

Clinical Predictors of Perforation in Patients with Acute Appendicitis

Aktar Hossain^{1*}, Israt Jahan², Kamrujjaman³, Moniruzzaman⁴, Ruhul Amin⁵, Tapas Chandra Mondal⁶, Jannatul Ferdous Juthi⁷

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*Corresponding author



ABSTRACT

Background: Acute appendicitis is the most common surgical emergency of the abdomen, and perforation significantly contributes to the morbidity, length of stay, and cost of the surgical procedure. The purpose of this study was to determine the clinical, laboratory, and sonographic factors associated with perforation of the appendix in patients with acute appendicitis. **Methods & Materials:** This cross-sectional analytical study was conducted at the Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from June 2017 to May 2018, with 60 patients who underwent appendectomy for acute appendicitis. Sociodemographic, clinical, laboratory, and ultrasonographic data were collected and analyzed using SPSS version 26. **Results:** 60 patients were found, 22 of whom (36.7%) had perforated appendicitis. In bivariate analysis, symptom duration >48 hours, fever $\geq 38^{\circ}\text{C}$, rebound tenderness, guarding/rigidity, leukocytosis $>15,000/\text{mm}^3$, neutrophilia $>75\%$, CRP $>10\text{ mg/L}$, and periappendiceal fluid on ultrasonography were significantly associated with perforation ($p < 0.05$). Multivariable analysis revealed that symptom duration >48 hours (AOR 5.82), fever $\geq 38^{\circ}\text{C}$ (AOR 3.76), guarding/rigidity (AOR 3.41), and periappendiceal fluid on ultrasonography (AOR 4.52) were independent risk factors for perforation. **Conclusions:** Delayed presentation, fever, guarding/rigidity, and periappendiceal fluid on ultrasonography are independent predictors of appendiceal perforation and can help guide the clinician to recognize high-risk patients who should be treated promptly with surgery.

Keywords: Acute appendicitis; Perforation; Predictors; Ultrasonography

1. Junior Consultant, Department of Surgery, District Sadar Hospital, Rajbari, Bangladesh (ORCID: 0009-0006-7529-9475)
2. Assistant Professor, Department of Physiology, Faridpur Medical College, Faridpur, Bangladesh
3. Assistant professor, Department of Surgery, District Sadar Hospital, Rajbari, Bangladesh
4. Consultant, Department of Surgery, Kushtia Medical College, Kushtia, Bangladesh
5. Honourable Medical Officer, Department of Anaesthesia, Kushtia Medical College, Kushtia, Bangladesh
6. Junior Consultant, Department of ENT, Rajbari Sadar Hospital, Rajbari, Bangladesh
7. Resident Medical Officer, Mediland Hospital & Diagnostic Center, Rajbari, Bangladesh

INTRODUCTION

Acute appendicitis is the most frequent surgical emergency of the abdomen in the world and makes up a significant proportion of unplanned admissions to general surgical units [1]. The age-standardized incidence of appendicitis has increased in many parts of the world in the last 30 years, especially in newly industrialized countries of Asia, the Middle East and sub-Saharan Africa, while it has remained stable in high-income countries [1,2]. The pooled population-based data also reveal significant geographic variation in incidence, which is correlated with urbanization and socioeconomic status, indicating that access to care and diagnostic pathways play a significant role in the detection and treatment of the disease [3]. Trend analyses based on the Global Burden of Disease framework show that case fatality has decreased consistently since 1990, but there are still significant regional differences in mortality and disability, with the greatest burden in lower-resource areas where diagnostic delay is prevalent [4]. Acute appendicitis can develop into perforation, the most serious complication, if left untreated or not diagnosed until it is too late. Perforated appendicitis is associated with significantly increased rates of surgical site infection, intra-abdominal abscess, prolonged hospitalization,

reoperation and mortality in vulnerable populations, compared with non-perforated appendicitis [5]. This progression is multifactorial and only partially understood, with reported associations of older age, male sex, medical comorbidities (diabetes, appendicolithiasis, and delay from onset of symptoms to surgical intervention) [5, 6, 7]. In children, each of the following has been reported as an independent predictor of perforation: longer duration of symptoms, higher fever, elevated inflammatory markers, and sonographic findings of a fecalith or free fluid [6, 8]. Elderly patients are also at a higher risk of perforation, which is often atypical and delayed by comorbid illness, and often have multiple comorbidities that further complicate the clinical picture [7, 8]. Delayed reporting further exacerbates this risk, as has been reported in resource-limited settings, and is recommended in international consensus guidance for prompt diagnosis and timely intervention [9, 10, 11]. In spite of this growing body of literature, there is no single clinical, laboratory, or radiological marker that reliably predicts perforation prior to operation, and published sets of predictors differ significantly between populations and healthcare settings, making them difficult to apply directly to routine emergency practice [4, 10]. Thus, a local knowledge of the

sociodemographic, clinical, laboratory, and sonographic parameters that differentiate perforated from non-perforated appendicitis is required to aid earlier diagnosis and prompt surgery referral. The purpose of this study was to determine the clinical risk factors for perforation in patients with acute appendicitis in order to guide risk stratification and to encourage timely treatment in those with a high risk of complicated appendicitis.

METHODS & MATERIALS

The study was a cross-sectional analytical study carried out at Sir Salimullah Medical College Mitford Hospital, Dhaka, from June 2017 to May 2018. Sixty patients (N = 60) of both sexes with a clinical diagnosis of acute appendicitis, confirmed during surgery and histopathology, were enrolled by consecutive non-probability sampling after informed written consent and ethical review committee approval. All patients of any age who were admitted to the hospital with a clinical diagnosis of acute appendicitis and underwent emergency appendectomy during the study period were included. Patients who were treated non-operatively or by interval appendectomy, those with an appendicular mass or abscess who were treated conservatively at presentation, pregnant patients, patients

with incomplete clinical, laboratory or operative records, and patients in whom histopathology did not confirm appendicitis were excluded from the analysis. The study variables included sociodemographic factors (age, sex, and residence), clinical factors (duration of symptoms, migratory right lower abdominal pain, nausea/vomiting, anorexia, fever $\geq 38^{\circ}\text{C}$, right iliac fossa tenderness, rebound tenderness, and guarding/rigidity), laboratory parameters (total white blood cell count, neutrophil proportion, and C-reactive protein), ultrasonographic findings (appendiceal diameter, periappendiceal fluid, and appendicolith), and intraoperative/histopathological findings (perforation status, operative appearance,

periappendiceal collection, localized peritonitis, and appendicolith identified intraoperatively or on histopathology). The data were entered and analyzed in SPSS (Statistical Package for the Social Sciences) version 26. Categorical variables were expressed as frequencies and percentages, and continuous variables as means with standard deviations or as categorized ranges for ease of comparison. The relationship between clinical, laboratory and sonographic parameters and perforation status was evaluated by the chi-square or Fisher's exact test as appropriate, and then by multivariable logistic regression analysis to determine independent predictors of appendiceal perforation, which were presented as adjusted odds ratios (AOR)

with 95% confidence intervals. Throughout the analysis, a p-value < 0.05 was regarded as statistically significant, and all tests were two-tailed.

RESULT

The sociodemographic profile of 60 patients with acute appendicitis is given in *Table I*. The largest age group was 21–30 years (22, 36.7%), followed by ≤ 20 years (14, 23.3%), 31–40 years (13, 21.7%), and > 40 years (11, 18.3%). Males predominated over females (37, 61.7% versus 23, 38.3%). The majority of patients were rural (35, 58.3%), with the remaining 25 (41.7%) from urban areas, and the study population was predominantly male.

Table I

Sociodemographic characteristics of patients with acute appendicitis, $n=60$.

Variable	Category	n (%)
Age, years	≤ 20	14 (23.3)
	21–30	22 (36.7)
	31–40	13 (21.7)
	> 40	11 (18.3)
Sex	Male	37 (61.7)
	Female	23 (38.3)
Residence	Rural	35 (58.3)
	Urban	25 (41.7)

The clinical presentation of the patients is summarized in *Table II*. Symptom duration was ≤ 24 hours in 21 (35.0%), 25–48 hours in 20 (33.3%), and > 48 hours in 19 (31.7%) patients. The most common findings were

migratory right lower abdominal pain (43, 71.7%), nausea/vomiting (39, 65.0%), anorexia (42, 70.0%) and right iliac fossa tenderness (56, 93.3%). Fever $\geq 38^{\circ}\text{C}$ was present in 26 (43.3%), rebound tenderness

in 29 (48.3%), and guarding/rigidity in 20 (33.3%) patients.

Table II

Clinical presentation of patients with acute appendicitis, $n=60$.

Variable	Category	n (%)
Duration of symptoms	≤ 24 hours	21 (35.0)
	25–48 hours	20 (33.3)
	> 48 hours	19 (31.7)
Migratory right lower abdominal pain	Present	43 (71.7)
	Absent	17 (28.3)
Nausea/vomiting	Present	39 (65.0)
	Absent	21 (35.0)
Anorexia	Present	42 (70.0)
	Absent	18 (30.0)
Fever $\geq 38^{\circ}\text{C}$	Present	26 (43.3)
	Absent	34 (56.7)
Right iliac fossa tenderness	Present	56 (93.3)
	Absent	4 (6.7)
Rebound tenderness	Present	29 (48.3)
	Absent	31 (51.7)
Guarding/rigidity	Present	20 (33.3)
	Absent	40 (66.7)

Laboratory and imaging features of the patients are summarized in *Table III*. Total white blood cell count was 10,001–15,000/ mm^3 in 26 (43.3%) patients, $> 15,000/\text{mm}^3$ in 20 (33.3%), and

$\leq 10,000/\text{mm}^3$ in 14 (23.3%). The neutrophil proportion was more than 75% in 38 (63.3%) patients, and C-reactive protein was more than 10 mg/L in 43 (71.7%). On ultrasonography, the diameter of the

appendix was more than 6 mm in 53 (88.3%) patients and periappendiceal fluid was seen in 25 (41.7%) patients and an appendicolith in 16 (26.7%) patients.

Table IIILaboratory and imaging characteristics of patients, $n=60$.

Variable	Category	n (%)
Total WBC count	$\leq 10,000/\text{mm}^3$	14 (23.3)
	10,001-15,000/ mm^3	26 (43.3)
	$>15,000/\text{mm}^3$	20 (33.3)
Neutrophil proportion	$\leq 75\%$	22 (36.7)
	$>75\%$	38 (63.3)
CRP	≤ 10 mg/L	17 (28.3)
	>10 mg/L	43 (71.7)
Ultrasonographic appendiceal diameter	≤ 6 mm	7 (11.7)
	>6 mm	53 (88.3)
Periappendiceal fluid on USG	Present	25 (41.7)
	Absent	35 (58.3)
Appendicolith on USG	Present	16 (26.7)
	Absent	44 (73.3)

Operative and pathological findings of the patients are presented in *Table IV*. Twenty-two (36.7%) patients were found to have perforation and 38 (63.3%) had non-perforated appendicitis. The operatively

appearing lesions were perforated in 22 (36.7%), inflamed in 21 (35.0%), and gangrenous without perforation in 17 (28.3%) patients. Periappendiceal collection was found in 18 (30.0%), localized

peritonitis in 21 (35.0%), and an appendicolith was found intraoperatively or pathologically in 17 (28.3%) patients.

Table IVOperative and pathological findings among patients with acute appendicitis, $n=60$.

Variable	Category	n (%)
Perforation status	Non-perforated	38 (63.3)
	Perforated	22 (36.7)
Operative appearance	Inflamed appendix	21 (35.0)
	Gangrenous appendix without perforation	17 (28.3)
	Perforated appendix	22 (36.7)
Periappendiceal collection	Present	18 (30.0)
	Absent	42 (70.0)
Localized peritonitis	Present	21 (35.0)
	Absent	39 (65.0)
Appendicolith identified intraoperatively/pathologically	Present	17 (28.3)
	Absent	43 (71.7)

The bivariate association between clinical and laboratory factors and perforation status is presented in *Table V*. Symptom duration >48 hours (59.1% versus 15.8%), fever $\geq 38^\circ\text{C}$ (72.7% versus 26.3%), rebound tenderness (72.7% versus 34.2%),

guarding/rigidity (59.1% versus 18.4%), WBC $>15,000/\text{mm}^3$ (54.5% versus 21.1%), neutrophils $>75\%$ (86.4% versus 50.0%), CRP >10 mg/L (90.9% versus 60.5%), and periappendiceal fluid (72.7% versus 23.7%) were significantly associated with

perforation ($p<0.05$). There was no significant association between age, sex or rural residence and perforation status.

Table V

Association of clinical and laboratory factors with appendiceal perforation.

Variable	Category	Perforated, $n=22$, n (%)	Non-perforated, $n=38$, n (%)	p-value
Age	≤ 30 years	10 (45.5)	26 (68.4)	0.081
	>30 years	12 (54.5)	12 (31.6)	
Sex	Male	15 (68.2)	22 (57.9)	0.430
	Female	7 (31.8)	16 (42.1)	
Rural residence	Yes	16 (72.7)	19 (50.0)	0.087
	No	6 (27.3)	19 (50.0)	
Symptom duration >48 hours	Yes	13 (59.1)	6 (15.8)	<0.001
	No	9 (40.9)	32 (84.2)	
Fever $\geq 38^\circ\text{C}$	Yes	16 (72.7)	10 (26.3)	<0.001
	No	6 (27.3)	28 (73.7)	
Rebound tenderness	Present	16 (72.7)	13 (34.2)	0.004
	Absent	6 (27.3)	25 (65.8)	
Guarding/rigidity	Present	13 (59.1)	7 (18.4)	0.001
	Absent	9 (40.9)	31 (81.6)	
WBC $>15,000/\text{mm}^3$	Yes	12 (54.5)	8 (21.1)	0.008
	No	10 (45.5)	30 (78.9)	
Neutrophils $>75\%$	Yes	19 (86.4)	19 (50.0)	0.005
	No	3 (13.6)	19 (50.0)	
CRP >10 mg/L	Yes	20 (90.9)	23 (60.5)	0.012
	No	2 (9.1)	15 (39.5)	
Periappendiceal fluid on USG	Present	16 (72.7)	9 (23.7)	<0.001
	Absent	6 (27.3)	29 (76.3)	

Table VI shows the multivariable logistic regression analysis of predictors of appendiceal perforation. Symptom duration >48 hours (AOR 5.82, 95% CI 1.55–21.87), fever $\geq 38^{\circ}\text{C}$ (AOR 3.76, 95% CI 1.10–

12.84), guarding/rigidity (AOR 3.41, 95% CI 1.02–11.42), and periappendiceal fluid on ultrasonography (AOR 4.52, 95% CI 1.27–16.08) were identified as independent predictors of perforation. WBC

>15,000/mm³ and CRP >10 mg/L were significant on bivariate analysis but not on multivariable analysis ($p>0.05$).

Table VI
Multivariable logistic regression analysis of predictors of appendiceal perforation.

Predictor	Category	Adjusted OR	95% CI	p-value
Symptom duration	>48 hours vs ≤ 48 hours	5.82	1.55–21.87	0.009
Fever	$\geq 38^{\circ}\text{C}$ vs $< 38^{\circ}\text{C}$	3.76	1.10–12.84	0.035
Guarding/rigidity	Present vs absent	3.41	1.02–11.42	0.047
WBC count	>15,000/mm ³ vs $\leq 15,000/\text{mm}^3$	2.74	0.81–9.27	0.104
CRP	>10 mg/L vs ≤ 10 mg/L	3.18	0.72–14.07	0.127
Periappendiceal fluid on USG	Present vs absent	4.52	1.27–16.08	0.020

DISCUSSION

In this study, 22 of 60 patients (36.7%) had perforation, which is similar to what has been reported by Alyhari et al. and Guan et al., where perforation rates are often reported at more than 30%, much higher than those usually reported in high-income health systems [12, 13]. This gap has been attributed less to the severity of the disease itself and more to the delay in seeking care and referral: a retrospective cohort of patients which showed that age <30 years, male sex, rural residence, and lower educational level were all associated with a high incidence of prehospital delay >48 hours, which is similar to the pattern of delayed presentation seen in the present cohort [12]. In this study, symptom duration > 48 hours was the strongest independent predictor of perforation (AOR 5.82), consistent with a previous study by Guan et al. and Pogorelic et al. in paediatric and adult patients that have shown symptom duration > 48 hours is independently associated with perforation, regardless of age [13, 14]. Similarly, fever $\geq 38^{\circ}\text{C}$ was an independent predictor (AOR 3.76), consistent with Guan et al. and Yang et al., who showed that high body temperature is an objective, reproducible marker of complicated disease in children and is effective even in the absence of laboratory facilities [13, 15]. Guarding/rigidity on abdominal examination was also an independent predictor of perforation (AOR 3.41), indicating the progression from focal to diffuse peritoneal irritation, which is characteristic of transmural necrosis and perforation of the appendiceal wall, and thus supports the ongoing importance of careful serial abdominal examination even in the era of immediate imaging access. Leukocytosis, neutrophilia and elevated C-reactive protein were each independently associated with perforation on bivariate analysis, but none remained so after adjustment for symptom duration, fever and examination findings. This attenuation is similar to other studies, which have shown that inflammatory markers are associated with overall disease severity, but their discriminative value for perforation alone is less pronounced after adjusting for

symptom duration and clinical signs, and combinations of markers have been found to be more discriminative than any single marker alone [16, 17]. Although not evaluated in this study, hyperbilirubinaemia has also been suggested as an adjunctive laboratory marker of perforation in several recent cohorts, highlighting the continued quest for a reliable, inexpensive laboratory marker that can be used where advanced imaging is not easily available [18,19]. Although ultrasonography overall was not as sensitive as it was specific for the diagnosis of perforation, complex or loculated periappendiceal fluid was an independent predictor of perforation in this cohort (AOR 4.52), as imaging-based studies have shown that this type of periappendiceal fluid has a particularly strong association with perforation, even when ultrasonography is negative [20, 21]. Notably, age and sex were not independently associated with perforation in this cohort, unlike several larger series that found that older age and geographic disadvantage were associated with delayed presentation and increased perforation risk, which may be due to the small size and referral pattern of a single-center series, and should be confirmed in larger, multicenter series [13, 22]. Together, these results suggest that a simple clinical and sonographic profile is more useful than laboratory testing in determining patients who are at high risk for perforation. They are consistent with the recommendations in the surgical literature for early evaluation and immediate surgical intervention after the clinical diagnosis of complicated appendicitis, as the timing and surgical technique used directly affect the postoperative course, complications, and hospital stay [23].

LIMITATIONS

The study was restricted to a single center and a small number of patients (N=60), which may reduce the generalizability and statistical power of the results, especially for age, sex, and place of residence.

CONCLUSION

Appendiceal perforation was present in over a third of patients with acute appendicitis in

this study. The presence of symptoms for more than 48 hours, fever $\geq 38^{\circ}\text{C}$, guarding/rigidity on examination, and periappendiceal fluid on ultrasonography were found to be independent predictors of perforation, whereas leukocytosis and C-reactive protein, although associated on bivariate analysis, did not remain independent. The results indicate that the use of easily obtained clinical and sonographic parameters, not laboratory markers, may assist the clinician in determining patients who are at high risk for perforation. These predictors should be identified early and prompt expedient surgical evaluation and intervention. The use of such a clinical-sonographic profile in routine emergency assessment could decrease the diagnostic delay and enhance the postoperative results. The early diagnosis and surgical removal of the appendix in high-risk patients continues to be the key to reducing the morbidity of complicated appendicitis.

RECOMMENDATIONS

These predictors should be validated in larger, multicenter, prospective studies, and a combined clinical-laboratory-sonographic scoring system for early prediction of appendiceal perforation is recommended.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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