

## Original Research Article

# Role of leucocytosis, hyperbilirubineamia, decreased mean platelet volume and increased international normalized ratio in prediction of complicated appendicitis

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## ABSTRACT

**Background:** A diagnostic approach for complicated appendicitis is still controversial. We analyzed the preoperative laboratory markers that may predict complicated appendicitis.

**Methods:** To study the role of leukocytosis, hyperbilirubinemia, decreased mean platelet volume (MPV) and increased international normalized ratio (INR) in the prediction of complicated appendicitis. Total 60 patients were enrolled and divided them into 2 groups, un-complicated (AUA) and complicated (ACA) acute appendicitis, each having 30 cases.

**Results:** Total leucocyte count (TLC) >10000 mm<sup>3</sup> was found in 70% of AUA cases and 80% of ACA cases serum bilirubin >1 mg/dl was found in 66.67% of AUA cases and 80 % of ACA cases. MPV <7.6 fL was found in 60% of AUA and 80% of ACA cases INR >1.2 was found in 20 % of AUA and 40% of ACA cases. TLC >10000/mm<sup>3</sup>, serum bilirubin >1 mg/dl and MPV <7.6 fL was found in 46.67% of AUA cases and 70 % of ACA cases.

**Conclusions:** Total leucocyte count, serum bilirubin and mean platelet volume have a predictive potential for the diagnosis of complicated appendicitis.

**Keywords:** Acute appendicitis, INR, MPV, Serum bilirubin, TLC

## INTRODUCTION

Appendicitis is a common surgical disease. The lifetime risk for having appendicitis is reported to be about 7 to 10%.<sup>1,2</sup> Usual management of appendicitis is a laparoscopic appendectomy, which has a lower complication rate, length of hospital stays, and mortality than open appendectomy.<sup>3,4</sup> However, morbidity or mortality even the after laparoscopic appendectomy could be happened.<sup>5-8</sup>

Many studies looked at managing uncomplicated appendicitis, including the use of antibiotics in

conservative management.<sup>9-11</sup> No definite method is currently available to differentiate complicated from uncomplicated appendicitis preoperatively, albeit several studies about predicting complicated appendicitis were published.<sup>12-15</sup>

A diagnostic approach for complicated appendicitis is still controversial. We analyzed preoperative laboratory markers that may predict complicated appendicitis.

Our focus in this study was on preoperative laboratory markers to predict whether they can complicate appendicitis or not.

## Objectives

This study seeks to investigate whether there is a statistically significant association between different investigations such as blood routine [including total leucocyte count (TLC), serum bilirubin, mean platelet volume (MPV) and international normalized ratio (INR)] and appendicitis (simple or perforated).

## METHODS

This prospective observational study was conducted after getting the ethical approval in the Department of General Surgery, Dr. S. N. Medical College and Associated Hospitals, Jodhpur, Rajasthan for management from January 2016 to December 2017. We assigned total 60 patients based on clinical and operative finding and these were divided into 2 groups [complicated appendicitis (AUA) and non-complicated appendicitis (ACA)], each having 30 patients.

We chose convenient sampling as those who were of >12 years of age with appendicitis proven by clinical findings and ultrasonography and excluded who are <12 years of age or who refused for admission and surgery and those who were terminally ill.

Details of cases were recorded including history and clinical examination. Investigations such as blood routine (including TLC, serum bilirubin, MPV and INR) and ultrasonography, computed tomography (CT) were done. The preoperative diagnosis was made. Based on intraoperative findings, periappendiceal abscess, gangrenous appendicitis was considered as ACA, whereas other findings were considered as AUA.

The results were analyzed using "Pearson Chi-square test".  $P < 0.05$  was considered significant.

## RESULTS

In both the groups, AUA and ACA, patients ranges between 21-30 years of age are most commonly affected, 53.33% and 46.67%, respectively, followed by age group 11-20 years with the incidence of 23.33% and 30%

respectively. The mean age in AUA group is 26.03 with a standard deviation (SD) of 7.58 and in ACA group mean age is 26.53 with 8.06 SD (Table 1).

**Table 1: Age wise distribution of AUA and ACA.**

Age (in years)	Uncomplicated (AUA)		Complicated (ACA)	
	No. of patients	%	No. of patients	%
11-20	7	23.33	9	30.00
21-30	16	53.33	14	46.67
31-40	5	16.67	5	16.67
>40	2	6.67	2	6.67
<b>Mean SD</b>	26.03±7.58		26.53±8.06	

As per Table 2, mean age for male in AUA group was 26.77 years with standard deviation of 8.57 and for female was 24.91 years with standard deviation of 5.97. In ACA group, mean age for male was 26.33 years with standard deviation of 6.68 and mean age for female was 27 with standard deviation of 11.11.

As per Table 3, out of 30 AUA cases, 21 (70%) had TLC >10,000 while 9 (30%) had TLC ≤10,000. Out of 30 ACA cases, 24 (80%) had TLC >10,000 while 6 (20%) had TLC ≤10,000. Out of 30 AUA cases, 20 (66.67%) had serum bilirubin >1 while 10 (33.33%) had serum bilirubin ≤1. Out of 30 ACA cases, 24 (80%) had serum bilirubin >1 while 6 (20%) had serum bilirubin ≤1. Out of 30 AUA cases, 18 (60%) had MPV <7.6 while 12 (40%) had MPV ≥7.6. Out of 30 ACA cases, 24 (80%) had MPV <7.6 while 6 (20%) had MPV ≥7.6. Out of 30 AUA cases, 6 (20%) had INR >1.2 while 24 (80%) had INR ≤1.2. Out of 30 ACA cases, 12 (40%) had INR >1.2 while 18 (60%) had INR ≤1.2.

Table 4 shows the mean TLC level in AUA patients was 10091±2344.7/mm<sup>3</sup> and in ACA patients were 13557.1±4031.6/mm<sup>3</sup>. The mean serum bilirubin level in AUA patients was 1.09±0.16 mg/dl and in ACA patients was 1.5±0.59 mg/dl. The mean MPV level in AUA patients was 7.49±0.39 fl and in ACA patients was 7.24±0.35 fl. The mean INR level in AUA patients was 1.11±0.13 and in ACA patients was 1.18±0.17.

**Table 2: Gender wise distribution in both groups.**

Sex	Uncomplicated (AUA)			Complicated (ACA)		
	No. of patients	Mean age	%	No. of patients	Mean age	%
Male	18	26.77±8.57	60.00	21	26.33±6.68	70.00
Female	12	24.91±5.97	40.00	9	27±11.11	30.00
<b>Total</b>	30		100.0	30		100.00

**Table 3: Outcome as per TLC, serum bilirubin, MPV and INR.**

Parameters	Values	Uncomplicated (AUA)		Complicated (ACA)	
		No. of patients	%	No. of patients	%
	≤10000	9	30	6	20

Continued.

Parameters	Values	Uncomplicated (AUA)		Complicated (ACA)	
		No. of patients	%	No. of patients	%
TLC (/mm <sup>3</sup> )	>10000	21	70	24	80
	Total	30	100	30	100
Serum bilirubin (mg/dl)	<1	10	33.33	6	20
	>1	20	66.67	24	80
	Total	30	100	30	100
Mean platelet volume (fL)	<7.7	18	60	24	80
	≥7.6	12	40	6	20
	Total	30	100	30	100
INR	≤1.2	24	80	18	60
	>1.2	6	20	12	40
	Total	30	100	30	100

**Table 4: Comparison of TLC, serum bilirubin, MPV and INR in both the groups.**

Parameters	Uncomplicated (AUA)	Complicated (ACA)	P value
	Mean SD	Mean SD	
TLC (/mm <sup>3</sup> )	10091±2344.7	13557.1±4031.6	0.0001
Serum bilirubin (mg/dl)	1.09±0.16	1.5±0.59	0.0006
MPV (fL)	7.49±0.39	7.24±0.35	0.012
INR	1.11±0.13	1.18±0.17	0.075

**Table 5: Comparison of patients having TLC >10000/mm<sup>3</sup>, serum bilirubin >1 mg/dl and MPV <7.6 fL with patients having TLC ≤10000/mm<sup>3</sup>, serum bilirubin ≤1 mg/dl and MPV ≥7.6 fL.**

Parameters	Uncomplicated (AUA)		Complicated (ACA)		P value
	No. of patients	%	No. of patients	%	
TLC >10000/mm <sup>3</sup> , serum bilirubin >1 mg/dl and MPV <7.6 fL	14	46.67	21	70	0.115
TLC ≤10000/mm <sup>3</sup> , serum bilirubin ≤1 mg/dl and MPV ≥7.6 fL	16	53.33	9	30	
Total	30	100	30	100	-

## DISCUSSION

Acute appendicitis is that the commonest explanation for “acute abdomen” in young adults. The appendectomy is the most often performed urgent abdominal operation and is usually the first major procedure performed by a surgeon in training.

The clinical diagnosis of acute appendicitis is corner stone; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 50% of cases, therefore, laboratory investigations provide significant complimentary aid in diagnosis as well as to differentiate between a non-complicated to complicated appendicitis. The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly as such procedures are associated with complications in 50% cases. Hence, the diagnosis of appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations.

The importance of specific elements within the clinical diagnosis of appendicitis is controversial. This study

analyzed the diagnostic value of various laboratory test leads to suspected complicated appendicitis.

The overall demographic findings of present study in terms of gender distribution was in-keeping with the finding of Ohene-yeboah et al, where, they found male and female proportions as 68.6 % and 31.4 % respectively.<sup>16</sup> In the present study (Table 2) collectively the percentage of male participants were 70% and the female were 30%, which corresponds with the study of Ohene-yeboah et al.

Increase in total leucocyte count and duration of the presentation can be a good marker of complicated appendicitis.<sup>17</sup> White blood cell count or C-reactive protein (CRP) values alone do not appear to provide any useful additional information to the surgeon. However, the sensitivity of the two combined tests is extremely high and normal values of both white blood cell count (WBCC) and CRP are impossible in pathologically confirmed appendicitis.<sup>18</sup> Assessment of appendix diameter and complete blood count parameters can be used together to increase the diagnostic value of AA.<sup>19</sup> The mean TLC level (Table 4) in AUA patients was 10091±2344.7/mm<sup>3</sup> and in ACA patients was 13557.1±4031.6 /mm<sup>3</sup> (p=0.0001) which was significantly higher.

A systematic Medline search was made from all published studies on the clinical and laboratory diagnosis of appendicitis. This meta-analysis of receiver-operator characteristic (ROC) areas and positive and negative likelihood ratios, of 28 diagnostic variables described in 24 studies are presented.<sup>20-24</sup>

Its conclusion was although all clinical and laboratory variables such as rebound and percussion tenderness, guarding and rigidity, migration, granulocyte count, proportion of polymorphonuclear blood cells, WBCC and CRP concentration were weak discriminators individually, they achieve a high discriminatory power when combined. Laboratory examination of the inflammatory response, clinical descriptors of peritoneal irritation, and a history of migration of pain yield the foremost important diagnostic information and will be included in any diagnostic assessment.<sup>20</sup>

Delayed or wrong diagnosis in patients with appendicitis may result in perforation and consequently increased morbidity and mortality. Serum bilirubin could also be a useful marker for appendicular perforation.<sup>21</sup> Elevated serum bilirubin for determining the danger of perforation in appendicitis has low sensitivity but higher specificity. This measure can therefore be used as a supplement in the diagnostic process.<sup>21</sup>

The mean serum bilirubin level (Table 4) in AUA patients was  $1.09 \pm 0.16$  mg/dl and in ACA patients was  $1.5 \pm 0.59$  mg/dl ( $p=0.0006$ , significantly higher). Sand et al in their study found the mean bilirubin levels in patients with appendicular perforation to be significantly higher than those with a non-perforated appendicitis. So the assessment of bilirubin levels must be a part of the initial evaluation of suspected appendicitis in the emergency room.<sup>22</sup>

Hyperbilirubinemia is the result of an imbalance between production and excretion of bilirubin by the liver. It may be because of hepatocellular, cholestatic or hemolytic diseases. The liver receives blood mainly through the portal venous system, portal blood carries nutrients and other substances absorbed from GIT including microorganisms and their product (toxins). Detoxification and immunological action of the reticuloendothelial system of the liver act as a first-line defense in clearing toxic substances, bacteria and its products. But when bacterial load overwhelms the Kupffer cell function, it's going to cause dysfunction or damage to hepatocytes (liver parenchyma). It reflects an increase in serum bilirubin alone or together with liver enzymes depending upon the sort, severity and site of the lesion.

In a retrospective cohort study conducted by Akturk et al on 221 patients who were operated, for acute appendicitis the total and indirect bilirubin levels were significantly higher in patients with perforated appendicitis compared with patients with simple appendicitis.<sup>23</sup> Elevated serum bilirubin had a sensitivity of 50.00 (95% CI 29.93 to 70.07)

and a specificity of 80.73 (95% CI 74.43 to 86.05) when predicting perforated appendicitis.<sup>23</sup> So appendicular perforation could also be accompanied with elevated serum bilirubin level.

Mean platelet volume (MPV) - a platelet parameter - might be an index of inflammation. In the present study, the mean MPV level (Table 4) in AUA patients was  $7.49 \pm 0.39$  fl and in ACA patients was  $7.24 \pm 0.35$  fL ( $p$  value=0.012). Danese et al speculated that the reduced MPV might be thanks to the consumption or sequestration of the massively activated platelets within the intestinal vasculature.<sup>23</sup> The results of a systemic meta-analysis showed a prominent decline of MPV levels in patients suffering from AA, compared to the control group (weighted mean difference -0.64; 95% CI, -0.74 to -0.54;  $p=0.037$ ).<sup>25</sup>

The mean INR level (Table 4) in AUA patients was  $1.11 \pm 0.13$  and in ACA patients were  $1.18 \pm 0.17$  ( $p=0.075$ ). Kim et al in a study a total of 234 patients reported elevated INR and serum CRP were related to complicated appendicitis ( $p=0.001$ ). On ROC curve analysis, the area under the curve (AUC) of CRP and INR were 0.796 and 0.723, respectively. They found that elevated INR and CRP were related to complicated appendicitis. Even though INR and CRP expanded essentially in patients with confounded a perforated appendix despite everything furthermore investigations to assess INR and CRP in patients experiencing moderate administration for an infected appendix are required.<sup>26</sup>

Hence, as per the Table 5, those patients who were having  $TLC > 10000/mm^3$ , serum bilirubin  $> 1$  mg/dl and  $MPV < 7.7$  fL are associated with complicated appendicitis.

Timing maybe an important effective factor that not measured its roll in current study. It may be possible that the time interval between onset of symptoms and presentation of the patients effect on the values of biomarkers, and the later a patient comes in, the higher the markers, and vice versa. Therefore, it is highly recommended to assess this important factor in further studies on this topic.

## CONCLUSION

Patients with clinical signs and symptoms of appendicitis and with TLC and serum bilirubin higher than the normal range and mean platelet volume lesser than normal range should be identified as having a higher probability of complicated appendicitis suggesting TLC, serum bilirubin and MPV have a predictive potential for the diagnosis of complicated appendicitis.

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