 5.33% in 51–60 years. The mean age of patients was 29.97±15.07 years.

Akbar *et al*. showed similar findings to ours [11]. Patients in age group of 11–25 yrs were 129 (44.8%), (26–40 yrs) were 112 (38.9%), of age (41–55 yrs) were 43 (14.9%). Similar findings were reported by Xharra *et al*. [12]. The age ranged from 5 to 59 years with the mean (standard deviation) being 19.7 years (±10.5), whereas 83.5% of patients were under 30 years old.

We had almost equal number of patients of both the genders with 48% males and 52% females. Akbar *et al*. showed 165 (57.3%) were male and 123 (42.7%) were female [11]. In a study by Xharra *et al*. males were 52.02%, females 47.97% [12]. The male: female ratio was 1.09:1 [13]. Panagiotopoulou *et al*. reported of the 1169 patients included in this study, 591 (50.6%) were female [13].

Table 1: Chief symptoms of patients and signs of illness

Parameters	No. of patients	Percentage
Symptoms		
RIF pain	75	100
Migrating pain	27	36
Vomiting	74	98.67
Fever	69	92
Signs		
RIF tenderness	75	100
Rebound tenderness	75	100
Guarding	15	20

RIF: Right iliac fossa

Table 2: Distribution of patients according to RIPASA and WBC count

Parameters	RIPASA >7.5	RIPASA <7.5	Total
Raised WBC (>11,000) cumm	21	0	21
Normal WBC	51	3	54
Total	72	3	75

RIPASA: Raja Isteri Pengiran Anak Saleha Appendicitis, WBC: White blood cell

Table 3: Distribution of patients according to RIPASA and CRP Levels

Parameters	RIPASA >7.5	RIPASA <7.5	Total
Raised CRP (>4) mg/L	49	3	52
Normal CRP	23	0	23
Total	72	3	75

RIPASA: Raja Isteri Pengiran Anak Saleha Appendicitis, CRP: C-reactive protein

Table 4: Distribution of patients according to WBC and CRP levels

Parameters	Normal CRP	Raised CRP (≥4) mg/L	Total
Normal WBC	17	37	54
Raised WBC (>11,000) cumm	6	15	21
Total	23	52	75

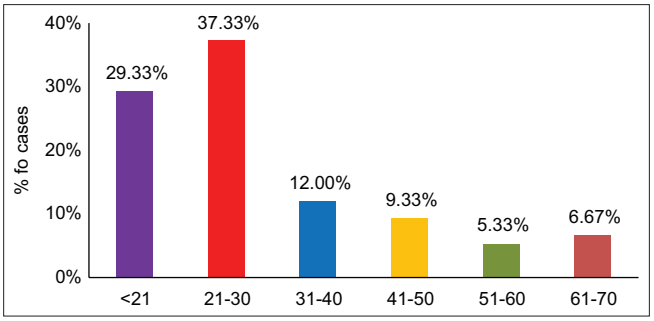
WBC: White blood cell, CRP: C-reactive protein

Table 5: Distribution of patients according to WBC and histopathology

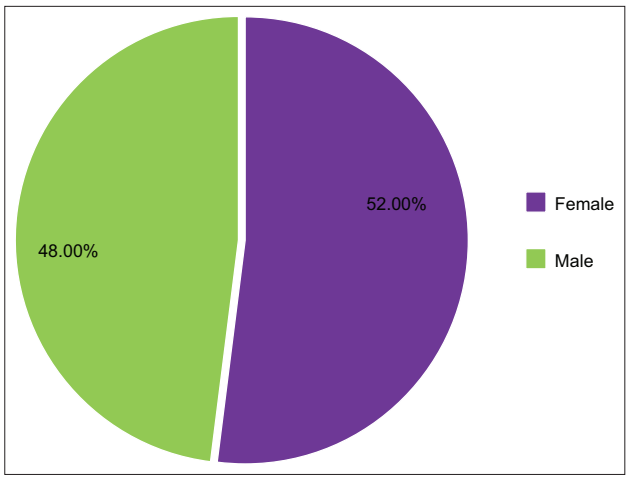
Parameters	Normal WBC		Raised WBC (>11,000) cumm	
Histopathology	No.	Percentage	No.	Percentage
Acute appendicitis	52	96.30	3	14.29
Acute suppurative appendicitis	2	3.70	7	33.33
Perforated appendix	0	0.00	6	28.57
Gangrenous appendicitis	0	0.00	5	23.81
Total	54	100.00	21	100.00

The chief presenting complaints were a history of RIF pain in all the patients, followed by a history of vomiting (98.67%), and fever in 92%. A history of migrating pain was observed in 36% of cases. On per abdomen examination, RIF tenderness and rebound tenderness were seen in all of the patients. Guarding was observed in 20% of them.

Ak *et al*. observed fever as the main presenting symptoms in 36.40% patients [14]. Xharra *et al*. observed nonspecific abdominal pain in 15 (8.7%), ruptured ovarian cysts 4 (2.3%), mesenteric lymphadenitis



Graph 1: Age distribution



Graph 2: Sex distribution

5 (2.9%), and urinary infection 1 (0.6%) as main symptoms [12]. Akbar *et al*. observed pain in the RIF, nausea/vomiting, migratory pain as the main symptoms and tenderness in RIF, abdominal guarding, rebound tenderness, rovsing sign, and fever as the main signs [11].

When we compared WBC counts according to RIPASA score, out of 75, 72 patients have raised RIPASA score, but out of these 75 patients, 21 were found with raised WBC. Out of 75 patients, 3 patients have decreased RIPASA score with normal WBC. WBC counts have a sensitivity of 29.17% and specificity of 100% with an accuracy of detection 32%.

Xharra *et al*. when the WBC count was assessed, the false positives were 4.62% and false negatives were 12.72% with a sensitivity of 85.1% and a specificity of 68%; the positive predictive value was 94% and the accuracy was calculated to be 82.6% [12].

The present study comprised 75 patients. Out of these 75, 72 patients have raised RIPASA score, but out of these 75 patients, 49 were found with raised CRP. Out of 75 patients, 3 had decreased RIPASA score. All 23 had normal CRP. Our results show that raised CRP counts have a sensitivity of 68.06% and specificity of 0% with a diagnostic accuracy of 65.33%.

In a study by Xharra *et al*. the serum CRP levels were normal in 22 patients with acute appendicitis [12]. Thus, the false-negative rate of CRP was 12.71%. Of the 25 patients with normal appendectomy, serum CRP levels were slightly elevated in 7 patients. A false-positive rate of CRP was 4.05%. Further, based on the surgeons' clinical impression, the diagnosis was true in 87.28% (n=151) and false in 12.72% (n=22) patients. In the present study, the positive predictive value of the CRP was 94.7%, specificity 72%, sensitivity 85.1%, and accuracy 83.2%. The accuracy of the CRP (83.2%) is not significantly greater than the WBC (82.6%).

According to Shoshtari *et al*. CRP measurement is very useful in the diagnosis of acute appendicitis, but it does not replace the clinical judgment of a surgeon [15].

In our study, 21 patients had raised WBC counts, out of them 15 patients had both raised WBC counts and raised CRP and 6 had normal CRP. 52 patients had raised CRP levels, out of them 15 patients had both raised WBC counts and raised CRP and 37 had normal WBC counts. 17 patients had both CRP and WBC counts in normal range, but were diagnosed to have appendicitis according to RIPASA score. Our results show that raised CRP and WBC counts had a sensitivity of 28.85% and specificity of 73.91% with a diagnostic accuracy of 42.67%.

Thus, in the emergency setting, a quick decision can be made upon seeing patients with RIF pain. Those with a RIPASA score >7.5 need admission and further management admission, while patients with a RIPASA score <7.0 can either be observed. With its high sensitivity (98%) and NPV (97.3%), the RIPASA score can also help to reduce unnecessary and expensive radiological investigations such as routine CT imaging.

WBC counts were normal in 96.3% of acute appendicitis cases, whereas in cases of perforated appendix, gangrenous appendicitis and acute suppurative appendicitis cases had raised WBC counts in 28.57%, 23.81%, and 33.33%, respectively.

There are in use different clinical classifications for the acute appendicitis (Yokoyama *et al.*) but, since the correlation of CRP values with histopathology findings was studied, they used the classification that combines the gross appearance of the appendix with the pathologic stage [16].

Total cases of acute appendicitis seen were 73.33% followed by acute suppurative appendicitis in 12%. Perforated appendix in 8% and gangrenous appendicitis in 6.67% of cases.

Limitations

There are potential limitations to this study.

Our study groups were chosen based on histological diagnoses, so patients who may have had appendicitis at the time of admission but were not operated on were excluded. This study, which was histologically based, did not examine patients who were taken to the operating room with a suspicion of having an appendicitis but who instead had another cause of peritonism, such as a malignancy or a gynecological cause.

CONCLUSION

It is concluded that the RIPASA score is a useful, basic, fast, and non-invasive diagnostic tool. Raised CRP and WBC counts had a sensitivity of 28.85% and specificity of 73.91% with a diagnostic accuracy of 42.67%.

The elevated CRP value was directly correlated with the degree of inflammation. The accuracy of the diagnosis of acute appendicitis is improved by CRP monitoring. When compared to WBC, CRP's diagnostic accuracy is not noticeably better. Elevated serum CRP levels have been seen to support the surgeon's clinical diagnosis.

When combined with WBC, CRP has good discriminatory power for appendicitis despite its inability to reliably predict acute appendicitis when used alone. However, a cutoff point for CRP that predicted perforated appendicitis could not be determined.

AUTHORS CONTRIBUTION

Equal contribution in all fields by all authors.

CONFLICTS OF INTERESTS

Nil.

AUTHORS FUNDING

Nil.

REFERENCES

1. McBurney C. IV. The incision made in the abdominal wall in cases of appendicitis, with a description of a new method of operating. Ann Surg 1894;20:38-43. doi: 10.1097/00000658-189407000-00004, PMID 17860070
2. Wagner JM, McKinney WP, Carpenter JL. Does this patient have appendicitis? JAMA 1996;276:1589-94, PMID 8918857
3. Sengupta A, Bax G, Paterson-Brown S. White cell count and C-reactive protein measurement in patients with possible appendicitis. Ann R Coll Surg Engl 2009;91:113-5. doi: 10.1308/003588409X359330, PMID 19102827
4. Owen TD, Williams H, Stiff G, Jenkinson LR, Rees BI. Evaluation of the Alvarado score in acute appendicitis. J R Soc Med 1992;85:87-8. doi: 10.1177/014107689208500211, PMID 1489366
5. Azaro EM, Amaral PC, Ettinger JE, Souza EL, Fortes MF, Alcântara RS, *et al*. Laparoscopic versus open appendicectomy: A comparative study. JSLS 1999;3:279-83. PMID 10694074
6. Williams GR. Presidential address: A history of appendicitis. With anecdotes illustrating its importance. Ann Surg 1983;197:495-506. doi: 10.1097/00000658-198305000-00001, PMID 6342553
7. Fitz RH. Perforating inflammation of the vermiform appendix. Am J Med Sci 1886;92:321-46.
8. Chong CF, Adi MI, Thien A, Suyoi A, Mackie AJ, Tin AS, *et al*. Development of the RIPASA score: A new appendicitis scoring system for the diagnosis of acute appendicitis. Singapore Med J 2010;51:220-5. PMID 20428744
9. McBurney C. Experiences with early operative interference in cases of diseases of the vermiform appendix. N Y Med J 1889;50:676-84.
10. Standring S. Gray's Anatomy: The Anatomical Basis of Clinical Practice. 40th ed. London: Churchill Livingstone, Elsevier; 2008.
11. Akbar I, Shehzad JA, Ali S. Diagnostic accuracy of Ripasa score. J Ayub Med Coll Abbottabad 2019;31:411-4. PMID 31535517
12. Xharra S, Gashi-Luci L, Xharra K, Veselaj F, Bicaj B, Sada F, *et al*. Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopathology findings in acute appendicitis. World J Emerg Surg 2012;7:27. doi: 10.1186/1749-7922-7-27, PMID 22866907
13. Panagiotopoulou IG, Parashar D, Lin R, Antonowicz S, Wells AD, Bajwa FM, *et al*. The diagnostic value of white cell count, C-reactive protein and bilirubin in acute appendicitis and its complications. Ann R Coll Surg Engl 2013;95:215-21. doi: 10.1308/003588413X13511609957371, PMID 23827295
14. Ak R, Doğanay F, Unal Akoğlu E, Akoğlu H, Uçar AB, Kurt E, *et al*. Predictive value of scoring systems for the diagnosis of acute appendicitis in emergency department patients: Is there an accurate one? HK J Emerg Med 2020;27:262-9. doi: 10.1177/1024907919840175
15. Shoshtari MH, Askarpour S, Alamshah M, Elahi A. Diagnostic value of Quantitative CRP measurement in patients with acute appendicitis. Pak J Med Sci 2006;22:300-3.
16. Yokoyama S, Takifuji K, Hotta T, Matsuda K, Nasu T, Nakamori M, *et al*. C-reactive protein is an independent surgical indication marker for appendicitis: A retrospective study. World J Emerg Surg 2009;4:36. doi: 10.1186/1749-7922-4-36, PMID 19878592