A prospective study of 70 cases evaluating the role of hyperbilirubinemia in acute inflammation of appendix

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Abstract
Acute Appendicitis is the most common general surgical emergency, and early surgical intervention improves outcomes. Despite the increased use of ultrasonography, computed tomography scanning and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%), as has the rate of appendiceal perforation. In an age accustomed to early and accurate preoperative diagnosis, acute appendicitis remains an enigmatic challenge and a reminder of the art of surgical diagnosis.

Aim: To evaluate the role of hyperbilirubinemia in Appendicitis

Material and methods: A prospective study of 70 clinically suspected cases of appendicitis admitted in surgical unit-6, Lata mangeshkar hospital, Nagpur were subjected to investigations to confirm the diagnosis from April 2011- April 2012. Data collected included total leucocyte count, liver function test and ultrasound. Subsequently these cases were operated and clinical diagnosis was confirmed by histopathology.

Results: Out of 70 cases, 41 were males and 29 were females. Their age ranged from 12 years to 60 years with average of 26.9 years. Duration of symptoms ranged from 1 day to maximum 8 days. All the cases diagnosed as acute appendicitis clinically. Per operatively, all cases had inflamed appendix. Among 70 cases, SB was raised in 42 (60%) cases where as 28 (40%) cases had normal SB level. It ranged from 1.2 mg/dL to 4.0 mg/dL. The average level of SB was 1.648 mg/dL.

Conclusion: Our study concludes that there was hyperbilirubinemia in 60% of the patients of acute appendicitis. Elevated serum bilirubin ranged from 1.2mg/dL - 4 mg/dL and was of mixed type. When compared to other studies there was no complicated appendicitis encountered in our study.

Keywords: appendicitis, hyperbilirubinemia, serum bilirubin

1. Introduction
The first appendicectomy was performed by Claudius Amyand, Surgeon to Westminster and St. George’s Hospitals and Sergeant Surgeon to George II, on a boy of 11 years of age in 1736.1 In 1886, Reginald Fitz of Boston correctly identified the appendix as the primary cause of right lower quadrant inflammation. He coined the term APPENDICITIS and recommended early surgical treatment of the disease.2 The inflamed Appendix results in the clinical syndrome known as Acute appendicitis. Appendicitis is relatively rare in infants and becomes increasingly common in childhood.3
It’s most frequently seen in patients in their second through fourth decades of life, with a mean age of 31.3 years and a median age of 22 years. There is a slight male: female predominance (1.2 to 1.3:1). Obstruction of the lumen is believed to be the major cause of acute appendicitis. Fecoliths are found in 40% of cases of simple acute appendicitis, 65% cases of gangrenous appendicitis without rupture and 90% cases of gangrenous appendicitis with rupture. Less common causes are hypertrophy of lymphoid tissue, inspissated barium from previous x-ray studies, tumors, vegetable and fruit seeds, and intestinal parasites. The appendix perforates about 48 hours after the onset of acute appendicitis. It has been suggested that delay in presentation is responsible for the majority of perforated appendices. Overall rate of perforation is 25.8%. Children <5 years and patients >65 years of age have highest rates of perforation. Appendicular perforation occurs most frequently distal to the point of luminal obstruction along the antimesenteric border.  

The Patho-physiology behind the elevation of Serum Bilirubin in Acute Appendicitis\textsuperscript{5-11}.

\begin{center}
\begin{itemize}
\item Acute Appendicitis
\item A non specific host immune response leading to oedema, increased intraluminal pressure and ischemic necrosis of mucosa causing gangrene and perforation
\item Transmigration/translocation of bacteria/toxins/cytokines
\item Either by direction invasion or through portal vein
\item endotoxemia / bacteremia
\item Invasion of Bacteria into the hepatic parenchyma interferes with the physiology of excretion of bile
\end{itemize}
\end{center}

Hyperbilirubinemia

The study on the association of hyperbilirubinemia with Appendicitis is being carried out recently and there are only a few studies in this regard. It was hypothesized that an association exists between the presence of hyperbilirubinemia and appendicitis and its complications\textsuperscript{5}.

2. Material and methods

A prospective analysis conducted at Lata mangeshkar hospital, Nagpur during April 2011- April 2012. 70 clinically suspected cases of acute appendicitis admitted in surgical unit-6 were subjected to investigations to confirm the diagnosis. Data collected included total leucocyte count, Serum bilirubin and ultrasound. Subsequently these cases were operated and clinical diagnosis was confirmed by histopathology. Clinical and investigative data were compiled and analyzed, and following observations were obtained. Routine Serum bilirubin test results were compared with laboratory reference values given in Table- 1.

2.1 Inclusion Criteria: Case with acute appendicitis and its complication with test negative for HBsAg and no past history of jaundice.

2.2 Exclusion Criteria: Case with acute appendicitis and its complication with test positive for HBsAg and/or past history of jaundice.

| Test         | Normal range |
|--------------|--------------|
| Serum Bilirubin Total | 1.1mg/dL    |
| Serum Bilirubin Direct   | 0.2mg/dL    |
3. Results

Clinical presentation and results of serum bilirubin is shown in table 2. We studied total 70 cases out of which 41 were males and 29 were females. Their age ranged from 12 years to 60 years. Age group distribution is shown in table 3. The average was 26.9 years. Duration of symptoms ranged from 1 day to maximum 8 days (table 4). All the cases diagnosed as acute appendicitis clinically (preoperatively), per operatively, all cases had inflamed appendix. Serum bilirubin revealed following results, Among 70 cases, SB was raised in 42 (60%) cases where as 28 (40%) cases had normal SB level (Fig.1, table 5). It ranged from 1.2 mg/dL to 4.0 mg/dL. The average level of SB was 1.648 mg/dL.

Table 2: Characteristics, clinical presentation and serum bilirubin

| S.N | Sex | Age | Duration of symptoms | Diagnosis | Serum bilirubin |
|-----|-----|-----|----------------------|-----------|-----------------|
|     |     |     |                      | Clinical/operative | Total (mg/dl) | Direct (mg/dl) | Indirect (mg/dl) |
| 1   | F   | 40  | 3d                   | AA        | 2.2             | 1.3           | 0.9               |
| 2   | M   | 40  | 2d                   | AA        | 1               | 0.7           | 0.3               |
| 3   | F   | 32  | 2d                   | AA        | 1.8             | 0.8           | 1.0               |
| 4   | F   | 20  | 2d                   | AA        | 3.1             | 0.8           | 2.3               |
| 5   | M   | 27  | 5d                   | AA        | 1.4             | 0.5           | 0.9               |
| 6   | M   | 15  | 3d                   | AA        | 4.0             | 2.1           | 1.9               |
| 7   | F   | 19  | 7d                   | AA        | 3.0             | 1.6           | 1.4               |
| 8   | M   | 12  | 5d                   | AA        | 2.8             | 1.2           | 1.6               |
| 9   | M   | 18  | 4d                   | AA        | 2.6             | 1.2           | 1.4               |
| 10  | F   | 32  | 3d                   | AA        | 0.64            | 0.31          | 0.33              |
| 11  | M   | 24  | 8d                   | AA        | 3.0             | 1.6           | 1.4               |
| 12  | M   | 30  | 6d                   | AA        | 2.56            | 1.62          | 0.94              |
| 13  | M   | 24  | 2d                   | AA        | 1.9             | 1.0           | 0.9               |
| 14  | M   | 35  | 2d                   | AA        | 1.9             | 1.0           | 0.9               |
| 15  | F   | 35  | 3d                   | AA        | 3.9             | 2.0           | 1.9               |
| 16  | F   | 26  | 1d                   | AA        | 0.4             | 0.2           | 0.2               |
| 17  | F   | 26  | 2d                   | AA        | 1.8             | 1.0           | 0.8               |
| 18  | M   | 40  | 2d                   | AA        | 0.6             | 0.3           | 0.3               |
| 19  | M   | 18  | 3d                   | AA        | 0.9             | 0.4           | 0.5               |
| 20  | M   | 23  | 1d                   | AA        | 2.8             | 1.2           | 1.6               |
| 21  | M   | 28  | 2d                   | AA        | 0.8             | 0.3           | 0.5               |
| 22  | M   | 35  | 3d                   | AA        | 1.1             | 0.5           | 0.6               |
| 23  | M   | 33  | 3d                   | AA        | 0.8             | 0.4           | 0.4               |
| 24  | M   | 27  | 1d                   | AA        | 1.2             | 0.6           | 0.6               |
| 25  | M   | 20  | 2d                   | AA        | 1.1             | 0.5           | 0.6               |
| 26  | M   | 18  | 3d                   | AA        | 1.1             | 0.5           | 0.6               |
| 27  | M   | 24  | 1d                   | AA        | 1.2             | 0.7           | 0.5               |
| 28  | F   | 35  | 3d                   | AA        | 0.9             | 0.4           | 0.5               |
| 29  | M   | 24  | 5d                   | AA        | 1.1             | 0.5           | 0.6               |
| 30  | M   | 30  | 3d                   | AA        | 0.8             | 0.4           | 0.4               |
| 31  | M   | 24  | 5h                   | AA        | 2.6             | 2.0           | 0.6               |
|   |   |   |   |   |
|---|---|---|---|---|
| 32 | M | 20 | 1d | AA |
| 33 | M | 22 | 1d | AA |
| 34 | F | 20 | 2d | AA |
| 35 | F | 35 | 3d | AA |
| 36 | M | 24 | 1d | AA |
| 37 | M | 17 | 1d | AA |
| 38 | F | 28 | 1d | AA |
| 39 | F | 35 | 8d | AA |
| 40 | F | 35 | 2d | AA |
| 41 | M | 17 | 1d | AA |
| 42 | F | 30 | 1d | AA |
| 43 | F | 19 | 2d | AA |
| 44 | F | 41 | 2d | AA |
| 45 | F | 30 | 1d | AA |
| 46 | F | 21 | 1d | AA |
| 47 | F | 40 | 1d | AA |
| 48 | M | 33 | 2d | AA |
| 49 | F | 29 | 3d | AA |
| 50 | M | 28 | 2d | AA |
| 51 | F | 34 | 2d | AA |
| 52 | M | 25 | 3d | AA |
| 53 | M | 22 | 4d | AA |
| 54 | F | 24 | 1d | AA |
| 55 | M | 24 | 3d | AA |
| 56 | F | 35 | 2d | AA |
| 57 | F | 30 | 2d | AA |
| 58 | F | 21 | 2d | AA |
| 59 | M | 32 | 2d | AA |
| 60 | F | 14 | 8d | AA |
| 61 | F | 18 | 1d | AA |
| 62 | M | 21 | 1d | AA |
| 63 | F | 50 | 2d | AA |
| 64 | M | 23 | 1d | AA |
| 65 | M | 23 | 3d | AA |
| 66 | M | 40 | 2d | AA |
| 67 | M | 15 | 3d | AA |
| 68 | M | 22 | 3d | AA |
| 69 | M | 26 | 3d | AA |
| 70 | M | 32 | 3d | AA |

|   |   |   |   |   |
|---|---|---|---|---|
|  |  |  |  |  |
Table 3: Age Group Wise Distribution of the Cases

| Age Group | No. of cases (%) |
|-----------|-----------------|
| 0-10      | Nil             |
| 11-20     | 14 (20)         |
| 21-30     | 34 (48.57)      |
| 31-40     | 20 (28.57)      |
| 41-50     | 02 (2.8)        |
| 51-60     | 0               |
| >60       | 0               |
| **Total** | **70 (100)**    |

Table 4: Duration of symptoms

| In Hours | No. of cases (%) |
|----------|-----------------|
| < 24     | 18 (25.71)      |
| 24 – 48  | 23 (32.85)      |
| 48 – 72  | 18 (25.71)      |
| >72      | 11 (15.71)      |
| **Total** | **70 (100)**    |

Table 5: Distribution of SB

| Serum Bilirubin Level | No. Of cases (%) |
|-----------------------|------------------|
| Raised serum bilirubin (Hyperbilirubinemia) | 42 (60) |
| Normal                | 28 (40)          |
| **Total No. Of cases (%)** | **70** |

4. Discussion

A retrospective study done in USC Medical Center, Los Angeles found elevated Bilirubin levels in 38% of cases and patients with Gangrene/perforation were significantly more likely to have Hyperbilirubinemia than those with Acute Appendicitis. The odds of appendiceal perforation are three times higher (odds ratio 2.6) for patients with Hyperbilirubinemia compared to those with normal Bilirubin levels\(^5\).
Another study conducted by Dept. of Surgery, Nepalgunj Teaching Hospital, Nepalgunj, Nepal found hyperbilirubinemia in 86.6% of the patients of acute appendicitis. The range of Hyperbilirubinemia ranged from 1.2mg – 8.4mg/dl with mixed type (Direct and Indirect) of Serum Bilirubin\(^6\).

A retrospective study conducted in Department of General & Visceral Surgery, Academic Teaching Hospital of the Ruhr University, Bochum, Germany found elevated bilirubin in all patients in the range of 0.1 – 4.3 mg/dl, while patients with Appendiceal perforation had Bilirubin in the range of 4.0 – 4.3 mg/dl\(^7\).

Study conducted by Dept. of Surgery, Nepalgunj Teaching Hospital, Nepalgunj, Nepal found elevated Total Serum Bilirubin (TSB) in 87% of cases. The mean of elevated serum Bilirubin was 2.26mg/dl and in patients with gangrenous or perforated appendix; elevation of TSB was found to be much higher\(^8\).

In our study, all the cases were diagnosed preoperatively with acute appendicitis. Intraoperatively all the cases had inflamed appendix. No gangrenous or perforated appendix was found. The serum bilirubin levels are elevated in 42 (60%). In almost all the raised serum bilirubin cases, both direct and indirect bilirubin level were raised. It was also observed in our study that there was no significant relation between duration of symptom and bilirubin level.

5. Conclusion

Our study concludes that there was hyperbilirubinemia in 60% of the patients of acute appendicitis. Elevated serum bilirubin ranged from 1.2mg/dL - 4 mg/dL and was of mixed type. When compared to other studies there was no complicated appendicitis encountered in our study.

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