

ROLE OF SERUM C REACTIVE PROTEIN, SERUM BILIRUBIN, TOTAL LEUKOCYTE COUNT AND NEUTROPHIL COUNT IN DIAGNOSIS OF ACUTE APPENDICITIS IN CHILDRENS, GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL

Udhayasankar V¹, Haris Vijila Rani M²

¹Assistant Professor, Department of Paediatric Surgery, Government Vellore Medical College Hospital, Vellore, Tamilnadu, India

²Associate Professor, Department of Paediatric Surgery, Government Vellore Medical College Hospital, Vellore, Tamilnadu, India

Received : 18/12/2023
Received in revised form : 20/02/2024
Accepted : 07/03/2024

Keywords:

Acute appendicitis, Serum C Reactive Protein, Serum Bilirubin, Total Leukocyte count, Neutrophil count.

Corresponding Author:

Dr. Udhayasankar V,

Email: drudhayasankar07@gmail.com

DOI:10.47009/jamp.2024.6.2.139

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 655-660



Abstract

Background: Acute Appendicitis is one of the most common Paediatric surgical emergency encountered in day to day surgical practice and in emergency. The following are methods for diagnosis of acute appendicitis - clinical, laboratory investigations and radiologically. In spite of advances in available methods results of negative appendectomy still there. The delay in diagnosis usually leads on to various complications that cause increase in both morbidity and mortality of the childrens. **Objectives:** To find out the specificity, sensitivity, predictive value of positive test and predictive value of negative test of CRP, Serum Bilirubin, Total leukocyte count, and Neutrophil count in diagnosis of acute appendicitis. To correlate HPE report with the blood investigations reports (CRP, Total serum bilirubin, Total leukocyte count, and neutrophil count). To establish the effect of combining all the investigation in same patients. To interpret the efficacy to improve the diagnosis and decision making of Acute appendicitis and hence reduce negative appendectomies with the help of these Investigations. **Materials and Methods:** In this study 100 patients with clinical features suggestive of acute appendicitis were included. Investigations Serum C Reactive Protein, Serum Bilirubin, Total Leukocyte Count and Neutrophil count is used for aiding the diagnosis and their post-operative Histo Pathological features were evaluated. Sensitivity, Specificity, Positive and Negative predictive value of individual tests and combining all the investigations in comparison with post-operative histopathological examination of appendectomy is analysed which was taken as the gold standard. **Result:** Among the 100 patients in the present study, CRP has the highest sensitivity and specificity (91.8%, 86.7%) followed by Serum Bilirubin (84.7%, 80%), Total Leukocyte Count (81.2%, 80%) and Neutrophil Count (81.2%, 86.7%). Combining all the four investigations increases the sensitivity and specificity of the tests (98.8%, 86.7%). **Conclusion:** CRP and Serum Bilirubin contains the important diagnostic information, so it always included in the diagnostic work up of acute appendicitis both complicated and uncomplicated. Sensitivity of TC and Neutrophil Count low individually. Combining all four investigations raises the sensitivity and specificity. If all four tests are negative acute appendicitis is very unlikely and surgery can be safely avoided in these patients thereby reducing the negative appendectomy rates.

INTRODUCTION

Acute abdominal pain with referral diagnosis of acute appendicitis is one of the most common paediatric surgical emergency presenting to the emergency department.^[1] The diagnosis of Acute appendicitis is made by clinical methods which

correlated with the laboratory investigations and radiological imaging. Radiological imaging Like CT abdomen is the most sensitive investigation. Laboratory investigations like CRP, Serum Bilirubin, Total count and Neutrophil count along with the clinical examination are sensitive on par with the radiological imaging to avoid negative appendectomies.^[2] Diagnosis of acute appendicitis

is still a mystery. There is increase in the negative appendicectomy rate of about 15 - 30 % seen in literature.^[3]

Objectives:

1. To find out the specificity, sensitivity, predictive value of positive test and predictive value of negative test of CRP, Serum Bilirubin, Total leukocyte count, and Neutrophil count in diagnosis of acute appendicitis.
2. To correlate HPE report with the blood investigations reports (CRP, Total serum bilirubin, Total leukocyte count, and neutrophil count)
3. To establish the effect of combining all the investigation in same patients.
4. To interpret the efficacy to improve the diagnosis and decision making of acute appendicitis and hence reduce negative appendicectomies with the help of these Investigations.

MATERIALS AND METHODS

Source of Data

This study was conducted in 100 patients as prospective analytical study. These 100 patients are clinically diagnosed to have acute appendicitis, and who were underwent emergency appendicectomy.

This study conducted in Govt.Vellore Medical college Hospital,Vellore, Department of Paediatric surgery, during the period from October 2021 to January 2024.

Inclusion Criteria

All the patients below 18 years of age diagnosed to have appendicitis included in this study and subjected for appendicectomy in Govt.Vellore Medical College, Vellore. All the patients underwent investigations CRP, Serum Bilirubin, Total Leukocyte count, Neutrophil count and post appendicectomy Histopathological examination.

Exclusion Criteria

1. Patients with co morbid conditions
2. Patients who were in conservative management.
3. Patients admitted for interval appendicectomy
4. Associated conditions where CRP, Serum Bilirubin, TC and Neutrophil count was elevated.

CRP more than 6mg/dl considered high, more than 11mg/dl considered very high. Serum Bilirubin of more than 1.4mg/dl considered high and more than 1.8mg/dl considered very high. Total WBC count of more than 10000 cells / cumm considered positive. Neutrophil count of more than 75% considered positive.

After getting informed consent patient subjected to Emergency Appendicectomy. Specimen subjected to histopathological examination.

Histopathologically positive cases among CRP positive cases considered to be True Positive. Histopathologically negative cases in same group considered false positives.

HPE positive cases among CRP negative considered False Negative. HPE negative cases considered True Negative. Similarly, Serum Bilirubin, Total WBC count and Neutrophil Count Individuals classified as True positives, False Positives, True negatives and False Negative.

$$\text{Sensitivity} = \frac{\text{TP} \times 100}{\text{TP} + \text{FN}}$$

$$\text{Specificity} = \frac{\text{TN} \times 100}{\text{TN} + \text{FP}}$$

$$\text{Predictive Value of Positive Test} = \frac{\text{TP} \times 100}{\text{TP} + \text{FP}}$$

$$\text{Predictive Value of Negative Test} = \frac{\text{TN} \times 100}{\text{TN} + \text{FN}}$$

RESULTS

In 100 patients were included in this study and underwent Emergency Appendicectomy.

Age distribution:

The maximum incidence of appendicitis seen between 10 to 15 years of age.

Sex Distribution:

In our study the number of male children's is 60, and female children's are 40 in number.

In present study out of 100 patients 85 patients has HPE positive, among 85 positive individuals CRP was elevated in 78 patients that is 91.8%. 7 patients had normal CRP value (x^2 Mc nemor = 10.9, $P < 0.001$) significant association in diagnosis of acute appendicitis. [Table 1, Figure 1]

In this study among 14 complicated patients, 12 patients had very high raise in CRP value 71%, whereas only 2 patients had very high CRP value in uncomplicated appendicitis. [Figure 2]

In present study CRP shows specificity of 86.7%, predictive value of positive test 97.5%, and predictive value of negative test 65%. [Figure 3]

In present study out of 100 patient's 85 patients has HPE positive, among 85 positive individuals serum bilirubin was raised in 72 patients that is 84.7%. 13 patients had normal serum bilirubin value (x^2 Mc nemor = 8.9, $P < 0.01$) significant association in diagnosis of acute appendicitis. [Table 2]

In this study among 14 complicated patients, 13 patients had very high raise in serum bilirubin value 92%, whereas only 1 patient had very high serum bilirubin value in uncomplicated appendicitis.

In present study serum bilirubin shows specificity of 80%, predictive value of positive test 96%, Negative predictive value 48%. [Figure 4]

In present study out of 100 patients 85 patients has HPE positive, among 85 positive individuals TC was raised in 69 patients that is 81.2%. 16 patients had normal Total count. (x^2 Mc nemor = 6.3, $P < 0.01$) significant association in diagnosis of acute appendicitis. [Table 3]

In present study total count shows specificity of 80%, predictive value of positive test 95%, predictive value of negative test 42%. As such in isolated TLC has low specificity, variety of causes increase the total count. [Figure 5]

In present study out of 100 patients 85 patients has HPE positive, among 85 positive individuals Neutrophil count was raised in 69 patients that is 81.2%. 16 patients had normal Total count. (x2 Mc memor = 6.3, P = <0.01) significant association in diagnosis of acute appendicitis. [Table 4]

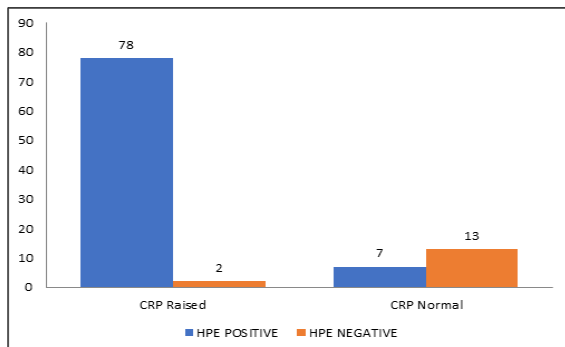


Figure 1: CRP with HPE Correlation

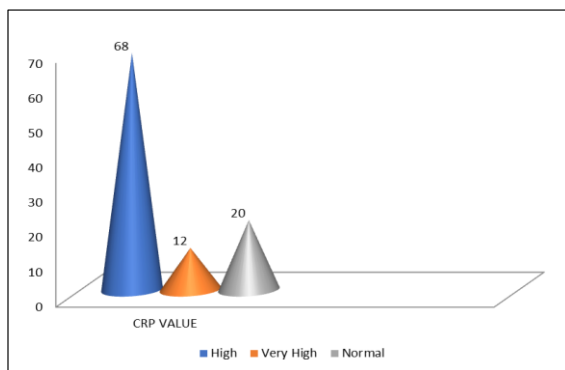


Figure 2: Distribution Of cases according to values of CRP

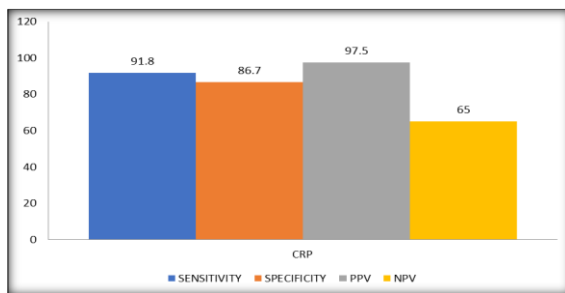


Figure 3: Sensitivity, Specificity, Predictive Value of Positive Test and Negative Test in Bar Diagram

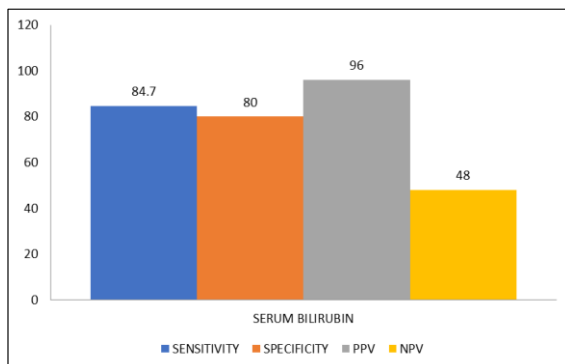


Figure 4: Sensitivity, Specificity, Predictive Value of Positive Test and Negative Test of Serum Bilirubin

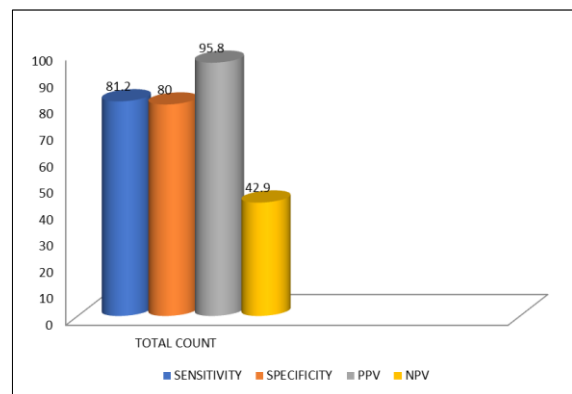


Figure 5: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value of Total Leukocyte Count

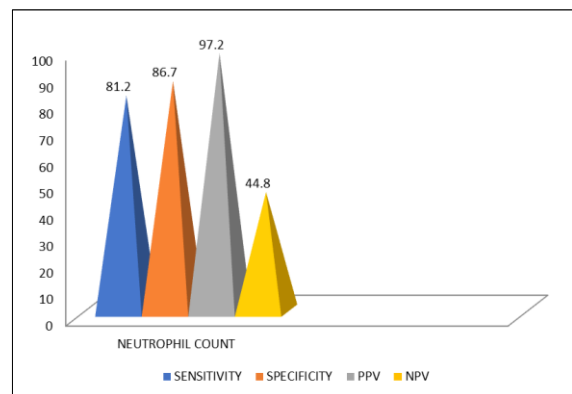


Figure 6: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value of Neutrophil Count

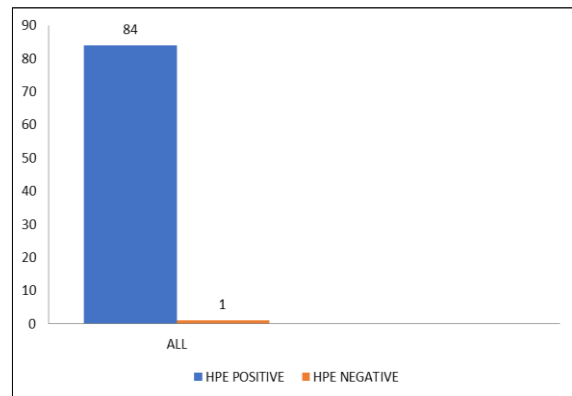


Figure 7: All Investigations with HPE Positive

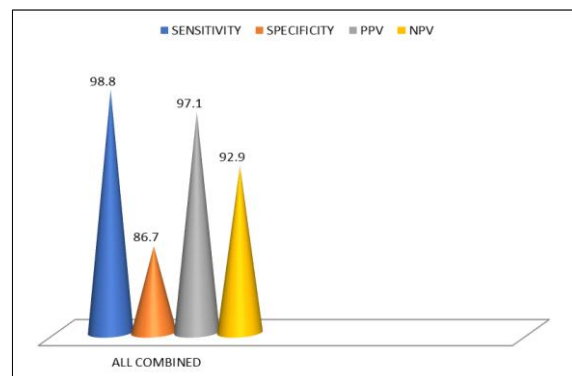


Figure 8: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value of All Combined

In present study Neutrophil count shows specificity of 86.7%, predictive value of positive test 97.2%, and predictive value of negative test 44.8%. As such in isolated Neutrophil count has low specificity, like total leukocyte count. [Figure 6]

In present study among 100 individuals, if all the four investigations positive , HPE positive goes up

to 84 individuals out of 85 that is sensitivity of 98.8%. [Table 5, Figure 7]

The specificity of combining all four investigations is 87.7%, predictive value of positive test is 97.7%, and predictive value of negative test is 92.9%. (χ^2 Mc nemor = 7.3, $P = <0.01$). [Figure 8].

Table 1: Role of Serum C Reactive Protein

CRP	HPE		Total
	Positive	Negative	
Positive	78TP	2FP	80
Negative	7FN	13TN	20
Total	85	15	100

Table 2: Role of Serum Bilirubin

Serum Bilirubin	HPE		Total
	Positive	Negative	
Positive	72TP	3FP	75
Negative	13FN	12TN	25
Total	85	15	100

Table 3: Role of Total WBC Count

Total Count	HPE		Total
	Positive	Negative	
Positive	69TP	3FP	72
Negative	16FN	12TN	28
Total	85	15	100

Table 4: Role of Neutrophil Count

Neutrophil Count	HPE		Total
	Positive	Negative	
Positive	69TP	2FP	71
Negative	16FN	13TN	29
Total	85	15	100

Table 5: Role of Combining All CRP, Serum Bilirubin, Total Count and Neutrophil Count

All	HPE		Total
	Positive	Negative	
Positive	84TP	2FP	86
Negative	1FN	13TN	14
Total	85	15	100

DISCUSSION

Kumar RV et al,^[4] 2011 conducted the study on diagnostic value of CRP in patient suspected to have appendicitis, found that there is increased sensitivity and specificity of CRP. Threshold for CRP raised if it increases more than 2.4mg/dl.

EminGurleyik et al,^[5] 1995 conducted study on diagnostic accuracy of CRP in the patients suspected to have acute appendicitis, they found that elevated serum CRP levels aids surgeons clinical diagnosis, and they recommended routine screening of CRP in suspected appendicitis patients.

Hyoung – Min Moon et al,^[6] 2011 conducted study on elevation of CRP levels >7mg/dl, associated with complicated appendicitis, this study proves that if elevation is there immediate and proper management should be advocated to reduce the disease progression and complications.

Gronroos and Gronroos et al,^[7] 1999 showed in their study acute appendicitis is unlikely if all the tests

were negative, and acute appendicitis is excluded with a 100% predictive value.

Ng and Lai,^[8]2002 found that if CRP, Total count and Neutrophil count is elevated , it is satisfactory to use these investigations in diagnosing acute appendicitis, shows specificity and positive predictive value.

Yang et al,^[9]2005 showed that if patient found to have all the investigations negative the diagnosis of acute appendicitis highly unlikely, and should be further evaluated with extra caution before proceeding in to surgery.

Norback and Harju et al,^[10] found that diagnostic efficacy of CRP, in means of sensitivity and specificity 84.4% and 48.5%. They found that CRP is most sensitive investigation which is a diagnostic marker of acute inflammatory conditions.

Ko et al,^[11]observed in their study that sensitivity and specificity of CRP around 95 and 51%. Also observed that sensitivity and specificity of Total WBC count 85.2% and 65%.

Khan et al,^[12]2004 observed among 110 individuals, the serum bilirubin value was increased in acute appendicitis, it is more specifically elevated in complicated appendicitis. Specificity of this study in complicated appendicitis is 80.6%, in uncomplicated acute appendicitis 56.36%.

Amallesh et al,^[13] in 2004 conducted a study on 192 patients. He observed that CRP was normal in 14 out of 33 negative HPE. The specificity and sensitivity of serum CRP was 42% and 91%. The PPV (raised CRP) was 88% and negative (normal CRP) NPV test is 48%. They concludes, neither raised nor normal CRP value is helpful in the diagnosis of acute appendicitis.

Schellekens DH et al,^[14] 2013 conducted study on 233 patients. They observed CRP and WBC were significantly higher in patients with Acute Appendicitis. But both the tests not concluded the cutoff points to differentiate acute appendicitis and other pathology. They only helpful in diagnosing the suspected acute appendicitis, to avoid negative appendicectomies.

Panagiotopoulou IG et al,^[15] in 2013 conducted retrospective study on 1,169 appendicectomies performed. They found that in perforated appendicitis, the median CRP level was significantly higher than that of Acute Appendicitis.

CRP showed the highest sensitivity 100% and negative predictive value of 100% for Complicated that is Perforated/Gangrenous appendicitis. They conclude that CRP has highest diagnostic accuracy in complicated appendicitis. This was further increased by combining Total leukocyte count.

Stefanutti G et al,^[16] in 2007 did a study on 100 childrens. Sensitivity of elevated Total leukocyte count is 60%. Sensitivity of elevated CRP alone was 86%. Sensitivity of combining both tests goes up to 98%. Sensitivity of combining both tests are extremely high. Normal values of both Total leukocyte count and CRP are very less in pathologically confirmed appendicitis.

Eryilmaz R et al,^[17] in 2001 did a study in 126 patients. They noticed that the mean CRP level was significantly higher in complicated appendicitis than with those presents with non-complicated appendicitis. The mean leucocyte count was significantly lower in patient with negative appendectomy. They noticed that sensitivity increased significantly if both CRP and TLC combined.

Oosterhuis et al,^[18] (1993) showed that serial CRP measurements helps to improve the diagnostic accuracy in patients with acute appendicitis. They observed that CRP and TLC both combined increase the diagnostic accuracy in patients with acute appendicitis.

Wu and coworkers,^[19] 2005, conducted retrospective study. They observed that combining CRP, Serum Bilirubin, TLC, and neutrophil count increases the sensitivity and PPV.

Marchand et al,^[20] study shows that diagnostic efficacy of leukocyte count, sensitivity of about 81%.

Agarwal et al,^[21] 2014 study showed that diagnostic efficacy of both CRP & TC, showing the sensitivity of 74.8% for CRP, 74.7% for TC, specificity of 66.7% for CRP, 54.7% for TC.

Sengupta et al,^[22] in 2009 co study showed that , on 98(75 females and 23 males) patients , for CRP sensitivity 65%, specificity 68% , positive predictive value (PPV) 34%, negative predictive value (NPV) 88%. For WBC alone 85,72,44,95 and if both combined 50,90,56 88

CONCLUSION

In the present study CRP estimation yielded a sensitivity of 91.8%, specificity of 86.7%, positive predictive value of 97.5%, and negative predictive value of 65%, in the diagnosis of acute appendicitis.

In this study serum bilirubin estimation yielded a sensitivity of 84.7%, specificity of 80%, positive predictive value of 96%, and negative predictive value of 48%.

The predictive value of negative test in our study is 100%, if all four tests were negative, the diagnosis of acute appendicitis can be excluded. In this group of patient's inspite of going for surgery, more conservative approach is needed. Deferring the surgery is considered in this group.

Therefore unnecessary appendicectomy in 15 patients, in whom the tests were true negative, could have been avoided, and thereby decreasing the morbidity to the patient.

Combining the all four tests increases the sensitivity, Specificity, and predictive value of positive test. The significance of combining the tests and their role in diagnosing acute appendicitis is found to be very high. These tests freely available in all the laboratories and even smaller set up of hospitals and also available for all the time.

Even with all available investigations Acute Appendicitis remains a diagnosis based on History and clinical examination. Clinical examination is indispensable in the diagnosis of acute appendicitis, all the investigations complement clinical skills and not replace it.

REFERENCES

1. Peranteau WH, Smink DS. Appendix, Meckel's and other small bowel diverticula. In: Zinner MJ, Ashley W. Stanley, editors. Maingot's Abdominal Operation. 12th ed. New York: The McGraw-Hill Companies; 2013. p. 623-40.
2. Chang F.C., Hogle H.H., Welling D.R.: The fate of the negative appendix. Am. J. Surg.1973;126:752-754
3. Pearson R.H. Ultrasonography for diagnosing appendicitis. Br Med. J. 1988;297:309-310
4. Kumar RV et al Diagnostic value of CRP in suspected acute appendicitis – prospective study. Indian J Med Sci,65(9)2011,399-405.
5. Gurleyik E, Guerleyik G, Unalmieser S. Accuracy of C-reactive protein measurement in diagnosis of acute

- appendicitis compared with surgeons clinical impression. *Dis colon rectum*.1995; 38:1270
6. Wu H-P, Lin C-Y, Chang C-F, Chang Y-J, Huang C-Y. Predictive value of C-reactive protein at different cutoff levels in acute appendicitis. *Am J Emerg Med*. 2005 Jul;23(4):449–53
 7. Grönroos JM, Grönroos P. A fertile-aged woman with right lower abdominal pain but unelevated leukocyte count and C-reactive protein. Acute appendicitis is very unlikely. *Langenbecks Arch SurgDtschGesFürChir*. 1999 Oct;384(5):437–40.
 8. Ng K-C, Lai S-W. Clinical analysis of the related factors in acute appendicitis. *Yale J Biol Med*. 2002 Feb;75(1):41
 9. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Role of leukocyte count, neutrophil percentage, and C-reactive protein in the diagnosis of acute appendicitis in the elderly. *Am Surg*. 2005;71(4):344-47.
 10. Nordback I, Harju E. Inflammation parameters in the diagnosis of acute appendicitis. *ActaChirScand* 1988; 154:43-8
 11. Ko YS, Lin LH, Chen DF. Laboratory aid and ultrasonography in the diagnosis of appendicitis in children. *Zhonghua Min Guo Xiao Erke Yi Xue Hui ZaZhi* 1995; 36: 415-9.
 12. Khan MN, Davie E, Irshad K: The role of white cell count and C-reactive protein in the diagnosis of acute appendicitis. *J Ayub Med Coll Abbottabad* 2004;16:17
 13. Amallesh T, Shankar M, Shankar R. CRP in Acute Appendicitis — Is It a Necessary Investigation? *Int J Surg*. 2004 May;2(2):88–9.
 14. Schellekens DHSM, Hulsewé KWE, van Acker BAC, van Bijnen AA, de Jaegere TMH, Sastrowijoto SH, et al. Evaluation of the Diagnostic Accuracy of Plasma Markers for Early Diagnosis in Patients Suspected for Acute Appendicitis. Lewis L, editor. *AcadEmerg Med*. 2013 Jul;20(7):703–10.
 15. Panagiotopoulou IG, Parashar D, Lin R, Antonowicz S, Wells A, Bajwa F, et al. The diagnostic value of white cell count, C-reactive protein and bilirubin in acute appendicitis and its complications. *Ann R CollSurg Engl*. 2013 Apr 1;95(3):215–21.
 16. Stefanutti G, Ghirardo V, Gamba P. Inflammatory markers for acute appendicitis in children: are they helpful? *Journal of pediatric surgery*. 2007;42(5):773-76.
 17. Eryilmaz R, Sahin M, Alimoglu The value of C-reactive protein and leucocyte count in preventing negative appendectomies. *Ulus Trauma Derg*. 2001;7:142–45.
 18. Oosterhuis WP, Zwinderman AH, Teeuwen M, van An del G, Oldenzel H, Kerkhoff JF, et al. C reactive protein in the diagnosis of acute appendicitis. *Eur J SurgActaChir*. 1993 Feb;159(2):115–9.
 19. Wu H-P, Lin C-Y, Chang C-F, Chang Y-J, Huang C-Y. Predictive value of C-reactive protein at different cutoff levels in acute appendicitis. *Am J Emerg Med*. 2005 Jul;23(4):449–53
 20. Marchand A, Van Lente F, Galen RS. The assessment of laboratory tests in the diagnosis of acute appendicitis. *Amer J ClinPathol* 1983; 80: 369-74
 21. CS Agarwal, S Adhikari. Role of C Reactive protein and leukocyte count in diagnosis of auteappendicitis, *Nepal Medical journal* 2008;10(1):11-15
 22. Sengupta A, Bax G, Paterson-Brown S. White Cell Count and C - reactive protein Measurement in Patients with Possible Appendicitis. *Ann R CollSurg Engl*. 2009 Mar;91(2):113–5