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Use of Different Haematological Parameter as a Predictor of Complicated Appendicitis

Dr. Md. Yeakub Hosain[1*], Dr. Md. Jakir Hossain[2], Dr. Md. Mahbub Azad[3], Dr. Shahin Reza[4], Dr. Mohmmad Shahin Kabir[5]

[1]MBBS, MS(Surgery), Registrar (Surgery), Department of Surgery, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh
[2]MBBS, FCPS(Surgery), Emergency Medical Officer, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh
[3]MBBS, FCPS(Surgery), Medical Officer, Department of Surgery, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh
[4]MBBS, MCPS(Surgery), FCPS(Surgery), Assistant Registrar (Surgery), Department of Surgery, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh
[5]MBBS, MS(Surgery), Registrar (Surgery), Department of Surgery, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh

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***Corresponding author:** Dr. Md. Yeakub Hosain
MBBS, MS(Surgery), Registrar (Surgery), Department of Surgery, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh

Abstract **Original Research Article**

Background: Acute appendicitis is the most common indication for emergency abdominal surgery. The diagnosis of appendicitis depends on the subjective criteria of clinical examination. However, distinguishing acute complicated appendicitis and uncomplicated is often difficult especially in the elderly population that usually not clinically specific unless it has developed into generalized peritonitis. Between the complicated and uncomplicated should be distinguished because of different surgical approaches. Haematological parameters are needed that would lead to early diagnosis. These tests are not only cheaper, but also feasible and available in peripheral hospitals compared to other supports such as USG, CT scan. ***Aims:*** To evaluate the predictive value of different haematological parameter in the diagnosis of acute complicated appendicitis. ***Methods:*** This prospective observational study was conducted in the Department of Surgery, Dhaka Medical College & Hospital over a period of one year. The patients who were admitted as suspected case of acute appendicitis are enrolled in this study. Data were collected in a pre-designed data collection sheet including particulars of the patients, detailed history, clinical examination, pre-existing co-morbidities and relevant investigations. ***Results:*** The mean age was found 27.66±10.62 years and 30.73±13.16 years in complicated and uncomplicated appendectomy. No significant difference of age between complicated and uncomplicated appendicectomy. Male patients were significantly higher in in complicated appendicitis group ($p<0.05$). Among 170 patients, 77 were found complicated appendicitis and 93 were uncomplicated appendicitis. There were statistically significant differences between the groups in WBC, NEU, LYM, NLR, CRP. The cut-off values of NLR, WBC, and NEU were 4.57, 15150x10^9/L, and 77.5x10^9/L, respectively for complicated appendicitis. The cut off value of CRP, platelet count was 4.50 mg/dl and 235.0 for complicated appendicitis. ***Conclusions:*** Elevated WBC, NEU, CRP and NLR may be considered useful biomarkers in assisting physical examination and other diagnostic methods in distinguishing severity of acute appendicitis.

Keywords: Acute appendicitis, Haematological parameter, abdomen.

INTRODUCTION

Appendicitis is the most common acute surgical disease of the abdomen [1]. Acute appendicitis is inflammation of the vermiform appendix due to lumen obstruction followed by bacterial infection. Acute appendicitis can be classified into two groups, namely complicated and uncomplicated. Complicated acute appendicitis (perforation, abscess, gangrene, and peritonitis) may be detected in 20% to 30% of all appendicitis patients [2]. It is related with increased risk of morbidity and mortality. Complicated appendicitis is associated with increased rate of wound infection, intra-abdominal abscess and postoperative ileus [3]. It is more common in elderly patients due to nonspecific clinical manifestations and co-morbidity. The high risk of complication also increases with increasing duration of symptoms [4].

The diagnosis of acute appendicitis depends on subjective criteria such as onset of symptoms, type of pain and physical examination. Distinguishing uncomplicated appendicitis with complication based on clinical findings is often difficult especially in elderly patients unless it has developed into generalized peritonitis. Investigations such as ultrasound or CT scan can help establish a diagnosis of complicated appendicitis and assist a surgeon to determine the approach of surgical technique [5].

Haematological parameter are needed that would lead to early diagnosis. They must be easily applicable everywhere, be cheap, non invasive and be reasonably accurate. These include white blood cell (WBC), neutrophil count, C-reactive protein (CRP), neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), platelet distribution width (PDW), red cell distribution width (RDW), and total serum bilirubin as a parameter for diagnosis of complicated appendicitis [6].

White cell counts such as neutrophils, and C-reactive protein are indicators of early inflammation in acute appendicitis [7]. Platelets are cytoplasmic fragments of bone marrow megakaryocytes with a diameter of 3-5micrometer and a volume of 4.5-11fL.Its dynamic functions are coagulation, hemostasis, inflammatory process, microbial host defence, wound healing, angiogenesis, and remodeling. Platelet indices are biomarkers of platelet activation.

Increased MPV indicates increased platelet diameter which can be used as a marker of production rate. PDW is an indicator of volume variability in platelet size and increased in the presence of platelet anisocytosis. Red cell distribution width (RDW) is the measurement of size variability of red cells. These blood parameters are related to inflammatory cases as in the case of appendicitis to distinguish between complicated and uncomplicated appendicitis [8]. Serum total bilirubin level also associated with appendicitis, presumably be due to the spread of bacteria or toxins through the portal vein from the GIT to the liver [9]. Study shows hyperbilirubinemia as a predictor of complicated appendicitis. Evidence shows that alteration of these haematological parameters are associated with appendicitis (McGowan *et al.*, 2013) [10]. This study will be conducted to evaluate the possibility.

OBJECTIVE

General Objectives:

- To evaluate the predictive value of different haematological parameter in the diagnosis of acute complicated appendicitis.

Specific Objectives:

- To assess the diagnostic accuracy of WBC, CRP, NLR, MPV, PDW, RDW and serum bilirubin, either individually or combined, in the prediction of complicated appendicitis.
- To compare among these parameters in rapid diagnosis of uncomplicated and complicated acute appendicitis.
- To make a recommendation for taking necessary measures to reduce morbidity and mortality of complicated acute appendicitis.

METHODOLOGY

Study Design: Prospective observational study

Period of Study: 01 (One) Year (01.07.2020-30.06.2021).

Place of Study: Department of Surgery, Dhaka Medical College & Hospital, Dhaka

Study Population: Patients those are admitted in Department of Surgery, DMCH & with a final diagnosis of acute appendicitis.

Selection Criteria:

Inclusion Criteria:

- Patients aged 14 years or older who was admitted in Department of Surgery, DMCH, with a diagnosis of acute appendicitis.
- Willing to be operated.
- Patient who was given consent for this study.

Exclusion Criteria:

- Patients with chief complaint of diffuse abdominal tenderness.
- Patients with other acute infectious diseases.
- Acute appendicitis with previous liver disease.
- Acute appendicitis with co-morbidity (heart disease, malignancy, diabetes mellitus, tuberculosis, AIDS, and auto immune diseases).
- Patients with severe sepsis or septic shock.

Method of Sampling: Purposing sampling (non randomized)

Sample Size: The sample size for this study would be-170.

Data processing and analysis:

All data were checked and edited after collection. Later, the data was put into the computer and analyzed with the help of trial version of software programme SPSS 26.0 (Statistical Package for Social Sciences) for windows and MS Excel work sheet. The measure of central tendency (Mean), measure of dispersion (Standard Deviation) and unpaired student's 't' test were calculated according to data distribution for continuous variables. Categorical data was reported as

numbers and percentage (%). Significant test of categorical variables was performed with Chi-square test with 95% confidence interval to make inference. Receiver operating characteristic (ROC) analysis and the area under the ROC curve (AUC) and 95% confidence intervals of haematological parameters were calculated to determine the best cut-off point. Then data were presented in the form of tables, graphs, frequency distribution and cross tabulation. P-value of less than 0.05 was considered as significant. Diagnostic performance was evaluated by sensitivity, specificity, positive predictive value, negative predictive value and accuracy or efficacy.

RESULTS

The study was conducted on 170 patients with a final diagnosis of acute appendicitis who had undergone an appendectomy. Of 170 patients, 77 were found complicated appendectomy and 93 were uncomplicated appendectomy.

Table-I: Comparison of age between complicated and uncomplicated appendectomy of the study patients (n=170)

Age group (years)	Complicated appendicitis (n=77)	Uncomplicated appendicitis (n=93)	p-value
16-25	38(49.4%)	39(41.9%)	
26-35	21(27.3%)	24(25.8%)	
36-45	11(14.3%)	21(22.6%)	
46-55	7(9.1%)	6(6.5%)	
56-65	0(0.0%)	3(3.2%)	
Total	77(100.0%)	93(100.0%)	
Mean±SD Range (min-max)	27.66±10.62 (16-50)	30.73±13.16 (16-65	0.101^{ns}

Data were expressed as frequency and percentage and mean±SD
Unpaired student t-test was performed to compare between two groups
ns = not significant

Table-I shows age of the study population, it was observed that maximum (49.4%) and 39(41.9%) patients belonged to 16-25 years followed by 27.3% and 25.8% patients age group 26-35 years in complicated and uncomplicated appendicectomy. The mean age was found 27.66±10.62 years and 30.73±13.16 years in complicated and uncomplicated appendectomy. No significant difference of age between complicated and uncomplicated appendicectomy (p>0.05).

Table-II: Association of gender between complicated and uncomplicated appendectomy of the study patients (n=170)

Gender	Complicated appendicitis (n=77)	Uncomplicated appendicitis (n=93)	p-value
Male	66(85.7%)	54(58.1%)	<0.001*
Female	11(14.3%)	39(41.9%)	
Total	77(100.0%)	93(100.0%)	

Figures in the parentheses indicate corresponding **percentage;**
Chi-squared Test (χ^2) was done to analyze the data**.**
*significant

Table-II showed the sex distribution of the study patients. The number of males and females in complicated appendicitis group was 66(85.7%) and 11(14.3%), respectively, and 54(58.1%) and 39(41.9%) in uncomplicated appendicitis group. Male patients were significantly higher in complicated appendectomy group (p<0.05).

Table-III: Comparison of haematological parameters between complicated and uncomplicated appendectomy of the study patients (n=170)

Haematologial parameters	Complicated appendicitis (n=77)	Uncomplicated appendicitis (n=93)	p-value
Total WBC (/mm^3)	18557.7±4788.5 (12100-29800)	14239.3±3017.2 (8300-21800)	<0.001*
Neutrophil (×10^9/L)	81.06±5.94 (60-93)	74.53±9.55 (53-86)	<0.001*
Lymphocyte (×10^9/L)	14.27±4.59 (6-28)	22.65±6.60 (13-38)	<0.001*

Haematologial parameters	Complicated appendicitis (n=77)	Uncomplicated appendicitis (n=93)	p-value
NLR	6.33±2.27 (2.83-14.17)	3.65±1.31 (1.39-6.23)	<0.001*
CRP (mg/dl)	7.62±2.77 (1.90-12)	2.80±2.39 (0.80-6)	<0.001*
Platelet count	259.14±59.61 (170-514)	233.19±55.30 (137-392)	0.004*
MPV (fL)	8.02±1.05 (6.35-9.89)	8.05±1.37 (5.60-10.90)	0.886
PDW (fL)	11.57±2.08 (7.90-16.30)	11.98±1.70 (9.80-16)	0.1259
RDW (%)	14.41±4.13 (3.50-22.10)	13.56±3.44 (5.12-20.30)	0.145

Data were expressed as mean±SD
Unpaired student t-test was performed to compare between two groups
*significant

Table III shows the comparisons of haematological parameters between the groups. There were statistically significant differences between the groups with respect to WBC, NEU, LYM, NLR, CRP, and platelet. The mean MPV, PDW, and RDW were not statistically significant between the groups.

Table-IV: Comparison of serum bilirubin between complicated and uncomplicated appendectomy of the study patients (n=170)

Variable	Complicated appendicitis (n=77)	Uncomplicated appendicitis (n=93)	p-value
Serum Bilirubin (mg/dL)	0.94±0.13 (0.71-1.32)	0.64±0.10 (0.46-0.77)	<0.001*

Data were expressed as mean±SD
Unpaired student t-test was performed to compare between two groups
ns = not significant

Independent t-test showed a higher significant difference in serum bilirubin levels in patients with acute complicated appendicitis (0.94±0.13) compared to uncomplicated appendicitis (0.64±0.10) with p <0.001, suggesting a significant association between increased serum bilirubin levels and complicated appendicitis.

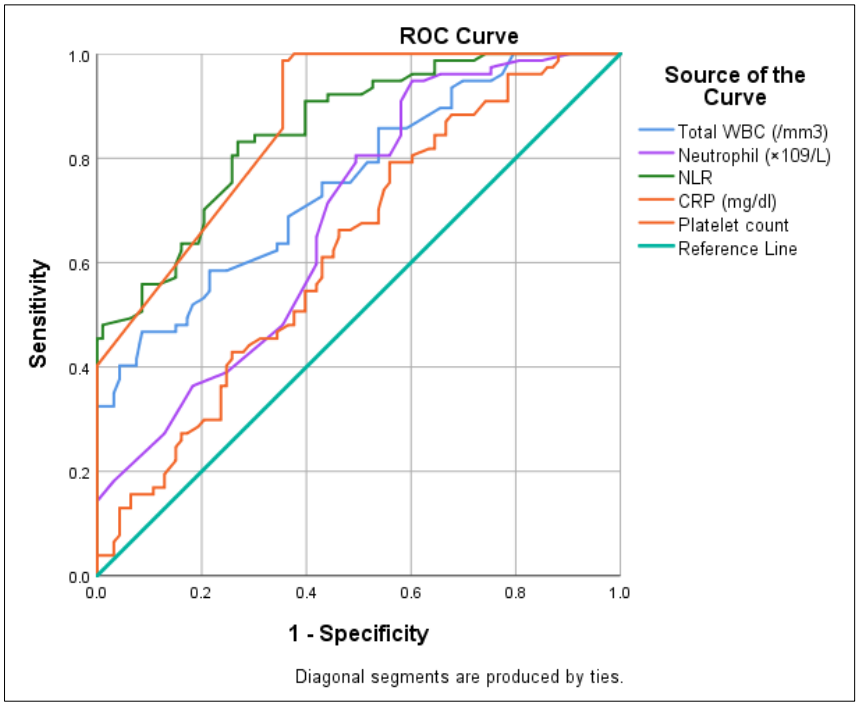

Figure-1: Receiver operating characteristic (ROC) curve analyses of significant parameters (NLR, WBC and NEU) for diagnosis of complicated appendicitis

Table V: Receiver operating characteristic curve (ROC) for the significant parameters in diagnosis of complicated appendicitis (n=170)

Test Result Variable(s)	AUC	Cut-off value	Sensitivity	Specificity	p-value	95% CI	
						Lower	Upper
Total WBC (/mm3)	.753	15150	68.8%	63.4%	.000	.681	.825
Neutrophil ($\times 10^9$/L)	.685	77.5	79.2%	51.5%	.000	.606	.763
NLR	.854	4.57	83.1%	73.1%	.000	.799	.908
CRP (mg/dl)	.868	4.50	97.4%	64.5%	.000	.818	.919
Platelet count	.625	235.0	61.0%	57.0%	.005	.542	.709

Diagnostic value of statistically significant parameters was analysed by using ROC analysis. The cut-off value of WBC in differential diagnosis of complicated appendicitis was 15150, with sensitivity of 68.8% and specificity of 63.4% (AUC: 0.753; 95% CI: 0.681–.825; p<0.001).

The cut-off value of neutrophil in differential diagnosis of complicated appendicitis was 77.5, with sensitivity of 79.2% and specificity of 51.5% (AUC: 0.685; 95% CI: 0.606–.763; p<0.001).

The cut-off value of NLR in differential diagnosis of complicated appendicitis was 4.57, with sensitivity of 83.1% and specificity of 73.1% (AUC: 0.854; 95% CI: 0.799– 0.908; p<0.001).

The cut-off value of CRP in differential diagnosis of complicated appendicitis was 4.50, with sensitivity of 97.4% and specificity of 64.5% (AUC: 0.868; 95% CI: 0.818– 0.919; p<0.001).

The cut-off value of platelet count in differential diagnosis of complicated appendicitis was 235, with sensitivity of 61.0% and specificity of 57.0% (AUC: 0.625; 95% CI: 0.542–.709; p=0.005).

DISCUSSION

In present study showed maximum (49.4%) and 39(41.9%) patients belonged to 16-25 years followed by 27.3% and 25.8% patients age group 26-35 years in complicated and uncomplicated appendicectomy. The mean age was found 27.66±10.62 years and 30.73±13.16 years in complicated and uncomplicated appendectomy. No significant difference of age between complicated and uncomplicated appendicectomy (p>0.05). Male patients were significantly higher in in complicated appendectomy group (p<0.05). In agreement this study Toktas *et al.*, (2017) reported the mean age of the AA cases was 28±9 years, and the mean age of control subjects was 29±10 years. Of the 30 acute appendicitis cases, 8 were female and 22 were male[11]. Age and gender were not significantly different among the groups. A total 68 (60.71%) patients were males and 44 (39.28%) were females, the male to female ratio being 1.5:1. The age range was 11-75 years, with a mean age of 27.6 years.

In present study demonstrated that statistically significant increased in complicated appendicitis compare to uncomplicated appendicitis respect to WBC, NEU, NLR, CRP, and platelet. The mean MPV, PDW, and RDW were not statistically significant between complicated and uncomplicated appendicitis. In accordance this study Sengul *et al.,* (2020) reported statistically significant differences between the groups with related to WBC, NEU, LYM, NLR and CRP. The mean MPV, PDW, and RDW were not statistically significant among the groups [12].

Acute appendicitis is one of the most common conditions requiring urgent surgery [13]. Whereas laboratory tests scoring systems, and imaging methods are used to diagnose acute appendicitis: Difficulties and delays in diagnosis in some cases may result in complications [14]. Therefore, researchers have focused on cheap, easy-to-use biomarkers with high diagnostic accuracy advocated that NLR is a useful predictor of appendicitis severity.

WBC is the most frequently used diagnostic laboratory test in acute appendicitis. Diagnostic value of statistically significant parameters was analysed by using ROC analysis. The cut-off value of WBC in differential diagnosis of complicated appendicitis was 15.15/mm^3, with sensitivity of 68.8% and specificity of 63.4% (AUC: 0.753; 95% CI: 0.681–.825; p<0.001). Sevinc *et al.*, (2016) analysed 3,392 acute appendicitis cases and found a WBC cut-off value of 11.900/mm3 (sensitivity 71.2%; specificity 67.2%) [15]. Bilici *et al.,* (2011) investigated the diagnostic value of WBC cut-off value of 11.000/mm3 (sensitivity 84%; specificity 89%) in paediatric cases [16].

In present study showed the cut-off value of NLR in differential diagnosis of complicated appendicitis was 4.57, with sensitivity of 83.1% and specificity of 73.1% (AUC: 0.854; 95% CI: 0.799–0.908; p<0.001). Kelly *et al.,* (2015) reported a NLR cut off value of 5.96 (sensitivity 62%; specificity 79%) to differentiate negative and positive appendectomy [17].

They also found a cut-off value of 6.35 (sensitivity 85%; specificity 48%) to discriminate complicated appendicitis. However, they showed a cut-off value of 7.53 (sensitivity 80%, specificity 55%) to diagnose perforation under the age of 18 years. A cut-off value of 3.0 (sensitivity 81.2%; specificity 53.1%) for acute appendicitis and 4.8 (sensitivity 78.4%; specificity 41.7%) for perforated appendicitis. According to the present results, NLR values were significantly different between the uncomplicated and complicated appendectomy groups ($p<0.001$). A cut-off value of 4.57 (sensitivity 83.1%; specificity 73.1%) was found for NLR to diagnose to diagnose complicated appendicitis.

Neutrophil count is one of the important parameters used for the differential diagnosis between uncomplicated appendicitis and complicated appendicitis. In this study, the cut-off value for neutrophil count was $7.75x10^9$/L (sensitivity 97.2%; specificity 51.5%) for complicated appendicitis. In accordance this study Sengul *et al.,* (2020) reported the cut-off value for neutrophil count was $10.3x10^9$/L (sensitivity 95.2%, specificity 76.7%) for complicated appendicitis [12]. Boshnak *et al.,* (2018) in a 200-patient prospective study, found a sensitivity of 72.4% and a specificity of 81.8 % for a cut-off level 9.4x109/L of neutrophil count for acute appendicitis [13]. In a study Bilici *et al.,* (2011) reported that neutrophil count had a sensitivity of 77% and a specificity of 91% for a cut-off level of >8 x109/L for diagnosing acute appendicitis [16].

C-reactive protein is an acute phase reactant and may be used as a diagnostic marker in acute inflammatory conditions. Studies in the literature have reported cut-off levels of CRP ranging between 0.5-1.7 mg/dL and having sensitivities of 38-91% and specificities of 26-98% (2014). The authors could not determine a cut-off level for CRP diagnostic of acute un-complicated appendicitis. However, we found a cut-off value of 1,3 mg/dL in acute complicated appendicitis (sensitivity 81%; specificity 80%).

In present study showed the cut-off value of platelet count in differential diagnosis of complicated appendicitis was 235, with sensitivity of 61.0% and specificity of 57.0% (AUC: 0.625; 95% CI: 0.542–.709; p=0.005). Recently, researchers have found a relationship between the changes in platelet indices and many inflammatory conditions, such as inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis, and atherosclerosis [18].

In present showed a higher significant difference in serum bilirubin levels in patients with acute complicated appendicitis (0.94±0.13) compared to uncomplicated appendicitis (0.64±0.10) with $p <0.001$, suggesting a significant association between increased serum bilirubin levels and complicated appendicitis. Research on hyperbilirubinemia as a predictor of perforated appendicitis has been performed by Chaudhary *et al.,* (2013) and serum bilirubin levels were suggested to be a potentially important adjunct in predicting the presence of perforated appendicitis [19]. The higher serum bilirubin levels were reported in patients with complicated acute appendicitis compared to uncomplicated acute appendicitis ($p<0.001$), which was consistent with present study.

CONCLUSION

Considering the adolescent age group, WBC, neutrophil, and NLR appear as useful serum biomarkers for diagnosing acute appendicitis. As for the distinction between uncomplicated and complicated appendicitis, WBC, Neutrophil, CRP, and NLR may be of use. A NLR cut-off level >4.57 may be helpful to make surgeons consider surgical treatment instead of antibiotic-based conservative management to prevent delays. MPV, RDW, and PDW, however, were not significantly helpful for that indication.

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