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Research Article

EVALUATION OF DIAGNOSTIC VALUE OF SERUM BILIRUBIN IN ACUTE APPENDICITIS AND ITS ROLE IN PREDICTING APPENDICULAR PERFORATION: A PROSPECTIVE STUDY

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Appendix, appendicitis, appendiceal perforation, hyperbilirubinemia.

A B S T R A C T

Background: The appendix is a small, tube like organ attached to the large intestine. Appendicitis is the swelling of the appendix. The condition is due to blockage inside the appendix which leads to increased pressure and inflammation. Serum bilirubin levels have been suggested as individual markers for appendicitis and acute appendicitis (AA) perforation (AP). **Aim and objectives:** To analyse relation between hyperbilirubinemia and acute appendicitis and to see how reliable it is as a diagnostic marker for AA or AP. **Material and methods:** A prospective observational study was conducted at Department of General Surgery, Patna Medical College, Patna during July 2014 to June 2016 in 156 patients thorough history were taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested Proforma. **Results:** Age Mean ± Standard deviation was 30.46 ± 9.62 with gender distribution was found that males i.e. 111 (71.15%) were more than female i.e. 45 (28.85%). Total bilirubin mean ± SD were 0.97 ± 0.31 mg/dl, it has difference in AA & AP i.e. 0.89 ± 0.42 & 1.51 ± 0.75 respectively. Hyperbilirubinemia in terms of sensitivity and specificity in AA was found to be 17.14% and 25.00% respectively. Positive Predictive Value, Negative Predictive Value and diagnostic accuracy of increased serum bilirubin in acute pancreatitiswas 2.48%, 73.09% and 24.21%.Similarly for AP it was found to be 81.25% and 83.57% respectively. Also Positive Predictive Value, Negative Predictive Value and diagnostic accuracy were 35.46%, 97.57% and 83.34%. **Conclusion:** Findings suggests serum bilirubin levels and liverenzyme to be a promising new laboratory marker for diagnosing acute appendicitis with perforation but acute appendicitis still – clinical.

INTRODUCTION

Appendicitis is the swelling (inflammation) of the appendix. The appendix is a small, tube like organ attached to the large intestine. The condition is due to blockage inside the appendix. The blockage leads to increased pressure and inflammation. Appendicitis can occur at any age but it is more common during childhood and adolescence [1]. Berengario Da Carpi, a surgeon and anatomist, was the first to describe the appendix in 1521. Morgagni in 1719 published a detailed description of appendix, its site and relation in his "AchersariaAnatomica". Verneys coined the term "vermiform appendix" in 1710. Vermiform means worm like. Claudius Amyand performed the first appendectomy on an 11-year-old child with a right scrotal hernia and a fistula in 1736. Hancock in 1848 successfully drained appendicular abscess in pregnant female during her eighth month of pregnancy. Reginald Fitz in 1886 first described acute appendicitis and also the first to use term appendicitis.

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In 1889, Chester McBurney described migratory pain as well as its localization along an oblique line from the anterior superior iliac spine to the umbilicus. McBurney described a right lower quadrant muscle-splitting incision for removal of the appendix in 1894 [1].

In Western countries appendicitis is associated with morbidity, mortality and significant costs to the healthcare system [2]. The life-time risk of appendicitis is 1 in 15 in the United States [2]. One third of appendicitis cases present to hospital with a perforated appendix [3]. Appendicitis related hospitalizations cost $3 billion in 1 year within the United States alone [4]. Every year 250,000 appendectomies are performed in United States. 1 in 15 people have the tendency of developing appendicitis during his lifetime and 7-10% of the subjects develop appendicitis primarily during the second and third decades of life. The lifetime danger of acute appendicitis is evaluated to be 7-8 percent [5]. Open appendectomy is normally performed for the cases of appendicitis but present days laparoscopic procedure has gained widespread popularity which was first performed by Semm in 1982. There has been a drastic reduction in morbidity and mortality in appendicitis in

20th century because of better obtainability of healthcare amenities that resulted in mortality has been decreased to lesser than 1% [6].The incidence of perforated appendicitis in adults has been reported from 13–37% or higher [6].

Serum markers such as C-reactive protein (CRP), white blood cell count (WBC), serum bilirubin, and liver transaminase levels have been suggested as individual markers for appendicitis and appendiceal perforation. In current practice, the diagnosis of acute appendicitis is mainly clinical, supported by laboratory and imaging studies. Ultrasonography and computed tomography (CT) may raise the diagnostic sensitivity to 66-100% and 90-100%, respectively, but these imaging practices entail several drawbackssuch as cost, radiation exposure, and operator dependency [7].

The aim of this study was to assess the association between hyperbilirubinemia in AA & AP and also assess other diagnostic tools in acute appendicitis.

Aim and objectives: To look into the connection between hyperbilirubinemia and acute appendicitis, as well as to see how reliable it is as a diagnostic marker for appendicular perforation.

MATERIAL AND METHODS

This prospective observational study was conducted at Department of General Surgery, Patna Medical College, Patna during July 2014 to June 2016. A total of 156 patients with fulfilment of inclusion criterias were taken into study and eligible patients were briefed about the nature of the study and a written informed consent was obtained from the consented patients. Thorough history was taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested Proforma.

Inclusion criterias

- All patients diagnosed as acute appendicitis clinically on admission.
- All patients diagnosed as appendicular perforation clinically on admission.
- For both these groups, only patients with histopathological report suggestive of acute appendicitis or appendicular perforation were included.

Exclusion criterias

- All patients documented to have a past history of Jaundice or Liver disease, chronic alcoholism (that is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years), Haemolytic disease and Acquired or congenital biliary disease.
- All patients with positive HBsAg
- All patients with cholelithiasis
- All patients with cancer of hepato-biliary system

For quantitative variables, mean and standard deviation were used, whereas for categorical variables, frequency and proportion were used. Data was also visualized using suitable diagrams such as bar graphs, pie graphs, and box plots. Through comparing mean values, the relation between categorical explanatory variables and the quantitative result was determined. The mean variations, as well as their 95% confidence intervals, were discussed. Cross-tabulation and percentage comparisons were used to determine the relationship between explanatory variables and categorical outcomes. The statistical significance was determined using the chi-square test. Statistical significance was described as a P value of less than 0.05.

RESULTS

Table 1 shows full analysis of age distribution in selected study population. It shows age Mean ± Standard deviation was 30.46 ±9.62 with lowest and highest value was 52 and 13 years. Kolmogorov-Smirnov test for Normal distribution found was D=0.1017 and it reject normality (P=0.0005).

Table 1 Descriptive analysis of age in study population (n=156).

Variable	AGE
Sample size	156
Lowest value	13
Highest value	52
Mean± Standard deviation	30.46±9.62
95% CI for the mean	28.94 to 31.98
Variance	92.52
Coefficient of Skewness	0.2356 (P=0.2198)
Coefficient of Kurtosis	-1.1504 (P<0.0001)
Kolmogorov-Smirnov test for Normal distribution	D=0.1017 Reject Normality (P=0.0005)

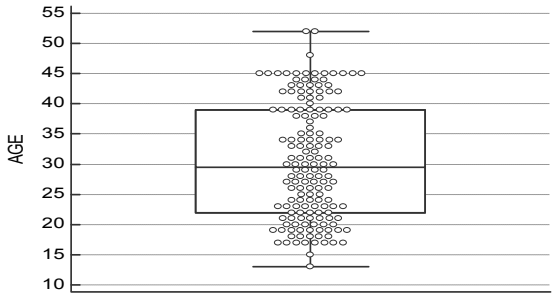

Figure 1 Showing Box and Whisker graph for Age in years

Table 2 Descriptive analysis of gender in the studied cases (n=156)

Gender	Number of Patients	Percentage
Male	111	71.15%
Female	45	28.85%

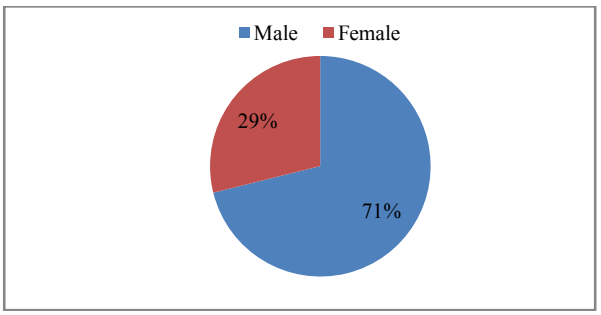

Figure 2 Descriptive analysis of gender in the study cases (n=156).

Table 2 shows gender distribution among study population and it was found that males i.e. 111 (71.15%) were more than female i.e. 45 (28.85%).

Table 3 Descriptive analysis of liver function test in study population (n=156)

Parameter	Mean ±SD	Median	Minimum	Maximum	S.E of Mean
Total Bilirubin	0.97 ± 0.31 For AA 0.89 ± 0.42 For AP 1.51 ± 0.75	0.97	0.41	1.92	0.02
Bilirubin Direct	0.36 ± 0.15	0.36	0.10	0.76	0.01
Bilirubin Indirect	0.61 ± 0.32	0.60	0.05	1.59	0.03
SGOT	28.16 ± 11.41	27.17	8.31	62.65	0.91

SGPT	27.85 ± 9.19	27.18	8.95	50.58	0.74
ALP	90.98 ± 30.25	89.55	24.43	164.41	2.42

Table 3 showed that in study population total bilirubin mean ± SD was 0.97 ± 0.31 mg/dl with maximum and minimum values were 1.92 & 0.41 mg/dl. But it has difference in AA & AP i.e. 0.89 ± 0.42&1.51 ± 0.75 respectively. Similarly for direct and indirect bilirubin the same values were 0.36 ± 0.15 mg/dl, 0.76 & 0.10 mg/dl, 0.61 ± 0.32, 1.59 & 0.05 mg/dl respectively. In view of liver enzymes table 3 shows that SGPT mean ± SD were 28.16 ± 11.41 IU/ml with maximum and minimum values were 62.65& 8.31 IU/ml. similarly for SGOT and ALP the same values were 27.85 ± 9.19, 50.58&8.95, 90.98 ± 30.25, 164.41& 24.43 IU/ml respectively.

Table 4 Descriptive analysis of TLC (/mm3) in study population (n=156)

Parameter	Mean ±SD	Median	Minimum	Maximum	S.E of Mean
TLC (/mm3)	11189.56 ± 4935.24	97000	1300	24,450	04.56

The mean TLC was 11189.56 ± 4935.24 in the study population, ranged between 1300 (/mm3) to 24,450 with Standard Error of Mean 04.56 as per Table – 4.

Table 5 Descriptive analysis of clinical diagnosis on in the study population (n=156).

Diagnosis	Number of Patients	Percentage
Acute appendicitis	140	89.74%
Appendiceal perforation	16	10.26%

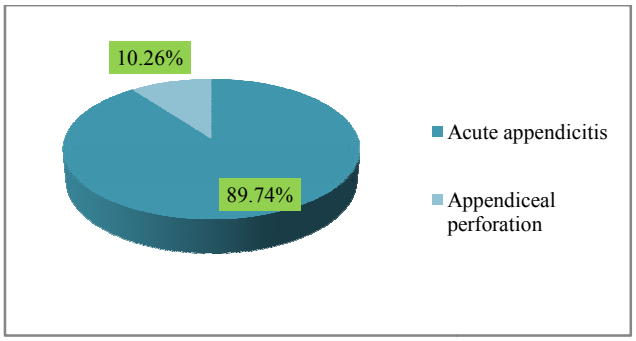

Figure 3 Descriptive analysis of clinical diagnosis on in the study population (n=156).

Table 6 shows that among the study population, 140 (89.74%) participants had Acute Appendicitis and 16 (10.26%) participants had appendicular perforation.

Table 6 Correlation of acute appendicitis and hyperbilirubinemia (n=156)

Hyperbilirubinemia	Acute appendicitis		Total	Chi-square	P-value
	Present	Absent			
Yes	24 (17.14%)	12 (75.00%)	36	27.0771	< 0.00001
No	116 (82.86%)	04 (25.00%)	120		
Total	140 (89.74%)	16 (10.26%)	156		

In acute appendicitis positive group, 24 (17.14%) had of hyper bilirubin, this proportion was 12 (75.00%) among acute appendicitis negative group. The difference in the proportion of hyper bilirubin between acute appendicitis was statistically significant (P-value <0.00001) as per Table - 6.

Table 7 Predictive analysis of hyperbilirubinemia in acute appendicitis

Statistics	Value	95% CI
Sensitivity	17.14%	11.30% to 24.42%
Specificity	25.00%	7.27% to 52.38%
Positive Likelihood Ratio	0.23	0.14 to 0.36
Negative Likelihood Ratio	3.31	1.41 to 7.77
Positive Predictive Value	2.48%	1.58% to 3.87%
Negative Predictive Value	73.09%	53.67% to 86.42%
Diagnostic Accuracy	24.21%	17.72% to 31.71%

Table 7 showed predictive analysis of hyperbilirubinemia in terms of sensitivity and specificity in AA was found to be 17.14% and 25.00% respectively. Similarly Positive Predictive Value and Negative Predictive Value was 2.48% and 73.09% respectively. Also found that diagnostic accuracy of increased serum bilirubin in acute pancreatitis was 24.21%.

Table 8 Correlation of Appendicular Perforation and hyperbilirubinemia (n=156)

Hyperbilirubinemia	Appendicular Perforation		Total	Chi-square	P-value
	Present	Absent			
Yes	13 (81.25%)	23 (16.43%)	36	33.988	< 0.00001
No	03 918.75%)	117 (83.57%)	120		
Total	16 (10.26%)	140 (89.74%)	156		

Table 8 shows that in Appendicular Perforation positive group, 13 (81.25%) had of hyper bilirubin, this proportion was 23 (16.43%) among Appendicular Perforation negative group. The difference in the proportion of hyper bilirubin between Appendicular Perforation was statistically significant (P-value <0.00001).

Table 9 Predictive analysis of hyperbilirubinemia in Appendicular Perforation

Statistics	Value	95% CI
Sensitivity	81.25%	54.35% to 95.95%
Specificity	83.57%	76.38% to 89.29%
Positive Likelihood Ratio	4.95	3.18 to 7.69
Negative Likelihood Ratio	0.22	0.08 to 0.62
Positive Predictive Value	35.46%	26.11% to 46.08%
Negative Predictive Value	97.57%	93.52% to 99.11%
Diagnostic Accuracy	83.34%	76.55% to 88.82%

Table 9 showed predictive analysis of hyperbilirubinemia in terms of sensitivity and specificity in AP was found to be 81.25% and 83.57% respectively. Similarly Positive Predictive Value and Negative Predictive Value was 35.46% and 97.57% respectively. Also found that diagnostic accuracy of increased serum bilirubin in appendicular perforation was 83.34%.

DISCUSSION

A prospective study done in 156 patients of acute pancreatitis clinical diagnosis in study period to evaluate implications of hyperbilirubinemia in acute pancreatitis or appendicular perforation cases. Mean age ± Standard deviation of presentation of acute pancreatitis in different studies:

Studies	Mean age± Standard deviation
Present study	30.46 ±9.62 years
D'Souza N *et al* [8] [2013]	29.4 years
Chandrasekaran D *et al* [9] [2019]	30.45±12.39 years
Patel D *et al* [10] [2014]	26 ± 13.4 years
Doraikannu D *et al* [11] [2020]	31.38 ± 15 years

Present study found males i.e. 111 (71.15%) were more than female i.e. 45 (28.85%), similarly Chandrasekaran D *et al* [9]

[2019] study, Patel D *et al* [10] [2014] & Doraikannu D *et al* [11] [2020] having 59%, 71% & 71.80% males than females. Total bilirubin over all in present study shows mean ± SD were 0.97 ± 0.31 mg/dl but for AA & AP i.e. 0.89 ± 0.42 & 1.51 ± 0.75 respectively. Similarly Chandrasekaran D *et al* [9] [2019] study showed Mean serum bilirubin level in appendicitis patients was 0.92±0.4 mg/dl when compared to perforated appendicitis which was 2.25±0.73 mg/dl. Doraikannu D *et al* [11] [2020] showed mean TLC was 10186.43 ± 4728.32 in the study population, ranged between 13 (/mm3) to 22540 (95% CI 9470.53 to 10902.33) which was comparable to present study. Emmanuel A *et al* [12] [2011], retrospective analysis of appendicectomies performed in two hospitals (n=472). They found that hyperbilirubinemia had a specificity of 88% and a positive predictive value of 91% for acute appendicitis. Also Chandrasekaran D *et al* [9] [2019] study found serum bilirubin as a predictor for appendicular perforation revealed Sensitivity of 93.3%, Specificity of 72.3%, with the Positive Predictive value 37.8%, Negative Predictive value 98.4%.Doraikannu D *et al* [11] [2020], when compared to acute appendicitis, hyper bilirubin had sensitivity of 15.93%, Specificity was 38.60%, False positive rate was 61.40%, False negative rate was 84.07%, Positive predictive value was 33.96%, Negative predictive value was 18.80% and the total diagnostic accuracy was 23.53%, which was comparable to present study.

CONCLUSION

Findings coming from present study suggests serum bilirubin levels and liverenzyme to be a promising new laboratory marker for diagnosing acute appendicitis with perforation; however diagnosis of acuteappendicitis remains essentially still – clinical. Its levels come out to bea credible aid in diagnosis of acute appendicitis and would be helpful investigation in decision making.

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