



Utility Of Serum Immature Granulocytes In Predicting Acute Appendicitis – An Indian Monocenter Retrospective Study

Dr. Sunderesh Kamal Chander.U, Dr. B Vinothkumar*, Dr. Yogalakshmi . E, Dr. Muthuvel. E

*Corresponding Author:
Dr. B .Vinothkumar

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Aim: To determine the reliability of immature granulocytes and neutrophils lymphocyte ratio in acute appendicitis. To compare these parameters between acute appendicitis patients and normal subjects

Study Design: A retrospective study

Place of Study: This study was carried out in Saveetha Medical College and Hospital, Tamil Nadu, India.

Methodology: A study was started after obtaining approval from the ethics committee. Out of 60 subjects, 30 patients underwent appendectomy and were histopathologically diagnosed with acute appendicitis. The remaining 30 subjects were normal healthy individuals. Demographic details, preoperative total leukocyte count, neutrophil per cent, lymphocyte per cent, neutrophil/lymphocyte ratio, and IG% were measured using an automated haematological analyzer XN 1000 and were compared with patients with acute appendicitis and normal subjects.

Conclusion: Our study showed the early diagnostic ability of immature granulocytes and neutrophils lymphocyte ratio for acute appendicitis was not significant.

Keywords: Acute appendicitis, Immature granulocytes, Total leukocyte count, neutrophil-lymphocyte ratio.

Introduction

The appendix is a finger-shaped tube approximately three inches long extending from the right side of the large intestinal region. The exact function of this appendix is not very clear. A condition in which the wall of the appendix becomes inflamed, edematous, and the lumen filled with pus, is known as appendicitis. Acute appendicitis is a medical emergency that needs immediate surgical intervention. If not untreated, there are high chances, the appendix will rupture spreading the infectious material into the abdominal cavity and pelvic cavity. Sometimes it leads to peritonitis, which will be a fatal complication if left untreated immediately. Appendicitis can strike at any age but is common between the ages of 15 and 35 years. It is very important to promptly assess the severity of appendicitis and we have different haematological parameters that can give an early estimate of disease

severity. However, clinical examination with a thorough physical examination remains vital to assess patients with unconfirmed acute appendicitis. Appendectomy surgical resection, whether a laparoscopic procedure or open is the most frequently performed surgical intervention worldwide[1]. After surgery, appendix tissue samples are taken to evaluate for histopathological examination for variable acute inflammation with a predominance of neutrophils; which involves some or all layers of the appendiceal wall and epithelial ulceration (Figure 1). However many times histology turned out to be negative either due to improper evaluation or resolve inflammatory response.

Immature granulocytes and neutrophils lymphocyte ratio have implications for patients with acute appendicitis, who do not routinely undergo radiological scanning in pregnant patients, or pediatric patients, and in some countries immediate

access to CT scans is limited. Immature white blood cells are immature granulocytes. However, our body is fighting an infection, it will increase more leukocyte blood cells will be immature. Immature granulocyte counts are often tests for patients that are highly susceptible to developing infections and inflammatory conditions. They may be accompanied by immunosuppression. Generally, an increase in the number of immature granulocytes will accompany raised absolute neutrophil counts. This study aimed to investigate the prognostic value of the immature granulocytes, and neutrophils lymphocyte ratio in acute appendicitis and determine its significance [2].

Material And Methods :

A retrospective study was carried out in line with research regulations, including the approval of the

Ethical Committee. The study includes 60 subjects, out of which 30 patients underwent appendectomy and were histopathologically diagnosed with acute appendicitis (group A). The remaining 30 subjects were normal healthy individuals(group B). The was conducted at Saveetha medical hospitals from December 2021 to March 2022. In these groups, the preoperative total leukocyte count, neutrophil count, and immature granulocyte counts were obtained using Sysmex Automated Analyzer NX1000. Neutrophil/lymphocyte (N/L) ratios were calculated by dividing Absolute neutrophil count and Absolute lymphocytes count. These haematological parameters were standardized by routine external and internal quality control checks. The demographic data and preoperative haematological parameters were analyzed and compared between these groups.

Figure 1 : Histopathological findings of Acute appendicitis

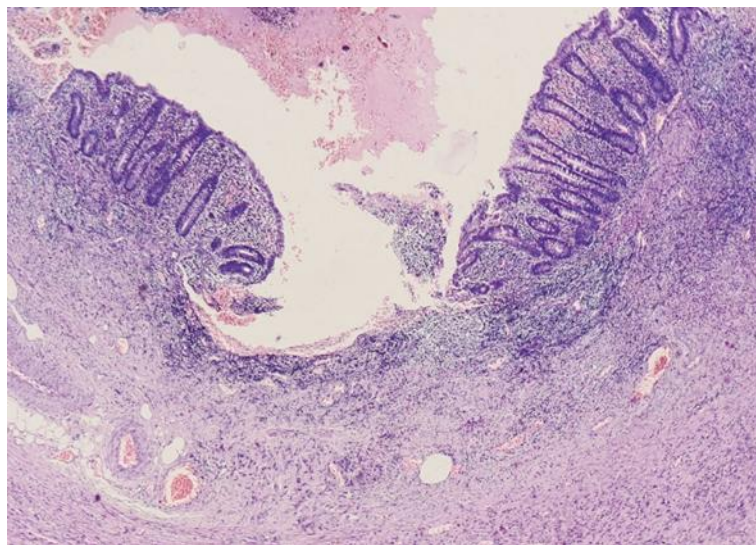
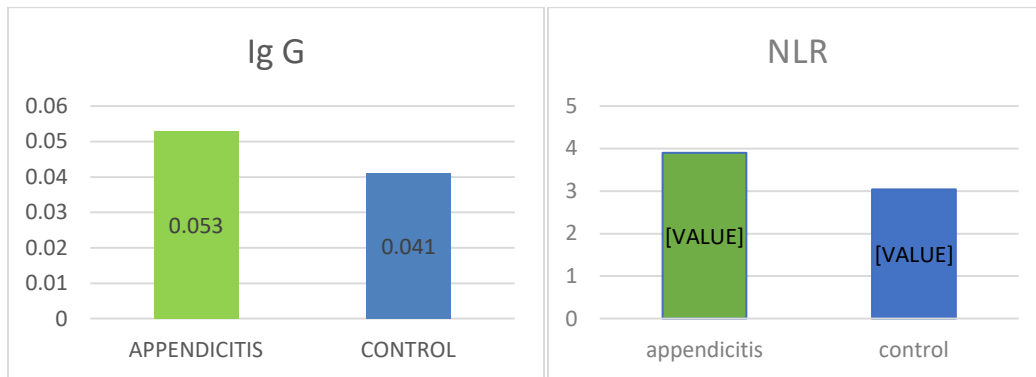


Table 1: Comparison of leukocyte parameters and immature granulocytes in the acute appendicitis group with the control group

Parameters	Acute appendicitis patients (n= 30)	Normal individual (n= 30)	P- value (0.05)
Age	30 ± 12	35 ± 17	0.19
WBC (x 10 ³ /µl)	7.4 ± 4.3	6.78 ± 2.4	0.17
Neutrophil count	67.9 ± 12.67	62.96 ± 15.71	0.18

Lymphocyte count	24.67± 11.27	21.62 ± 6.38	0.20
Immature granulocyte percentage	0.053 ± 0.02	0.041± 0.03	0.10
Neutrophil lymphocyte ratio	3.9 ± 3.09	3.04 ± 1.35	0.15

Figure 2a & b



Results :

In our study, out of a total of 60 cases, 30 were acute appendicitis patients (proven by histopathological examination) and another 30 were normal individuals (control). In acute appendicitis case, WBC count was 7.4 ± 4.3 , Neutrophil count was 67.9 ± 12.67 , Lymphocyte count was 24.67 ± 11.27 , Immature granulocyte percentage was 0.053 ± 0.02 , Neutrophil lymphocyte ratio was 3.9 ± 3.09 . In control, WBC count was 6.78 ± 2.4 , Neutrophil count was 62.96 ± 15.71 , Lymphocyte count was 21.62 ± 6.38 , Immature granulocyte percentage is 0.041 ± 0.03 , Neutrophil lymphocyte ratio is 3.04 ± 1.35 . On comparison between these group P-value for WBC count was 0.17, Neutrophil count was 0.18, Lymphocyte count was 0.20, Immature granulocyte percentage was 0.10, and Neutrophil lymphocyte ratio was orifice. P-value greater than 0.05 means which was not statistically significant in all parameters and the null hypothesis was not rejected (Table 1).

Discussion :

Obstruction of the appendiceal orifice leads to an increase in intraluminal and intramural pressure, resulting in small vessel occlusion and lymphatic

stasis which leads to a wall of the appendix being ischemic and necrotized. Recent studies have demonstrated that the Immature granulocyte and neutrophil-lymphocyte ratio can be used as an effective inflammatory marker in acute appendicitis. Due to recent technologies, it has been possible to detect the percentage and number of IG due to technical developments in automated haematological analyzers. NLR and immature granulocytes are inexpensive, simple biomarkers that can be studied in almost any medical centre and have recently been used in many diseases, including inflammatory conditions. In a retrospective study increased neutrophil ratio, was detected as a good diagnostic marker in acute appendicitis. The sensitivity of the neutrophil ratio has been 60.1% and specificity 76.9% in diagnosing acute appendicitis. The neutrophil ratio seems to be a better inflammatory marker in acute appendicitis. A neutrophil rate above 85% has been associated with advanced appendicular inflammation. However, the neutrophil ratio was not a proper laboratory test to predict complicated appendicitis. The neutrophil-to-lymphocyte ratio (NLR) is a simple and easy-calculated biomarker to asses the inflammatory status. It gives values about two inflammatory cells since NLR will be useful in

predicting appendicitis and its severity. Hajibandeh et al. Demonstrated a study that children with NLR > 8.8 are at higher risk of appendicitis [3,4,5].

Immature granulocytes have recently become easily measurable. Immature granulocytes are generated and differentiated in bone marrow, and their presence in peripheral granulocyte circulation indicates greatly increased bone marrow activation due to an inflammatory condition. Measurement of immature myeloid cells such as bands has been considered clinically useful for the diagnosis of infection and inflammatory conditions. However, most the medical centre have stopped performing manual band counts because they were proven to be inaccurate and imprecise. But the major problem with the band count is the inability to reproducibly identify band neutrophils. The literature contains at least three different definitions of a band neutrophil, leading to unacceptably wide observer variability [6,7,8,9].

Other immature granulocytes including metamyelocytes, myelocytes, and promyelocytes have better morphological definition and together can be used as an alternative to the band count. Immature granulocytes are usually not detected in healthy individuals but are elevated in patients with acute appendicitis, infections, acute inflammatory disorders, and tissue necrosis. [10,11] Usually, an increase in IG is accompanied by an increase in the absolute neutrophil count. However, in a trial with 403 patients, Park et al. discovered that the sensitivity of IG% was insufficient for the diagnosis of acute appendicitis and did not give any significant advantage when compared to other inflammatory markers. In contrast, another investigation comprising 438 patients reported that the IG value was a quick, easy-to-access, and reliable measure in both the diagnosis of Acute appendicitis and Subacute appendicitis [12,13].

Conclusion

The present study showed immature granulocytes and neutrophils lymphocyte ratio is not a conclusive biomarker for patients with acute appendicitis, and it has no additional benefits over other inflammatory markers. A combination of clinical history data, physical examinations, and laboratory investigation are needed to establish for early diagnosis of acute appendicitis. Further studies are required to assess whether combining these parameters with other

commonly used biomarkers such as CRP, Tumor Necrosis Alpha, Alpha 1-Glycoprotein, leukocyte elastase complex, and Interleukine-6,8 would result in a better predictive value.

Limitations of the study

There were some limitations in our study. Firstly, this was a retrospective study and done small scale. Secondly, it was not possible to include the time from the onset of symptoms to the collection of samples, which is an important limiting factor.

Disclaimer

The products used for this research are commonly and predominantly used products in our area of research and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

Ethical approval

This study was approved by the Ethics Committee of Saveetha Medical and Hospital.

Acknowledgement

I sincerely thank Saveetha Medical College and Hospital, Chennai, for their continued support in the procurement of the data. I also extend heartfelt gratitude to, all the faculties in the Department of Pathology, Especially to my research guide Dr Yogalakshmi. E and to my HOD Dr Chitra Srinivasan. We thank all patients who participated in this study. Thanks to all health care workers in our hospital for their efforts in caring for these patients.

Reference

1. Bhangu A, Soreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. *Lancet*. 2015;386:1278-1287.
2. Mathews EK, Griffin RL, Mortellaro V, et al. Utility of immature granulocyte percentage in pediatric appendicitis. *J Surg Res*. 2014;190:230-234.
3. Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Trobs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg*. 2006;6:15.

4. McGowan DR, Sims HM, Zia K, Uheba M, Shaikh IA. The value of biochemical markers in predicting a perforation in acute appendicitis. *ANZ J Surg.* 2013;83:79-83.
5. Hajibandeh, S., Hajibandeh, S., Hobbs, N., and Mansour, M. (2020). Neutrophil-to-lymphocyte Ratio Predicts Acute Appendicitis and Distinguishes between Complicated and Uncomplicated Appendicitis: A Systematic Review and Meta-Analysis. *Am. J. Surg.* 219 (1), 154–163. doi:10.1016/j.amjsurg.2019.04.018
6. Unal Y. A new and early marker in the diagnosis of acute complicated appendicitis: immature granulocytes. *Ulus Travma Acil Cerrahi Derg.* 2018;24:434-9.
7. Park JS, Kim JS, Kim YJ, et al. Utility of the immature granulocyte percentage for diagnosing acute appendicitis among clinically suspected appendicitis in adult. *J Clin Lab Anal.* 2018;32:e22458.
8. Ha, S.O.; Park, S.H.; Park, S.H.; Park, J.S.; Huh, J.W.; Lim, C.M.; Koh, Y.; Hong, S.B.; Jang, S. Fraction of immature granulocytes reflects severity but not mortality in sepsis. *Scand. J. Clin. Lab. Investig.* 2015, 75, 36–43.
9. Geest, P.J.; Mohseni, M.; Brouwer, R.; van der Hoven, B.; Steyerberg, E.W.; Groeneveld, A.B. Immature granulocytes predict microbial infection and its adverse sequelae in the intensive care unit. *J. Crit. Care* 2014, 29, 523–527.
10. Guraya SY, Al-Tuwaijri TA, Khairy GA, Murshid KR. Validity of leukocyte count to predict the severity of acute appendicitis. *Saudi Med J.* 2005;26:1945–1947.
11. Coleman C, Thompson JE Jr, Bennion RS, Schmit PJ. White blood cell count is a poor predictor of the severity of disease in the diagnosis of appendicitis. *Am Surg.* 1998;64:983–985.
12. Khan A, Riaz M, Kelly ME, Khan W, Waldron R, Barry K, et al. Prospective validation of neutrophil-to-lymphocyte ratio as a diagnostic and management adjunct in acute appendicitis. *Ir J Med Sci.* 2018 May;187(2):379-384.
13. Kahramanca S, Ozgehan G, Seker D, Gökce EI, Seker G, Tunç G, Küçükpınar T, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. *Ulus Travma Acil Cerrahi Derg.* 2014 Jan;20(1):19-22