

A PROSPECTIVE CROSS-SECTIONAL STUDY OF HYPERBILIRUBINEMIA AS A PREDICTOR OF SEVERITY OF ACUTE APPENDICITIS

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ABSTRACT

Early identification of severe acute appendicitis remains challenging despite advances in clinical assessment and imaging. Hyperbilirubinemia has appeared as a probable biochemical marker for forecasting disease severity and may assist in making decisions prior to surgery. To evaluate the correlation between the RIPASA score and serum bilirubin as a predictor of the severity of acute appendicitis. This prospective cross-sectional study comprised 77 patients with acute appendicitis confirmed by histology. RIPASA severity, appendiceal perforation, and histological results were all linked with preoperative blood total, direct, and indirect bilirubin levels. Mann-Whitney U, Chi-square, Pearson correlation, Kruskal-Wallis, and receiver operating characteristic (ROC) curve analyses were among the statistical tests used. While direct and indirect bilirubin fractions did not substantially correlate with illness severity, total blood bilirubin did demonstrate a significant correlation with increasing RIPASA severity ($p = 0.004$). Hyperbilirubinemia was not significantly associated with appendiceal perforation, and ROC analysis demonstrated limited predictive performance for perforation. Total bilirubin showed better discriminatory ability than direct and indirect bilirubin but was not an independent predictor. A straightforward, affordable, and easily accessible supplementary biomarker for determining the severity of acute appendicitis is serum total bilirubin. However, rather than being employed as a stand-alone predictor of appendiceal perforation, it should be evaluated in conjunction with clinical evaluation and the RIPASA score.

KEYWORDS: Hyperbilirubinemia, Acute Appendicitis, Serum bilirubin, RIPASA score, Appendiceal perforation

1. INTRODUCTION

Acute appendicitis is one of the most common causes of severe abdominal pain that require emergency surgery globally. It impacts people of all ages and continues to be a major reason for emergency room admissions. Appendectomy surgery is a standard surgical procedure, however, if there is a late diagnosis or inappropriate management, the disease can progress to gangrene, perforation, formation of intra-abdominal abscesses, peritonitis, and sepsis potentially resulting in increased morbidity and healthcare burden following surgery. As such, early detection of patients who are prone to complicated appendicitis is still a great challenge in the field of emergency surgery (Ambre & Chavan, 2018).

With the use of laboratory tests and radiographic imaging, the diagnosis of acute appendicitis is mostly determined clinically. By integrating clinical characteristics laboratory measurements, physical examination, scoring systems of clinical particularly the Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score have improved diagnostic accuracy. Even the current diagnostic methods have not been effective in distinguishing uncomplicated appendicitis from complicated disease prior to surgery. Hence, there has been considerable effort into developing the identification of simple, low cost, readily available biochemical markers that can help the clinician to determine the severity of the disease prior to operative intervention (Zosimas et al., 2021).

One laboratory test that has shown promise in forecasting the strictness of acute appendicitis is hyperbilirubinemia. Patients with appendiceal infections are considered to have high blood bilirubin levels because of mechanical obstruction brought on by bacterial endotoxemia and a systemic inflammatory response. The endotoxins produced by gram negative bacteria interfere with the transport of bilirubin to the hepatocytes and to the bile, thus producing a transient cholestasis and a rise in plasma bilirubin. Hepatic dysfunction can worsen as inflammation progresses and leads to gangrene or perforation, causing increased levels of bilirubin (Akai et al., 2019).

Multiple prospective studies have shown that patients with complicated or perforative appendicitis have significantly higher serum bilirubin levels than those with uncomplicated appendicitis, indicating more severe appendiceal inflammation, and bilirubin may be considered a marker of advanced appendiceal inflammation (Bakshi & Mandal, 2021; Kar et al., 2022). These findings have also been observed in the paediatric population, in which the presence of higher bilirubin levels was linked to a higher risk of perforation and poor outcome of appendectomy (Pogorelič et al., 2021). Additionally, bilirubin has shown to have a higher specificity than some routine inflammatory markers as an addition to clinical assessment in the diagnosis of acute appendicitis (Zosimas et al., 2021).

The practicality of bilirubin as a indicator for complex appendicitis has been validated by recent research. The sensitivity of hyperbilirubinemia ranged from high to moderate, with moderate diagnostic accuracy of hyperbilirubinemia in identifying appendiceal perforation, according to a systematic review and diagnostic meta-analysis (Gavriilidis et al., 2019). Similarly, another more recent systematic review found that elevated bilirubin might be a valuable complementary marker to aid in the diagnosis of complicated appendicitis when used with clinical assessment and other blood markers (Czyszczonek et al., 2025). Furthermore, biochemical parameters, especially hyponatremia, have been suggested to be associated with other biochemical changes and may help further identify patients with increased risk of complicated appendicitis (Shuaib et al., 2022). Furthermore, there have been reports that higher levels of bilirubin are associated with perforated appendicitis, which has been seen in clinical investigations, again supporting the use of bilirubin as a tool for risk stratification prior to surgery (Iftikhar et al., 2019).

Hyperbilirubinemia and complex acute appendicitis have been linked in prior research; however, previously reported diagnostic performance ranges across different study populations and different clinical settings. Patients' characteristics, laboratory cut-off values, and diagnostic criteria have led to conflicting findings about the clinical utility of serum bilirubin as an independent predictor of disease severity (Akai et al., 2019; Gavriilidis et al., 2019). Furthermore, there are very few prospective studies that have evaluated the relationship between validated clinical severity measures and blood bilirubin levels (e.g., RIPASA score) with operative and histopathological results. Hence, more prospective studies are needed to assess the potential of serum bilirubin to predict the severity of acute appendicitis and aid early clinical decision-making (Bakshi & Mandal, 2021; Czyszczonek et al., 2025). Thus, the study's goal is to ascertain if blood bilirubin might be a novel laboratory marker to help diagnose and gauge the harshness of appendicitis.

Objective

To correlate levels of serum bilirubin with the Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score to establish the relation among severity of acute appendicitis and serum bilirubin.

2. METHODOLOGY

2.1 Study Setting and Design

Over the course of six months, the potential cross-sectional study was carried in the general surgery department of Yenepoya Medical College Hospital (YMCH), Deralakatte, Mangalore, after getting clearance from the Institutional Ethics Committee. Patients who were detected with acute appendicitis in the casualty and outpatients' department were selected as study subjects after taking their informed written consent.

2.2 Study Population

This research included 77 individuals who had appendectomies due to clinically suspected instances of acute appendicitis. The diagnosis was made from the clinical findings and confirmed by the histopathological examination of the specimen.

2.3 Eligibility Criteria

Individuals greater than 5 years old undergoing appendectomy due to suspected acute appendicitis confirmed by histopathology were part of the study. Those individuals who were younger, had underlying hepatobiliary diseases such as hepatitis, gallstones, and cirrhosis, had haemolytic disorders like sickle cell anaemia and thalassemia, did not send appendiceal specimens for histopathological analysis, and had negative histopathological appendicitis were not included in the investigation.

2.4 Sampling Technique and Sample Size

The size of sample was analysed using the standard equation for calculation of proportion at 7% margin of error and 95% confidence level, and a presumed prevalence from a past study giving a minimum sample size of 77 respondents. Participants were consecutively recruited among the eligible cases presenting within the study duration through convenient sampling technique.

2.5 Study Procedure

RIPASA score system was used to clinically assess each subject after the patients gave their written consent. Serum levels of total, haemoglobin, total leukocyte count, platelet count, direct, and indirect bilirubin, C-reactive protein, liver function tests, and urinalysis were among the preoperative biochemical tests performed on the participants. In addition, ultrasound or CT scans were done where necessary. Subsequently, all the subjects underwent an appendectomy operation, and the findings from the procedure were recorded. Histopathological examination of the resected appendiceal specimen was done.

2.6 Outcome Measures

The association between the degree of acute appendicitis as resolved by the RIPASA score and the serum bilirubin level was the main outcome. The secondary goals were the link between bilirubin fractions and clinical and laboratory factors, the relationship between bilirubin levels and appendiceal perforation, and the diagnostic value of serum bilirubin in predicting disease severity using ROC curve analysis.

2.7 Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 24 and Jamovi version 2.6.23 were used to analyse and visualise the data after it was imported into Microsoft Excel. Frequency and percentage were used to characterise categorical variables, and the Chi-Square test or Fisher's exact test were used for analysis. The mean $\pm$ standard deviation and the median with interquartile range were used for description of continuous variables. Pearson correlation was used to evaluate the connection between various variables. The Mann-Whitney U and Kruskal-Wallis tests were used to compare the groups. The Receiver Operating Characteristic (ROC) curve, which also looked at sensitivity, specificity,

AUC, and optimal cut-off values, was used to assess the diagnostic capability of serum bilirubin. A p-value of less than 0.05 was used as the significance threshold.

3. RESULTS

3.1 Study Population's baseline features

The research comprised 77 individuals with acute appendicitis as determined by histopathology. Prior to analysing the association among blood bilirubin level and illness cruelty, the research population was evaluated by looking at the patients' baseline demographic and clinical features. Figure 1 and Table 1 show the research patients' clinical and demographic characteristics. The research population's demographic features, including the participants' age and gender distribution, are shown in Figure 1.

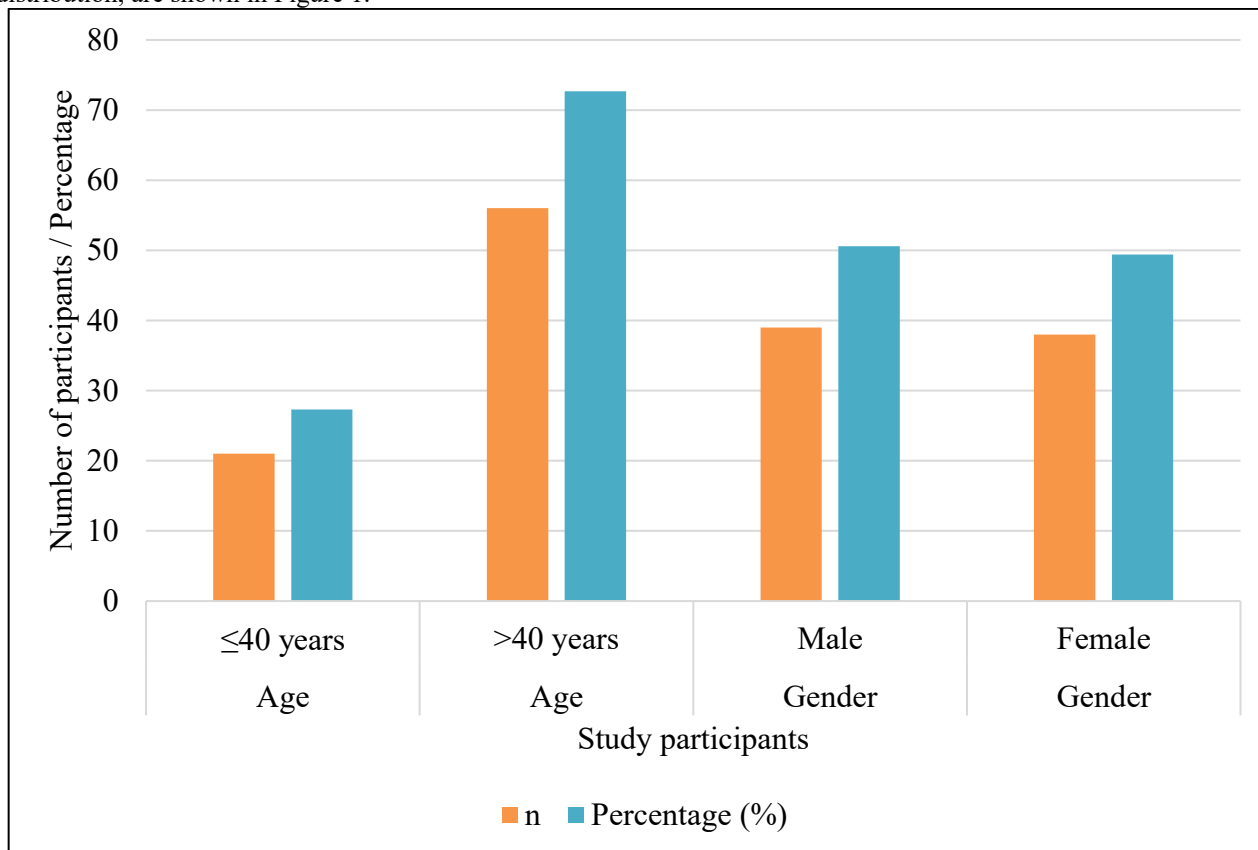


Figure 1. Distribution of age and gender among the study participants

The participants involved in this study belonged to both age groups and were almost equally divided between males and females. The demographic features have been described in detail in Table 1 below.

Table 1. Research participants' baseline clinical features (N = 77)

Variable	Category	n (%)
Duration of symptoms	≤48 hours	20 (26.0)
	>48 hours	57 (74.0)
Presenting symptoms*	Right iliac fossa pain	77 (100.0)
	Nausea and vomiting	53 (68.8)
	Migration of pain	36 (46.8)
	Fever	30 (39.0)
	Anorexia	30 (39.0)
Clinical signs*	Right iliac fossa tenderness	72 (93.5)
	Rebound tenderness	40 (51.9)
	Rovsing's sign	29 (37.7)
	Guarding	15 (19.5)

*Multiple responses were recorded.

Clinical manifestations of the study participants have been described in Table 1 below. The most common clinical manifestations included right iliac fossa pain and tenderness; other manifestations include nausea/vomiting, pain migration, fever, and anorexia. The majority of patients reported having symptoms for more than 48 hours before to presentation, which is noteworthy.

3.2 Laboratory Profile and Disease Characteristics

Laboratory studies and features of disease of the study subjects were assessed to define the biochemical profile and severity of disease of the subjects at presentation. This forms the baseline laboratory and pathological profile of the subjects. The laboratory and disease profile of the subjects are shown in Figure 2 and Table 2. The serum bilirubin profile is shown in Figure 2, whereas other laboratory tests, severity of disease, surgical findings, and histopathology results have been listed in Table 2.

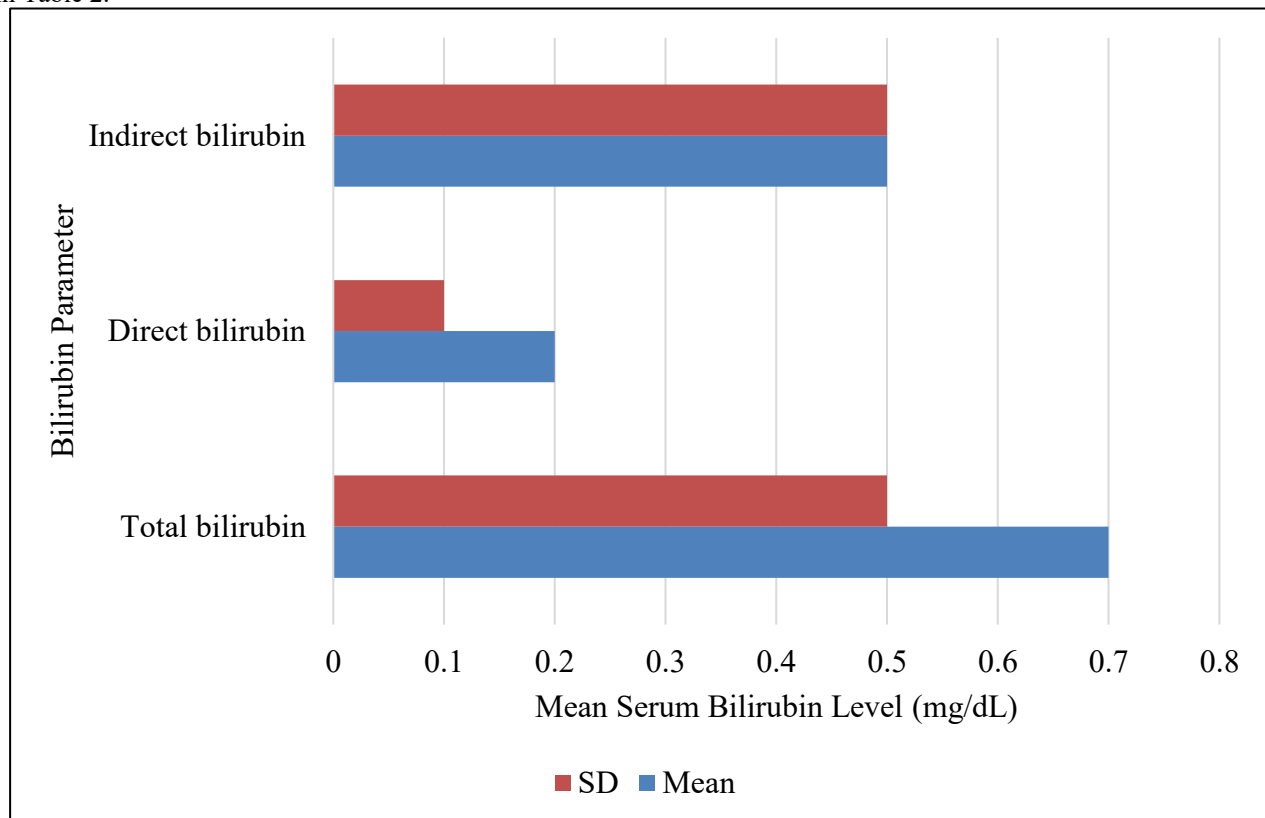


Figure 2. Mean ($\pm$ SD) direct, and indirect bilirubin, serum total levels among the study participants

Fig. 2 shows the serum bilirubin profile of the subjects involved in the experiment. The highest mean was observed for total bilirubin, followed by indirect bilirubin, while direct bilirubin had the lowest mean level.

Table 2. Laboratory profile and disease characteristics of the study participants (N = 77)

Variable	Category/Value
Other laboratory parameters (Mean $\pm$ SD)	
Haemoglobin (g/dL)	13.1 $\pm$ 1.8
Total leukocyte count (cells/mm ³)	9400 $\pm$ 3400
Platelet count (lakh/mm ³)	2.85 $\pm$ 0.60
C-reactive protein (mg/L)	20.3 $\pm$ 43.4
RIPASA severity, n (%)	
Low	10 (13.0)
Moderate	27 (35.1)
High	40 (51.9)
Appendiceal perforation, n (%)	
No	59 (76.6)
Yes	18 (23.4)
Histopathological diagnosis, n (%)	
Acute appendicitis	39 (50.6)
Other appendiceal pathologies*	38 (49.4)

*Includes subacute, chronic, recurrent, resolving appendicitis, and other histopathological variants identified on histopathological examination.

The rest of the laboratory indices and the disease features have been outlined in Table 2. High RIPASA severity classification was seen in the majority of cases, however, from a histological perspective, the most frequent diagnosis was acute appendicitis.

3.3 Distribution of Hyperbilirubinemia Among Study Participants

To find out how many of those suffering from acute appendicitis had hyperbilirubinemia, the serum total bilirubin levels of the subjects were assessed. This data is presented in Table 3 where participants were classified on the basis of normal and elevated serum total bilirubin levels.

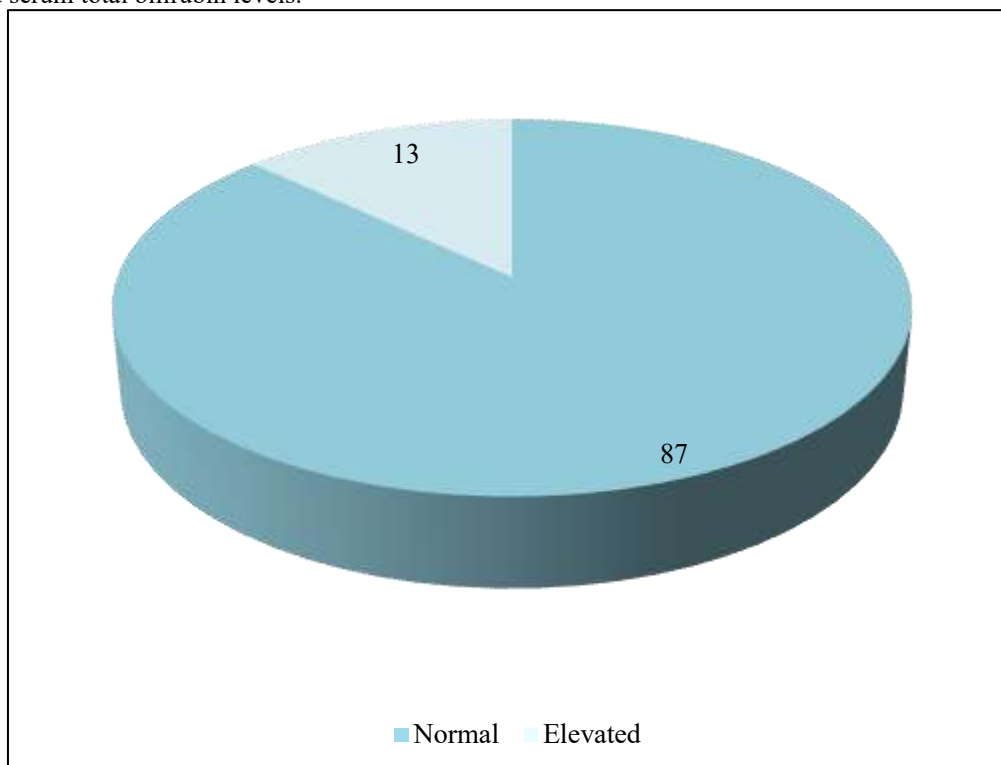


Figure 3. Distribution of serum total bilirubin levels among the study participants

Figure 3 showed that the majority of the time, the levels of total serum bilirubin were within the normal range (87.0%; n=67) compared to those in 13.0% of the patients where hyperbilirubinemia was seen (n=10). This demonstrates that the presence of increased serum levels of bilirubin was not common in patients of acute appendicitis.

3.4 Association Between Hyperbilirubinemia and Severity of Acute Appendicitis

Using the RIPASA scoring scale, the association among the degree of acute appendicitis and total bilirubin was evaluated. The patient distribution based on the normal and raised serum bilirubin levels in terms of RIPASA severity scores is presented in Table 4 below.

Table 4. Association among serum total bilirubin levels and RIPASA severity categories

RIPASA severity	Normal bilirubin n (%)	Elevated bilirubin n (%)	p-value
Low	10 (100.0)	0 (0.0)	0.063
Moderate	20 (74.1)	7 (25.9)	
High	37 (92.5)	3 (7.5)	

Pearson's Chi-square test

The distribution of serum bilirubin levels differed between the RIPASA severity categories; however, the relationship was not statistically significant, as shown in Table 4.

3.5 Comparison of Bilirubin Fractions Across RIPASA Severity Categories

To investigate the association among the severity of acute appendicitis and serum bilirubin fractions, bilirubin fractions in the serum were examined throughout the RIPASA severity classifications. Figure 4 shows the average serum total, direct, and indirect bilirubin fractions throughout the RIPASA severity classifications.

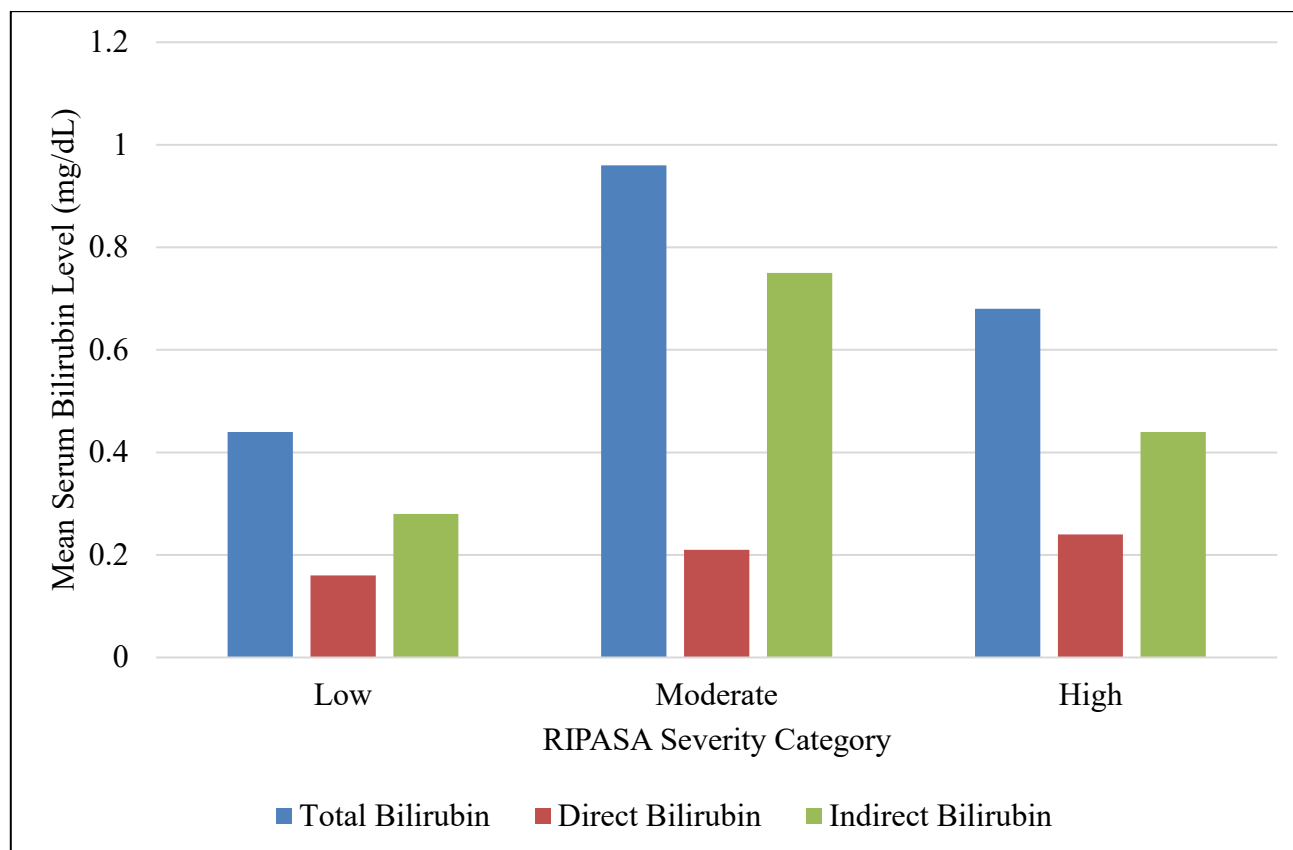


Figure 4. Mean serum total, direct, and indirect bilirubin levels according to RIPASA severity categories

The mean level of total bilirubin rose from 0.44 mg/dL in the low severity group to 0.96 mg/dL in the moderate severity group and 0.68 mg/dL in the high cruelty group, as shown in Figure 4 below. The mean level of direct bilirubin of 0.16 mg/dL, the modest brutality group had a mean level of 0.21 mg/dL, and the high harshness group had a mean level of 0.24 mg/dL. Similarly, the average amount of indirect bilirubin rose from 0.28 mg/dL in the group with low severity to 0.75 mg/dL in the group with moderate cruelty and decreased to 0.44 mg/dL in the group with high severity. Overall, the total bilirubin showed the largest difference between the RIPASA severity categories and the highest statistical significance ($p = 0.004$). On the other hand, no statistical significance was shown for direct ($p = 0.068$) and indirect ($p = 0.064$) bilirubin variations.

3.6 Association Between Hyperbilirubinemia and Appendiceal Perforation

To establish a relationship between hyperbilirubinemia and appendiceal perforation, the relationship between serum total bilirubin and appendiceal perforation was analyzed. The distribution of patients based on their serum total bilirubin levels (normal or high) among those who had appendiceal perforation and those who did not is shown in Table 6.

Table 6. Association between serum total bilirubin levels and appendiceal perforation

Serum total bilirubin	No perforation n (%)	Perforation n (%)	p-value
Normal	53 (89.8)	14 (77.8)	0.231
Elevated	6 (10.2)	4 (22.2)	

Pearson's Chi-square test.

While increased serum bilirubin was noted to be common in patients with appendiceal perforation, the relationship between increased serum bilirubin and perforation was statistically insignificant (Table 6).

3.7 Comparison of Bilirubin Fractions According to Perforation Status

Serum bilirubin fractions were compared in patients having appendiceal perforation and non-perforating appendicitis to identify their association with appendiceal perforation. The mean values of total, indirect and direct bilirubin in serum regarding appendiceal perforation are depicted in Figure 5.

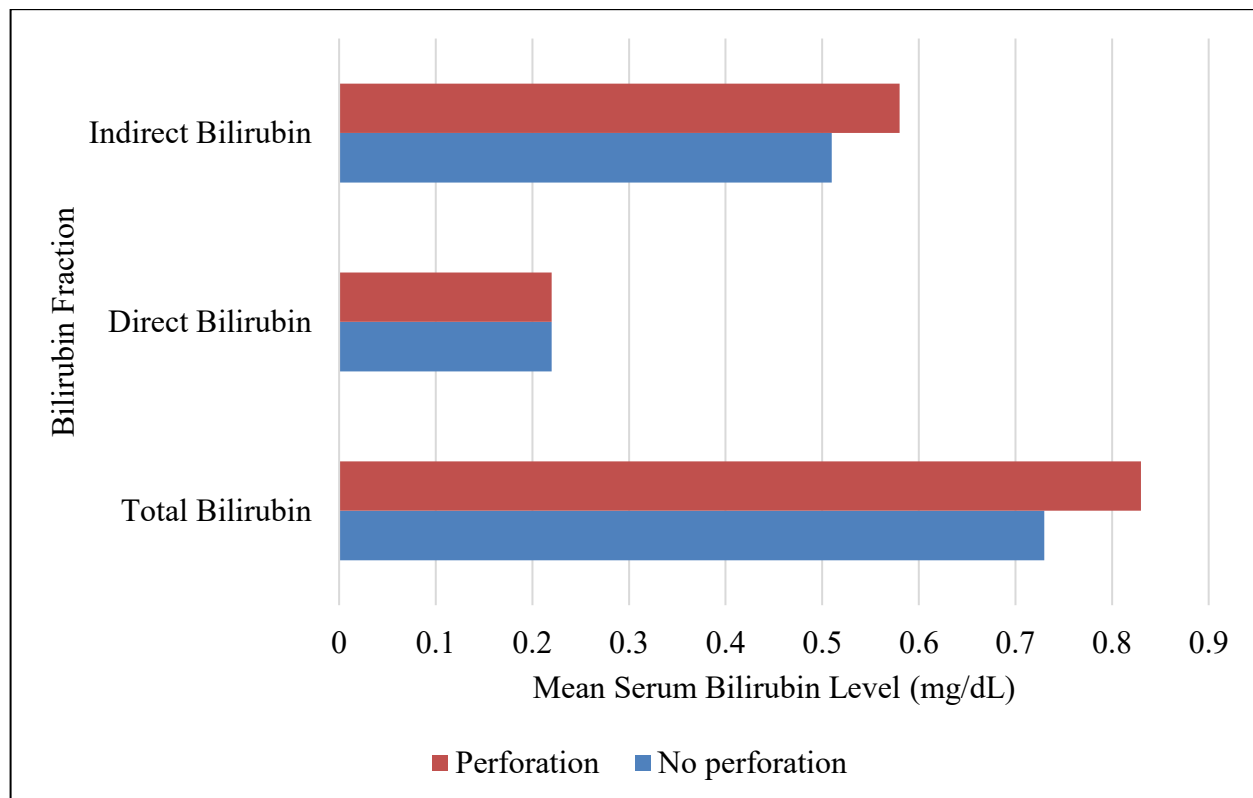


Figure 5. Mean serum total, direct, and indirect bilirubin levels according to appendiceal perforation status

Figure 5 illustrates that the average total bilirubin level was 0.73 mg/dL for those without a ruptured appendix and 0.83 mg/dL for those who had one. Both groups' mean direct bilirubin levels were 0.22 mg/dL, whereas their mean indirect bilirubin levels were 0.51 mg/dL and 0.58 mg/dL, respectively. The mean of both groups' direct bilirubin levels were 0.22 mg/dL, whereas their mean indirect bilirubin levels were 0.51 mg/dL and 0.58 mg/dL, respectively.

3.8 Correlation Between Bilirubin Levels and Clinical Parameters

There was significant correlation found between bilirubin fractions and laboratory parameters chosen for correlation analysis. Only direct bilirubin fraction correlated positively with the RIPASA score among the bilirubin fractions, while the RIPASA score correlated significantly positively with CRP (C-reactive protein) and total white blood cell count, as described in Table 8.

Table 8. Correlation of bilirubin fractions with laboratory parameters and RIPASA score

Variable	Hb	TLC	Platelet count	CRP	RIPASA score
Total bilirubin	0.364 (0.001)	0.420 (<0.001)	-0.346 (0.002)	0.196 (0.088)	-0.020 (0.860)
Direct bilirubin	-0.127 (0.270)	-0.018 (0.876)	0.125 (0.279)	0.015 (0.900)	0.266 (0.019)
Indirect bilirubin	0.370 (0.001)	0.399 (<0.001)	-0.352 (0.002)	0.181 (0.115)	-0.077 (0.504)
RIPASA score	-0.089 (0.441)	0.278 (0.014)	0.139 (0.227)	0.243 (0.033)	

Pearson's correlation coefficient (r) values are displayed, with the p-value enclosed in parenthesis.

Correlation analysis found significant correlations between different fractions of bilirubin and selected laboratory indices. Of different fractions of bilirubin, only direct bilirubin exhibited a significant positive correlation with RIPASA score while RIPASA score had significant positive correlations with total leukocytes count and C-reactive protein (Table 8).

3.9 Diagnostic Performance of Bilirubin in Predicting Severity of Acute Appendicitis

The analysis of ROC curve was used to evaluate the prediction performance of various bilirubin fractions in serum in the diagnosis of appendiceal perforation. Table 9 displays the cutoff values, sensitivity, specificity, AUC, and p-values. Figure 6 displays the ROC curves.

Table 9. Serum bilirubin fractions' diagnostic efficacy in anticipating appendiceal perforation

Parameter	Cut-off (mg/dL)	Sensitivity (%)	Specificity (%)	AUC (95% CI)	p-value
Total bilirubin	0.650	44.4	59.3	0.562 (0.414–0.709)	0.430
Direct bilirubin	0.250	33.3	61.0	0.499 (0.336–0.662)	0.990
Indirect bilirubin	0.450	38.9	64.4	0.556 (0.408–0.704)	0.474

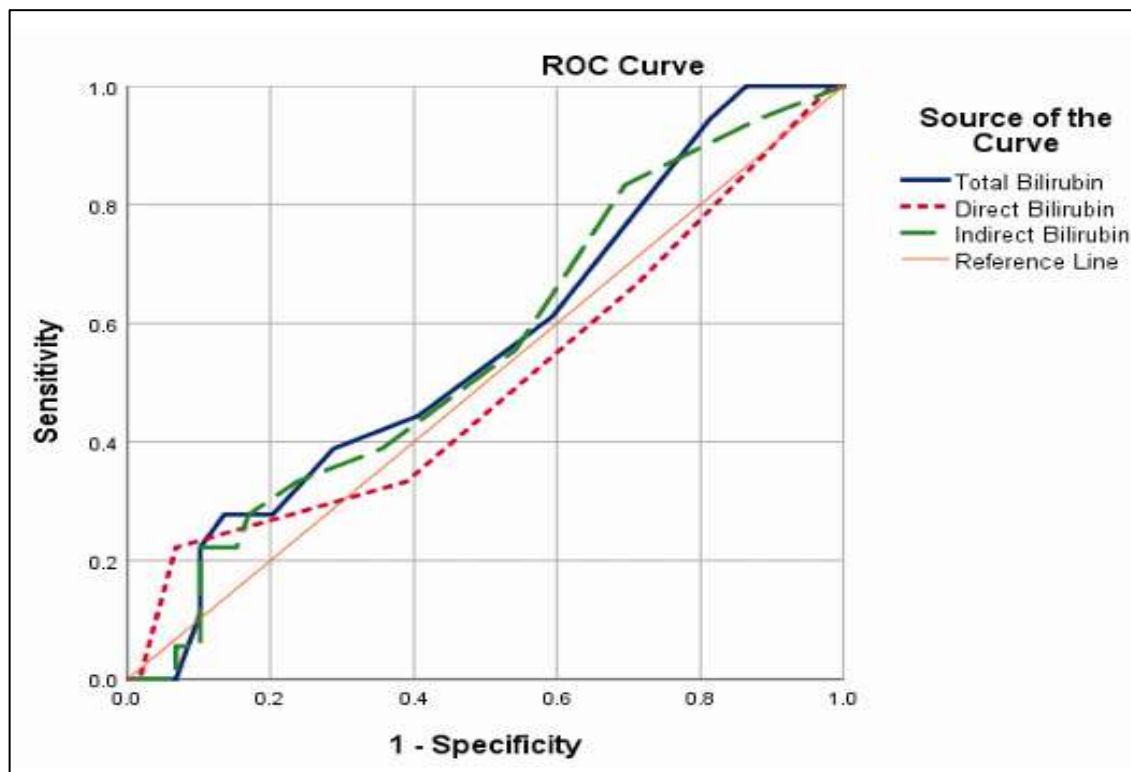


Figure 6. ROC curves display the analytical performance of serum total, direct, and indirect bilirubin for predicting appendiceal perforation

The ROC curve analysis indicated that there was a poor diagnostic capability of serum bilirubin fractions for the diagnosis of appendiceal perforation. From the examined markers, the serum total bilirubin was found to have the greatest AUC, but the direct and indirect bilirubins had equal discriminatory capacity. Nevertheless, none of the bilirubin fractions possessed statistical predictive power for appendiceal perforation (Table 9 and Figure 6).

4. DISCUSSION

In order to gauge the brutality of acute appendicitis, we looked at serum bilirubin levels as a laboratory measure in this prospective cross-sectional research. The majority of patients were in the high RIPASA severity grade while a small number of patients had hyperbilirubinemia. The severity of the condition was significantly correlated with total serum bilirubin levels, although neither direct nor indirect bilirubin levels were significantly different between severity groups. Patients with perforation of the appendix had slightly higher bilirubin levels, but no difference was seen between individual levels of bilirubin and perforation. Additionally, receiver operating characteristic (ROC) curves showed that bilirubin parameters were not particularly discriminatory for predicting perforation, indicating that serum bilirubin is not a reliable indicator of perforation on its own. The high association between total serum bilirubin level and the severity of the RIPA indicates that severe appendiceal inflammation may affect hepatic bilirubin metabolism by endotoxin-induced hepatocellular dysfunction. In contrast, there was no discernible change between the direct and indirect bilirubin percentages, suggesting that total bilirubin is a better measure of the overall inflammatory response. Thus, serum total bilirubin can be used as an additional tool to be used along with more available clinical assessment tools, but not as a sole diagnostic tool.

The patients' total and indirect bilirubin levels were somewhat elevated with perforated appendix, but this was not statistically significant and ROC analysis showed poor predictive capacity. These results suggest that serum bilirubin alone is not enough to predict perforation and that as the disease progresses, so will bilirubin increase. But rather, they must be read in conjunction with clinical parameters, inflammatory markers and imaging tests and must be used in conjunction with a validated scoring system like RIPASA, to better assess the patients and to stratify the risk before the surgery.

The present results are in general agreement with previous studies that have assessed indicator of complicated appendicitis is serum bilirubin. Kaur et al. (2025) and Gelevski (2025) reported that higher serum bilirubin levels were linked to increased severity of the disease and might help to recognize complicated appy. Patil et al. (2024), Agrawal et al. (2023) and Rodríguez-Aguilera et al. (2023) reported that high serum bilirubin levels were associated with higher severity of the disease and may be useful in recognizing complicated appy. Likewise, Ahmed et al. (2020), Alaradi et al. (2020), Khan and Asad (2020), Elshoura et al. (2018) and Singh et al. found that hyperbilirubinemia can enhance diagnostic accuracy in conjunction with typical clinical findings.

Some of the studies focused on appendiceal perforation and found greater associations than the present study. According to the study of Vetri et al. (2022), Koirala et al. (2022), Azizoglu et al. (2023), Nishat et al. (2025) and Elafandy and Singh (2025), levels of serum bilirubin were often significantly elevated in patients with perforated appendicitis; thus, hyperbilirubinemia may be useful for predicting perforation. However, there was no discernible correlation between

bilirubin levels and perforation in the current investigation, with the exception of limited rises. The differences could be due to variations in study design, patient characteristics, sample size, timing of the laboratory evaluation, and criteria for complicated appendicitis. Even though the ability of total bilirubin to predict perforation was not strong in the current investigation, the substantial association among total bilirubin and the RIPAS severity suggests that bilirubin is an indicator of the degree of inflammation.

Serum bilirubin estimation is cheap, fast and is readily available in routine use in the emergency surgical practice. In the light of the current study, total serum bilirubin could be helpful in combination with clinical examination, RIPASA scoring, inflammatory markers, and radiological investigations to provide some useful information about the severity of acute appendicitis. Bilirubin was found to be a poor predictor of appendiceal perforation, but with its use in the routine surgical evaluation may help select those patients who need closer follow-up and prompt surgical intervention. Thus, serum bilirubin should be considered alongside, but not as a primary, diagnostic test in the acute appendicitis diagnosis.

The current study has many drawbacks. The sample size was modest and it was carried out at a single tertiary care facility which could restrict the generalisability of the outcomes. Serum bilirubin levels were only measured once and not throughout the disease process. Although pre-defined eligibility criteria excluded potential confounding factors which may influence bilirubin metabolism, this was not possible to fully remove them. Furthermore, the current study solely used the RIPASA score to assess the association amid bilirubin and illness severity and other inflammatory markers and multicenter validation were not undertaken. Multicentre studies are recommended on a larger scale in the future, which include many biochemical parameters and a uniform diagnostic criterion, to validate the clinical significance in further detail of hyperbilirubinemia in complicated acute appendicitis.

5. CONCLUSION

The present prospective cross-sectional investigation aimed to evaluate hyperbilirubinemia's potential as a predictor of acute appendicitis severity. The findings demonstrated a strong relationship between total bilirubin and the assessed degree of illness by the RIPASA scoring system, indicating an increase in inflammation severity in acute appendicitis with increased bilirubin levels. However, no significant relationships were observed with disease severity for the direct and indirect bilirubin fractions. Patients who have perforation had slightly elevated bilirubin concentration, but neither hyperbilirubinemia nor any of the individual bilirubin fractions had a statistically noteworthy suggestion with perforation, and the study of the receiver operating characteristic curve revealed a low diagnostic value. These findings suggest that serum total bilirubin is a practical, affordable, and readily accessible laboratory parameter that may also be used as a supplement to the clinical evaluation and already available diagnostic tools when assessing patients with acute appendicitis. Bilirubin should not be used as a single test to diagnose complicated appendix or appendiceal perforation, however. It is increased in clinical significance when used in combination with clinical presentation, RIPASA scoring, inflammatory markers, and imaging studies. Future prospective, to validate these findings, multicenter trials with bigger patient groups are required, to provide a consensus on the bilirubin threshold values and to clarify the significance of the serum bilirubin level in the context of broader diagnostic and management methods for acute appendicitis patients' early diagnosis and risk assessment.

REFERENCES

1. Agrawal, A., Khan, S., Khare, R., & Sahu, A. (2023). Relationship Between Hyperbilirubinemia And Acute Appendicitis-An Observational Study. *Surgical Chronicles*, 28(1).
2. Ahmed, F. A., Aljirdabi, N. S., & Almahari, S. A. (2020). Hyperbilirubinemia in acute appendicitis. *Bahrain Medical Bulletin*, 42(4).
3. Akai, M., Iwakawa, K., Yasui, Y., Yoshida, Y., Kato, T., Kitada, K., ... & Iwagaki, H. (2019). Hyperbilirubinemia as a predictor of severity of acute appendicitis. *Journal of International Medical Research*, 47(8), 3663-3669.
4. Alaradi, J., Rahman Alharmi, R. A., Alqaseer, A., Ahmed, F. A., Aljirdabi, N. S., & Almahari, S. A. (2020). Hyperbilirubinemia in Acute Appendicitis. *Bahrain Medical Bulletin*, 42(4).
5. Ambre, S. R., & Chavan, S. (2018). Hyperbilirubinemia as a diagnostic marker for acute appendicitis. *International Surgery Journal*, 5(6), 2091-2096.
6. Azizoğlu, M., Okur, M. H., Aydoğdu, B., Orbay, T. M., Bakir, A. C., Klyuev, S. A., ... & Risteski, T. T. (2023). Hyperbilirubinemia is a predictor of appendiceal perforation in children: A meta-analysis. *Academic Journal of Health Sciences*, 38(4), 64-68.
7. Bakshi, S., & Mandal, N. (2021). Evaluation of role of hyperbilirubinemia as a new diagnostic marker of complicated appendicitis. *BMC gastroenterology*, 21(1), 42.
8. Czysteczon, A., Maczkowski, B., Tkaczyk, A., Drozd, M., Boral, W., Mikler, S., ... & Maczkowski Sr, B. (2025). Hyperbilirubinemia as a Marker for Complicated Acute Appendicitis: A Systematic Review. *Cureus*, 17(9).
9. Elafandy, A., & Singh, S. (2025). Bilirubin as a Diagnostic Factor in Acute Appendicitis. *Cureus*, 17(10).
10. Elshoura, A. A., Abo-Ryia, M. H., Elsadany, A., Saber, S. A., & Mousa, G. I. (2018). Prospective Assessment of Elevated Serum Bilirubin Level in Diagnosis of Acute Appendicitis. *Adv Surg Sci*, 6, 27-30.
11. Gavriilidis, P., de'Angelis, N., Evans, J., Di Saverio, S., & Kang, P. (2019). Hyperbilirubinemia as a predictor of appendiceal perforation: A systematic review and diagnostic test meta-analysis. *Journal of clinical medicine research*, 11(3), 171.
12. Gelevski, R. (2025). Hyperbilirubinemia as a biomarker for complicated appendicitis: a retrospective study. *Macedonian Journal of Anaesthesia*, 9(2), 51-57.

13. Iftikhar, M., Qureshi, U., Khan, J. S., & Shafique, S. (2019). Hyperbilirubinemia as an indicator of complicated appendicitis. *International Journal of Surgery and Medicine*, 5(2), 58-58.
14. Kar, S., Behera, T. K., Jena, K., Sahoo, A. K., BEHERA, T., & JENA Sr, K. U. M. A. R. M. A. N. I. (2022). Hyperbilirubinemia as a possible predictor of appendiceal perforation in acute appendicitis: a prospective study. *Cureus*, 14(2).
15. Kaur, M., Singh, G., Khurana, S., & Singh, G. (2025). Hyperbilirubinemia as a Diagnostic Marker for Acute complicated Appendicitis.
16. Khan, S., & Asad, H. (2020). ASSESSMENT OF ACCURACY OF HYPERBILIRUBINEMIA IN EARLY DIAGNOSIS OF ACUTE APPENDICITIS IN OUR POPULATION. *Pakistan Armed Forces Medical Journal*, (1), S54.
17. Koirala, D. P., Gupta, A. K., Dahal, G. R., Shrestha, B. M., Shrestha, S., Neupane, S., & Pokharel, R. P. (2022). Role of hyperbilirubinaemia as a predictor of complicated appendicitis in paediatric population. *African Journal of Paediatric Surgery*, 19(2), 61-64.
18. Nishat, O., Pooja, K., & Shivam, P. P. (2025). Diagnostic Value of Hyperbilirubinemia in Acute Appendicitis and Appendiceal Perforation. *European Journal of Cardiovascular Medicine*, 15, 322-327.
19. Patil, L. S., Yashawini, P. M., Sujay, D. J., & Nikhil, M. (2024). Elevated Serum Bilirubin as a Predictor of Acute Appendicitis-A cohort study. *European Journal of Cardiovascular Medicine*, 14, 642-646.
20. Pogorelić, Z., Lukšić, A. M., Mihanović, J., Đikić, D., & Balta, V. (2021). Hyperbilirubinemia as an indicator of perforated acute appendicitis in pediatric population: A prospective study. *Surgical Infections*, 22(10), 1064-1071.
21. Rodríguez-Aguilera, O., Cervantes-Ortiz, R. J., & Torres-Medina, V. (2023). Serum bilirubin levels as a predictor of severity in acute appendicitis. *Hypertension*, 4, 6-8.
22. Shuaib, A., Alhamdan, N., Arian, H., Sallam, M. A., & Shuaib, A. (2022). Hyperbilirubinemia and hyponatremia as predictors of complicated appendicitis. *Medical Sciences*, 10(3), 36.
23. Singh, J., Kathpal, K., Chalotra, V., Sharda, S., & Chalotra, V. Hyperbilirubinemia: A diagnostic tool for acute appendicitis & its complication.
24. Vetri, R., Sainath, S., Kannichamy, V., & Banerjee, A. (2022). Hyperbilirubinemia as a predictor of perforated appendicitis. *Journal of Surgery and Research*, 5(3), 468-471.
25. Zosimas, D., Lykoudis, P. M., Strano, G., Burke, J., Al-Cerhan, E., & Shatkar, V. (2021). Bilirubin is a specific marker for the diagnosis of acute appendicitis. *Experimental and therapeutic medicine*, 22(4), 1-5.