



Diagnostic accuracy of serum bilirubin levels for perforated and simple appendicitis.

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INTRODUCTION

Appendicitis is one of the commonest causes of abdominal pain among patients referred to the emergency departments and appendectomy is one of the frequent surgical procedures reported.¹ The appendicitis is a global disease with its incidence declining in the western countries compared to developing countries where its incidence is increasing averaging >200 patients per 100,000 population.² However, its diagnosis may be elusive due to lack of pathognomonic sign or symptom thus leading to delay diagnosis and surgery which may cause complications³ such as perforation, abdominal abscess, urinary retention, small bowel obstruction and peritonitis thus causing increased morbidity and mortality of the patients.⁴

The reported mortality of simple acute appendicitis is 0.3% increasing 6% in cases

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ABSTRACT... Objective: To determine the diagnostic accuracy of serum bilirubin levels as predictor of perforated and simple appendicitis. **Study Design:** Cross Sectional study. **Setting:** Surgical Unit Aziz Bhatti Shaheed Teaching Hospital Gujrat. **Period:** June 2019 to December 2019. **Material & Methods:** This study was conducted after approval of ethical committee and informed consent of patients. Serum Bilirubin level on photometric testing using 2,4-dichloroaniline were determined. Histopathological examination was considered as a gold standard for diagnosing and categorizing patients as having acute appendicitis and acute appendicitis with perforated appendix. Serum Bilirubin levels and final histopathological reported were compared to determine diagnostic accuracy of serum Bilirubin levels. **Results:** The mean age of patient was 33.41 ± 12.46 years. In this study 153(47.81%) patients were male and 167 (52.19%) patients were female. Sensitivity and specificity for Serum Bilirubin were 88.62% and 94.42%. The mean serum bilirubin level was 36.72 ± 41.05 years. The minimum and maximum serum bilirubin level was 5.00 and 169.00. The positive predictive value was 90.83% and negative predictive value was 93% with diagnostic accuracy of 92.19%. **Conclusion:** Hyperbilirubinemia can be utilized for early diagnosis of appendiceal perforation and can identify the nature of appendicitis for better management.

Key words: Appendicitis, Hyperbilirubinemia, Perforated Appendicitis.

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with perforation.⁵ Recent literature has reported negative appendectomy rate of 22.8% and many surgeons believe it as inevitable.⁶ The mortality in acute appendicitis has been associated with negative appendectomies and complicated appendicitis.⁷ A recent local study showed that acute appendicitis is more common during summers in Pakistan⁸ however epidemiological data in general population is lacking.

Alvarado Score along with the clinical features and laboratory analyses are used in diagnosis of acute appendicitis.⁹ Hyperbilirubinemia is associated with appendicitis and it might be a useful preoperative investigation to identify patients with appendiceal perforation and gangrene.¹⁰ One study determined the specificity and sensitivity of bilirubin in diagnosing complicated acute appendicitis keeping cut off value of > 20 $\mu\text{mol/l}$ to be 74.02% and 80%.¹¹ Another study at same

cut off limit showed sensitivity, specificity, positive and negative predictive value to be 100%, 92.9%, 72.7%, 100% respectively.¹²

Few local studies are available for diagnostics accuracy of serum bilirubin levels for complicated appendicitis. Thus the objective of study is to determine the diagnostic accuracy of serum bilirubin levels for predicting perforated and simple appendicitis.

MATERIAL & METHODS

This cross-sectional validation study was conducted at the emergency Surgical Unit Aziz Bhatti Shaheed Teaching Hospital Gujrat from 8-6-2019 till 7-12-2019. Ethical approval was taken from ethical committee of hospital (01-06-2019) and informed consent was taken from patients. Non probability consecutive sampling was done. Patients of age 18-60 of either gender presenting with signs and symptoms of acute appendicitis within 7 days were included in the study. Those patients who were undergone other emergency laparotomy where appendicectomy was also performed as part of the procedure or if they had a history of confirmed hepatitis or liver disease or if they were known to have persistently deranged LFTs when assessed on available medical records were excluded from study.

Patient were diagnosed as a case of appendicitis on basis of signs and symptoms which included pain in the right iliac fossa with any of anorexia, nausea, vomiting, fever >37.3 degree centigrade, tenderness and rebound tenderness in right iliac fossa. If patient with appendicitis had serum bilirubin > 20.0 $\mu\text{mol/l}$, they were considered to have perforated appendicitis on serum bilirubin. Perforated appendicitis on histopathology was defined as having a visible perforation or an inflamed appendix with evidence of microscopic perforation.

The demographic information like name, age, sex, address was obtained. Blood sample was drawn with help of staff nurse and was sent to hospital laboratory for determination of serum Bilirubin level on photometric testing using 2,4-dichloroaniline. After collecting report nature of appendicitis were

labeled as perforated or non-perforated. Final histopathological examination was considered as a gold standard for diagnosing and categorizing patients as having acute appendicitis and acute appendicitis with perforated appendicitis. Serum Bilirubin levels and final histopathological reported was compared to determine diagnostic accuracy of serum Bilirubin levels. The data was collected on given attached proforma.

All collected data was entered and analyzed using SPSS version 20. For quantitative variables like age of patients, duration of pain, Serum Bilirubin levels were presented as mean \pm SD. For qualitative variables like gender of patients, diagnosis of appendicitis on histopathology and Serum Bilirubin levels were presented as frequencies and percentages. Diagnosis of appendicitis on histopathology, Serum Bilirubin levels were tabulated in the form of 2 \times 2 table to calculate sensitivity, specificity, predictive values for the positive and negative value of both scores taking results of histopathology as gold standard. Data was stratified by age and duration of pain to address effect modifiers. Post stratification diagnostic accuracy was applied to see significance of these effect modifiers. Post stratification chi square test was applied. P-value ≤ 0.05 was considered as significant.

RESULTS

A total of 320 patients were included in the study. The mean age of patient was 33.41 ± 12.46 years. A total of 126 (39.38%) patients were 18-35 years old and 194 (60.62%) were 36-40 years old. In this study 153 (47.81%) patients were male and 167 (52.19%) patients were female.

The mean duration of pain was 3.92 ± 1.97 days. 147 (45.94%) patients suffered from pain for 1-3 days and 173 (54.06%) patients told that they suffer from pain for 4-7 days. The mean serum bilirubin level was $36.72 \pm 41.05 \mu\text{mol/l}$. The range of serum bilirubin level was from 5 to 169 $\mu\text{mol/l}$. The serum bilirubin level was >20 $\mu\text{mol/l}$ in 120 (37.50%) patients and it was seen $\leq 20 \mu\text{mol/l}$ in 200 (62.50%) patients. 123 (38.44%) patients were diagnosed with perforated appendicitis and 197 (61.56%) were diagnosed with non-perforated

appendicitis histopathologically.

Serum bilirubin level >20 µmol/l was seen in 109 patients having perforated appendicitis and in 11 patients with non-perforated appendicitis. Serum bilirubin level ≤20 µmol/l was seen in 14 patients with perforated appendicitis and in 186 patients with non-perforated appendicitis. Sensitivity and specificity for Serum Bilirubin >20 µmol/l were 88.62% and 94.42% respectively. The positive predictive value was 90.83% and negative predictive value was 93% with diagnostic accuracy of 92.19% as described in Table-I.

		Histopathological Findings		Total
		Perforated	Non-perforated	
Serum Bilirubin	>20 µmol/l	109	11	120
	≤20 µmol/l	14	186	200
Total		123	197	320

Table-I. Comparison of histopathological findings and serum bilirubin level.

Sensitivity	88.62%
Specificity	94.42%
Positive Predictive Value	90.83%
Negative Predictive Value	93%
Diagnostic Accuracy	92.19%

There is significant association between histopathology findings and serum bilirubin level regardless of gender and age moreover the overall diagnostic accuracy was high. (Table-II and III).

	Serum Bilirubin	Histopathological Findings		P-Value
		Perforated	Non-perforated	
18-35 Years	>20 µmol/l	75	6	<0.0001
	≤20 µmol/l	10	103	
36-40 Years	>20 µmol/l	34	5	<0.0001
	≤20 µmol/l	4	83	

Table-II. Comparison of histopathological findings and serum bilirubin level with respect to age.

	Age (years)	
	18-35	36-46
Sensitivity	88.24%	89.47%
Specificity	94.5%	94.32%
Positive Predictive Value	92.59%	87.18%
Negative Predictive Value	91.15%	95.4%
Diagnostic Accuracy	91.75%	92.86%

Duration of Pain (days)	Serum Bilirubin	Histopathological Findings		P- Value
		Perforated	Non-perforated	
1-3	>20 µmol/l	60	4	<0.0001
	≤20 µmol/l	7	76	
4-7	>20 µmol/l	49	7	<0.001
	≤20 µmol/l	7	110	

Table-III. Comparison of histopathological findings and serum bilirubin level with respect to duration of pain (days).

	Duration (days)	
	1-3	4-7
Sensitivity	89.55%	87.5%
Specificity	95%	94.02%
Positive Predictive Value	93.75%	87.5%
Negative Predictive Value	91.57%	94.02%
Diagnostic Accuracy	92.52%	91.91%

DISCUSSION

This study shows that serum bilirubin levels can be used as predictors of perforated appendicitis with high sensitivity and specificity with no statistically significant association with age and duration of symptoms. The patients with previous history of deranged serum bilirubin levels or hepatitis were not included in this study. However the previous studies have determined that acute perforated appendicitis is more in male gender, age > 60 years and delayed presentation.¹³

In the study of Sand et al a total of 538 patients, hyperbilirubinemia (>1 mg/dL) was found in 134 of 538 (24.9%) having sensitivity and specificity of bilirubin for the preoperative diagnosis of appendiceal perforation to be 65% and 86% respectively and PPV for appendiceal perforation to be 51%.⁵ However the results of this study are different from that of Sand et al. It shows higher

sensitivity, specificity and positive predictive value. These results may differ due different geographical areas involved in study as well as different sample size.

Sandstorm et al. demonstrated that high bilirubin levels have specificity of 83%, PPV of 86% in diagnosis of acute appendicitis. However in complicated appendicitis and simple appendicitis they showed a PPV of 66% and 81% respectively.¹⁴ Their study also has a lower specificity and PPV in diagnosis of acute perforated appendicitis as compared to this study. This may be attributed to small sample size in their study.

One recent study by Iqbal et al. conducted in Pakistan showed that serum bilirubin has sensitivity of 76.96% and specificity of 91.35% in cases of perforated appendicitis. They also showed a PPV of 74.07%.¹⁵ Although the sensitivity is higher in this study as compared to Iqbal et al.; the specificity is comparable to this study. They also had lower PPV as compared to this study. The difference may be due to small sample size in their study. However they also studied other parameters in diagnosis of perforated and gangrenous appendicitis.

In the study of Khan et al. it was observed that patients with gangrenous or perforated appendicitis had greater elevation of serum bilirubin as compared to simple suppurative acute appendicitis. The specificity, sensitivity, PPV and NPV were 100%, 82.07%, 100% and 17.3% respectively.¹⁶ The sensitivity and specificity in our study is lower that of reported by Khan et al. These differences may be due to difference in sample sizes. Another recent study also described serum bilirubin as a reliable marker of diagnosis of acute perforated appendicitis.¹⁷

However there are contradictions noted in recent literature. One recent study by Kanlioz et al. demonstrated that serum bilirubin can only be used as supportive to diagnosis of perforated appendicitis but not as a predictor and diagnostic tool.¹⁸ Another meta-analysis also determined that serum bilirubin is not a useful diagnostic tool in diagnosing perforated appendicitis.¹⁹ These

studies contradict the results of this study.

This study shows that serum bilirubin with value of $> 20 \mu\text{mol/l}$ can be used as an effective marker for early diagnosis of perforated appendicitis with high sensitivity, specificity, PPV, NPV and overall diagnostic accuracy is good. However there are contradictory studies present in recent literature.^{18,19} Thus there is need for further studies in evaluating the role of serum bilirubin as a diagnostic tool for perforated appendicitis on a larger scale. There is also a need for large epidemiological studies for perforated appendicitis in Pakistan as data is limited. This is a single center limited study. Further large scale studies should be done.

CONCLUSION

The sensitivity and specificity of serum bilirubin was higher than that of histopathology findings so hyperbilirubinemia can be utilized for early diagnosis of appendiceal perforation and better management during surgery.





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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Muhammad Naeem	Planned the research, designed questionnaire, Data collection.	
2	M. Mudassar Liaqat	Manuscript writing, Critical review of manuscript.	
3	Syed Saleem Raza	Data collection, Review of manuscript.	
4	Zulakha Nadeem	Data collection, Data Entry.	
5	Syed M. Ali Shah	Data analysis, Critical review of manuscript.	