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## ORIGINAL ARTICLE

## The Diagnostic Value of Hyperbilirubinemia And Total Leucocyte Count in the Evaluation of Acute Appendicitis

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## ABSTRACT

**Background:** Acute appendicitis (AA) is a common abdominal emergency encountered in general surgery. In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and can be confirmed by laboratory tests and ultrasonography. However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases, either the diagnosis is missed or the patient's normal appendix is operated on, leading to increase in mortality and morbidity.

**Aims:** It is to evaluate the importance of total leukocyte count (TLC) and total serum bilirubin (TSB) in the diagnosis of clinically suspected cases of AA.

**Settings And Design:** This is a prospective study conducted at the Department of Surgery at NGMC, Teaching Hospital, Nepalgunj, Nepal, from December 2004- Jan 2008.

**Methods And Material:** 122 patients suspected of having appendicitis at clinical evaluation underwent prospective evaluations which included laboratory tests (TLC, LFT, Urine analysis) and ultrasonography (USG) of the abdomen. They were operated on and their diagnosis was confirmed per-operatively and post-operatively by histo-pathological examination. Laboratory results, operative findings and histo-pathological findings were compiled, analyzed and compared with reference values. The TLC and total serum bilirubin (TSB) were considered positive for appendicitis when their values were greater than  $10^{10}$  cell/cmm and  $> 1.1$  mg/dL, respectively.

**Results:** The ages ranged from 8-73 years with a mean of 29.36 years. Out of 122 patients, 21(17.81%) cases belonged to the early group of cases (reported  $<24$  hours after the onset of the symptoms), while 101(82.78%) cases belonged to the delayed group of cases (reported  $>24$  hours after the onset of the symptoms). The histological examination revealed that of the 122 specimens, 118(96.72%) had a positive histology for AA, while 4 (3.22%) had normal histology. TLC was elevated in 93 (76.22%) cases and it was normal in 29 (23.77%) cases. Among the cases that had elevated TLC, only 91(97.84%, CI  $14010 \pm 254$ ) had a positive histology for AA, while the remaining 2 (2.15%) had normal histology. Among 29 cases that had normal TLC, 27 had positive histology for AA, while the remaining 2 had normal histology. The specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and overall diagnostic accuracy are 50%, 77%, 97.8%, 7.4% and 76.22%, respectively. TSB was elevated in 95 cases (77.86%, CI  $2.06 \pm 0.73$ ), while it was within normal limits in 27 (22.13%) cases. Among the cases that had elevated TBS, all had positive histology for AA, while in cases with normal TBS, 23 had a positive histology for AA, while 4 had normal histology. The specificity, sensitivity, PPV, NPV, and overall diagnostic accuracy are 100%, 80%, 100%, 14% and 81.14%, respectively Liver enzyme changes if any, were not helpful in the diagnosis.

**Conclusion:** Elevated TSB (without severe changes in liver enzymes) was found to be a better laboratory test with 100% specificity, 80% sensitivity and 81.14% overall diagnostic accuracy than TLC with 50% specificity, 77% sensitivity and 76.22% overall diagnostic

accuracy in the diagnosis of AA. But the diagnosis can be further improved if positive results of either tests alone or in combination are taken into consideration. This will reduce the missing rate of AA without increasing the rate of negative appendicectomies.

**Key Words:** Hyperbilirubinaemia, Total Leukocyte Count, Total Serum Bilirubin, Acute Appendicitis

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Appendicitis is the most common cause of acute abdominal pain that necessitates surgical intervention in the Western world and around Kathmandu valley in Nepal<sup>1, 2</sup>. The clinical diagnosis of acute appendicitis is based primarily on symptoms and physical findings. However, this diagnosis is often difficult and up to 50% of the patients hospitalized for possible appendicitis do not actually have this disorder. Authors of large prospective studies reported a 22%-30% removal rate of normal appendices at surgery<sup>3-6</sup>. To reduce the frequency of unnecessary appendectomy, the importance of laboratory findings that include both white blood cell (WBC) counts and C-reactive protein (CRP) values has been stressed<sup>7-9</sup>, and the use of USG as a diagnostic tool for appendicitis has been widely evaluated<sup>10-13</sup>. Various scores combining clinical features and lab investigations have also been developed and are good enough to reach the diagnosis. These are the Alvarado score<sup>14</sup> and the Modified Alvarado score<sup>15</sup>. Recently, elevation in serum bilirubin, was reported, but the importance of the raised total has not been stressed<sup>17</sup>.

It is well established that when microbes invade the body, leucocytes defend it. This leads to increase in the leucocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of 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.<sup>18-24</sup>

### Aim

To evaluate the specificity, sensitivity, PPV, NPV and diagnostic accuracy of TLC and TSB in the diagnosis of acute appendicitis.

### Material And Methods

This is a prospective study conducted at Nepalgunj Medical College, Teaching Hospital, Nepalgunj, Nepal, from December 2004 to January 2008. Consecutive patients suspected of having appendicitis at clinical evaluation underwent prospective evaluations which included laboratory tests (TLC, LFT, Urine analysis) and USG of the abdomen. They were operated on and their diagnosis was confirmed per-operatively and post-operatively by histo-pathological examination. Laboratory results, operative findings and histo-pathological findings were compiled, analyzed and compared with the reference values. The TLC and TSB were considered positive for acute appendicitis when their values were greater than  $10^{10}$  cell/cmm and  $> 1.1$  mg/dL, respectively.

### Criteria of selection for the cases:

Patients with a history of alcohol intake with AST/ALT  $< 2$  or no history of alcohol and hepatotoxic drug intake, those who were HBsAg negative or those with no past history of jaundice with acute appendicitis were included in the study, whereas patients with a history of alcohol intake and AST/ALT  $> 2$ , a history of hepatotoxic drug intake, those which were HBsAg positive and /or those with a past history of jaundice and acute appendicitis were excluded from the study.

## Observations

A total of 122 patients were included in the present study. Their ages ranged from 8-73 years with a mean age of 29.36 years. The male to female ratio in adults and children were 1.57: 1:: 3.8:1, respectively. The commonest age group was 30 -40 years in adult patients. Out of the 122 cases, 21(17.81%) belonged to the early group of cases (duration of the onset of the symptoms- <24hours), while 101 (82.87%) belong to the delayed group of cases (duration of the onset of symptoms- >24 hours). Among the 21 early cases, 2 reported <12 hours, while the rest of the 19 reported >12 hours for the onset of symptoms [Table/Fig 1], [Table/Fig 2], [Table/Fig 3].

**(Table/Fig 1) Distribution of the cases in Different age groups (n=122)**

Age Group	No. (%)
0-10	05 (4.09%)
10-20	22 (18.03%)
20-30	34(27.86%)
30-40	37 (30.32%)
40-50	14 (11.47%)
50-60	07 (5.73%)
> 60	03 (2.45%)
<b>Total</b>	<b>122 (100%)</b>

**(Table/Fig 2) Sex wise distribution of the cases (n=122)**

Sex	No. (%)
<b>Adult</b>	
Male	60(49.18%)
Female	38 (31.14%)
<b>Child</b>	
Male	19 (15.57%)
Female	05 (4.09%)
<b>Total</b>	<b>122 (100%)</b>

**(Table/Fig 3) Distribution of cases according to duration of symptoms (n=122)**

Duration of Symptoms in hours	No. (%)
0-24	
<12	02(1.65%)
>12	21(17.21%)
5-48	26(21.31%)
49-72	53(43.44%)
>72	20(16.39%)
<b>Total</b>	<b>122 (100%)</b>

Histological examination reports revealed that out of the 122 appendix specimens, 118 (96.72%) had a positive histology for AA, while the remaining 4(3.22%) had normal histology [Table/Fig 4].

**(Table/Fig 4) Distribution of the cases according to level of TSB and TLC (n=122)**

Type of appendix	TSB		TLC	
	<1.1mg/dL No. (%)	>1.1mg/dL No. (%)	<10000cell/cc No. (%)	>10000cell/cc No. (%)
Acute Appendicitis	16 (13.11%)	70 (57.37%)	2(1.63%)	84(68.85%)
Gangrenous Appendix	2 (01.63%)	12 (9.83%)	11(9.01%)	3(2.45%)
Perforated Appendix	5 (04.09%)	13(10.61%)	14(11.47%)	49(3.27%)
Normal Appendix	4 (03.27%)	Nil	2(1.63%)	2(1.63%)
<b>Total</b>	<b>27 (22.13%)</b>	<b>95 (77.86%)</b>	<b>29(23.77%)</b>	<b>93(76.22%)</b>

Of the 122 patients, 93 were found to have elevated TLC (76.22%) (18early&75 delayed) and it was normal in 29 (23.77%) (3 early&26 delayed) cases. Among the cases that had elevated TLC, only 91(97.84%, CI 14010±254) had a positive histology for AA and the remaining 2(2.15%) had normal histology. Among 29 cases that had normal TLC, 27 had a positive histology for AA, while the remaining 2 had normal histology. The specificity, sensitivity, PPV, NPV and DA are 50%, 77%, 97.8%, 7.4% and 76.22%, respectively [Table/Fig 5].

(Table/Fig 5) Sensitivity and specificity, positive and negative predictive value of TLC in AA (n=1122)

TLC	Histopathology			Specificity = 50% Sensitivity = 77% PPV= 97.8% NPV=7.4% DA= 76.22%
	Normal	AA	Total	
<b>Elevated</b> >10 <sup>10</sup> cell/cmm	2 (FP)	91 (TP)	93	
<b>Normal</b>	2 (TN)	27(FN)	29	
<b>Total</b>	<b>4</b>	<b>118</b>	<b>122</b>	

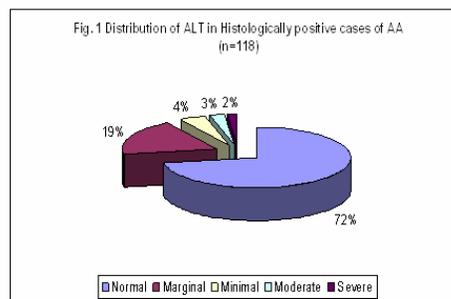
Of the 122 patients, 95 were found to have elevated TSB (77.86%, CI 2.06±0.73) (17early &78delayed), while it was within normal limits in 27 (22.13%) cases. Among the cases that had elevated TSB, all had a positive histology for AA, while in cases with normal TBS, 23 had positive histology for AA, while 4 had normal histology. The specificity, sensitivity, PPV, NPV, and DA are 100%, 80%, 100%, 14% and 81.44%, respectively [Table/Fig 6].

(Table/Fig 6) Sensitivity and specificity, positive and negative predictive value of TSB in AA (n=122)

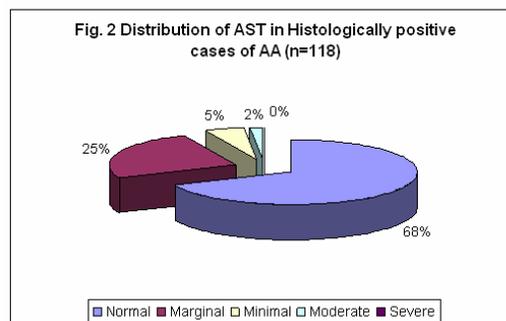
TSB	Histopathology			Specificity = 100% Sensitivity = 80% PPV= 100% NPV= 14% DA= 81.14%
	Normal	AA	Total	
<b>Elevated</b> >1.1mg/dL	Nil (FP)	95 (TP)	87	
<b>Normal</b>	4 (TN)	23 (FN)	23	
<b>Total</b>	<b>4</b>	<b>118</b>	<b>122</b>	

Liver enzymes e.g. serum alanine amino transferase (ALT/SGPT) was normal in 86(70.49%), marginally elevated (<1time) in 26(21.31%), minimally elevated (>1-<2time) in 5(4.09%), moderately elevated (<3times) in 3(2.45%) and severely elevated (>3times) in 2(1.63%) of the cases. Serum aspartate aminotransferase(AST/SGOT) was normal in 75(61.47%), marginally elevated (<1time) in 37(30.32%), minimally elevated (>1time-<2times) in 8(6.55%), moderately elevated (3times) in 1(0.84%) and no case of severe elevation was observed. Age and sex adjusted ALP was normal in 62(50.81%), slightly elevated (1 time) in 46(37.70%), moderately elevated (< 2 times) in 9(7.37%) and severely elevated (>2 times) in 5(4.09%) of the cases [Table/Fig 7], [Table/Fig 8], [Table/Fig 9].

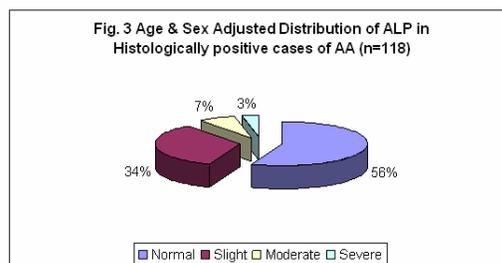
(Table/Fig 7) Distribution of ALT in Histologically Positive cases of AA (n=118)



(Table/Fig 8) Distribution of AST in Histologically Positive cases of AA (n=118)



(Table/Fig 9) Age and Sex Adjusted Distribution of ALP in Histologically Positive Cases



## Discussion

A majority of the cases are reported to the hospital only 24 hours after the onset of symptoms. Histopathological reports of the appendix specimens revealed that 96.27% had a positive histology for AA, whereas TLC and TSB were elevated in 76.22% and 77.86% of the cases, respectively. This indicates that the elevation of both TLC and TSB strictly does not follow the acute inflammation of the appendix.

If TLC alone is taken into consideration to reach the diagnosis in a clinically suspected case of AA, then there is a possibility that about 1.7% results could be false positive (elevation of TLC without inflammation of appendix) and 22.13% results could be false negative (positive

histology without elevation of TLC), which means that there are chances that 1.7% normal appendices will be removed, while in 22.13% of the cases, the diagnosis will be missed.

If TSB alone is taken into consideration to reach the diagnosis in a clinically suspected case of AA, there will be no false positive results, but there could be 18.85% false negative results, which means that none of the normal appendices will be removed, but in 18.85% of the cases, the diagnosis will be missed.

On comparing both test results, TSB was found to be a better test than TLC, because the missing percentage of the diagnoses was nearly similar in both tests (22.13% Vs 18.85%), but the percentage of negative appendectomy with TSB was nil as compared to TLC (1.7%).

If both are elevated, both TLC and TSB are taken into account to reach the diagnosis in clinically suspected cases of AA. The correct diagnosis is usually made only in 55% of the cases. This is because both the tests do not show elevated values at the same time in 45% of the cases. This can cause the real diagnosis to be missed out in too many cases, while if both test results show elevated values which are taken into account either alone or together, the chances of a correct diagnosis is increased to 99.3% and the chances of a missed diagnosis is reduced to <1% at the expense of 1.7% unnecessary appendectomies (false positive cases). This is much higher than either of the two tests individually and together. Thus, in cases where TLC is normal, TSB can be used as an alternative lab test, or vice versa, to reach the diagnosis. This may reduce the rate of missed diagnoses without increase in the percentage of negative appendectomies<sup>7,25</sup>.

## Conclusion

Elevated TSB (without severe changes in liver enzymes) is a better laboratory test (with 100% specificity, 80% sensitivity and 81.14% overall diagnostic accuracy) than TLC (with 50% specificity, 77% sensitivity and 76.22% overall diagnostic accuracy) in the diagnosis of AA. But, the diagnostic accuracy is further improved if positive results of either tests alone or in combination are taken into consideration for the

diagnosis. This will reduce the rate of missed diagnoses of AA without increasing negative appendectomies.

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