

Study the Changes in Hematological Parameters as Diagnosis Tool in Acute Appendicitis

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Abstract: The present study was designed to study the changes in hematological parameters in acute appendicitis patients (AA). The target population of this study was 40 male individuals from Al-Yarmouk Teaching Hospital and positive control group composed of 20 colitis male patients, and a negative control group composed of 20 healthy male individuals with the same age range. The diagnosis was made by the consultant medical staff, which based on a history, symptoms, clinical examination and other investigation. Blood samples were collected from each patient and control then used for analysis of white blood cell (WBC), lymphocyte, neutrophil, mean platelet volume (MPV), and erythrocyte sedimentation rate (ESR). The results demonstrate high significant difference in WBC, neutrophil, and ESR of AA patients compared with the control groups. There is no significant difference in lymphocyte of AA patients compared with control groups. A significant decrease in the MPV of AA patients compared with negative control group and no significant differences with positive group.

Keywords: White blood cell (WBC), lymphocyte, neutrophil, mean platelet volume (MPV), erythrocyte sedimentation rate (ESR), acute appendicitis

1. Introduction

Acute appendicitis (AA) is one of the most frequent underlying conditions in patients presenting with acute abdominal pain at the emergency department, it might occur at any age (Liu *et al.*, 2017). The etiology remains uncertain, but possible causes include luminal obstruction blocking the escape of mucosal secretions and leading to an increase in pressure, causing engorgement and stasis that can lead to necrosis and eventually perforation (Baird *et al.*, 2017).

White blood cells (WBC), or leukocytes, are cells of the immune system involved in defending the body against both infectious disease and foreign materials (Rashid, 2013). Intervals for WBC counts and relative percentages and absolute cell counts vary by patient age and hospital population (Chabot-Richards and George, 2014).

Neutrophils are well recognized during acute inflammation. They are typically the first leukocytes to be recruited to an inflammatory site and are capable of eliminating pathogens by multiple mechanisms (Kolaczowska and Kubes, 2013). As such, the neutrophils in the blood rapidly migrate to the infected site and, to compensate for neutrophil consumption, the bone marrow increases neutrophil production (Honda *et al.*, 2016).

Lymphocytes are the cornerstone of the adaptive immune system. Their absence causes severe immunodeficiency and renders individuals unable to thrive in a 'germ-filled' world (Reiner and Adams, 2014). They can be altered in many primary immune diseases or diseases with secondary involvement of the immune system (Tosato *et al.*, 2013).

Mean platelet volume (MPV), which reflects the size of platelets, is an accepted marker of platelet function (Cure *et al.*, 2014). It is one of the most widely used surrogate markers of platelet function and has been shown to reflect inflammatory burden and disease activity in several diseases including pre-eclampsia, acute pancreatitis, unstable angina,

myocardial infarction, and systemic inflammation such as ulcerative colitis and Crohn's disease (Kucuk and Kucuk, 2015).

Erythrocyte sedimentation rate (ESR) was first described in 1921 by Westergren (Al-lmi, 2013). It is widely used as a screening test for patients with acute and chronic inflammatory diseases. Although it is nonspecific diagnostic test, but it is a marker for neonatal infection, it is used in monitoring and follow-up of certain groups of patients, such as those with rheumatoid arthritis, polymyalgia, rheumatic and Hodgkin's disease, where disease activity is mirrored by changes in the ESR (Adhikari *et al.*, 2017).

Therefore, the aim of the present study is to determine the changes in hematological parameters in AA patients as compared with negative and positive controls. These parameters included WBC, lymphocytes and neutrophils counts as well as MPV and ESR values.

2. Materials and Methods

Subjects

The target population of this study was 40 male individual from Al-Yarmouk Teaching Hospital, Baghdad, Iraq during the period between November 2017 & March 2018 with age ranged between 15 to 40 years. The patients were diagnosed with AA by the consultant medical staff, according to clinical examination and symptoms. A positive control group was composed of 20 colitis male patients with the same age range, and a negative control group was composed of 20 healthy male individuals also with the same age range.

Collection of Blood Samples

Blood samples were obtained by venipuncture, using 5ml disposable syringe from patients and control groups. Drawing the blood into a test tube containing an anticoagulant (EDTA) to stop it from clotting.

Hematological Assay

Determination of WBC, Lymphocyte, Neutrophil, and MPV was carried out by auto hematology analyzer and estimation of ESR by wintrobe method.

Statistical Analysis

The Statistical Analysis System- SAS (2012) program was used to study of difference factors in study parameters. LSD test was used to significant compare between means. Estimate of correlation coefficient in this study between difference parameters (SAS, 2012).

3. Results

The results of the present study show a high significant ($p < 0.01$) increase in the means of WBC in AA patients compared with positive and negative control. The means of WBC count are 9.98 ± 0.74 , 8.13 ± 0.67 and $6.99 \pm 0.43 \times 10^3 \text{ cell}/\mu\text{L}$ in AA patients, positive and negative control groups, respectively. While there is non-significant difference in the means of lymphocyte count in AA patients compared with positive and negative control. The means of lymphocyte count are 1.99 ± 0.24 , 2.24 ± 0.21 and $2.07 \pm 0.16 \times 10^3 \text{ cell}/\mu\text{L}$ in AA patients, positive and negative control groups, respectively. There is also a highly significant ($p < 0.01$) increase in neutrophil count in AA patients compared with negative control. The means of neutrophil count are

6.59 ± 0.64 and $4.09 \pm 0.35 \times 10^3 \text{ cell}/\mu\text{L}$ in AA patients and negative control, respectively. In addition, there is no significant difference in neutrophil count in AA patients compared with positive control. The mean of neutrophil count in positive control is $5.18 \pm 0.70 \times 10^3 \text{ cell}/\mu\text{L}$. While there is no significant difference in neutrophil count in positive control compared with negative control (Table 1).

Concerning the results in Table (2), they show a highly significant ($p < 0.01$) decrease in MPV means in AA patients compared with negative control. The means of MPV are 8.49 ± 0.62 and $11.45 \pm 0.35 \text{ fL}$ in AA patients and negative control, respectively. While there is highly significant ($p < 0.01$) decrease in the MPV in positive control compared with negative control and no significant difference in MPV means in AA patients compared with positive control. The mean of MPV in positive control is $9.48 \pm 0.62 \text{ fL}$.

Table (2) also demonstrate a high significant ($p < 0.01$) increase in the means of ESR in AA patients compared with positive and negative control. The means of ESR are 26.94 ± 5.94 , 9.70 ± 2.50 and $10.76 \pm 2.92 \text{ mm}/\text{hr}$ in AA patients, positive and negative control groups, respectively. While there is no significant difference in ESR means in positive control compared with negative control.

Table 1: The counts of WBC, lymphocytes and neutrophils in AA patients and negative and positive controls

Groups	No.	Mean \pm SE		
		WBC count ($\times 10^3 \text{ cells}/\mu\text{L}$)	Lymphocytes count (%)	Neutrophils count (%)
Negative control (-ve)	20	6.99 ± 0.43 B	2.07 ± 0.16 A	4.09 ± 0.35 B
Positive control (+ve)	20	8.13 ± 0.67 B	2.24 ± 0.21 A	5.18 ± 0.70 AB
Patients	40	9.98 ± 0.74 A	1.99 ± 0.24 A	6.59 ± 0.64 A
LSD value	---	1.778 **	0.591 NS	1.627 **
P-value	---	0.0044	0.702	0.0098

** ($P < 0.01$), NS: Non-Significant.
 Means having with the different letters in same column differed significantly.

Table 2: The means of MPV and ESR in AA patients and negative and positive controls

Groups	No.	Mean \pm SE	
		MPV (fL)	ESR (mm/h)
Negative control (-ve)	20	11.45 ± 0.35 A	10.76 ± 2.92 B
Positive control (+ve)	20	9.48 ± 0.62 B	9.70 ± 2.50 B
Patients	40	8.49 ± 0.62 B	26.94 ± 5.94 A
LSD value	---	1.536 **	11.277 **
P-value	---	0.0009	0.0058

** ($P < 0.01$).
 Means having with the different letters in same column differed significantly.

convenient inflammatory markers presented in CBC have been studied to evaluate their value in establishing the diagnosis of acute appendicitis. Similar to literature, we found that WBC count was significantly higher in AA patients, the increased WBC count is the earliest and the most frequently diagnosis tool used in acute appendicitis (Boshnak *et al.*, 2017). Several reports suggest that an elevated leukocyte count is usually the earliest laboratory test to indicate appendiceal inflammation, and most of the patients with acute appendicitis present with leukocytosis (Al-gaithy, 2017).

With the objective of an earliest and most accurate diagnosis of acute appendicitis, mainly in most advanced stages, some authors have described the relation of the percentage of polymorphonuclear leucocytes with necrosis and appendix perforation (Anderson *et al.*, 1999; Anderson and Anderson, 2008; Keske *et al.*, 2008). According to those authors a value of segments above 85% would be related to the advanced stages of appendix infection (Goulart *et al.*, 2012).

Grönroos *et al.* (1994) were the first to report that an increased leukocyte count was a very early marker of

4. Discussion

Appendectomy is one of the most common procedures done in surgical emergency, differential diagnosis of acute appendicitis is still a matter of debate in some atypical cases where delayed or inaccurate diagnosis may lead to several complications (Jones *et al.*, 2004). Radiological imaging modalities that help in the decision for surgery may not confirm the diagnosis or may not be available in some hospitals (Terasawa *et al.*, 2004; Al-Khayal and Al-Omran, 2007). For this reason, inexpensive, readily available, and

appendiceal inflammation in adult patients. Further, Yokoyama *et al.* (2009) reported that WBCs counts and neutrophil percentage are not useful for surgical indication.

In addition, the results of the present study show that there is no significant difference in lymphocyte count in AA patients compared with controls. Goulart *et al.* (2012) no relevant data was found in literature comparing lymphopenia and evolution stage of appendix infection.

Our results showed that neutrophil percentage were elevated in the vast majority of patients with acute appendicitis. Consequently. Both WBC count and neutrophil percentage are not specific for acute appendicitis. Leukocytosis is a non-specific reaction caused by acute or chronic inflammation, acute physical or emotional stress and several other conditions. This is reflected in several reports and in the present study by a rather low specificity for acute appendicitis. Increases in neutrophil percentage also can occur in various bacterial infections. Therefore, a raised leucocyte count or neutrophil percentage cannot effectively support the diagnosis of acute appendicitis (Yang *et al.*, 2006).

There are a few studies regarding the role of MPV in AA diagnosis in children and adults, albeit with variable results (Albayrak *et al.*, 2011; Bilic *et al.*, 2011; Uyanik *et al.*, 2012; Narci *et al.*, 2013). A study comparing a healthy adult control group and an adult patients group with AA found significantly lower MPV level, and our study is similar to the previous study that MPV is lower than controls. However, the complicated appendicitis group had a lower MPV measurement value compared to other groups. The reduction in MPV levels was explained as the sequestration of larger thrombocytes in the vascular segments of the inflamed intestines (Danese *et al.*, 2004). However, as there are not many studies on this subject, it is clear that further studies should be conducted in this field (Bozkurt *et al.*, 2015).

ESR was highly increased significantly and that similar to study done by Dahmardehei *et al.* (2013) were studied that ESR had significant statistical correlation with pathological diagnosis of acute appendicitis.

Berenji *et al.* (2010) found that sensitivity and positive predictive value of ESR can strengthen the clinical diagnosis of acute appendicitis. In Shukla *et al.* (2015) study the association of ESR and acute appendicitis was shown to be significant with value. According to many unspecific studies, the review of ESR in the diagnosis of acute appendicitis has been very time-consuming and does not have high value. Today, the use of time-consuming and costly diagnostic procedure in the diagnosis of appendicitis has been limited and patients and their health care providers prefer to use technologies with lower costs and side-effects (Dahmardehei *et al.*, 2013).

Conclusion

Elevated WBC, neutrophil counts and ESR may be used as diagnostic tests in cases of acute appendicitis, while lymphocyte and MPV levels were not useful as diagnostic markers.

References

- [1] Liu S., Pei F., Wang X., Li D., Zhao L., Song Y., Chen Z. and Liu B. (2017). "The immune impact of mimic endoscopic retrograde appendicitis therapy and appendectomy on rabbits of acute appendicitis." *Oncotarget* 8(39): 66528-66539.
- [2] Baird D., Simillis C., Kontovounisios C., Rasheed S. and Tekkis P. (2017). "CLINICAL UPDATES Acute appendicitis."
- [3] Rashid B. (2013). "Relation ship between increased WBC with increased lipid profile in blood." *Diyala Journal of Medicine* 5(2): 83-90.
- [4] Chabot-Richards D. and George T. (2014). "Leukocytosis." *International journal of laboratory hematology* 36(3): 279-288.
- [5] Kolaczowska E. and Kuberski P. (2013). "Neutrophil recruitment and function in health and inflammation." *Nature Reviews Immunology* 13(3): 159.
- [6] Honda T., Uehara T., Matsumoto G., Arai S. and Sugano M. (2016). "Neutrophil left shift and white blood cell count as markers of bacterial infection." *Clinica Chimica Acta* 457: 46-53.
- [7] Reiner S. and Adams W. (2014). "Lymphocyte fate specification as a deterministic but highly plastic process." *Nature Reviews Immunology* 14(10): 699.
- [8] Tosato F., Bernardi D., Sanzari M., Pantano G. and Plebani M. (2013). "Biological variability of lymphocyte subsets of human adults' blood." *Clinica Chimica Acta* 424: 159-163.
- [9] Cure M., Cure E., Yuce S., Yazici T., Karakoyun I. and Efe H. (2014). "Mean platelet volume and vitamin D level." *Annals of laboratory medicine* 34(2): 98-103.
- [10] Kucu K. E. and Kucu K. I. (2015). "Mean platelet volume is reduced in acute appendicitis." *Turkish journal of emergency medicine* 15(1): 23-27.
- [11] Al-Imi A.: Effect of erythropoietin on haematological and biochemical indices in patient with chronic kidney disease, doctor of philosophy, Iraq, University of Baghdad, College of Science, Biology Department- Zoology/Physiology, 2013, 20.
- [12] Adhikari B., Patra S., Chanda C. and Shrivastava R. (2017). "Erythrocyte sedimentation rate, measurement by capillary tube method, (Micro-ESR)-best method for neonate and small children." *J Med Sci Clin Res* 5(05): 22135-22137.
- [13] SAS. (2012). *Statistical Analysis System, User's Guide*. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.
- [14] Jones K., Penn A., Dunn L., Nadalo L. and Mangram A. (2004). "Are negative appendectomies still acceptable?" *The American journal of surgery* 188(6): 748-754.
- [15] Terasawa T., Blackmore C., Bent S. and Kohlwe R. (2004). "Systematic review: computed tomography and ultrasonography to detect acute appendicitis in adults and adolescents." *Annals of internal medicine* 141(7): 537-546.
- [16] Al-Khayal K. and Al-Omran M. (2007). "Computed tomography and ultrasonography in the diagnosis of equivocal acute appendicitis. A meta-analysis." *Saudi medical journal* 28(2): 173-180.
- [17] Boshnak N., Boshnaq M. and Elgohary H. (2017). "Evaluation of Platelet Indices and Red Cell Distribution

- Width as New Biomarkers for the Diagnosis of Acute Appendicitis." *Journal of Investigative Surgery*: 1-9.
- [18] Al-gaithy Z. (2012). "Clinical value of total white blood cells and neutrophil counts in patients with suspected appendicitis: retrospective study." *World Journal of Emergency Surgery* 7(1): 32.
- [19] Andersson R., Hugander A., Ghazi S., Ravn H., Offenbart S., Nystrom P. and Olaison G. (1999). "Diagnostic value of disease history, clinical presentation, and inflammatory parameters of appendicitis." *World journal of surgery* 23(2): 133-140.
- [20] Andersson M. and Andersson R. (2008). "The appendicitis inflammatory response score: a tool for the diagnosis of acute appendicitis that outperforms the Alvarado score." *World journal of surgery* 32(8): 1843-1849.
- [21] Keskek M., Tez M., Yoldas O., Acar A., Akgul O., Gocmen E. and Koc M. (2008). "Receiver operating characteristic analysis of leukocyte counts in operations for suspected appendicitis." *The American journal of emergency medicine* 26(7): 769-772.
- [22] Goulart R., Silvério G., Moreira M. and Franzon O. (2012). "Main findings in laboratory tests diagnosis of acute appendicitis: a prospective evaluation." *ABCD. Arquivos Brasileiros de Cirurgia Digestiva (São Paulo)* 25(2): 88-90.
- [23] Grönroos J., Forsstrom J., Irjala K. and Nevalainen T. (1994). "Phospholipase A2, C-reactive protein, and white blood cell count in the diagnosis of acute appendicitis." *Clinical chemistry* 40(9): 1757-1760.
- [24] Yokoyama S., Takifuji K., Hotta T., Matsuda K., Nasu T., Nakamori M., Hirabayashi N., Kinoshita H. and Yamaue H. (2009). "C-Reactive protein is an independent surgical indication marker for appendicitis: a retrospective study." *World Journal of Emergency Surgery* 4(1): 36.
- [25] Yang H., Wang Y., Chung P., Chen W., Jeng L. and Chen R. (2006). "Laboratory tests in patients with acute appendicitis." *ANZ journal of surgery* 76(1-2): 71-74.
- [26] Albayrak Y., Albayrak A., Albayrak F., Yildirim R., Aylu B., Uyanik A., Kabalar E. and Guzel I. (2011). "Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis." *Clinical and Applied Thrombosis/Hemostasis* 17(4): 362-366.
- [27] Bilici S., Sekmenli T., Göksu M., Melek M. and Avci V. (2011). "Mean platelet volume in diagnosis of acute appendicitis in children." *African health sciences* 11(3).
- [28] Uyanik B., Kavalci C., Arslan E., Yilmaz F., Aslan O., Dede S. and Bakir F. (2012). "Role of mean platelet volume in diagnosis of childhood acute appendicitis." *Emergency medicine international* 2012.
- [29] Narci H., Turk E., Karagulle E., Togan T. and Karabulu K. (2013). "The role of mean platelet volume in the diagnosis of acute appendicitis: a retrospective case-controlled study." *Iranian Red Crescent Medical Journal* 15(12).
- [30] Danese S., Motte C. and Fiocchi C. (2004). "Platelets in Inflammatory Bowel Disease: Clinical, Pathogenic, and Therapeutic Implications." *American Journal Of Gastroenterology* 99: 938.
- [31] Bozkurt S., Köse A., Erdogan S., Bozali G., Ayrik C., Arpaci R., Özgür A., Dündar G. and Türkmenoglu O. (2015). "MPV and other inflammatory markers in diagnosing acute appendicitis." *J Pak Med Assoc* 65(6): 637-641.
- [32] Dahmardehei M., Khazaei A., Vahab M. and Sargazimoghadam M. (2013). "Diagnostic Value of Leukocytosis, ESR and CRP in Patients with Suspected Acute Appendicitis." *Zahedan Journal of Research in Medical Sciences* 15(7): 59-63.
- [33] Berenji M., yarabbi A., EshaghHoseini N., GhaziSaeadi R. and Vagharian V. (2010). "Association rate of leukocytosis increased CRP and ESR with acute appendicitis." *EBNESINA* 13(1): 24-27.
- [34] Shukla S., Baweja I., Gupta R., Chawla I., Bal M. and Bodal V. (2015). "Estimation of ESR, CRP, TLC and DLC in 200 Suspected Cases of Acute Appendicitis." *Research Journal of Pharmaceutical, Biological and Chemical Sciences.* 6(2): 732-737.