Original Article

Correlation between Alvarado score and preoperative serum hyperbilirubinemia as a new diagnostic modality for severity of acute appendicitis

Sami Mufeed, Hany Maurice, Poula R.R. Hanna and Hitham H. Mohey

Department of General and Laparoscopic Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt.

ABSTRACT

Introduction: Acute appendicitis is a prevalent abdominal emergency that necessitates immediate surgery. The most common emergency procedure carried out globally is an appendectomy.

Objective: To assess the clinical significance of the preoperative correlation between the Alvarado score and serum hyperbilirubinemia and to evaluate their ability to predict the severity of acute appendicitis clinically.

Patients and Methods: This cross-sectional analytic study was performed at the Department of General Surgery Emergency of a tertiary hospital in the period between June 2022 and March 2023. This study was carried out on 208 cases with acute appendicitis.

Results: The mean age of participants was 29.17±14.452 years, predominantly males (54.8%). About two-thirds of the cases (67.8%) underwent open appendectomy, 58 (27.9%) underwent laparoscopic appendectomy, and nine (4.3%) underwent laparoscopic and then converted to open appendectomy. More than half of the cases were categorized as probably appendicitis by Alvarado score. There was a statistically significant difference comparing Alvarado's scores and the pathological findings of the participants (*P=0.021*). No statistically significant differences were recorded between Alvarado score findings and preoperative serum bilirubin levels.

Conclusion: The study found an association between Alvarado's score and pathology findings. However, no statistically significant differences were recorded between the Alvarado score and preoperative serum bilirubin levels.

Key Words: Acute appendicitis, Alvarado score, preoperative serum hyperbilirubinemia, severity of appendicitis.

Received: 5 July 2024, **Accepted:** 21 July 2024, **Published:** 4 October 2024

Corresponding Author: Hytham H. Mohey, MD, Department of General & Laparoscopic Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt. **Tel.:** +20 100 887 6772, **E-mail:** dochytham@gmail.com

ISSN: 1110-1121, October 2024, Vol. 43, No. 4: 1579-1586, © The Egyptian Journal of Surgery

INTRODUCTION

Acute appendicitis is a prevalent abdominal emergency that necessitates immediate surgery. The most common emergency procedure carried out globally is an appendectomy[1,2].

About 80% of the time, skilled physicians correctly diagnose appendicitis[3]. A number of biochemical markers, such as procalcitonin, interleukin-6, C-reactive protein, and white blood cell count, have been employed to enhance the clinical diagnosis of acute appendicitis. Nevertheless, it can occasionally be difficult to diagnose appendicitis since the typical symptoms and indicators may not be present[4].

There is a critical need for a predictor of the severity of acute appendicitis because postoperative risks of morbidity and mortality, in addition to longer hospital stays, are linked to delayed identification and treatment of severe appendicitis. A number of scoring methods, including the Alvarado score, have been proposed for appendicitis, taking into account laboratory results, physical examination findings, and clinical characteristics[5].

Moreover, an imbalance between the liver's production and excretion of bilirubin leads to hyperbilirubinemia, which could be a novel diagnostic tool for appendix perforation[6]. In cases of acute appendicitis, hyperbilirubinemia that is not brought on by biliary blockage or liver dysfunction might be seen. The clinical utility of hyperbilirubinemia in diagnosing acute appendicitis is still debatable despite certain research reporting on its effectiveness[7,8].

Hence, our goals were to determine the clinical importance of the preoperative connection between serum bilirubin level and Alvarado score and to evaluate their predictive power for acute appendicitis severity.

PATIENTS AND METHODS:

The work is a diagnostic accuracy cross-sectional analytic study carried out in the General Surgery

DOI: 10.21608/EJSUR.2024.301872.1114

Emergency Unit at a Tertiary Hospital. The study was conducted between June 2022 and March 2023 and included 208 patients clinically diagnosed with acute appendicitis. We excluded patients with gallbladder stones, hyperbilirubinemia secondary to a known cause (hepatic diseases, hepatic viruses, hepatotoxic drugs, etc.), and any other cause of sepsis.

Ethical consideration: the study protocol was reviewed and permitted by the institutional research and ethics committee. After participants were adequately briefed on the study's goals, their written informed consent was obtained. The participant was free to withdraw from the study at any moment; participation was entirely voluntary. According to the Declaration of Helsinki, all steps of data collecting, entry, and analysis were conducted in a highly confidential and private manner.

Steps of the procedure

Every patient had a thorough history-taking process that covered their past, present, and personal histories. A meticulous physical examination was done to assess vital signs, cardiovascular, neurological, and respiration assessment, as well as a local abdominal examination. Laboratory workup done included complete blood picture, serum electrolytes (Na, K), C-reactive protein, international normalized ratio, kidney function test, and liver test profile. The liver function tests included serum albumin, alanine aminotransferases and serum aspartate, serum bilirubin, and prothrombin time.

Radiological assessment was done through abdominal-pelvic ultrasound (US) to assess the liver size and the gallbladder status, as well as the appendix, in addition to the assessment of other intraabdominal organs.

Within 30 min of the patient's arrival at the hospital, blood samples were taken, and radiological examinations were completed 2 h later. These patients underwent emergency open or laparoscopic appendectomy after being initially stabilized. Operative details of the duration and severity of acute appendicitis were documented. Ultimately, postoperative histological analysis verified the clinical diagnosis by classifying patients into positive cases (acute appendicitis with perforation/gangrene) and negative cases (acute appendicitis with a normal appendix or acute uncomplicated appendicitis).

At least one additional visit to the outpatient clinic was made in addition to the postoperative follow-up at the hospital.

Calculating the Alvarado score

Alvarado determined that three physical signs – tenderness, rebound pain, and elevation of temperature – two laboratory findings – leukocytosis and shift of the formula to the left – and three symptoms – migration of pain in the right iliac fossa, anorexia, and nausea/vomiting – were helpful in the diagnosis of acute appendicitis. He then ranked the signs and symptoms based on their diagnostic weight.

A total score of 5 or 6 is consistent with the diagnosis of acute appendicitis; a score of 7 or 8 suggests probable appendicitis, and a score of 9 or 10 suggests very probable appendicitis[9] (Table 1).

Table 1: The Alvarado scoring system for acute appendicitis

	Alvarado score
Symptoms	
Migratory RIF pain	1
Nausea/vomiting	1
Anorexia	1
Signs	
Right iliac fossa tenderness	2
Elevation of temperature	1
Rebound tenderness RIF	1
Laboratory findings	
Leukocytosis	2
Neutrophilic shift to the left (>75%)	1
	Total score=10
Sum	
0–4	Not likely appendicitis
5–6	Equivocal
7–8	probable appendicitis
9–10	very probable appendicitis

Sample size: the required sample size was determined using the Open Epi calculator. A 95% confidence interval, 5% accuracy, and 80% power indicate that a minimum sample size of 173 should be needed. After factoring in 20% to account for possible nonresponse, 208 patients were assessed to be the final sample size. The patients will be recruited via a convenience sampling technique.

Statistical methods

Utilizing the 24th edition of IBM® SPSS® (Statistical Package for the Social Sciences), Chicago, USA, version 24. data entry, processing, and statistical analysis were completed. Quantitative data were presented as mean, median, SD, and interquartile range; qualitative data were presented as percentage and frequency. The following significance tests were applied: Spearman's correlation, Wilcoxon's, χ^2, logistic regression analysis, and Kruskal–Wallis. Data were shown, and appropriate analysis was carried out based on the kind of data (parametric and

nonparametric) that were collected for every parameter. To determine the statistical significance of a nonparametric variable's difference between more than two research groups, the Kruskal–Wallis test was employed. One-way analysis of variance is for continuous variables with normal distribution. Following analysis of variance, the Tukey test was used for post-hoc analysis, followed by the Mann–Whitney U test. *P values* were regarded as statistically significant if they were less than 0.05.

RESULTS:

This study involved 32 patients who fulfilled the inclusion criteria presenting with acute appendicitis. The mean age of the investigated population is 29.17±14.452 years. Among the included patients, 54.8% were males. The majority of the study participants did not suffer any comorbidities (87%), while 13% had comorbidities, as shown in (Table 2).

Analysis of the clinical presentation of the studied group shows that 202 (97.1%) had right iliac fossa tenderness, 200 (96.2%) had rebound tenderness, 147 (70.7%) had anorexia, 158 (76.0%) had nausea/vomiting, 57(27.4%) had migration of pain, and 20 (9.6%) had fever.

About two-thirds of the cases (67.8%) underwent open appendectomy, 58 (27.9%) underwent laparoscopic appendectomy, and nine (4.3%) underwent laparoscopic then converted to open appendectomy.

Regarding intraoperative findings, 141 (67.8%) patients were found to be uncomplicated, 68 (32.7%) were perforated, nine (4.3%) were gangrenous, and two (1.0%) were autolyzed fecalith.

In contrast, the pathology finding of the studied group shows that 39 (18.8%) were catarrhal, 62 (29.8%) were perforated, 14 (6.7%) were gangrenous, and eight (3.8%) were gangrenous and perforated.

The time the patients took before presentation had a mean value of 2.77±3.223 days. Hospital stays ranged between 1 and 14 days, with a mean value of 2.60±1.983 days. By analyzing the results of the preoperative serum bilirubin levels of the studied group, they showed a mean value of 1.13±0.612 mg/dl.

Calculated Alvarado scores among the patients revealed that 21 were categorized as not likely appendicitis, 43 as equivocal, 121 as probably appendicitis, and 23 as highly likely appendicitis. The relation between Alvarado score and pathology findings shows statistically significant differences between the categories of Alvarado score and pathology outcomes (*P=0.021*). The results clarify that 62% of the patients scored as not likely appendicitis by Alvarado score were negative appendices by pathological examination, 44% of the patients scored as equivocal by Alvarado score were negative appendices by pathological examination, 37% of the patients scored as probably appendicitis by Alvarado score were negative appendices by pathological examination and only 34% of the patients scored as highly likely appendicitis by Alvarado score were negative appendices by pathological examination as shown in (Table 3, Fig. 1).

On the other hand, the relation between Alvarado score and preoperative serum bilirubin levels shows no statistically significant differences between the categories of Alvarado score findings and their corresponding bilirubin levels among the study patients (Table 4).

Table 2: Preoperative, intraoperative, pathological characteristics and complications among study participants

	N=208 [*n* (%)]
Comorbidity	
Free	181 (87.0)
HTN	12 (5.8)
DM	11 (5.3)
Cardiac	8 (3.8)
Hypothyroidism	3 (1.4)
Stroke	2 (1.0)
G٦PD	1 (0.5)
Intraoperative finding	
Not complicated	141 (67.8)
Perforated	68 (32.7)
Gangrenous	9 (4.3)
Autolyzed, Fecalith	2 (1.0)
Hi؟topathological finding	
Negative	85 (40.9)
Perforated	62 (29.8)
Catarrhal	39 (18.8)
Gangrenous	14 (6.7)
Gangrenous and perforated	8 (3.8)
Complication	
None	194 (93.3)
Ascending colon injury	2 (1.0)
Burs؟ abdomen	2 (1.0)
Cecal injury	2 (1.0)
Wound infection+ICU	2 (1.0)
Wound infection	2 (1.0)
Re-exploration	2 (1.0)
Readmission, collection	2 (1.0)

Table 3: Relation between Alvarado score and both pathology findings and serum bilirubin level among study participants

	Alvarado score [*n* (%)]				
	Not likely appendicitis (*N*=21)	Equivocal (*N*=43)	Probably appendicitis (*N*=121)	Highly likely appendicitis (*N*=23)	*P* value
Pathology finding					
Negative	13 (61.9)	19 (44.2)	45 (37.2)	8 (34.8)	0.021
Perforated	5 (23.8)	8 (18.6)	41 (33.9)	8 (34.8)	
Catarrhal	1 (4.8)	12 (27.9)	19 (15.7)	7 (30.4)	
Gangrenous	2 (9.5)	0	12 (9.9)	0	
Gangrenous and perforated	0	4 (9.3)	4 (3.3)	0	
Bilirubin					
Range	0.32–1.91	0.18–2.10	0.15–2.64	0.15–2.50	0.350
Mean±SD	1.19±0.459	0.96±0.649	1.17±0.624	1.12±0.583	

Table 4: Relation between Alvarado score and both pathology findings and serum bilirubin level among study participants.

	Alvarado score								*P-value*
	Not likely appendicitis (n=21)		Equivocal (n=43)		Probably appendicitis (n=121)		Highly likely appendicitis (n=23)		
Pathology Finding	No.	%	No.	%	No.	%	No.	%	
Negative	13	61.9	19	44.2	45	37.2	8	34.8	0.021
Perforated	5	23.8	8	18.6	41	33.9	8	34.8	
Catarrhal	1	4.8	12	27.9	19	15.7	7	30.4	
Gangrenous	2	9.5	0	0	12	9.9	0	0	
Gangrenous and perforated	0	0	4	9.3	4	3.3	0	0	
Bilirubin									
Range	0.32–1.91		0.18–2.10		0.15–2.64		0.15–2.50		0.350
Mean±SD	1.19±0.459		0.96±0.649		1.17±0.624		1.12±0.583		

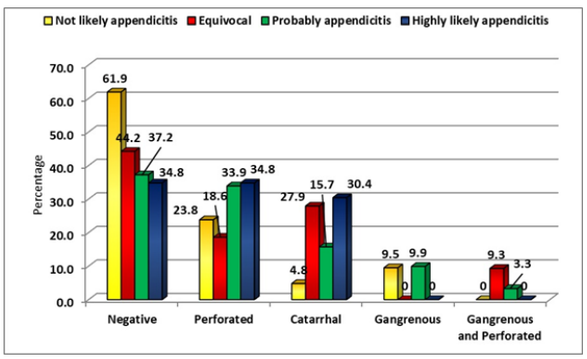

Fig. 1: Relation between Alvarado's score and pathology findings.

DISCUSSION

One of the most frequent causes of urgent surgery is appendicitis[10]. The diagnosis of the appropriate stage of acute appendicitis determines whether surgery is necessary[11–15]. In an effort to discover potential markers of complex appendicitis, a number of tests and scoring systems have been investigated[10,14,16–18]. Yet, there is a significant rate of missing cases, and none of the existing approaches can be employed as standalone diagnostic tools[19]. The useful tool of assessment is the preoperative hyperbilirubinemia in cases with complicated appendicitis, but this has been studied only in a few research[20–22].

This cross-sectional analytic study's primary goals were to evaluate the clinical significance of serum hyperbilirubinemia and the Alvarado scoring system for appendicitis as predictors of the severity of acute appendicitis. The study involved 208 participants.

The mean age, according to the present study, was 29.17±14.452 years. Male cases were predominant, with 54.8%. Comparable with these results, recent studies showed that the cases diagnosed with acute appendicitis were young adults with means in the second and third decades of age and males being predominant (up to 60%)[23,24].

Regarding the clinical presentation of the studied group, especially those discussed in the Alvarado scoring system, it was revealed that almost all

patients (202; 97.1%) presented with right iliac fossa tenderness, 200 (96.2%) had rebound tenderness, 147 (70.7%) had anorexia, 158 (76.0%) had nausea/vomiting, and 57 (27.4%) had migration of pain. Also, the time before the presentation to hospital had a mean value of 2.77±3.223 days.

This is consistent with Yeşiltaş *et al*.[25], who stated that acute appendicitis has the symptoms of migratory pain to the right lower quadrant, anorexia, vomiting, and nausea, rebound tenderness, and fever. Moreover, Kalliakmanis *et al*.[26] evaluated acute appendicitis symptoms and reported that pain migration to the right iliac fossa, loss of appetite, periumbilical pain, fever, rebound tenderness, and local rigidity were statistically correlated with histopathological severity ($P<0.05$).

The current study showed that roughly two-thirds of the cases (141; 67.8%) underwent open appendectomy, 58 (27.9%) underwent laparoscopic, and nine (4.3%) underwent laparoscopic then converted to open appendectomy, making the larger part of the study cohort undergoing an open procedure. In line with these findings, a large study analyzing the findings among 1316 patients showed that the most common procedure was open appendectomy among 1081 (82.1%) patients, and the remaining 235 (17.9%) patients underwent laparoscopic appendectomy[27]. However, other research shows that laparoscopic procedures were performed more than open techniques among their study cohorts, reaching 86.2% of all performed procedures[28].

Hospital stay ranged between 1 and 14 days with a mean value of 2.60±1.983 days among the present study population. Comparable with these findings, a study showed that length of stay ranged from 1 to 19 days postopen appendectomy[29]. Also, Halaseh *et al*.[28] showed that their study patients stayed an average of 3.08 days in the hospital, although most of their patients underwent laparoscopic technique, which allows for shorter duration of hospital stays.

The current study showed that more than two-thirds of the patients (141; 67.8%) were not complicated appendicitis cases with intraoperative evaluation, while those complicated were in the form of perforation, gangrenous appendix, or autolyzed appendix (32.7, 4.3, and 1.0%, respectively). In concordance, several studies showed that noncomplicated acute appendicitis formed the majority (>70% of cases, reaching 90% in some studies), and less than 25% had complications in the form of perforation, gangrene, or purulent appendix[25,30,31].

Regarding postoperative complications, the present study showed that 93.3% have no complications. The complications found were ascending colon injury, burst abdomen, cecal injury, wound infection with or without ICU admission, the need for re-exploration and readmission. Comparable with these results, Kim *et al*.[32] demonstrated that 124 patients, or 9.8% of the total, experienced postoperative sequelae related to complicated appendicitis. Wound infection was the most frequent consequence (6.1%).

However, according to Omari and colleagues, 21% of the study sample experienced postoperative complications. They observed that the number of complications in the perforated group of patients was three times higher than that of the nonperforated group, with 33 (75%) and 11 (25%) patients, respectively[33].

Analyzing the findings of histopathological examination of the specimens of the studied group, revealed that more than 40% were negative specimens; however, 29.8% were perforated, 18.8% were catarrhal, 6.7% were gangrenous, and 3.8% were gangrenous and perforated. In a large study, which included 2364 cases involving acute appendicitis, catarrhal appendicitis represented 18.5%, suppurative appendicitis 12.7%, gangrenous appendicitis 45.7%, and perforated appendicitis 23%[34].

After the calculation of Alvarado scores, more than half of the patients (58%) were categorized as probably appendicitis. Most importantly, after analyzing the factors associated with the Alvarado scoring system, the current study revealed that there was a statistically significant association between Alvarado score findings and pathology findings.

In concordance with the current study, Yeşiltaş *et al*.[25], Talabi *et al*.[35], and Memon *et al*.[36] showed that there was a marked association between Alvarado score and pathology findings. Also, Al-Tarakji *et al*.[37] showed that there was statistical significance between Alvarado risk stratification with histopathology and intraoperative grades ($P=0.001$ each).

In contrast, Sousa-Rodrigues *et al*.[38] revealed that there was no connection between Alvarado's score and pathology findings. The disagreement may be because of the difference in sample size and inclusion criteria.

On the other hand, the present study could not find statistically significant differences between Alvarado score findings and serum bilirubin levels.

As far as we are aware, this is the first study that tested the correlation between Alvarado score and bilirubin level. Despite the lack of significance, this correlation needs to be retested with larger studies. However, several studies were conducted to test the correlation between bilirubin levels and complicated appendicitis. Our findings were supported in this aspect by Ahmed

et al.[30], who found no significant correlation between high bilirubin levels and complicated appendicitis. This is consistent with previous investigations by Chambers *et al*.[39], Kanlioz and Karatas[40], and Yeşiltaş *et al*.[25], in which it was concluded that bilirubin could not be utilized independently to expect perforated or complicated appendicitis; however, it still can be used as a supporting factor to other parameters.

CONCLUSION

The current study showed that surgical management, either with laparoscopic or open approaches, was safe and effective in the management of acute appendicitis. The study results failed to find a significant correlation between Alvarado's score and bilirubin level. On the other hand, there was a significant linkage between Alvarado's score and histopathological findings.

Recommendations

The authors recommend that future research should have a larger sample size and include multicenter studies to validate our findings.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Smith PH. The diagnosis of appendicitis. Postgrad Med J 1965; 41:2.

2. Cusheiri A, Grace PA, Darzi A, Borley N, Rowley D. Disorders of small intestine and vermiform appendix. Clinical Surgery. 2nd ed. UK: Blackwell Publishing Ltd. 2003;405.

3. Maa J. The Appendix. In: Beauchamp RD, Evers Townsend BM, Mattox KL, eds. Sabiston Textbook of Surgery. 18th ed. Philadelphia, PA: Saunders Elsevier; 2008. 1333–1347.

4. Chaudhary P, Kumar A, Saxena N, Biswal UC. Hyperbilirubinemia as a predictor of gangrenous/perforated appendicitis: a prospective study. Annals of gastroenterology: quarterly publication of the Hellenic Society of Gastroenterology. 2013;26(4):325.

5. Son CS, Jang BK, Seo ST, Kim MS, Kim YN. A hybrid decision support model to discover informative knowledge in diagnosing acute appendicitis. BMC Medical Informatics and Decision Making. 2012 Dec;12:1-4.

6. Eren T, Tombalak E, Ozemir IA, Leblebici M, Ziyade S, Ekinci O, *et al*. Hyperbilirubinemia as a predictive factor in acute appendicitis. European Journal of Trauma and Emergency Surgery. 2016 Aug;42:471-6.

7. Vaziri M, Pazouki A, Tamannaie Z, Maghsoudloo F, Pishgahroudsari M, Chaichian S. Comparison of pre-operative bilirubin level in simple appendicitis and perforated appendicitis. Medical journal of the Islamic Republic of Iran. 2013 Aug;27(3):109.

8. Sevinç MM, Kınacı E, Çakar E, Bayrak S, Özakay A, Aren A, *et al*. Diagnostic value of basic laboratory parameters for simple and perforated acute appendicitis: an analysis of 3392 cases. Ulus Travma Acil Cerrahi Derg 2016; 22:155–162.

9. Pisano M, Capponi MG, Ansaloni L. Acute Appendicitis. Current trends in diagnostic and therapeutic options. In: Microbiology for Surgical Infections [Internet]. Elsevier; Academic Press; 2014 p. 97–110. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780124116290000064.

10. Bhangu A, Søreide K, Saverio DS. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet 2015; 386:1278–1287.

11. Wang V, Kriger D, Fanous E. Should all complicated appendicitis be treated the same? The answer is no. Am Surg 2019; 85:1179–1183.

12. Hajibandeh S, Hajibandeh S, Hobbs N. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: a systematic review and meta-analysis. Am J Surg 2020; 219:154–163.

13. Rawolle T, Reismann M, Minderjahn MI. Sonographic differentiation of complicated from uncomplicated appendicitis. Br J Radiol 2019; 92:20190102.

14. Avanesov M, Wiese NJ, Karul M. Diagnostic prediction of complicated appendicitis by combined clinical and radiological appendicitis severity index (APSI). Eur Radiol 2018; 28:3601–3610.

15. Imaoka Y, Itamoto T, Takakura Y. Validity of predictive factors of acute complicated appendicitis. World J Emerg Surg 2016; 11:48.

16. Farooqui W, Pommergaard HC, Burcharth J. The diagnostic value of a panel of serological markers in acute appendicitis. Scand J Surg 2015; 104:72–78.

17. Deiters A, Drozd A, Parikh P. Use of the Alvarado score in elderly patients with complicated and uncomplicated appendicitis. Am Surg 2019; 85:397–402.

18. Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. J Investig Surg 2018; 31:121–129.

19. Kabir SA, Kabir SI, Sun R. How to diagnose an acutely inflamed appendix; a systematic review of the latest evidence. Int J Surg 2017; 40:155–162.

20. Giordano S, Pääkkönen M, Salminen P. Elevated serum bilirubin in assessing the likelihood of perforation in acute appendicitis: a diagnostic meta-analysis. Int J Surg 2013; 11:795–800.

21. Adams HL, Jaunoo SS. Hyperbilirubinaemia in appendicitis: the diagnostic value for prediction of appendicitis and appendiceal perforation. Eur J Trauma Emerg Surg 2016; 42:249–252.

22. Chaudhary P, Kumar A, Saxena N. Hyperbilirubinemia as a predictor of gangrenous/ perforated appendicitis: a prospective study. Ann Gastroenterol. 2013; 26:325–331.

23. Husssin M, Kumar D, Ahmed R, Kazim E, Zubair M. Comparison of appendicits inflammaroty response (AIR) score with alvarado score in the diagnosis of acute appendicitis. Pak J Surg 2019; 35:4.

24. Bakshi S, Mandal N. Evaluation of role of hyperbilirubinemia as a new diagnostic marker of complicated appendicitis. BMC Gastroenterol 2021; 21:1–6.

25. Yeşiltaş M, Karakaş DÖ, Gökçek B, Hot S, Eğin S. Can Alvarado and appendicitis inflammatory response scores evaluate the severity of acute appendicitis? Turk J Trauma Emerg Surg 2018; 24:6.

26. Kalliakmanis V, Pikoulis E, Karavokyros IG, Felekouras E, Morfaki P, Haralambopoulou G, *et al*. Acute appendicitis: the reliability of diagnosis by clinical assessment alone. Scand J Surg 2005; 94:201–206.

27. Akbulut S, Koç C, Şahin TT, Şahin E, Tuncer A, Demyati K, *et al*. An investigation into the factors predicting acute appendicitis and perforated appendicitis. Turk J Trauma Emerg Surg 2021; 27:4.

28. Halaseh SA, Kostalas M, Kopec C, Nimer A. Bilirubin as a predictor of complicated appendicitis in a district general hospital: a retrospective analysis. Cureus 2022; 14:9.

29. Ximenes AM, Mello FS, Lima-Júnior ZB, Ferreira CF, Cavalcanti AD, Dias-Filho AV. Hospitalization time after open appendectomy by three different surgical techniques. Arq Brasil Cirurg Dig (São Paulo) 2014; 27:188–190.

30. Ahmed FA, Aljirdabi NS, Almahari SA. Hyperbilirubinemia in acute appendicitis. Bahrain Med Bull 2020; 42:4.

31. Surel AA, Güngörer B. The predictors of complicated acute appendicitis: large unstained cells, gamma-glutamyl transferase, monocyte to platelet ratio, age and gender. J Health Sci Med 2020; 4:477–481.

32. Kim JY, Kim JW, Park JH, Kim BC, Yoon SN. Early versus late surgical management for complicated appendicitis in adults: a multicenter propensity score matching study. Ann Surg Treat Res 2019; 97:103–111.

33. Omari AH, Khammash MR, Qasaimeh GR, Shammari AK, Yaseen MK, Hammori SK. Acute appendicitis in the elderly: risk factors for perforation. World J Emerg Surg 2014; 9:1–6.

34. Tayfur MA, Balci MG. Pathological changes in appendectomy specimens including the role of parasites: a retrospective study of 2400 cases of acute appendicitis. Nig J Clin Pract 2019; 22:270–275.

35. Talabi AO, Adedeji TA, Sowande OA, Adejuyigbe O. Predictive values of Alvarado score, serum C-reactive protein, and white blood cell count in the diagnosis of acute appendicitis: a prospective study. Ann Pediatr Surg 2021; 17:1–7.

36. Memon ZA, Irfan S, Fatima K, Iqbal MS, Sami W. Acute appendicitis: diagnostic accuracy of Alvarado scoring system. Asian J Surg 2013; 36:144–149.

37. Al-Tarakji M, Zarour A, Singh R, Ghali MS. The role of Alvarado score in predicting acute appendicitis and its severity in correlation to histopathology: a retrospective study in a Qatar population. Cureus 2022; 14:e26902.

38. Sousa-Rodrigues CF, Rocha AC, Rodrigues AK, Barbosa FT, Ramos FW, Valões SH. Correlation between the Alvarado Scale and the macroscopic aspect of the appendix in patients with appendicitis. Rev Colégio Brasil Cirurgiões 2014; 41:336–339.

39. Chambers AC, Bismohun SL, Davies H, White P, Patil AV. Predictive value of abnormally raised serum bilirubin in acute appendicitis: a cohort study. Int J Surg 2015; 13:207–210.

40. Kanlioz M, Karatas T. The relationship of perforated appendicitis with total and direct bilirubin. Cureus 2019; 11:12.