



Research Article

Ankara Med J, 2020;(4):790-797 // doi 10.5505/amj.2020.66934

EVALUATION OF URINE ANALYSIS IN ADULTS WITH SIMPLE AND COMPLICATED APPENDICITIS BASİT VE KOMPLİKE APANDİSİTLİ ERİŞKİNLERDE İDRAR ANALİZİNİN DEĞERLENDİRİLMESİ

 Handan Özen Olcay¹,  Emine Emektar¹,  Meral Tandoğan¹
 Tuba Şafak¹,  Hakan Bulus²,  Yunsur Cevik¹

¹Ankara Keçiören Eğitim ve Araştırma Hastanesi, Acil Tıp Kliniği

²Ankara Keçiören Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği

Yazışma Adresi / Correspondence:

Handan Özen Olcay (e-mail: hozen84@hotmail.com)

Geliş Tarihi (Submitted): 27.02.2020 // Kabul Tarihi (Accepted): 20.10.2020



Öz

Amaç: Akut apandisit sık görülen abdominal acillerden biridir. Bu çalışmada yetişkin acil servis popülasyonunda basit apandisit ve komplike apandisiti ayırmada rutin idrar tahlilinin kullanılabilirliğini değerlendirmeyi amaçladık.

Materyal ve Metot: Çalışmaya 18 yaş üzeri patolojik tanısı akut apandisit olan ve acil serviste idrar analizi yapılmış hastalar dahil edildi. Eksik verisi olan hastalar çalışma dışı bırakıldı. Patoloji raporlarına göre, hastalar basit ve komplike apandisit olarak sınıflandırıldı.

Bulgular: Basit apandisit grubu ile karşılaştırıldığında komplike apandisit grubunda, idrar keton cisimleri, protein ve nitrit sayımı anlamlı olarak daha yüksekti (tüm değerler için $p < 0,05$). Çok değişkenli lojistik regresyon analizinde, keton cisimleri ve idrar nitrit pozitifliği komplike apandisit varlığını tahmin etmede istatistiksel olarak anlamlı bulundu (tüm değerler için $p < 0,001$).

Sonuç: İdrar analizi, akut batından şüphelenilen hastalarda yapılan rutin testlerden biridir. Bu nedenle, biz idrar tahlilinde idrarda keton ve nitrit pozitifliğinin komplike apandisit açısından uyarıcı olabileceğini düşünüyoruz.

Anahtar Kelimeler: Akut apandisit, idrar analizi, keton, nitrit

Abstract

Objectives: Acute appendicitis is one of the common abdominal emergencies. We aimed in this study to evaluate whether routine urinalysis may use in discriminating between simple appendicitis and complicated appendicitis in the emergency department.

Materials and Methods: Patients over 18 years of age with a pathological diagnosis of acute appendicitis and those who underwent urine analysis in the emergency department were included in the study. Patients with missing data were excluded. According to pathology reports, patients were classified as simple and complicated appendicitis.

Results: Compared to simple appendicitis, the complicated appendicitis group had significantly higher urine ketone body, protein, and nitrite counts on admission ($p < 0.05$ for all parameters). Urine ketone bodies and positive urine nitrite were found to predict statistically significant complicated appendicitis in multivariate logistic regression analysis (for all values $p < 0.001$).

Conclusion: Urine analysis is one of the routine tests performed in patients with suspected acute abdomen. Therefore, we think that especially urine ketone bodies and positive urine nitrite in urine analysis may be a warning for complicated appendicitis.

Keywords: Acute appendicitis, ketone, nitrite, urine analysis.

Introduction

Acute appendicitis (AA) is one of the most common surgical emergencies. In about 7% of the population, AA may occur at any time of their lifetime. AA is an inflammation usually caused by obstruction of the vermiform appendix.^{1,2} It is known that delayed treatment is associated with high mortality and morbidity, also early diagnosis and treatment is lifesaving.³

In the literature, appendicitis is classified as simple and complicated.⁴ According to this classification a suppurative appendix is considered as simple appendicitis, however gangrenous appendicitis, perforated appendicitis, and periappendicular abscess are considered as complex appendicitis. In simple appendicitis congestion, color changes, increased diameter, exudate, and pus can be seen macroscopically; transmural inflammation, ulceration, or thrombosis, with or without extramural pus can be seen microscopically. Friable appendix with purple, green, or black color changes and transmural inflammation with necrosis are pathological findings of gangrenous appendicitis. Untreated gangrenous appendicitis eventually becomes perforated. Similarly, periappendicular abscesses with transmural inflammation with pus also carry a high risk for postoperative complications.^{4,5} Diagnostic methods purposes principally to confirm the diagnosis of AA, and after to classify simple or complex diseases.⁶

Biomarkers are used to support patients' physical examination and clinical history when a diagnosis of AA is suspicious. No laboratory test, such as white blood cell count, C-reactive protein, or procalcitonin, can diagnose AA with high specificity and sensitivity.⁷ Although urinalysis is a part of the routine evaluation in patients presenting with acute abdominal pain, its role in the diagnosis of AA is still unclear.¹ This study aimed to identify whether routine urine analysis may inform in discriminating between simple appendicitis and complicated appendicitis in the adult emergency department population.

Materials and Methods

Before our retrospective study, local ethics committee approval was obtained (09/10/2019, 2012-KAEK-15/1940). All patients older than 18 years old who were admitted to our emergency department between 01.04.2014–31.03.2019 and diagnosed with acute appendicitis and operated in the general surgery clinic were included in the study. Patients with no urine test and missing data were excluded from the study. Patients' demographic data, urine analysis results, surgical notes, and pathology reports were obtained by scanning the hospital data system and patient files. Urine analysis was performed on BT URICELL 1280-1600 devices (BT products, İzmir, Turkey).

The urine analysis tests detect and measure the specific gravity (SG), pH, leukocyte esterase, protein, nitrite, ketone, erythrocyte, and leukocyte value.

According to pathology reports, patients were classified as simple and complicated appendicitis. Perforated appendicitis, gangrenous/necrotic appendicitis, and periappendicular abscesses were accepted as complicated appendicitis.

Statistical analysis

Data were analyzed using IBM SPSS16.0 (Chicago, IL, USA) statistical program. Kolmogorov Smirnov test was used to determine whether the distribution of discrete and continuous numerical variables was suitable for normal distribution. As the data did not conform to the normal distribution, median values, and interquartile range (IQR, 25% -75) were shown, and categorical variables were shown as the number of cases and (%). Categorical variables were evaluated by Chi-square and continuous variables were evaluated by the Mann Whitney U test. A univariate logistic regression model was developed to predict the risk of complicated appendicitis. After each independent variable was tested in the univariate model, a multivariate logistic regression model was included with statistically significant variables ($p < 0.20$). The multivariate regression model was evaluated by the Hosmer Lemeshow test. Results were considered statistically significant for $p < 0.05$.

Results

During the study period, 1198 patients were identified who supply the inclusion criteria of having undergone appendectomy for suspected acute appendicitis. 397 patients were excluded due to lack of data and urine analysis. 323 (40.32%) of the 801 patients included in the study were female and the median age of all patients was 30 (IQR 25-75: 24-39). Ketone positivity was detected in urine analysis of 141 (%17.60) patients. According to pathology reports, 569 (71.04%) patients were simple and 232 (28.96%) were complicated appendicitis. Demographics and some laboratory results of all patients are shown in Table 1. Comparison of characteristics and urine parameters among patients with simple appendicitis and complicated appendicitis were shown in Table 2. We found that nitrite, ketone, protein positivity, and urine specific gravity were statistically higher in urine analysis compared to simple appendicitis in complicated appendicitis patients ($p < 0.001$ for all values).

Multivariate logistic regression analysis was performed to examine the effects of variables in Table 2 with other variables. In the multivariate model, protein positivity, ketone positivity, specific gravity, nitrite positivity, urine erythrocyte count, as well as age and gender parameters, with p values of 0.20 and below, were included.

After the model associated with the Hosmer-Lemeshow test is seen to be fit statistical analysis revealed that positive urine ketone bodies and positive urine nitrite were important parameters for predicting complicated appendicitis (for all values $p < 0.001$) (Table 3).

Table 1. Demographic and laboratory data of patients n (%), median (IQR 25-75%)

Gender	
Female n (%)	323 (40.32%)
Age [median (IQR 25-75)]	30 (24-39)
Urine test analysis [n (%)]	
Nitrite positivity	39 (4.86%)
Leukocyte esterase positivity	158 (19.72%)
Ketone positivity	141 (17.60%)
Urine Ketone positivity [n (%)]	141 (100%)
-Ketone +1 positivity	92 (65.26%)
-Ketone +2 positivity	30 (21.27%)
-Ketone +3 positivity	19 (13.47%)
Urine test analysis [median (IQR 25-75)]	
Erythrocyte value	1 (0.9-2.05)
Leukocyte value	1 (0.45-2)
Specific gravity	1021 (1015-1027)
pH value	6 (5.5-6.5)
Pathology results [n (%)]	
Simple appendicitis	569 (71.04%)
Complicated appendicitis	232 (28.96%)
-Gangrenous/necrotic appendicitis	170 (21.22%)
-Perforated appendicitis	96 (11.98%)

Table 2. Comparison of characteristics and urine parameters among patients with simple appendicitis and complicated appendicitis n (%), median (IQR 25-75%)

	Simple appendicitis (n= 569)	Complicated appendicitis (n=232)	p value
Age [median (IQR 25-75)]	30 (23.5-38.5)	31 (24-42)	0.206
Gender [n (%)]			
Female	242 (42.53%)	81 (34.91%)	0.046
Urine test analysis [n(%)]			
Ketone positivity	76 (13.35%)	65 (28.01%)	<0.001
Protein positivity	48 (8.43%)	43 (18.53%)	<0.001
Nitrite positivity	11 (1.93%)	28 (12.06%)	<0.001
Leukocyte esterase positivity	106 (18.62%)	52 (22.41%)	0.222
Urine test analysis [median (IQR 25-75)]			
Erythrocyte value	1 (0.9-2)	1 (1-3)	0.133
Leukocyte value	1 (0.45-2)	1 (0.6-2.7)	0.253
Specific gravity	1020 (1015-1026)	1023 (1015-1028)	0.003
pH value	6 (5.5-6.5)	6 (5.5-6.5)	0.943

Table 3. Multivariate regression analysis of urine analysis in patients with complicated appendicitis

	Wald	P-value	Odds Ratio	(95%CI)
Age	5.07	0.024	1.02	(1.00-1.03)
Gender	8.27	0.004	0.60	(0.43-0.85)
Protein positivity	4.61	0.032	1.72	(1.05-2.81)
Ketone positivity	15.29	<0.001	2.26	(1.50-3.40)
Specific gravity	3.14	0.076	1.01	(1.00-1.02)
Nitrite positivity	22.40	<0.001	6.41	(2.97-13.84)
Erythrocyte value	0.48	0.486	1.00	(1.00-1.00)

Discussion

Early diagnosis of AA is not always easy, also diagnostic methods may not always be sufficient to distinguish between simple and complicated appendicitis. There may not be enough imaging methods to diagnose AA in rural areas, however, sometimes ultrasound and tomography may not help diagnose AA.⁴⁻⁶ Therefore, simple and cheap auxiliary tests are still needed to make a diagnosis. In this study, we think that the two parameters analyzed in urine analysis can be useful in predicting complicated appendicitis. In our study, 71.04% of the patients, who underwent appendectomy, were simple appendicitis and 28.96% were complicated appendicitis. These findings were consistent with the literature.⁵ Complicated appendicitis was determined from the pathology reports and surgical notes of the patients according to the pathological classification in the review published by Bhangu et al.⁴ According to pathology reports, 12% of our patients were perforated. The perforation rate in the literature is similarly 13-20%.⁸

In this study, we found that urine ketone bodies, nitrite, and protein positivity were significant factors in complicated appendicitis. In our regression analysis, we found that the incidence of complicated appendicitis was 2.25 times more in ketone positive patients. Similarly, Chen et al. found that ketone, nitrite, and protein positivity were significantly higher in child patients with perforated appendicitis.⁹ As we know, ketone bodies increase in urine in cases such as hunger, diabetes mellitus, dehydration, high fever, vomiting, diarrhea, severe liver disease.^{10,11} Ketone positivity in patients with appendicitis may also be due to hunger, nausea, and vomiting, which are expected symptoms of acute appendicitis. Complicated appendicitis may result in more severe loss of appetite and vomiting than simple ones, and our findings may be explained by this condition. Patients with complicated appendicitis may present with more severe clinical findings than simple patients, and positive ketone and nitrite parameters detected during urinalysis at the time of admission may stimulate the emergency physician for complicated appendicitis.

In the literature, it has been reported that in acute appendicitis, urinary tract infection may be caused by peritoneal irritation due to urinary tract compression.¹² This may be the reason for the significantly higher

nitrite positivity in patients with complicated appendicitis. We think that; patients with positive ketone and nitrite in urine analysis who are at higher risk of perforation could be operated on earlier.

According to classical knowledge, the treatment of appendicitis is surgical appendectomy. However, recent studies have reported that simple appendicitis can be managed with medical treatment without surgery.^{13,14} At this point, the distinction between simple and complicated appendicitis becomes more important in the diagnostic process.

Furthermore, a simple or a perforated patient may affect the surgeon's choice of surgical method.¹⁵ Additionally, early diagnosis of appendicitis may prevent perforation, abscess, and postoperative complications, as well as may reduce hospital stay and costs.

In the literature, there are many studies investigating laboratory parameters predicting complicated appendicitis. Some studies have shown that CRP levels correlate with the severity of appendix inflammation and may be sensitive to predict appendix perforation.^{16,17} Yang et al. reported that higher white blood cell count, CRP level, neutrophil percentage, and low serum sodium level could be used to predict perforated appendicitis.¹⁸ There are also studies showing that the neutrophil-lymphocyte ratio is a promising marker that can predict both the diagnosis and severity of appendicitis.¹⁹ In the literature, there is no test to detect complicated appendicitis with 100% sensitivity and specificity before surgery, so there is still a need for further studies on auxiliary tests.

In conclusion, urine analysis is one of the routine tests performed in patients with suspected acute abdomen. Therefore, we think that especially urine ketone bodies and positive urine nitrite in urine analysis may be warning for complicated appendicitis without increasing the cost.

Limitations

There are a few limitations to be considered regarding this study. First, this is a single-center retrospective study. The relationship between urine parameters and the degree of perforation, gangrene, or necrosis could not be determined due to the limited pathology reports.

References

1. Soldo I, Radisic Biljak V, Bakula B, Bakula M, Simundic AM. The diagnostic accuracy of clinical and laboratory parameters in the diagnosis of acute appendicitis in the adult Emergency department population: a case control pilot study. *Biochem Med* 2018;28:30712.
2. Tannoury J, Abboud B. Treatment options of inflammatory appendiceal masses in adults. *World J Gastroenterol* 2013;19:3942-50.
3. Van Dijk ST, Van Dijk AH, Dijkgraaf MG, Boermeester MA. Meta-analysis of in-hospital delay before surgery as a risk factor for complications in patients with acute appendicitis. *Br J Surg* 2018;105:933-45.
4. Bhangu A, Søreide K, DiSaverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis and management. *Lancet* 2015;386:1278-87.
5. Van den Boom AL, de Wijkerslooth EML, Mauff KAL, et al. Interobserver variability in the classification of appendicitis during laparoscopy. *Br J Surg* 2018;105:1014-9.
6. Perez KS, Allen SR. Complicated appendicitis and considerations for interval appendectomy. *JAAPA* 2018;31:35-41.
7. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg* 2013;100:322-9.
8. Andersson RE, Hugander A, Thulin AJ. Diagnostic accuracy and perforation rate in appendicitis: association with age and sex of the patient and with appendectomy rate. *Eur J Surg* 1992;158:37-41.
9. Chen YC, Zhao LL, Lin YR, Wu KH, Wu HP. Different urinalysis appearances in children with simple and perforated appendicitis. *Am J Emerg Med* 2013;31:1560-3.
10. Misra S, Oliver NS. Utility of ketone measurement in the prevention, diagnosis and management of diabetic ketoacidosis. *Diabet Med* 2014;32:14-23.
11. Cevik Y, Corbacioglu SK, Cikrikci G, Oncul V, Emektar E. The effects of Ramadan fasting on the number of renal colic visits to the emergency department. *Pak J Med Sci.* 2016;32(1):18-21.
12. Maio G, Aragona F, Cisternino A, Calabrò A, Ostardo E, Artibani W. Urological Manifestations of Acute Appendicitis: Report of Two New Cases. *Urol Int* 1992;48:242-4.
13. Becker P, Fichtner-Feigl S, Schilling D. Clinical Management of Appendicitis. *Visc Med* 2018;34:453-8.
14. Dhillon NK, Barmparas G, Lin TL, et al. Unexpected Complicated Appendicitis in the Elderly Diagnosed with Acute Appendicitis. *Am J Surg* 2019;218:1219-22.

15. Kim HY, Park JH, Lee SS, Lee WJ, Ko Y, Andersson RE et al. CT in Differentiating Complicated From Uncomplicated Appendicitis: Presence of Any of 10 CT Features Versus Radiologists' Gestalt Assessment. *Am J Roentgenol* 2019;213:1-9.
16. Eriksson S, Granstrom L, Carlstrom A. The diagnostic value of repetitive preoperative analyses of C-reactive protein and total leucocyte count in patients with suspected acute appendicitis. *Scand J Gastroenterol* 1994;29:1145-9.
17. Dueholm S, Bagi P, Bud M. Laboratory aid in the diagnosis of acute appendicitis. *Dis Colon Rectum* 1989;32:855-9.
18. Yang J, Liu C, He Y, Cai Z. Laboratory Markers in the Prediction of Acute Perforated Appendicitis in Children. *Emerg Med Int* 2019;2019:1-4.
19. Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg* 2012;97:299-304.