INTRODUCTION
Acute appendicitis comes under one of the most frequently encountered cause of “Acute abdomen”.1-2 Appendicectomy is the most frequently performed emergency abdominal operation and is often the first major procedure performed by a surgeon in training. Experienced clinicians accurately diagnose appendicitis based on a combination of history, physical examination and laboratory studies about 80% of the time.3

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In spite of advances in the radiological and laboratory investigations the diagnosis of Appendicitis still remains a dilemma. Although most patients with Acute Appendicitis can be easily diagnosed, in some cases the sign and symptoms are variable and a firm diagnosis can be difficult. This is particularly true where the appendix is retrocaecal or retroileal. The percentage of appendicectomies performed where appendix subsequently found to be normal varies 15-50% and postoperative complications can occur in up to 50% of these patients. Delay in diagnosis of Acute Appendicitis leads to perforation and peritonitis and increased mortality. Perforation ranges 50-90% in various series.

To supplement the clinical diagnosis and to reduce the frequency of unnecessary
Appendicectomy, the importance of laboratory investigations like White Blood Cell (WBC) counts and C-reactive protein (CRP) values has been stressed.\textsuperscript{4} The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.\textsuperscript{5} However up to date there is no confirmatory laboratory marker for the pre-operative diagnosis of acute appendicitis and appendicular perforation. Recently, elevation in serum bilirubin was reported, but the importance of the raised total bilirubin has not been stressed in appendicitis.\textsuperscript{6} It is well established that when microbes invade the body, leukocytes defend it. This leads to increase in the leukocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of pro-inflammatory cytokines such as TNF-alpha, IL6 and cytokines. These reach the liver via Superior mesenteric vein (SMV) and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow.\textsuperscript{7}

In view of the above context, the present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute uncomplicated appendicitis and also, to see whether elevated bilirubin levels have a predictive potential for the diagnosis of complicated (necrotising and perforated) appendicitis.

MATERIALS AND METHODS
This is a cross sectional study conducted in the Department of General Surgery, S.S.G.Hospital, Baroda during the period of January 2013 to October 2013.

Sampling method
The sample size was calculated based on the following formula.

\[
\text{n} = \frac{Z^2 \times p \times q}{d^2}
\]

Where,
\begin{align*}
Z & = 1.96 \approx 2 \text{ (considering confidence as } 95\%) \\
p & = \text{prevalence (prevalence} \text{ is taken as } 50\% \text{ as exact prevalence is not known)} \\
q & = 100 - p \text{ that is, } 50\% \\
d & = \text{Absolute error which was } 10\%
\end{align*}

A total of 100 patients with clinical diagnosis of acute uncomplicated appendicitis or complicated appendicitis were studied based on the following criteria.

**Inclusion Criteria**
All patients diagnosed as acute uncomplicated or complicated appendicitis clinically on admission, operated upon and confirmed by histopathological examination were included.

**Exclusion**
- 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).
- Hemolytic disease.
- Acquired or congenital biliary disease.
- Patients with positive HBsAg.
- Patients with cholelithiasis.
- Patients with cancer of hepato-biliary system.

The serum bilirubin and LFTs were carried out using the Semi Auto Analyser (erbachem V2) machine available in the hospital and HbsAg was tested by ELISA. The patients were operated, intraoperative findings were noted and the specimen was sent to the department of Pathology for Histopathological examination. Histopathological diagnosis of either acute appendicitis or necrotising appendicitis was noted.

**Ethics**
Ethical clearance was obtained from “The Scientific And Ethical Review Committee” of the institution for the study. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or complicated appendicitis under Department of General Surgery, SSGH, Baroda during the study period were screened for eligibility.

**STATISTICAL ANALYSIS**
The data obtained was tabulated on Microsoft excel spreadsheet and analysed.
as below.

- Patients with clinical diagnosis of acute uncomplicated appendicitis having hyperbilirubinemia were expressed in percentage as:

  Patients with clinical diagnosis of acute uncomplicated appendicitis with elevated Serum bilirubin level

  All patients with clinical diagnosis of acute uncomplicated appendicitis

  Mean of the level of elevation of Serum bilirubin was calculated for patients with clinical diagnosis of acute appendicitis.

- Patients with clinical diagnosis of complicated appendicitis having hyperbilirubinemia were expressed in percentage as:

  Patients with clinical diagnosis of complicated appendicitis with elevated Serum bilirubin

  All patients with clinical diagnosis of complicated appendicitis

  Mean of the level of elevation of Serum bilirubin were calculated for patients with clinical diagnosis of complicated appendicitis.

  A hypothesis was made based on the observation of the level of the two means.

RESULTS

Out of 100 patients enrolled for the study, 71 patients (71%) were males while the remaining 29 patients (29%) were females. The overall mean age of all 100 patients was 26 ± 13.4 years (range, 12.6–39.4 years). The average age in males and females was 26.9 ± 13.0 years (range, 13.9–39.9 years) and 24.9 ± 14.3 years (range, 10.6–39.2 years) respectively. 32 patients (32%) had Total Leukocyte count less than 11,000/mm³ while 68 patients (68%) counts above 11,000/mm³. The mean Total bilirubin of all 100 patients was 1.3 ± 0.45 mg/dL (range, 0.85–1.75 mg/dL) while the Direct bilirubin was 0.7 ± 0.3 mg/dL (range, 0.4–1.0 mg/dL) and indirect bilirubin was 0.6 ± 0.28 range (0.32–0.88). The mean SGPT was 19.8 ± 5.95 U/L (range, 13.85–25.75 U/L). 18 patients (18%) of all 100 patients were found to have normal bilirubin levels (≤ 1.0 mg/dL), while 82 patients (82%) had raised bilirubin levels (> 1.0 mg/dL). Out of 25 patients diagnosed as complicated appendicitis 23 patients (92%) had raised bilirubin levels (> 1.0 mg/dL), while the remaining 02 patients (8%) had normal levels (≤ 1.0 mg/dL). Histopathologically, 75 patients (75%) were confirmed as Acute Uncomplicated appendicitis while 25 patients (25%) were diagnosed as complicated appendicitis. The mean bilirubin levels in patients diagnosed with Acute uncomplicated appendicitis was 1.19 ±0.33 mg/dL (range, 0.86–1.52 mg/dL) while in patients diagnosed with complicated appendicitis was 1.78 ±0.48 mg/dL (range, 1.3–2.26 mg/dL). The Direct bilirubin and Indirect bilirubin in patients diagnosed with Acute uncomplicated appendicitis were 0.64 ± 0.26 mg/dL and 0.54 ± 0.20 respectively. The Direct bilirubin and Indirect bilirubin in patients diagnosed with complicated Appendicitis were 0.94 ±0.33 mg/dL and 0.79 ± 0.39 mg/dL respectively. 49 patients (65.33%) of the total patients diagnosed with Acute uncomplicated appendicitis (n=75) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 26 patients (34.67%) had normal bilirubin levels (≤ 1.0 mg/dL). Similarly, 23 patients (92%) of the total patients diagnosed with complicated Appendicitis (n=25) were found to have elevated bilirubin levels (> 1.0 mg/dL) while 02 patients (8%) had normal bilirubin levels (≤ 1.0 mg/dL).

DISCUSSION

Obstruction of the lumen is believed to be the major cause of acute appendicitis. Faecoliths are the usual cause of obstruction. Less common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites. The bacteriology of normal appendix is similar to that of
normal colon. The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia coli* and *Bacteroids fragilis*. However a wide variety of both facultative and anaerobic bacteria may be present.

**Table No.13. COMPARISON FOR SEX INCIDENCE IN VARIOUS STUDIES**

<table>
<thead>
<tr>
<th>Various studies</th>
<th>M:F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study (2013) n=100</td>
<td>2.4 : 1</td>
</tr>
<tr>
<td>Marudanayagam et al(^{12}) (2006) n=2660</td>
<td>1.5 : 1</td>
</tr>
<tr>
<td>Samsi et al(^{20}) (1969) n=100</td>
<td>2 : 1</td>
</tr>
</tbody>
</table>

In the present study of the 100 patients enrolled for the study, 71 patients (71%) were males while the remaining 29 patients (29%) were females. This correlates with the male preponderance seen in other studies.

**Table No.14 COMPARISON FOR AGE INCIDENCE IN VARIOUS STUDIES**

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Marudanayagamet al(^{12}) (2006) in % (n = 2660)</th>
<th>Present study in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 10</td>
<td>16.46</td>
<td>9</td>
</tr>
<tr>
<td>11 – 20</td>
<td>35.09</td>
<td>30</td>
</tr>
<tr>
<td>21 – 30</td>
<td>19.2</td>
<td>32</td>
</tr>
<tr>
<td>31 – 40</td>
<td>13.7</td>
<td>12</td>
</tr>
<tr>
<td>Over 40</td>
<td>15.2</td>
<td>17</td>
</tr>
</tbody>
</table>

The mean age in our study population (100 patients) was 26.4 ± 13.39 years (range, 13.01–39.79 years). Majority of the patients (62%) in present study were in 2\(^{nd}\) and 3\(^{rd}\) decades of life. This is consistent with other studies as well as with the quoted incidence in literature.

**Table 15: COMPARISON FOR TOTAL COUNT IN VARIOUS STUDIES**

<table>
<thead>
<tr>
<th>STUDIES</th>
<th>WBC COUNT (&gt; 11,000/cmm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present Study (n=100)</td>
<td>68%</td>
</tr>
<tr>
<td>Emmanuel et al(^{18}) (n=472)</td>
<td>93%</td>
</tr>
<tr>
<td>Ghimire et al(^{20}) (n=141)</td>
<td>55%</td>
</tr>
</tbody>
</table>

The total leukocyte count was found elevated (>11,000/cmm) in 68 patients (68%) of the total 100 patients. The mean of TLC count in all patients was 12467 ± 3278.82/mm\(^3\) (range, 6318 - 13742/mm\(^3\)). This correlates with other studies.

**Table No. 16 COMPARISON FOR SERUM BILIRUBIN IN VARIOUS STUDIES**

<table>
<thead>
<tr>
<th>References</th>
<th>Total Bilirubin &gt; 1.0 mg/dl complicated appendicitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study (n=100)</td>
<td>65.33% 92%</td>
</tr>
<tr>
<td>Khan et al(^{6}) (n=110)</td>
<td>56.36% 80.6%</td>
</tr>
<tr>
<td>Emmanuel et al(^{18}) (n=472)</td>
<td>29% 60%</td>
</tr>
<tr>
<td>Young Hong etal(^{21}) (n=1195)</td>
<td>62% 90%</td>
</tr>
</tbody>
</table>

Hyperbilirubinemia (> 1.0 mg/dL) in our study was found in 82 patients (82%) of all the 100 patients (n=100) enrolled in the study, while 18 patients (18%) had normal bilirubin levels (≤1.0mg/dL) range, (0.85 – 1.75 mg/dL), which was above the normal range (≤1.0mg/dL) considered for the study, hence indicating the occurrence of hyperbilirubinemia.

The mean of Direct bilirubin was 0.7±0.3 mg/dL (range, 0.4-1.0 mg/dL) while that of Indirect bilirubin was 0.6±0.28 mg/dL (range, 0.32 – 0.88 mg/dL).

Amongst the patients diagnosed with Acute uncomplicated appendicitis(n=75), 49 patients (65.33%) were found to have elevated bilirubin (>1.0 mg/dL) while only 26 patients (34.67%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with complicated appendicitis (n=25), 23 patients (92%) had bilirubin elevated (>1.0 mg/dL), while only 2 patients (8%) had normal levels (<1.0 mg/dL). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute uncomplicated appendicitis (65.33%) or complicated appendicitis (92%).

The mean bilirubin levels in patients diagnosed with Acute uncomplicated appendicitis was 1.3±0.45 mg/dL (range, 0.75 – 2.05 mg/dL) while in patients
Evaluation of hyperbilirubinemia as a new diagnostic marker for acute appendicitis

diagnosed with complicated appendicitis was 1.78±0.48 mg/dL (range, 0.74–3.06 mg/dL). Hence, we see that patients with complicated appendicitis had higher levels of bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible of having complicated appendicitis than those with normal or slightly elevated total serum bilirubin.

Appendicitis were 0.7±0.3 mg/dL and 0.54±0.2 respectively. Similarly, direct bilirubin and indirect bilirubin in patients diagnosed with complicated appendicitis were 0.94±0.33 mg/dL and 0.79±0.39 mg/dL respectively. Sensitivity of bilirubin in predicting acute uncomplicated appendicitis and complicated appendicitis was 65.33% and 92% respectively.

REFERENCES:
Evaluation of hyperbilirubinemia as a new diagnostic marker for acute appendicitis


26. Samsi AB, Adarkar NY, Kamat RS. A study of 100 consecutive cases of acute appendicitis - with their histopathological findings. Ind J Surg1969 November-December;574-78.

