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A STUDY TO EVALUATE THE ASSOCIATION OF HYPERBILIRUBINEMIA IN PATIENTS WITH APPENDICULAR PERFORATION

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Abstract

Background: Appendicular perforation is a serious complication of acute appendicitis, often associated with increased morbidity. Early identification of perforation is crucial for timely surgical intervention. Recent evidence suggests that hyperbilirubinemia may serve as a predictive marker for appendicular perforation.

Objectives: To evaluate the association between serum total bilirubin levels and appendicular perforation in patients undergoing appendectomy.

Methods: A prospective cross-sectional observational study was conducted at the Department of General Surgery, Gadag Institute of Medical Sciences, Karnataka, from June 2023 to November 2024. A total of 140 patients, aged 18–70 years, presenting with suspected acute appendicitis/perforation were enrolled. Clinical, biochemical, and radiological data were collected. Serum total bilirubin was measured on admission and re-evaluated on the 7th post-operative day. Final diagnosis was confirmed by histopathology. Data were analyzed using SPSS v21 with a significance level of $p \leq 0.05$.

Results: Out of 140 patients, 30 (21.4%) had histopathologicaly confirmed appendicular perforation. Hyperbilirubinemia was significantly more common in these patients ($p < 0.05$). A positive correlation was observed between serum total bilirubin and total leukocyte count ($r = 0.325$, $p = 0.000$) and SGOT levels ($r = 0.180$, $p = 0.033$). No significant correlation was noted between bilirubin and SGPT or ALP. Most patients (97.1%) presented with right iliac fossa pain, and 29.3% had symptoms lasting five days.

Conclusion: Serum total bilirubin may be a useful adjunct marker in the early detection of appendicular perforation, particularly in resource-limited settings. While not diagnostic alone, hyperbilirubinemia in the absence of liver disease should raise clinical suspicion for perforation and prompt early surgical intervention.

Keywords: Acute appendicitis, Appendicular perforation, Hyperbilirubinemia, Serum bilirubin, Predictive marker, Inflammation.

INTRODUCTION:

Acute appendicitis is one of the most common surgical emergencies worldwide, with a lifetime incidence of approximately 7–8% [1]. While the majority of cases are straightforward, complications such as appendicular perforation can significantly increase morbidity and mortality, particularly in patients who present late or with atypical symptoms [2]. The diagnosis of appendicular perforation remains a challenge, especially in resource-limited settings, where advanced imaging modalities may not always be available. Hence, identifying simple, cost-effective, and accessible biomarkers is crucial to aid early diagnosis and improve patient outcomes.

Recent studies have highlighted the potential role of hyperbilirubinemia as an indicator of appendicular perforation [3–5]. Bilirubin, a breakdown product of hemoglobin, is primarily processed by the liver. Elevated serum bilirubin levels in the absence of underlying hepatobiliary disease may reflect systemic inflammatory responses or microbial translocation, both of which are common in gastrointestinal perforations [6]. The proposed pathophysiological mechanism involves translocation of endotoxins from gram-negative bacteria (e.g., *E. coli*) during appendiceal inflammation or perforation, which impairs hepatocyte excretory function and leads to an increase in serum bilirubin levels [7].

Several studies have demonstrated a statistically significant association between total serum bilirubin levels and complicated appendicitis, particularly perforated appendicitis [8–10]. These findings suggest that hyperbilirubinemia could serve as a surrogate marker for perforation, aiding in surgical decision-making and early intervention. However, the utility of bilirubin as a predictive marker still varies across populations, and the magnitude of association requires further exploration.

Given the limitations of clinical diagnosis and the variable availability of advanced imaging, this study was conducted to evaluate the association between hyperbilirubinemia and appendicular perforation in patients undergoing appendectomy at a tertiary care center. By correlating bilirubin levels with clinical and histopathological findings, the study aims to assess whether hyperbilirubinemia can be used as a reliable adjunct in identifying patients at higher risk of perforation.

MATERIALS AND METHODS:

1. Study Design:

This study was designed as a prospective cross-sectional observational study to evaluate the association between hyperbilirubinemia and appendicular perforation. The prospective nature allowed for real-time data collection and follow-up, while the cross-sectional aspect enabled analysis at the time of hospitalization and early post-operative period.

2. Study Setting:

The study was conducted in the Department of General Surgery, Gadag Institute of Medical Sciences, a tertiary care teaching hospital in Gadag, Karnataka. The hospital caters to a large catchment area and is well-equipped with diagnostic, surgical, and post-operative facilities.

3. Study Duration:

The study was carried out over 18 months, from June 2023 to November 2024. This period ensured adequate patient enrollment, diagnosis confirmation, treatment, and follow-up.

4. Study Participants:

Inclusion Criteria:

1. Patients aged 18–70 years with clinical suspicion of acute appendicitis or appendicular perforation.
2. Patients undergoing emergency appendectomy.
3. Histopathological confirmation of appendicitis/perforation.
4. Patients who gave written informed consent.

Exclusion Criteria:

1. Patients with chronic liver diseases (e.g., cirrhosis, fibrosis).
2. History of alcohol-related liver disease or chronic alcoholism.
3. Patients with hemolytic anemia or other hemolytic disorders.

4. Known cases of biliary tract disease or biliary atresia.
5. Patients with viral hepatitis (e.g., HBsAg positive).
6. History of hepatotoxic drug intake.
7. Patients with gastrointestinal malignancies**.**
8. Pregnant women were excluded due to potential procedural risks.

5. Study Sampling:
A **purposive sampling** technique was employed. All eligible patients admitted with clinical suspicion of acute appendicitis or appendicular perforation and meeting inclusion criteria during the study period were enrolled.

6. Sample Size Calculation:
A total of **140 patients** were included in the study. The sample size was determined based on the estimated prevalence of appendicular perforation, with adjustment made for potential dropout to ensure adequate statistical power.

7. Study Groups:
As this was an observational study, no control or interventional groups were formed. Patients were classified retrospectively based on their bilirubin levels and the presence or absence of appendicular perforation to assess their association.

8. Study Parameters:
a. **Clinical Parameters:** Vital signs (pulse, BP, respiratory rate), duration of symptoms, abdominal signs.
b. **Biochemical Parameters:** Serum total bilirubin, Complete blood count, Liver function tests (SGOT, SGPT, ALP), Peripheral smear, HbsAg, Urine analysis
c. **Radiological Investigations:** Ultrasonography (to evaluate appendiceal status and perforation).
d. Post-operative Parameters: Complications, wound infection, and bilirubin levels reassessed on the 7th post-operative day**.**

9. Study Procedure:
After ethical approval and written informed consent, eligible patients were recruited.
-Upon admission, blood samples were collected within 30 minutes for baseline laboratory investigations.
- Ultrasonography was performed within 2 hours of admission.
-All patients underwent emergency appendectomy after stabilization.
-Specimens were sent for histopathological confirmation.
-Post-operatively, patients were monitored for 5 days in the ward.
-A follow-up bilirubin test was performed on the 7th post-operative day during outpatient review.

10. **Data Collection:**
A structured proforma was used to record all clinical findings, investigation results, intra-operative notes, and post-operative progress. Data were compiled daily by the investigator and verified against case sheets and lab reports.

11. **Data Analysis:**
-Data were entered into Microsoft Excel and analyzed using SPSS version 21.
- Descriptive statistics (mean, SD, percentages) were used for continuous and categorical variables.
-Chi-square test was applied to assess associations between categorical variables.
-A **p-value ≤0.05** was considered statistically significant.

12.**Ethical Considerations:**
The study received approval from the Institutional Ethics Committee of Gadag Institute of Medical Sciences. Participation was voluntary, and informed consent was obtained. Confidentiality was maintained throughout. No additional invasive procedure was performed apart from routine clinical

management. The study adhered to the principles of Declaration of Helsinki, ensuring that the rights, well-being, and privacy of patients were protected.

RESULTS AND OBSERVATIONS:

Table 1: Duration of Symptoms

Duration	Frequency	Percent
1 DAY	11	7.9
10 DAYS	1	0.7
12 DAYS	2	1.4
15 DAYS	4	2.9
2 DAYS	2	1.4
3 DAYS	24	17.1
4 DAYS	30	21.4
5 DAYS	41	29.3
6 DAYS	16	11.4
7 DAYS	6	4.3
8 DAYS	3	2.1
Total	140	100.0

Table 2: Site of Pain

Pain Site	Frequency	Percent
ALL QUADRANTS OF ABDOMEN	1	0.7
RIGHT ILIAC FOSSA	136	97.1
RIGHT ILIAC FOSSA AND RIGHT HYPOCHONDRIUM	2	1.4
RIGHT ILIAC FOSSA AND HYPOGASTIRUM	1	0.7
Total	140	100.0

Table 3: Clinical Signs, Comorbidities, and Diagnosis in Patients with Appendicular Conditions (n = 140)

Parameter	Category	Frequency	Percentage (%)
Fever	Absent	95	67.9%
	Present	45	32.1%
Vomiting	Absent	78	55.7%
	Present	62	44.3%
Diabetes Mellitus	Absent	138	98.6%
	Present	2	1.4%
Hypertension	Absent	140	100.0%
	Present	0	0.0%
Temperature	Nil	96	68.6%
	Present	44	31.4%
Pallor	Absent	136	97.1%
	Present	4	2.9%

Icterus	Absent	124	88.6%
	Present	16	11.4%
Cyanosis	Absent	140	100.0%
	Present	0	0.0%
Clubbing	Absent	140	100.0%
	Present	0	0.0%
Lymphadenopathy	Absent	140	100.0%
	Present	0	0.0%
Pedal Oedema	Absent	140	100.0%
	Present	0	0.0%
Tuberculosis	Absent	140	100.0%
	Present	0	0.0%
Thyroid Disorder	Absent	140	100.0%
	Present	0	0.0%
Diagnosis	Acute Appendicitis	110	78.6%
	Appendicular Perforation	30	21.4%

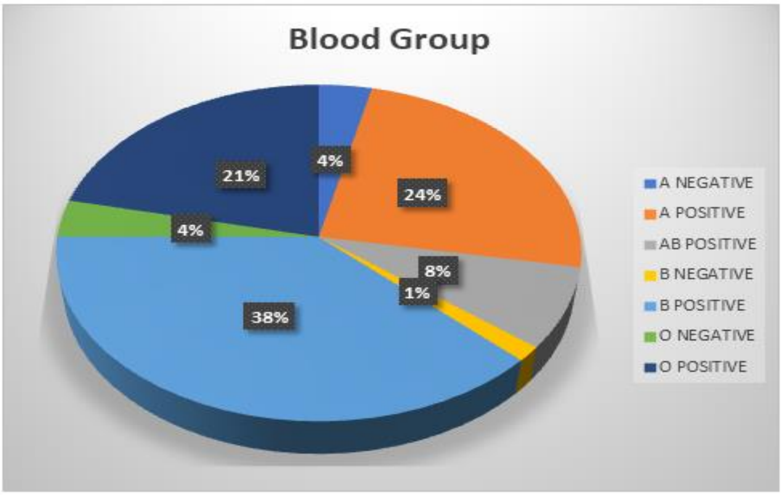

Figure 1: Distribution of Blood Groups in Patients with Appendicular Perforation

Table:4 Clinical, Comorbid, Diagnostic, and Lab Findings in Patients with Appendicular Conditions (n = 140)

Parameter	Category	Frequency	Percentage (%)
Fever	Absent	95	67.9%
	Present	45	32.1%
Vomiting	Absent	78	55.7%
	Present	62	44.3%
Diabetes Mellitus	Absent	138	98.6%
	Present	2	1.4%
Hypertension	Absent	140	100.0%
	Present	0	0.0%
Temperature	Nil	96	68.6%
	Present	44	31.4%

Pallor	**Absent**	**136**	**97.1%**
	Present	**4**	**2.9%**
Icterus	**Absent**	**124**	**88.6%**
	Present	**16**	**11.4%**
Cyanosis	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
Clubbing	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
Lymphadenopathy	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
Pedal Oedema	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
Tuberculosis	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
Thyroid Disorder	**Absent**	**140**	**100.0%**
	Present	**0**	**0.0%**
HIV Status	**Negative**	**139**	**99.3%**
	Positive	**1**	**0.7%**
Hepatitis B Status	**Negative**	**140**	**100.0%**
	Positive	**0**	**0.0%**
Diagnosis	**Acute Appendicitis**	**110**	**78.6%**
	Appendicular Perforation	**30**	**21.4%**
Ultrasound Report	**Acute Appendicitis**	**127**	**90.7%**
	Appendicular Perforation	**13**	**9.3%**
Histopathology Report	**Acute Appendicitis**	**110**	**78.6%**
	Appendicular Perforation	**30**	**21.4%**

Table 5: Surgical Procedures Performed

Surgical Procedure	**Frequency**	**Percent**
LAPAROSCOPIC APPENDICECTOMY	**74**	**52.9**
OPEN APPENDICECTOMY	**66**	**47.1**
Total	**140**	**100.0**

Table 6: Descriptive Statistics of Laboratory Parameters in Patients with Appendicular Perforation

Descriptive Statistics					
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Total count	**140**	**1176**	**29880**	**11274.17**	**4984.139**
HB	**140**	**5.1**	**104.0**	**13.586**	**7.9277**
Platelet count	**140**	**0.59**	**2018.00**	**17.0124**	**170.33289**
Total Bilirubin	**140**	**0.20**	**6.70**	**1.1503**	**0.85014**
SGOT	**140**	**0.2**	**100.0**	**27.733**	**14.3654**
SGPT	**140**	**5.0**	**355.0**	**26.520**	**36.7852**
ALP	**140**	**17.0**	**433.0**	**98.689**	**62.1622**
Postoperative Day 1	**140**	**0.20**	**6.70**	**1.1660**	**0.84574**

Bilirubin					
Postoperative Day 7 Bilirubin	140	0.2	11.0	1.234	1.1328

Table 7: Correlation of Total Bilirubin with Clinical Parameters in Patients with Appendicular Perforation:

		Total Bilirubin
Age	Correlation	0.215*
	P value	0.011
	N	140
Pulse Rate	Correlation	0.016
	P value	0.847
	N	140
SBP	Correlation	-0.086
	P value	0.311
	N	140
DBP	Correlation	-0.069
	P value	0.417
	N	140
Saturation	Correlation	-0.035
	P value	0.681
	N	140

Table 8: Correlation of Total Bilirubin with Laboratory Parameters in Patients with Appendicular Perforation

		Total Bilirubin
Total count	Correlation	0.325**
	P value	0.000
	N	140
HB	Correlation	0.003
	P value	0.976
	N	140
Platelet count	Correlation	-0.015
	P value	0.859
	N	140
SGOT	Correlation	0.180*
	P value	0.033
	N	140
SGPT	Correlation	0.006
	P value	0.944
	N	140
ALP	Correlation	0.014
	P value	0.867

	N	**140**
Postoperative Day 1 Bilirubin	**Correlation**	**0.993****
	P value	**0.000**
	N	**140**
Postoperative Day 7 Bilirubin	**Correlation**	**0.016**
	P value	**0.853**
	N	**140**

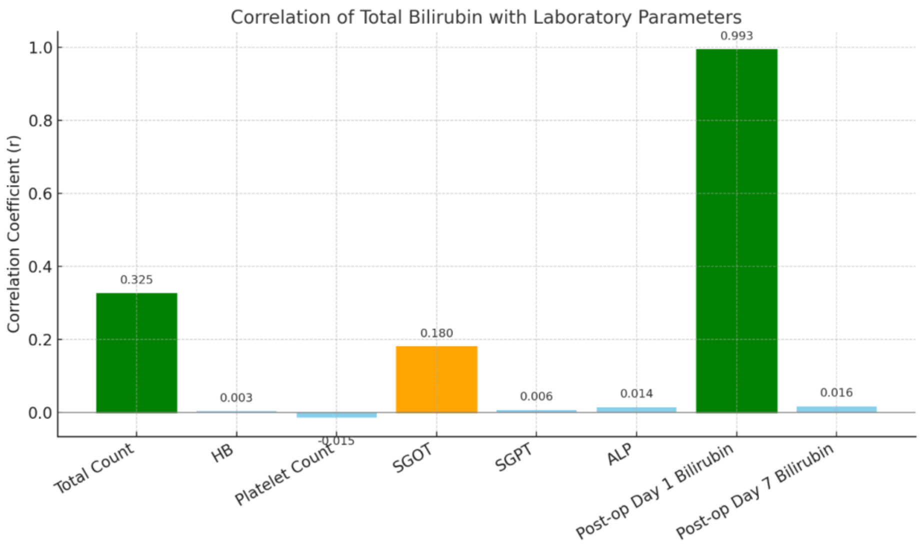

Figure 2: Correlation of total bilirubin with various laboratory parameters in patients with appendicular perforation

DISCUSSION:

The present study was conducted to evaluate the association of hyperbilirubinemia with appendicular perforation, aiming to determine if serum bilirubin could serve as a biochemical marker for complicated appendicitis. Among 140 patients included in the study, 30 (21.4%) were confirmed to have appendicular perforation, and 16 patients (11.4%) had clinically detectable icterus, which was significantly associated with elevated serum bilirubin levels.

Our findings are consistent with earlier studies, such as that of Sand et al. [3], who demonstrated that hyperbilirubinemia was significantly associated with appendiceal perforation, suggesting a sensitivity of 70% and specificity of 86%. Similarly, Estrada et al. [5] in their study found that total bilirubin >1 mg/dL was a statistically significant marker in predicting appendicular perforation with a positive predictive value (PPV) of 90%.

In our study, the mean total bilirubin level was 1.16 mg/dL, which increased slightly to 1.23 mg/dL by the 7th post-operative day. Importantly, a strong positive correlation was found between total bilirubin and total leukocyte count ($r = 0.325$, $p < 0.001$), highlighting that hyperbilirubinemia coincides with the inflammatory response in complicated appendicitis. This is consistent with the hypothesis that endotoxins released during appendiceal inflammation impair hepatocellular bile secretion, resulting in elevated bilirubin levels [6,7].

Interestingly, no significant correlation was observed between serum bilirubin and liver enzymes such as SGPT, ALP, or SGOT, reinforcing that the elevated bilirubin in these cases is not due to intrinsic liver disease, but rather is likely due to bacterial endotoxemia or systemic inflammation. Kucuk et al. [6] also reported similar findings where bilirubin elevation occurred without significant hepatocellular damage.

Another important finding in our study was that ultrasonographic detection of perforation was relatively low (9.3%), while histopathology confirmed it in 21.4% of cases, suggesting that clinical and biochemical indicators like bilirubin may provide a useful adjunct in identifying perforated appendicitis when imaging is inconclusive. This supports results from Eren et al. [8], who emphasized that relying on bilirubin levels in combination with clinical features could enhance early diagnosis and reduce complication rates.

Though hyperbilirubinemia alone may not be sufficient to diagnose appendicular perforation, its incorporation into clinical decision-making—especially in resource-limited settings—can guide the urgency of surgical intervention. The absence of underlying liver disease in our cohort strengthens the conclusion that elevated bilirubin is associated with appendicular perforation rather than liver dysfunction.

However, there are limitations to this study. Being a single-center study, its generalizability is limited, and the use of purposive sampling may introduce selection bias. Future multicentric, randomized studies are warranted to validate these findings across diverse populations and to develop a bilirubin-based scoring system for appendicitis severity assessment.

CONCLUSION:

This prospective observational study demonstrates a significant association between **h**yperbilirubinemia and appendicular perforation in patients undergoing emergency appendectomy. Elevated serum total bilirubin, in the absence of pre-existing hepatobiliary disease, was observed more frequently in patients with perforated appendicitis**,** suggesting its potential as a biochemical marker for complicated cases.

Given that serum bilirubin testing is inexpensive, easily available, and rapidly performed, it can serve as a valuable adjunct to clinical and radiological evaluation, especially in settings with limited diagnostic resources. Incorporating bilirubin levels into the preoperative assessment may aid in early identification of perforation, improving surgical planning and potentially reducing post-operative complications.

However, while hyperbilirubinemia may support clinical suspicion, it should not be used in isolation. Larger, multicentric studies are warranted to further validate its predictive value and to explore its role in risk stratification and surgical decision-making in acute appendicitis.

REFERENCES:

1. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. *Lancet*. 2015;386(10000):1278–87.
2. Sammalkorpi HE, Mentula P, Leppäniemi A. A new adult appendicitis score improves diagnostic accuracy of acute appendicitis—a prospective study. *BMC Gastroenterol*. 2014;14:114.
3. Sand M, Bechara FG, Holland-Letz T, et al. Diagnostic value of hyperbilirubinemia as a predictive factor for appendiceal perforation in acute appendicitis. *Am J Surg*. 2009;198(2):193–8.
4. Khan S. Evaluation of hyperbilirubinemia in diagnosis of acute appendicitis. *Int J Surg*. 2011;9(2):101–4.
5. Estrada JJ, Petrosyan M, Barnhart J, et al. Hyperbilirubinemia in appendicitis: a new predictor of perforation. *J Gastrointest Surg*. 2007;11(6):714–8.
6. Kucuk A, Kucuk AO, Uslukaya O. Role of bilirubin in acute appendicitis. *World J Gastroenterol*. 2016;22(4):1067–72.

7. Bolandparvaz S, Vasei M, Owji SM, et al. Is hyperbilirubinemia a predictive factor for complicated appendicitis? *Iran Red Crescent Med J*. 2014;16(3):e10235.
8. Eren T, Tombalak E, Ozeren M, et al. Hyperbilirubinemia as a predictive factor in acute appendicitis. *Eurasian J Emerg Med*. 2014;13(4):149–53.
9. Khan A, Khan MS, Sheikh ZA. Diagnostic accuracy of hyperbilirubinemia as a marker of complicated acute appendicitis. *Pak J Surg*. 2014;30(3):209–12.
10. Chaudhary P, Cheema IA, Ahmad R, et al. Hyperbilirubinemia: a new predictive marker for complicated appendicitis. *Ann Pak Inst Med Sci*. 2015;11(4):193–7.