J Surg Res 2021; 4 (3): 441-449 *DOI: 10.26502/jsr.10020153*

Research article

Diagnostic Precision of C-Reactive Protein Levels, Neutrophil Count and Total Leukocyte Count in Identifying Acute Appendicitis Clinically

Lal Bux Brohi[1,2], Mehwish Mooghal[1,2*], Hussain Ahmed[3], Waseem Ahmad Khan[1,2], Jalil Malik[1,2], Tariq Mahmood Malik[1,2], Wajiha Khan[4], Kamran Rahim[1,2], Asrar Ahmad[1,2], Rana Hassan Javaid[1,2], Hina Tahseen[1,2]

[1]Department of Surgery, PNS Shifa Hospital, Karachi, Pakistan

[2]Department of Surgery, Bahria University Medical and Dental College, Karachi, Pakistan

[3]Armed Forces Institute of Urology, Rawalpindi, Pakistan

[4]Dow University of health Sciences, Karachi, Pakistan

[*]**Corresponding author:** Mehwish Mooghal, Department of surgery, PNS Shifa Hospital, Karachi, Pakistan.

Received: 13 August 2021; **Accepted:** 23 August 2021; **Published:** 25 August 2021

Citation: Lal Bux Brohi, Mehwish Mooghal, Hussain Ahmed, Waseem Ahmad Khan, Jalil Malik, Tariq Mahmood Malik, Wajiha Khan, Kamran Rahim, Asrar Ahmad, Rana Hassan Javaid, Hina Tahseen. Diagnostic precision of C-reactive protein levels, neutrophil count and total leukocyte count in identifying acute appendicitis clinically. Journal of Surgery and Research 4 (2021): 441-449.

Abstract

Objective

To identify diagnostic precision of C-reactive proteins levels, neutrophils and total leukocyte count in diagnosing acute appendicitis clinically, taking histopathology as a benchmark.

Methods

After permission from hospital's ERC, the data collection was carried out at surgical department PNS Shifa over a period of Six months (13 October 2020 to 13 April 2021). Suspected patients of acute appendicitis reporting to OPD and emergency who were diagnosed clinically as having acute appendicitis were included in study. WBC count of >10,000 cells/mm^3 and neutrophil count of >75% and CRP >6 mg/dl was considered positive. Histopathology reports

of all clinical suspected patients were collected and compared with the laboratory tests done preoperatively to determine their diagnostic accuracy.

Results

Mean age was 38.45(SD ± 6.32) with C. I (37.31...36.27) years. Out of 121 patients 50 (41.32%) were male and 71 (58.62%) were female. Diagnostic precision of CRP, TLC, neutrophils was (79.34%,76.03%,72.73%) in diagnosing acute appendicitis with sensitivity level of (80.88%,79.49%,74.36%), specificity (77.36%,69.77%,69.77%), PPV (82.09%,82.67,81.69) and NPV was found to be (75.93%,65.22%,60.0%) by using histology as benchmark.

Conclusion

It is to be concluded that combined C-reactive protein, TLC and neutrophils count yielded high diagnostic precision with high sensitivity and specificity as compare to CRP, TLC and NC separately. Combined CRP, TLC and NC is cheap, readily available and non-invasive imaging modality that is reasonably good and relatively comparable with the histopathology in diagnosing of acute appendicitis.

Keywords: Appendicitis/ diagnosis; C-Reactive Protein; leukocyte count; Neutrophil; Histologic technique

1. Background

Acute appendicitis is amidst the most prevailing cause of right iliac fossa pain and surgical abdomen presenting to emergency departments worldwide and remains one of the most common diseases dealt with by the general surgeon, with lifetime liability of 8.6% to 12%in men and 6.7% to 23.1% in women [1]. The tendency to have an episode of acute appendicitis is higher in juvenile and young adult population, but the incidence of complicated appendicitis shows divergence among different age groups. Although classic/straightforward cases of acute appendicitis are easy to manage, real dilemma lies in diagnosing and managing the cases of atypical/complicated appendicitis. Clinical diagnosis alone leads to relatively unacceptable negative appendectomy rates of 15 to 30% [1]. The diagnosis is rather more difficult among female population of productive age [2,3]. In this review article, the diagnostic considerations of the disease are reassessed with special highlight on difficulties in clinical accuracy of the diagnostic parameters. Early surgical intervention is the key to prevent appendicular perforation, but unnecessarily high rates of negative appendectomies can eventually leads to unavoidable morbidity and even mortality [4,5]. The conventional use of computed tomography (CT) abdomen in cases of diagnostic dilemma has helped to curtail the number of negative appendectomies [6,7]. Studies showed that preoperative use of CT seems to be of more aid and help to reach a diagnosis among women of age 45 years or younger [4,5]. However, the diagnostic delay which is encountered by using the CT scan as adjunct can sometimes delay clinically apparent cases of acute appendicitis, and therefore can even heighten up the risk for perforation/complications [8]. Moreover, unconventional use of CT is associated with elevated risk of cancer especially in a population who are exposed to radiation hazard at younger age, as incidence of acute appendicitis is more in younger population [9]. In a study, the prevalence of acute appendicitis was found 23.5% by using CT scan as adjunct modality [10]. In another study, analysis of combination of CRP, WBC, neutrophil count with

ultrasonography was done which concluded an increase in sensitivity and specificity of overall results (100%, 80%) [11]. In another study, the sensitivity and specificity of combined TLC, CRP and percentage of neutrophil count in diagnosis of acute appendicitis was 88.04% and 94.44% [12]. Appendectomy is the most commonly performed emergency surgery and is done by almost every surgeon during the initial period of his training. Since the definitive description of the clinical findings of acute appendicitis made by Fitz in 1886, and McBurney's report to the New York Surgical Society in 1899, surgical removal of the diseased appendix has long been considered the standard of care for the treatment of acute appendicitis. With the exception of laparoscopic techniques, relatively little has changed in the surgical technique of appendectomy since the days of McBurney and Senn. The rationale of our study is to determine the most precise and sensitive investigation which aid to improve the diagnosis of appendicitis and decision-making and hence decrease negative appendectomy rate also. There are multiple studies available, which were conducted in different hospitals and found these inflammatory markers helpful in diagnosis of suspected cases of appendicitis. We want to conduct this study in our hospital if we would find high sensitivity and specificity of CRP, WBC count, neutrophil count in detecting appendicitis so in future we will develop management guidelines and treatment protocols to detect appendicitis by using C-reactive proteins, neutrophils count and total leukocyte count alone as an investigation modality in patients.

2. Materials and Methods

This was a descriptive Cross-Sectional Study, carried out at Surgical department PNS SHIFA Karachi , over a period of six months after approval of ethical review committee from 13 October 2020 to 13 April 2021. All patients who were enrolled in study were informed about the main concept of the research, anticipated time duration, procedures to be undertaken, participant's decision to deny to participate/withdraw from the research once it has started, as well as the anticipated consequences and risk/benefit ratio. By taking sensitivity=88.04%,12 specificity=94.44%,12 P=23.5%,10 d=10% for sensitivity, d= 4% for specificity and 95% confidence level. The calculated sample size was 121 patients. Non-Probability Consecutive Sampling technique was used. Our inclusion criteria were :

- Patients of either gender.
- Patient with 5-12 years of age for paediatrics.
- Patient with 13-60 years of age for adults.
- Clinically suspected patients of acute appendicitis (right sided abdominal pain on the basis of Visual analogue scale ≥ 7 pain score and any one or more of the following:

o Guarding: tensing of abdominal wall musculature.

o Fever ≥ 100 ^{0}F.

o Positive Rebound Tenderness.

Exclusion criteria of our patients were :

- Known immunosuppressed/ immunocompromised patients.
- Patients taking steroids.
- Patients with serum creatinine > 1.5 mg/dl
- Patients admitted for interval appendicectomy (resolved acute phase).
- Diagnosed cases where inflammatory markers are already raised like rheumatoid arthritis, glomerular nephritis, SLE, IBD on the basis of clinical record.
- Pregnant women

Patients included in the study were subjected to carry

out C-reactive proteins and blood complete picture including differential leukocyte count, neutrophil count preoperatively and their results were evaluated. WBC count of ≥ 10,000 cells/mm3 and neutrophil count of ≥ 75% was considered significant. CRP ≥ 6 mg/dl was considered significant. Histopathology reports of all clinically suspected patients was collected and compared with the laboratory tests carried out preoperatively to determine their diagnostic accuracy. All data including age, gender, fever, clinical examinations, white blood cell count, total leukocyte count, neutophil count was recorded on a Performa. The effect modifiers and biasness was controlled by ensuring proper adherance to inclusion and exclusion criteria. Patient's data was assembled and scrutinized through statistical package for Social Sciences (SPSS) Version 21. Frequency and percentage was interpreted for qualitative variables like gender, clinical findings (fever, tenderness, rebound), findings of CRP, TLC, neutrophil count and histopathology. Mean ± SD were calculated for quantitative variable i.e. age. Sensitivity, specificity, positive predictive value(PPV) and negative predictive value(NPV) and diagnostic accuracy of the diagnostic tests was also calculated by using 2 X 2 table. Stratification with respect to age and gender was done. Post stratification diagnostic accuracy, sensitivity, specificity, PPV(positive predictive value) and NPV(negative predictive value) were calculated. Post stratification chi squire test was applied by using $P \leq 0.05$ as significant.

3. Results

In this study 121 patients were included to assess the diagnostic precision of C-reactive proteins, neutrophil count and total leukocyte count in the identifying suspected cases of acute appendicitis taking histopathology as gold standered and the results were analyzed as Mean ± SD of age was 38.45±6.32 with C.I (37.31…….36.27) years. Out of 121 patients 50(41.32%) were male and 71 (58.62%) were female. Fever was noted in 58(48%) while 63(52%) had normal temperature. Positive tenderness in right lower quadrant was found in 85(70.25%). Rebound tenderness was noted in 77 (63.63%) patients while 44 (36.3%) had no rebound tenderness. Diagnostic accuracy of CRP was 79.34% in diagnosis of acute appendicitis with sensitivity 80.88%, specificity 77.36% , PPV 82.09% and NPV was found to 75.93% by using histopathology as gold standard. Diagnostic accuracy of TLC was 76.03% in diagnosis of acute appendicitis with sensitivity 79.49%, specificity 69.77% PPV 82.67% and NPV was found to 65.22% by using histopathology as gold standard. Diagnostic accuracy of neutrophil count was 72.73% in diagnosis suspected cases of acute appendicitis with sensitivity 74.36%, specificity 69.77% PPV 81.69% and NPV was found to 60.0% by using histopathology as gold standard. Diagnostic accuracy of combined C-reactive proteins, total leukocyte count and neutrophil count was 89.26% in diagnosis of acute appendicitis with sensitivity 84.75%, specificity 93.55% PPV 92.59% and NPV was found to 86.57% by using histopathology as gold standard. Stratification of age and gender were done with respect to combined C-reactive proteins, neutrophil count and total leukocyte count and separately as well to assess diagnostic accuracy, sensitivity, specificity, positive and negative predictive value as shown in Table 1 and 2.

For Age Group 8--40 (n=85)		95% Confidence Interval		For Age Group > 40 (n=36)		95% Confidence Interval	
	%	Lower	Upper		%	Lower	Upper
Sensitivity	85.37	0.75	0.96	Sensitivity	83.33	0.62	1.04
Specificity	93.18	0.86	1	Specificity	91.67	0.8	1.03
Prevalence of disease	48.24	0.38	0.59	Prevalence of disease	33.33	0.18	0.49
Positive Predictive value	92.11	0.835	1	Positive Predictive value	83.33	0.62	1.04
Negative Predictive value	87.23	0.78	0.97	Negative Predictive value	91.67	0.8	1.02
Overall accuracy**	89.41	0.83	0.96	Overall accuracy**	88.89	0.79	0.99

Table 1: Stratification of age group with respect to combined CRP, TLC, Neutrophil count, n=121

For Male (n=50)		95% Confidence Interval		For Female (n=71)		95% Confidence Interval	
	%	Lower	Upper		%	Lower	Upper
Sensitivity	83.33	0.68	0.98	Sensitivity	83	0.73	0.94
Specificity	88.46	0.76	1.01	Specificity	86.96	0.73	1.01
Prevalence of disease	48	0.34	0.62	Prevalence of disease	67.61	0.57	0.78
Positive Predictive value	86.96	0.73	1.01	Positive Predictive value	93.02	0.85	1.01
Negative Predictive value	85.19	0.72	0.99	Negative Predictive value	71.43	0.55	0.88
Overall accuracy**	86	0.76	0.96	Overall accuracy**	85.41	0.76	0.93

Table 2 : Stratification of gender with respect to combined CRP, TLC, Neutrophil count, n=121

4. Discussion

This cross-sectional study is carried out at Surgical department PNS SHIFA hospital Karachi. In this study 121 patients were included to assess the diagnostic precision of C-reactive proteins, neutrophil count and total TLC in the identifying suspected acute appendicitis clinically while taking histopathology as gold standard. The prevailing ages for acute appendicitis among both genders remains 20-35 years, the data that corresponds to the literary work that is carried out for acute appendicitis and highlights its peak incidence years i.e., teens and early 20's [1]. Acute appendicitis remains the most familiar surgical acute abdomen presenting to emergency setups requiring surgery [1], but due to the dearth of availability of accurate diagnostic investigations, the dilemma persists in its confirmation which resulted in unacceptably high negative appendectomy rates (15-30%), which in consonance with literature, the reported clinical precision is 70-95% which is

subjected to clinical expertise and skills of the surgeons [1,4]. This can handicap an already overburdened health care structure of our region, as needless surgical procedures can utilize the hospital resources with resultant unfavourable socio-economic outcomes and yieldness [3,4]. As a routine, acute appendicitis is clinically diagnosed by relying on patient's history and examination, eliciting signs and symptoms of pain RIF, nausea, vomiting, fever, rebound tenderness at McBurney's point, psoas and obturator's sign. Majority gives history of peri-umbilical pain which afterwards shift to RIF. But problem remains, as above mentioned clinical findings vary from patient to patient with resultant misdiagnosed cases, which according to the literature are reportedly as high as 20% [1,2]. In this article diagnostic precision of combined C-reactive proteins, TLC and neutrophil count was 89.26% in cases of acute appendicitis with sensitivity 84.75%, specificity 93.55%, PPV 92.59% and NPV 86.57% by using histopathology as gold standard. A study reported negative appendectomy rate of 15.3% with added increase in length of hospital stay, financial burden to both patient and health care system with infectious sequela of the surgery [4]. Similarly, S Scammell et al in their study found out the negative appendicectomy rate of 16.5% while perforated cases were near 23.7%. They suggested to use ultrasound as a pre-operative adjunct to decrease the rates of negative appendectomies as it gives a high sensitivity of 83.3% and specificity of 97.4%, especially in younger population [5]. In the current study diagnostic accuracy of TLC was 76.03% in diagnosis of acute appendicitis with sensitivity 79.49%, specificity 69.77% PPV 82.67% and NPV was found to 65.22% by using histopathology as gold standard. Haider Kamran et al stressed on the significance and role of TLC as a clinical adjunct investigation to help diagnose cases of acute appendicitis, but not to use it as a single criterion [17]. Gülten Kiyak et al in their study proposed that raised TLC with or without using ultrasound as a pre-operative protocol had aided in diagnosing acute appendicitis cases particularly among female patients of fertile age group [18-20]. Our study also depicts that TLC has more sensitivity over CRP in acute appendicitis patients which correlates with the results of other studies and also with Shehzad Ahmed Abbasi et al. which confirmed about supremacy of TLC over ultrasound in both sensitivity and diagnostic accuracy. Our results indicated p value of TLC as 0.00 which is statistically significant, this high turnout value further adds to its clinical implications [8,20], but at the same time our study also proposed that the sole diagnostic criteria to use TLC as a diagnostic tool can be an overestimation, therefore combination of TLC with other diagnostic parameters like CRP, neutrophils and ultra sound is needed to increase the specificity and sensitivity of the diagnosis [8,9,13,17,20-22]. Same is proposed by Arshad Kamal and his colleagues, that clinical score of TLC is heightened when it is used in combination with neutrophils and CRP [8,9,13,17-21]. Furthermore, it has been proposed in the literature that in cases where there is a diagnostic dilemma, clinical assessment always has a upper hand if compared to TLC alone. In routine practice, differential count shows shift to left which depicts increased neutrophils percentage in patients with acute appendicitis. This specific clinical picture proclaims body's response of inflammation to diseased appendix. A number of articles have reported neutrophilia of ≥75% as a significant finding in more than 75% of the patients. In our study diagnostic precision of neutrophil count was 72.73% in diagnosing acute appendicitis with sensitivity of 74.36%, specificity 69.77% PPV 81.69%

and NPV of 60.0%. Similarly Adnan A. Mohammed and colleagues also addressed in their article that they observed increased neutrophil response in patients who present with acute appendicitis. Subsequently as the disease progresses, more bacterial invasion occurs along the layers of appendix there is a generalized increase in TLC alongwith the pre-existing neutrophilia. Therefore, the diagnostic supremacy of TLC is increased if the neutrophil percentage is taken into account [23]. In another study it was summarized that neutrophils percentage was correlated to different stages of appendicitis.16 While S. Ali and colleagues noticed in their research that elevated neutrophil percentage when used alone was less sensitive (58.52%) and specific (61.90%). When neutrophils percentage is alone taken into account its sensitivity ranges between 60-84%, but if combined TLC and Neutrophil percentage is used the sensitivity reached around 87%. Our study elaborated a clear association between neutrophil count and acute appendicitis but when compared to TLC, it is less sensitive and specific. Although the p value was statistically significant. Furthermore ,when the percentage of neutrophils is united with CRP, TLC and ultra sound the overall sensitivity and specificity of investigations is positively increased, which greatly improves the chances to correctly diagnose acute appendicitis in equivocal cases [5,19]. CRP is an acute phase reactant protein, which upon any inflammatory/infectious trigger inside the body is produced by the hepatocytes depicting body's response to a diseased state. It starts to elevate in concentration within 8-12 hours of onset of any acute infection/inflammation and level peaks at 24-48 hours and persists elevated till the triggering process lasts. On/off many research articles have been published to evaluate its significance and role in acute appendicitis patients. The observed anticipated values of CRP during the episode of acute appendicitis vary in sensitivity and specificity among different studies i-e. 40-99% and 27-90% respectively [12,13]. Many researchers proposed in their work that a CRP value within a limit signifies a normal appendix without inflammation [12,13-16]. In current literature diagnostic accuracy of CRP was 79.34% in diagnosis of acute appendicitis with sensitivity 80.88%, specificity 77.36%, PPV 82.09% and NPV was found to be 75.93% by using histopathology as gold standard. In a recent published study it is stated that CRP is a better lab indicator when combined with neutrophil count and TLC in diagnosing complicated/equivocal cases of acute appendiceal inflammation. Elevated concentrations of CRP with or without elevated TLC/neutophil count mandated exploration, and in many cases combination of these investigations deferred the use of CT scan as a pre-operative investigation, therefore it is suggested to go for CRP along with TLC and neutrophils as a pre-operative investigation for cases in which the diagnosis is equivocal. Another author reported the same results that CRP had the highest sensitivity and specificity of the tests that they performed for acute appendicitis 90%, 80% respectively. Also the combination of CRP with TLC elevates the diagnostic value of the investigations with sensitivity and specificity of 96.25%, 80% respectively. Shefki Xharra et al, Shozo Yokoyama et al and Adnan A. Mohammed et al also stressed on the idea that raised CRP levels were more diagnostic than neutrophils and TLC and were directly correlated to the severity of appendiceal inflammation. Our P value for CRP was significant which shows its probable association with acute appendicitis directly, but when comparison is done with TLC, it is less sensitive. Our study also concluded that combination of CRP with other parameters like TLC and

neutrophils reported higher sensitivity and specificity. It is to be stressed here that CRP is not a replacement of clinical diagnosis, but it be incorporated as an adjunct investigation due to its clinical importance ,cost effectiveness and readily availability. Our limitation of study was that we used a simple cut off value for CRP to label our patients as positive or negative only. Many studies have demonstrated the direct link between serum CRP levels and the severity of disease/appendicitis [13,23]. Also we did not include ultrasound and CT scans as a protocol in our study, the role of these investigations is already known in equivalent cases [10,11]. By using the laboratory levels of CRP, neutrophils and TLC as a protocol for any new research, we can work on to find the severity of appendicitis and can find a link between the these parameters. And henceforth a new guideline for the surgical management of acute appendicitis can be formulated using these laboratory parameters as a pre-operative routine.

5. Conclusion

It is to be concluded that combined CRP, TLC and neutrophil count was having high diagnostic accuracy with high sensitivity and specificity as compare to CRP, TLC and neutrophil count separately. Although histopathology is the gold standard in diagnosing acute appendicitis. Combined CRP, TLC and NC is cheap, readily available and non-invasive imaging modality that is reasonably good and relatively comparable with the biopsy in diagnosis. However, combined CRP, TLC and NC is better in determining the extent of the disease and its complications.

Acknowledgement: None to declare

Disclaimer: None to Declare

Conflict of interest: None to Declare

Funding disclosure: None to Declare

References

1. Sammalkorpi HE, Mentula P, Leppaniemi A. A new adult appendicitis score improves diagnostic accuracy of acute appendicitis: a prospective study. BMC Gastroenterol 14 (2014): 114.

2. Hoffmann J, Rasmussen OO. Aids in the diagnosis of acute appendicitis. Br J Surg 76 (1989): 774-779

3. Seetahal SA, Bolorunduro OB, Sookdeo TC, et al. Negative appendectomy: a 10-year review of a nationally representative sample. Am J Surg 201 (2011): 433-437.

4. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg 137 (2002): 799.

5. Scammell S, Lansdale N, Sprigg A, et al. Ultrasonography aids decision-making in children with abdominal pain. Ann R Coll Surg Engl 93 (2011): 405-409.

6. Cuschieri J, Florence M, Flum DR, et al. The SCOAP Collaborative. The SCOAP Collaborative included: Negative appendectomy and imaging accuracy in the Washington state surgical care and outcomes assessment program. Ann Surg 248 (2008): 557-563.

7. Coursey CA, Nelson RC, Patel MB, et al. Making the diagnosis of acute appendicitis: do more preoperative CT scans mean fewer negative appendectomies? a 10-year study. Radiol 254 (2010): 460-408.

8. Busch M, Gutzwiller FS, Aellig S, et al. In-hospital delay increases the risk of perforation in adults

with appendicitis. World J Surg 35 (2011): 1626-1633.

9. David S Huckins, Karen Copeland. Diagnostic accuracy of combined WBC, ANC and CRP in adult emergency department patients suspected of acute appendicitis. The American Journal of Emergency Medicine 44 (2021): 401-406.

10. Pickhardt PJ, Lawrence EM, Pooler BD, et al. Diagnostic performance of multidetector computed tomography for suspected acute appendicitis. Ann Int Med 154 (2011): 789-796.

11. Sahu SS, Kumar P, Chaubey D, et al. Accuracy of C-reactive protein, neutrophil count,total leukocyte count and ultrasonogram in diagnosis of acute appendicitis. Int J Sci Stud 2 (2014): 191-197.

12. Shafi SM, Afsheen M, Reshi FA. Total leucocyte count, C-reactive protein and neutrophil count: diagnostic aid in acute appendicitis. Saudi J Gastroenterol 15 (2009): 117

13. Shefki X, Lumturije GL, Kumrije X, et al. Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopathology findings in acute appendicitis. World J Emerg Surg 7 (2012): 27.

14. Shozo Y, Katsunari T, Tsukasa H, et al. C-Reactive protein is an independent surgical indication marker for appendicitis: a retrospective study. World J EmergSurg 4 (2009): 36

15. Anshuman S, George B, Simon PB. White cell count and C-reactive protein measurement in patients with possible appendicitis. Ann R Coll SurgEngl 91(2009): 113-115.

16. Rafael NG, Gilson de SS, Marcelo BM, et al. Main findings in laboratory tests diagnosis of acute appendicitis: a prospective evaluation. Arq Bras Cir Dig 25 (2012): 88-90.

17. Haider K, Danish N, Aamir N, Mohammad H, Mukhtar A, Ulas K. role of total leukocyte count in diagnosis of acute appendicitis J Ayub Med Coll Abbottabad 20 (2008): 70-71.

18. Gülten K, Birol K, Ali ÖD, et al. Evaluation of Ohmann and Eskelinen scores, leukocyte count and ultrasonography findings for diagnosis of appendicitis. Turkish J Trauma &Emerg Surg 15 (2009): 77-81.

19. S Ali, O Shah, M Shah, et al. Role Of Total Leukocyte Count, Neutrophil Percentage, C-Reactive Protein And Ultrasonography In The Diagnosis Of Acute Appendicitis. The Internet J Surg 24 (2009): 12.

20. Shehzad AA, Ahmed HM. Diagnostic Accuracy of Total Leucocyte Count and Ultrasound in the Diagnosis of Acute Appendicitis. J Rawal.Med 16 (2012): 147-149.

21. Arshad K, Shafiullah. Significance of total leucocyte count in the diagnosis of acute appendicitis in children. Gomal J Med Sci 9 (2011): 23-29.

22. Sarmad RK, Kahlan RK. Is there a relationship between histopathological features of acute appendicitis and preoperative acute inflammatory markers. International J of Adv Research 2 (2014): 967-973.

23. Adnan AM, Nuredin AD, Saleh MA, et al. The diagnostic value of C-reactive protein, white blood cell count and neutrophil percentage in childhood appendicitis. Saudi Med J 25 (2004): 19-24.

24. Hopkinsmedicine.org. Computed Tomography (CT or CAT) Scan of the Abdomen | Johns Hopkins Medicine Health Library (2015).

25. Shyam S, Prabhat K, Digamber C, et al. Accuracy of C-reactive Protein, Neutrophil Count, Total Leukocyte Count and USG in Diagnosis of Acute Appendicitis. Intern J. Sci Study 2 (2014): 10.