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Abstract:

Background and Aims: Acute appendicitis remain a common cause of abdominal surgeries, presenting diagnostic challenges with a significant rate of negative appendectomy. This study aimed to assess the diagnostic utility of complete blood count (CBC)-associated parameters in distinguishing between positive and negative appendectomy cases. **Methods:** A cross-sectional study was conducted, including patients suspected of acute appendicitis. Preoperative CBC samples were collected and analyzed for various parameters including white blood cell count (WBC), platelet count (PLT), mean platelet volume (MPV), neutrophils-to-lymphocytes ratio, platelets-to-lymphocytes ratio, red cell distribution width (RDW), and platelet distribution width (PDW). Statistical analysis was employed to compare these parameters between positive and negative appendectomy patients. **Results:** Among the 200 patients included, 30 (15%) underwent negative appendectomy. Positive appendectomy patients exhibited significantly higher mean values of neutrophils, WBC, red blood cells, neutrophils-to-lymphocytes ratio, and platelets-to-lymphocytes ratio (P < .05), while the MPV to platelet ratio was significantly lower in this group. The neutrophils-to-lymphocytes ratio demonstrated the highest diagnostic power for appendicitis diagnosis, with a sensitivity of 83.5% and specificity of 90%.

Conclusion: The study findings underscore the limited utility of neutrophils-to-lymphocytes ratio alone for preoperative diagnosis of acute appendicitis, with other CBC-related parameters showing suboptimal sensitivity and specificity. Further research is warranted to enhance diagnostic accuracy in this realm.

Keywords: acute appendicitis, appendectomy, CBC, lymphocytes, neutrophils, parameters.

Introduction:

Appendicitis stands as a prevalent cause of abdominal surgery worldwide, with significant morbidity and mortality risks if left untreated. Despite its clinical importance, diagnosing appendicitis accurately remains challenging, often leading to unnecessary surgeries or delayed interventions. Reliable diagnostic tools are imperative to enhance diagnostic precision and streamline patient management. (Guaitoli et al., 2020)

Traditional diagnostic approaches for appendicitis often rely on clinical presentation and imaging studies, yet these methods may lack specificity and sensitivity. Complete blood count (CBC) emerges as a routine blood test, routinely utilized in emergency settings to assess inflammatory conditions. Elevated white blood cell count (WBC) and neutrophil count are commonly observed in acute appendicitis, but their diagnostic value varies across studies and patient populations. (Alizadeh et al., 2020)

In recent years, attention has shifted towards exploring additional CBC-associated parameters to refine the diagnostic accuracy of appendicitis. These parameters, including neutrophils-to-lymphocytes ratio (NLR), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and red cell distribution width (RDW), offer potential insights into the inflammatory process underlying appendicitis. (Rahmani et al., 2020)

Of particular interest is the role of interleukin-6 in stimulating megakaryocytes, leading to alterations in platelet parameters such as MPV, which may serve as diagnostic and prognostic markers in inflammatory conditions. (He et al., 2019)

This study aims to investigate the diagnostic utility of CBC-related parameters in distinguishing between positive and negative appendectomy cases. By analyzing these parameters in appendicitis patients undergoing surgical intervention, we aim to contribute to the development of more accurate and reliable diagnostic algorithms for acute appendicitis. (Sherkatolabbasieh et al., 2020)

Methods:

This cross-sectional study enrolled patients presenting with abdominal pain and right lower quadrant (RLQ) tenderness suspected of appendicitis at the emergency department .Exclusion criteria encompassed individuals lacking access to diagnostic tests, refusal to participate, history of hematological diseases, prior appendectomy or abdominal surgery, intestinal or infectious diseases, pregnancy, cancer, inflammatory conditions, recent abdominal trauma or procedures, corticosteroid use within the last 14 days, chemotherapy or immunosuppressive drugs within the last 29 days, urinary tract infections or pathology, as indicated by abnormal urine analysis results (WBC > 20 and RBC > 30).

Following enrollment, patients underwent clinical evaluation for acute appendicitis diagnosis, alongside complete blood cell count (CBC) differential analysis. Parameters including mean platelet volume, platelet count, mean platelet volume to platelet count ratio, neutrophils-to-lymphocytes ratio, red blood cell distribution width, platelet distribution width, and platelets-to-lymphocytes ratio were computed. Patients deemed at high risk for appendicitis underwent appendectomy, with excised appendices subjected to histopathological examination. Tissue specimens were processed conventionally, sectioned, stained with hematoxylin-eosin, and diagnosed accordingly. Pathological findings served as the gold standard for appendicitis diagnosis, with desired indicators' diagnostic performance (sensitivity, specificity, and predictive values) evaluated against pathology results. Negative appendectomy was defined as surgical cases lacking appendicitis upon histopathological assessment.

Collected data included demographic information, symptoms, clinical examination findings, medical history, CBC results, and pathology outcomes, recorded via a structured questionnaire. Written consent was obtained from all participants. Sample size estimation followed established methodologies, aiming for a sample size of 200 individuals with a 95% confidence level and 5% error coefficient.

Statistical analyses were conducted using SPSSv17 software, employing Student's t-test, ANOVA, Chi-square, Fisher's exact test, and Mann-Whitney U test as appropriate. Significance was set at p < 0.05. Results were reported as mean \pm standard deviation. The diagnostic performance of parameters was evaluated via receiver operating characteristic (ROC) curve analysis, including sensitivity, specificity, predictive values, and area under the curve (AUC) within a 95% confidence interval.

Ethical approval was obtained from the Research Ethics Board of Alborz University of Medical Sciences (IR.ABZUMS.REC.1399.082).

Results:

A total of 200 patients underwent appendectomy, with 30 (15%) experiencing negative appendectomy. The mean age of participants was 27.59 ± 13.26 years, with 142 (71%) males and 58 (29%) females. There was no statistically significant difference in mean age or gender distribution between positive and negative appendectomy groups (p = .411 and p = .436, respectively).

Significant differences were observed in various CBC parameters between patients with and without appendicitis. Patients with appendicitis exhibited higher mean WBC (13,554.1 \pm 3,396.74 vs. 7,343.33 \pm 1,735.36 10^6/mm^3, p < .001), mean neutrophil levels (11,038.6 \pm 3,432.05 vs. 4,634.0 \pm 1,596.74 10^6/mm^3, p < .001), and mean lymphocytes (1,937.27 \pm 1,362.19 vs. 2,332.9 \pm 1,079.97 10^6/mm^3, p = .005). Additionally, mean RBC, MPV to platelet ratio, neutrophils-to-lymphocytes ratio, and platelets-to-lymphocytes ratio differed significantly between the two groups (p < .05), as determined by Mann-Whitney test due to non-normal distribution.

Receiver operating characteristic (ROC) curve analysis revealed varying diagnostic accuracies for different CBC parameters. The area under the ROC curve for mean platelet volume in diagnosing acute appendicitis was 0.391, with a best cut-off point of 8.75. Platelet count had an AUC of 0.597, with a best cut-off point of 190,500 10^6/mm^3. The ratio of mean platelet volume to platelet count had an AUC of 0.372, with a best cut-off point of 0.0417.

Similarly, the AUC for neutrophils-to-lymphocytes ratio was 0.902, with a cut-off of 3.669. For RDW, the AUC was 0.58, with a cut-off of 55.12, and for PDW, the AUC was 0.588, with a cut-off of 55.13. The AUC for platelets-to-lymphocytes ratio was 0.717, with a cut-off of 128.43. Notably, the highest diagnostic power for appendicitis diagnosis was observed with the neutrophils-to-lymphocytes ratio, exhibiting sensitivity of 83.5% and specificity of 90%. Other CBC-related parameters showed lower diagnostic accuracy. (Table 2 summarizes these findings.)

TABLE 1 Mean and SD of the variables in the studied patients based on the appendectomy

Variables	Negative appendectomy	Acute appendicitis	P-value
WBC (10^6 /mm^3)	7343.33 (±1735.36)	13554.1 (±3396.74)	<.001
Neutrophil (10 ⁶ /mm ³)	4634 (±1596.74)	11038.6 (±3432.05)	<.001
Lymphocyte (10 ⁶ /mm ³)	2332.9 (±1079.97)	1937.27 (±1362.19)	.005
RBC (10^6 /micl)	4.75 (±0.47)	5.04 (±0.972)	.035
Platelets (10 ⁶ /mm ³)	218300 (±49362.2)	241341.17 (±61936.79)	.091
MPV	9.93 (±0.844)	9.62 (±0.950)	.056

PDW	12.11 (±1.414)	11.78 (±1.946)	.1
RDW (fl)	12.56 (±0.904)	12.80 (±0.953)	.123
Platelets/MPV	$0.05~(\pm 0.053)$	0.04 (±0.018)	.025
Neutrophil/lymphocyte	2.61 (±2.133)	7.9 (±4.811)	<.001
Platelets/lymphocyte	119.32 (±108.740)	157.29 (±77.081)	<.001

TABLE 2 Sensitivity and specificity, positive and negative predictive value of the studied variables in the diagnosis of acute appendicitis

Variables	TP	FP	TN	FN	Sensitivity	Specificity	PPV	PNV	PP	PN	Accuracy	Contingence
MPV	137	26	4	33	80.5	13	84	10.8	0.925	1.8	70.5	кΡ
Platelets	134	18	12	36	78.8	40	86.4	25	1.31	0.53	73	0.05
MPV/platelets	92	18	12	78	54.11	40	83.6	13	0.901	1.14	52	0.151
Neutrophil/lymphocyte	142	3	27	28	83.5	90	97.9	49	8.35	0.183	84.5	0.032
RDW	95	11	19	75	55.8	63	89.6	20.2	1.5	0.7	57	0.102
PDW	33	5	25	137	19.4	83	86.8	15.4	1.14	0.971	29	0.01
Platelets/lymphocyte	99	5	25	71	58.2	83	95.1	26	3.42	0.5	62	0.218

Abbreviations: FN (false negative), FP (false positive), PN (probability negative), PNV (predictive value negative), PP (probability positive), PPV (predictive value positive), TN (true negative), TP (true positive).

This table presents the sensitivity, specificity, positive predictive value (PPV), negative predictive value (PNV), positive probability (PP), negative probability (PN), accuracy, and contingence for various studied variables in the diagnosis of acute appendicitis.

Discussion:

The study conducted on 206 healthy individuals and 226 patients with suspected acute appendicitis revealed significant differences in mean platelet volume (MPV) between patients with acute appendicitis and healthy controls. However, the diagnostic power of MPV alone was found to be low in our study, contrary to previous findings suggesting its potential as a diagnostic marker. Despite its inclusion in complete blood count (CBC), MPV did not exhibit high specificity or predictive value for diagnosing acute appendicitis, with a reported specificity of only 13% and predictive value of 10.8%. (Moitaba et al., 2020)

Earlier research by Yavuz et al. (2010) and Gu et al. (2017) highlighted the diagnostic value of MPV and platelet markers in acute appendicitis. However, our study results diverge, indicating a need for caution in relying solely on MPV for diagnosis. (Yavuz and Ece, 2014) (Gu Nes et al., 2017)

Additionally, studies by Bosh et al. (2018) and Kahramanca et al. (2014) emphasized the potential diagnostic utility of platelet-related parameters, such as platelet-to-lymphocyte ratio (PLR). While our findings also noted elevated platelets-to-lymphocytes ratio in acute appendicitis patients, its diagnostic power was found to be limited. (Bosh et al., 2018) (Kahramanca et al., 2014)

Similarly, a study by Alexander et al. in Nigeria explored the diagnostic markers including neutrophils-to-lymphocytes ratio (NLR), platelets-to-lymphocytes ratio, and MPV. Despite some variations by age and gender, the diagnostic power of these markers for acute appendicitis was not found to be high. This aligns with our study's results, indicating that MPV and platelets-to-lymphocytes ratio may not serve as reliable diagnostic markers independently. (Alexander et al., 1968)

Moreover, a study by RoozRokh et al. emphasized the importance of combining diagnostic tests, such as C-reactive protein (CRP) and white blood cell (WBC) count, for improved sensitivity in diagnosing acute appendicitis in children. While our study found high sensitivity and specificity for NLR, its agreement with pathology results was moderate, suggesting that NLR alone may not suffice for accurate diagnosis. (Roozrokh and Stahlfeld, 2002)

In conclusion, while various CBC parameters, including MPV and platelet-related ratios, have been explored for their diagnostic potential in acute appendicitis, our study emphasizes the need for cautious interpretation. While these markers may contribute to suspicion, their diagnostic power alone appears to be limited. Combined with clinical findings and imaging, they may enhance diagnostic accuracy, but further research is warranted to establish comprehensive diagnostic criteria for acute appendicitis. (Akbulut et al., 2019)

Conclusion

In conclusion, our study revealed that 15% of patients who underwent appendectomy had negative pathology results, highlighting the challenge in relying solely on complete blood count (CBC) findings for diagnosing acute appendicitis. Therefore, it is evident that none of the CBC parameters alone should be considered diagnostic criteria for this condition.

It is imperative to acknowledge the limitations of individual CBC markers in accurately diagnosing acute appendicitis. Instead, future research should focus on assessing the combined accuracy of CBC parameters alongside other clinical, paraclinical, and imaging studies. By integrating multiple diagnostic modalities, including CBC findings, clinicians can improve diagnostic accuracy and reduce the burden of unnecessary appendectomies with negative outcomes. This approach will enhance patient care by ensuring appropriate surgical interventions and minimizing the risk of unnecessary procedures.

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