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The Role of Lymphocyte-to-Monocyte Ratio Levels in Diagnosis of Appendicitis in Children

Çocuklarda Apendisit Tanısında Lenfosit Monosit Oranı Değerinin Rolü

ABSTRACT

Objective:
Appendicitis is the most common surgical disease with right lower abdominal pain in pediatric age. This study aimed to investigate the diagnostic value of lymphocyte monocyte ratio (LMR) in appendicitis in children.

Material and Methods:
A total of 150 patients under the age of 18 who were admitted to the hospital and given blood samples due to reasons of non-inflammatory conditions and were proved to have appendicitis (non-complicated or complicated) between 2017 and 2020 were analyzed retrospectively. Patients were classified into three subgroups: Group 1 (healthy children without any inflammation, n=50), Group 2 (non-complicated appendicitis, n=50) and Group 3 (complicated appendicitis, n=50).

Results:
The median LMR level was significantly lower in the non-complicated and complicated appendicitis groups than in group 1 (p=0.00). The cut-off value of LMR on admission to predict non-complicated appendicitis was 2.98 with a sensitivity of 94% and a specificity of 96% (area under the curve, 0,960, p= 0.000). The cut-off value of LMR on admission to predict complicated appendicitis was 2.15 with a sensitivity of 96% and a specificity of 72% (area under the curve, 0,865, p= 0.000).

Conclusion:
This study shows that the LMR ratio may be helpful with high sensitivity and specificity in diagnosing appendicitis.

Key Words:
Appendicitis, Children, Inflammation, Lymphocyte-to-monocyte ratio

ÖZ

Amaç:

Apendisit, çocuk yaş grubunda sağ alt kadran ağrısının en sık cerrahi hastalığıdır. Bu çalışmanın amacı, çocuklarda apendisitte lenfosit monosit oranının (LMO) tanısal değerini araştırmaktır.

Gereç ve Yöntemler:

2017-2020 yılları arasında 18 yaşından küçük inflamatuar olmayan nedenlerle hastaneye başvurup kanları alınan ve apendisit (komplike olmayan veya komplike olan) tanısı almış toplam 150 hasta retrospektif olarak incelendi. Hastalar Grup 1 (inflamasyonu olmayan sağlıklı çocuklar, n=50), Grup 2 (komplike olmayan apendisit, n=50) ve Grup 3 (komplike apendisit, n=50) olmak üzere üç alt gruba ayrıldı.

Bulgular:

Ortalama LMO düzeyinin komplike olmayan ve komplike apendisit gruplarında Grup 1'e göre anlamlı olarak düşük olduğu görüldü (p=0.000). LMO'nun komplike olmayan apandisiti öngörmek için başvurudaki cut-off değeri 2,98'dir, duyarlılığı %94 ve özgüllüğü %96'dır (eğrinin altındaki alan, 0,960, p= 0.000). LMO'nin başvuruda komplike apandisiti öngörmek için cut-off değeri 2,15, duyarlılığı %96 ve özgüllüğü %72 idi (eğri altındaki alan, 0,865, p= 0.000).

Sonuç:

Bu çalışma, LMO oranının yüksek duyarlılık ve özgüllük ile apandisit tanısının koyulmasında yardımcı olabileceğini göstermektedir.

Anahtar Kelimeler:

Apandisit, Çocuk, İnflamasyon, Lenfosit monosit oranı

INTRODUCTION

Appendicitis is the most common surgical disease with right lower abdominal pain in pediatric age (1–3). The diagnosis of appendicitis is led by detailed medical history, physical examination, blood parameters and imaging methods such as ultrasound and computed tomography (3, 4). The diagnosis of appendicitis can still be clinically challenging because of the non-specific presentation of the disease (5). Despite the increasing incidence of appendicitis in the literature, misdiagnoses or late diagnoses result in perforation, abscess formation and a high rate of negative appendectomies (6).

Complete blood count (CBC) is used for diagnosing medical conditions (7). The laboratory tests such as white blood cells (WBC), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP) as valuable parameters of inflammatory conditions have been used for a long time to help the diagnosis (3). NLR and lymphocyte-to-monocyte ratio (LMR), calculated with CBC, have been investigated as potential biomarkers for various diseases (7). Among these, WBC and CRP are non-specific blood parameters for the diagnosis of appendicitis. These inflammatory markers can also elevate with other non-surgical abdominal diseases (2). Therefore, diagnostic discrimination between appendicitis and non-surgical diseases is difficult. In conclusion, there is a need for inflammatory markers which can be helpful for diagnosis. Other inflammatory markers such as NLR and LMR may also be useful for evaluating systemic inflammatory status (3, 8).

This study aimed to investigate the evaluation of LMR levels during stages of appendicitis and compare the results with the healthy control group. WBC, CRP and NLR were also studied and correlation with LMR was evaluated in the diagnosis of appendicitis.

MATERIAL and METHODS

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Ankara Medical Faculty Ethical Committee, Ankara University (i11-706-20). One hundred and fifty patients under the age of 18 who were admitted to the Pediatric Emergency Clinic and Pediatric Surgery Clinic between 2017 and 2020 were recorded retrospectively. Patients were classified into three groups. Each group included 50 patients. Group 1 was non-inflammatory conditions (appealed with non-abdominal pain which was an inguinal hernia, undescended testes, etc., and taken blood samples before surgery), Groups 2 and 3 were inflammatory conditions which were diagnosed with non-complicated appendicitis and complicated appendicitis, respectively. Radiologic imaging and clinical status were the decisive points for groups 2 and 3. Pathological specimen results were controlled with the radiological and surgical diagnosis for groups 2 and 3. Excluded criteria for this study were as follows: age above 18 years, another different reason for abdominal pain such as urinary tract infection, gastroenteritis, or hematologic disease. Demographic and laboratory data were recorded. WBC and CRP levels were studied in all groups, and LMR and NLR values were calculated.

Statistical Analysis

The data were analyzed using SPSS for Windows (SPSS 23.0 IBM, Amarok, NY, USA). Normally distributed data in more than two groups were compared with ANOVA and a Kruskal-Wallis variant analysis was used for the data that were not normally distributed. The Spearman test was used for correlation analysis. The strongest correlations were presented, as indicated by the Spearman test $r>0.6$ and $r<0.6$. ROC curve was used to determine whether LMR levels had characteristics to distinguish appendicitis from the other group. The cut-off value (the value at the point where sensitivity and selectivity were the highest was determined as the cut-off value) was calculated. p values <0.05 were considered statically significant.

RESULTS

The study included a total of 150 children younger than 18 years of age who were admitted for various reasons with non-inflammatory disease and appendicitis to the pediatric emergency clinic and pediatric surgery outpatient clinic, respectively. Group 1 was chosen from the 50 healthy children admitted to the pediatric surgery outpatient clinic. Groups 2 and 3 were selected from the 50 children for each group; patients were admitted to the pediatric emergency clinic for abdominal pain and diagnosed with non-complicated and complicated appendicitis. A random numbers table was used for choosing the patients. According to gender, 85 (56.6%) of 150 patients were males and 65 (43.4%) were females. There were no statistical differences between groups for gender (p=0.054). The mean ages of groups 1, 2 and 3 were 11.74, 11,5, and 9,96 years, respectively. The mean WBC, median CRP, LMR, and NLR levels are shown in Table I.

Table I. Gender, Median age, Mean WBC levels, Median CRP levels, Median NLR levels and Median LMR levels

	Group 1 (n=50)	**Group 2 (n=50)**	**Group 3 (n=50)**
Gender	23M /27F	36M / 14F	26M / 24F
Median Age (Min.-Max.)	12 (4-17)	11 (5-17)	10 (2-17)
Mean WBC levels (Min.-Max.)	6.920±1.465 (4.250-10.200)	16.351±5.147 (5.300-27.200)	17.847±5.721 (3.010-32.730)
Median CRP levels (Min.-Max.)	0.85 (0.10-11.90)	9.75 (0.20-151.70)	138.15 (16.90-380.90)
Median NLR levels (Min.-Max.)	1.31 (0.30-4.96)	6.35 (0.92-44.40)	8.43 (2.60-39.64)
Median LMR levels (Min.-Max.)	5.43 (3.51-10.40)	1.94 (0.90-5.32)	1.29 (0.41-2.90)

The WBC was significantly higher in groups 2 and 3 than in group 1 (p=0.000). There were no statistical differences between groups 2 and 3 (p=0.617). The CRP level for group 3 was significantly higher than group 1 and group 2 (p=0.000). The median NLR value was significantly higher in group 2 and 3 patients than group 1 patients in the preoperative hemogram parameters (p=0.000). There were statistical differences between group 2 and group 3 (p=0.012). The median LMR level was significantly lower in non-complicated and complicated appendicitis groups than in group 1 (p=0.000). There were statistical differences between group 2 and group 3 (p=0.001).

LMR levels correlated significantly with WBC and CRP (p=0.00). A strong negative correlation was found in WBC (r Spearman= - 0.688) and CRP (r Spearman= - 0.684) (Table II).

Table II. Correlations of LMR,WBC,CRP and NLR LMR

LMR			
Variable	**n**	**r**	**P (<0.05)**
WBC	150	-.688	.000
CRP	150	-.684	.000
NLR	150	-.827	.000

According to ROC analysis, the cut-off value of LMR on admission to predict non-complicated appendicitis was 2.98 with a sensitivity of 94% and a specificity of 96% (area under the curve, 0,960, p= 0.000, Figure 1).

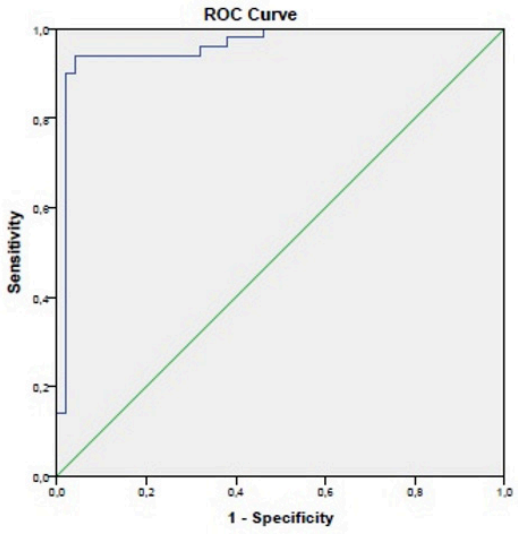

Figure 1. ROC analyses of the diagnostic capability of LMR for non-complicated appendicitis

The cut-off value of LMR on admission to predict complicated appendicitis was 2.15 with a sensitivity of 96% and a specificity of 72% (area under the curve, 0,865, p= 0.000, Figure 2).

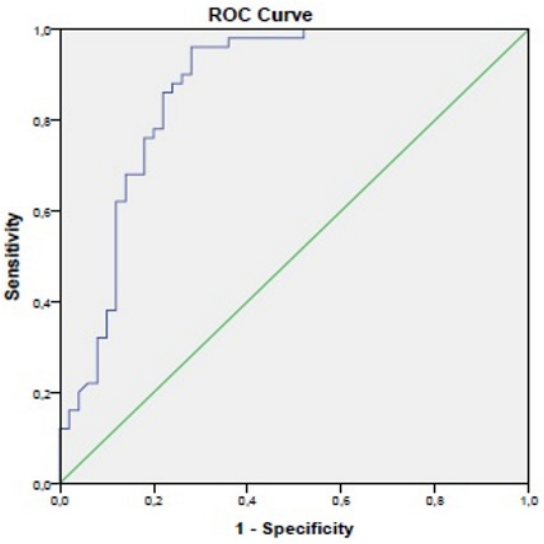

Figure 2. ROC analyses of the diagnostic capability of LMR for complicated appendicitis

DISCUSSION

Diagnosis of appendicitis depends on physical examination together with blood parameters and radiologic evaluation. This study demonstrated that LMR levels are decreased in the non-complicated and complicated appendicitis group compared to the healthy group. Regarding this result, decreased LMR levels may be helpful for the diagnosis of appendicitis in children.

Early diagnosis of appendicitis may sometimes be difficult in children who are admitted with abdominal pain. But this situation is important to prevent complications such as perforation, wound infection, and abscess formation which are associated with increased morbidity and mortality rates (9). WBC, CRP, and NLR which are used as simple parameters for helping the diagnosis, usually improve inflammation processes (3, 10, 11). Unfortunately, there are still no 100% specific and sensitive blood parameters for the diagnosis of appendicitis (3). Wither et al. showed that the sensitivity and specificity of WBC were 69.6% and 43.1%, respectively and the CRP was 95.4% and 24.5%, respectively (12). Kaiser et al. and Shafi et al. also showed that WBC and CRP increased in appendicitis (9, 13). In this study, WBC and CRP levels in the appendicitis group were significantly higher than in the healthy group.

Several studies have shown that NLR, a more sensitive parameter than WBC and CRP, increased in appendicitis (14-16). In this study, NLR levels were higher in children with non-complicated and complicated appendicitis than in group 1 and the levels were highest in complicated appendicitis.

Besides these biomarkers, LMR has been reported as an inflammation marker that may decrease acute or chronic inflammation such as ulcerative colitis, and ovarian tumors (8, 17). This study found that LMR levels for complicated appendicitis were lower than for non-complicated appendicitis. LMR levels over 2.98 have high specificity (96%) and sensitivity (94%) for non-complicated appendicitis. LMR levels over 2.15 have high sensitivity (96%) and acceptable specificity (72%) for complicated appendicitis. These results show that LMR levels accurately distinguish non-complicated and complicated appendicitis in children.

Radiologic evaluation is the commonly preferred method for diagnosis of appendicitis (2). Tuncer et al. showed that the sensitivity and specificity of ultrasound were 91.25% and 60%, respectively (2). The disadvantage of ultrasound is that sonographic evaluation is subjective and unavailable in all hospitals (5). Another radiologic evaluation is computed tomography (CT), which may be counted as an ideal method for diagnosis of appendicitis. Doria et al. showed that the sensitivity and specificity of CT were 94% and 95%, respectively (18). Although CT has higher sensitivity and specificity than ultrasound, exposure to high-level radiation is a significant disadvantage for children (19). For this reason, a specific blood test that gives more accurate results may be needed.

Study Limitations

The limitation of this study was its retrospective nature. The indefinite duration of inflammation at the time of blood sampling might also have affected the analysis and may be counted as another limitation.

CONCLUSION

Diagnosis of appendicitis is still a challenge to emergency physicians and surgeons. Hemogram is a cost-effective and easily applicable parameter for all hospitals. WBC, NLR, and LMR levels are procured easily from hemogram for helping to diagnose acute abdominal pain. LMR levels are significantly lower in non-complicated appendicitis than in healthy children and lowest in complicated appendicitis. LMR may be a novel potential marker for the diagnosis of appendicitis which is identified as non-complicated and complicated appendicitis. Concerning these results, negative appendectomies may be reduced with the help of these biomarkers.

Ethics Committee Approval:
This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Ankara University Medical Faculty Ethical Committee, Ankara University (approval number: i11-706-20).

Informed Consent:
All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:
Concept – K.B., U.A.; Design – K.B., E.E., P.X.; Supervision – K.B., U.A..; Resources – P.X., E.E.; Materials – P.X.; Data Collection and/or Processing – K.B., P.X.; Analysis and/ or Interpretation – E.E., U.A.; Literature Search – G.G., M.B.K., M.Ç.; Writing Manuscript – K.B., E.E., U.A.; Critical Review - G.G., M.B.K., M.Ç

Conflict of Interest:
The authors have no conflict of interest to declare.

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REFERENCES

1. Özdamar MY, Karavaş E. Acute mesenteric lymphadenitis in children: findings related to differential diagnosis and hospitalization. Arch Med Sci 2020; 16(2):313–20.

2. Tuncer AA, Cavus S, Balcioglu A, Silay S, Demiralp İ, Calkan E, Altin MA, Eryilmaz E, Karaisaoglu AO, Bükülmez A, Dogan İ, Embleton DB, Cetinkursun S. Can mean platelet volume, Neutrophil-to-Lymphocyte, Lymphocyte-to-Monocyte, Platelet-to-Lymphocyte ratios be favourable predictors for the differential diagnosis of appendicitis? J Pak Med Assoc 2019; 69(5):647–54.

3. Ates U, Bahadir K, Ergun E, Gollu G, Durmaz M, Gunay F, Erguder I, Bingol-Kologlu M, Yagmurlu A, Dindar H, Cakmak M. Determination of Pentraxin 3 levels in diagnosis of Appendicitis in children. Pediatr Int 2020; 62(5):624-8.

4. Çağlayan F, Çakmak M, Çağlayan O, Çavuşogˇlu T. Plasma D -Lactate Levels in Diagnosis of Appendicitis. J Investig Surg 2003; 16(4):233–7.

5. Glass CC, Rangel SJ. Overview and diagnosis of acute appendicitis in children. Semin Pediatr Surg 2016; 25(4):198–203.

6. Salö M, Roth B, Stenström P, Arnbjörnsson E, Ohlsson B. Urinary biomarkers in pediatric appendicitis. Pediatr Surg Int 2016; 32(8):795–804.

7. Moosmann J, Krusemark A, Dittrich S, Ammer T, Rauh M, Woelfle J, Metzler M, Zierk J. Age- and sex-specific pediatric reference intervals for neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, and platelet-to-lymphocyte ratio. Int J Lab Hematol 2022; 44(2):296–301.

8. Okba AM, Amin MM, Abdelmoaty AS, Ebada HE, Kamel A, Allam A, Sobhy O. Neutrophil/lymphocyte ratio and lymphocyte/monocyte ratio in ulcerative colitis as non-invasive biomarkers of disease activity and severity. Autoimmun Highlights 2019; 10(1):4.

9. Kaiser M, Schroeckenfuchs M, Castellani C, Warncke G, Till H, Singer G. The diagnostic value of hepcidin to predict the presence and severity of appendicitis in children. J Surg Res. 2018; 222:102-7.

10. Huckins DS, Simon HK, Copeland K, Spiro DM, Gogain J, Wandell M. A novel biomarker panel to rule out acute appendicitis in pediatric patients with abdominal pain. Am J Emerg Med 2013; 31(9):1368–75.

11. Lee SK, Lee SC, Park JW, Kim S-J. The utility of the preoperative neutrophil-to-lymphocyte ratio in predicting severe cholecystitis: a retrospective cohort study. BMC Surg 2014; 14(1):100.

12. Wither AS, Grieve A, Loveland JA. Correlation of white cell count and CRP in acute appendicitis in paediatric patients. S Afr J Surg 2019; 57(4):40.

13. Shafi S, Afsheen M, Reshi F. Total leucocyte count, C-reactive protein and neutrophil count: Diagnostic Aid in acute appendicitis. Saudi J Gastroenterol 2009; 15(2):117.

14. Oztan MO, Aksoy Gokmen A, Ozdemir T, Müderris T, Kaya S, Koyluoglu G. Pentraxin-3: A strong novel biochemical marker for appendicitis in children. Am J Emerg Med 2019; 37(10):1912–6.

15. Markar SR, Karthikesalingam A, Falzon A, Kan Y. The diagnostic value of neutrophil: Lymphocyte ratio in adults with suspected acute appendicitis. Acta Chir Belg 2010; 110(5):543–7.

16. Yazici M, Ozkisacik S, Oztan MO, Gürsoy H. Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. Turk J Pediatr 2010; 52(4):400–3.

17. Lu C, Zhou L, Ouyang J, Yang H. Prognostic value of lymphocyte-to-monocyte ratio in ovarian cancer. Medicine (Baltimore) 2019; 98(24):e15876.

18. Doria AS, Moineddin R, Kellenberger CJ, Epelman M, Beyene J, Schuh S, Babyn PS, Dick PT. US or CT for Diagnosis of Appendicitis in Children and Adults? A Meta-Analysis. Radiology 2006; 241(1):83–94.

19. Çetinkaya E, Erdoğan A, Akgül Ö, Çelik C, Tez M. High serum cancer antigen 125 level indicates perforation in acute appendicitis. Am J Emerg Med 2015; 33(10):1465–7.