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Original Contribution

Different urinalysis appearances in children with simple and perforated appendicitis

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ABSTRACT

Purpose: This study aimed to determine whether routine urinalysis may serve as a tool in discriminating between acute appendicitis and perforated appendicitis in children.**Basic procedures:** We prospectively collected 357 patients with clinically suspected acute appendicitis. Urinalysis was performed in patients with clinically suspected acute appendicitis before surgical intervention. Routine urinalysis is composed of 2 examinations: chemical tests for abnormal chemical constituents and microscopic tests for abnormal insoluble constituents. Receiver operating characteristic curves for urine white blood cell (WBC) counts and urine red blood cell (RBC) counts in distinguishing between patients with simple appendicitis and patients with perforated appendicitis were also analyzed.**Main findings:** Urine ketone bodies, leukocyte esterase, specific gravity, pH, WBC, and RBC counts were all significant parameters among patients with normal appendices, simple appendicitis, and perforated appendicitis (all $P < .05$). Based on multivariate logistic regression analysis, positive urine ketone bodies and nitrate were significant parameters in predicting perforated appendicitis ($P = .002$ and $P = .008$, respectively). According to the results of receiver operating characteristic curves, the appropriate cutoff values were 2.0/high-power field for urine RBC counts and 4.0/high-power field for urine WBC counts in predicting perforated appendicitis in children.**Principal conclusions:** Routine urinalysis may serve to aid in discriminating between simple and perforated appendicitis. Clinically, we believe that these urine parameters may aid primary emergency physicians with decision making in patients with clinically suspected appendicitis.

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1. Introduction

Appendicitis is the most frequent surgical etiology among children presenting to emergency departments (EDs) with abdominal pain over the right lower quadrant [1,2]. However, despite intensive research and discussion, rapid, accurate diagnosis of pediatric appendicitis remains an elusive challenge [2–4]. A clinical decision to operate leads to the removal of a normal appendix in 10% to 20% of the cases [5,6]. Although diagnostic imaging has been used with increasing frequency, it has limitations such as exposure to ionizing radiation, availability of skilled technicians at all hours, and high costs

[7,8]. Moreover, some cases are not straightforward, leading to equivocal results [9–11]. In general, a normal appendix found during appendectomy represents a misdiagnosis; a delayed diagnosis of acute appendicitis may lead to perforation and peritonitis. Thus, improving diagnostic accuracy is desirable both for timely diagnosis and for reducing the number of unnecessary appendectomies.

Although preoperative laboratory tests are fast, cheap, and more available, the predictive value of the serum biomarkers is still far from favorable in diagnosing appendicitis in children. Therefore, many studies have been conducted to find out whether any other parameters could increase the diagnostic accuracy of acute appendicitis. In some studies, equivocal urinalysis results have been reported [12,13]. However, the correlation between urinalysis and appendicitis is still unclear. Therefore, in this study, we aimed to determine whether routine urinalysis may serve as a helpful tool in discriminating between acute appendicitis and perforated appendicitis in children.

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2. Methods

2.1. Patient participants

This was a prospective study of pediatric patients who presented with right lower quadrant abdominal pain at 2 medical hospitals in central Taiwan between 2005 and 2009. Children younger than 18 years with suspected appendicitis who underwent urinalysis were enrolled in this study. Children who did not undergo urinalysis and who had definitely bacterial growth from the culture of urine were both excluded. The histopathologic criteria for the appendicitis diagnosis were defined as transmural invasion of granulocytes. Perforated appendicitis was defined as a preoperative diagnosis of perforation, or a localized abscess. In addition, a patient was defined as having a normal appendix (1) when a nonsurgical patient discharged from the ED was followed up by a telephone interview 2 weeks after the index visit to confirm that the diagnosis of appendicitis could be ruled out or (2) when an uninflamed appendix was found in a patient who had undergone surgery (a normal appendectomy). The study was approved by the institution's Human Subjects Review Committee. Informed consent was obtained from all study participants.

3. Methods

This was a prospective observational cohort study and did not intend to influence the indications and timing of the surgical approach. Urinalysis was performed in patients with clinically suspected acute appendicitis before surgical intervention. Routine urinalysis is composed of 2 examinations: chemical tests for abnormal chemical constituents and microscopic tests for abnormal insoluble constituents. Urine test strip analysis was performed by the automated urinalysis systems - the Sysmex UF-1000i (URISYS 2400, Roche Diagnostics). These test strips detect and measure specific gravity (SG), pH, leukocyte esterase, occult blood (OB), and ketones [10]. Urine sedimentation may contain cells, casts, and crystals and is examined microscopically after centrifugation of a urine sample. Because the number of elements found in each high-power field (HPF) may vary considerably from one field to another, several fields are averaged. The red blood cell (RBC) and white blood cell (WBC) counts were performed manually by counting and averaging the mean cells in 5 fields. Receiver operating characteristic (ROC) curves for urine WBC counts and urine RBC counts in predicting patients with perforated appendicitis were also analyzed.

3.1. Statistical analysis

The *t* test, Mann-Whitney *U* test, Fisher exact test, multivariate logistic regression analysis, and ROC curves were used for statistical

analysis. The differences between the groups are presented as 95% confidence intervals (CIs). Probability levels lower than .05 were considered significant. We also examined the test parameters including sensitivity (Sn), specificity (Sp), the area under the ROC curve (AUC), positive likelihood ratio (LR⁺), and negative LR (LR⁻) at the various cutoff values. The AUC, calculated using the trapezoidal rule, was considered a global measure of the diagnostic value of that parameter. Both LR⁺ and LR⁻ were calculated for the best cutoff values. The criterion value indicated the value corresponding to the highest accuracy (minimal false-negative and false-positive results). Statistical analyses were performed using SPSS software (version 15.0; SPSS Inc, Chicago, IL).

4. Results

4.1. Characteristics of the study subjects

During the study period, a total of 424 children with suspected appendicitis who underwent urinalysis were enrolled in the study. Of them, 67 patients who did not use our outpatient clinic for follow-up were excluded from this study. The remaining 357 pediatric patients younger than 18 years were recruited for further analysis; they comprised 158 boys (44.3%) and 199 girls (55.7%), with a mean age of 11.1 ± 4.2 years. Among the 357 patients, 205 had histologically proven simple appendicitis, 49 had perforated, and 53 had normal appendices.

5. Main results

In Table 1, urine ketone bodies, leukocyte esterase, SG, pH, urine WBC, and urine RBC were all significant parameters among patients with normal appendices, simple appendicitis, and perforated appendicitis (all *P* < .05). In addition, children with perforated appendicitis had a significantly higher percentage of positive ketone bodies (*P* = .003), positive OB (*P* = .024), positive nitrate (*P* < .001), and positive leukocyte esterase (*P* = .003) than did those with simple appendicitis. Moreover, children with perforated appendicitis had significantly lower urine pH (*P* = .003), greater SG (*P* = .003), more WBC counts (*P* = .012), and more RBC counts (*P* = .002) than did those with simple appendicitis. Furthermore, based on the results of multivariate logistic regression analysis, the diagnostic values of the urine parameters in predicting perforated appendicitis are shown in Table 2. We found that positive urine ketone bodies and positive urine nitrate were significant parameters in predicting perforated appendicitis (*P* = .002 and *P* = .008, respectively). The odds ratio of positive urine ketone bodies for perforated appendicitis was 2.866, but the odds ratio of positive urine nitrate was as high as 9.493. ROC curves for urine WBC counts and urine RBC counts in predicting patients with

Table 1
Comparison of urine parameters among patients with normal appendices, simple appendicitis, and perforated appendicitis

Variable	Normal appendices (n = 53), no. (%)	Simple appendicitis (n = 255), no. (%)	Perforated appendicitis (n = 49), no. (%)	<i>P</i> ^a	<i>P</i> ^b
Gender					
Male	23 (44.3)	141 (55.3)	26 (53.1)	.120	.684
Female	30 (55.7)	114 (44.7)	23 (46.9)		
Urinalysis					
Ketone	11 (21.2)	77 (30.2)	22 (44.9)	.001	.003
OB	16 (30.5)	83 (32.5)	23 (46.9)	.061	.024
Nitrate	1 (1.9)	11 (4.3)	10 (20.4)	.060	<.001
Leukocyte esterase	10 (18.9)	44 (17.3)	15 (30.6)	.013	.003
	Mean ± SD	Mean ± SD	Mean ± SD	<i>P</i>	<i>P</i>
pH	6.61 ± 0.88	6.40 ± 0.97	6.11 ± 0.83	<.001	.003
SG	1.018 ± 0.009	1.020 ± 0.009	1.023 ± 0.009	<.001	.003
WBC (HPF)	1.42 ± 2.03	1.96 ± 4.07	3.08 ± 3.53	.042	.012
RBC (HPF)	1.89 ± 4.06	4.60 ± 15.03	9.64 ± 23.21	.002	.002

^a Compared among normal appendices, simple appendicitis and perforated appendicitis.

^b Compared between simple appendicitis and perforated appendicitis.

Table 2

Multivariate logistic regression analysis of urinalysis in patients with perforated appendicitis

Parameters	Sn	Sp	LR ⁺	LR ⁻	OR	95% CI	P
Ketone	0.46	0.79	2.19	0.68	2.866	1.466-5.602	.002
OB	0.44	0.70	1.47	0.80	1.511	0.659-3.467	.330
Nitrate	0.20	0.98	10.00	0.82	9.493	1.790-50.337	.008
Leukocyte esterase	0.30	0.83	1.76	0.84	1.054	0.499-2.224	.891

OR, odds ratio.

perforated appendicitis are shown in Fig. The AUC of urine RBC counts appeared as 0.62, and the AUC for urine WBC counts showed as 0.56 (Table 3). The appropriate cutoff values were 2.0/HPF for urine RBC counts and 4.0/HPF for urine WBC counts in predicting perforated appendicitis in children.

6. Discussion

Abdominal pain is one of the most common presenting symptoms of children brought to the pediatric ED [6]. Causes of abdominal pain in children range from simple etiologies to potentially catastrophic ones. Distinguishing appendicitis from other disorders is difficult, particularly in young children [2,4,6]. However, early diagnosis of appendicitis can not only prevent perforation, abscess formation, and postoperative complications but also decrease cost by decreasing hospitalization time [4,10]. Imaging techniques have been shown to be particularly accurate for diagnosing appendicitis; however, they are not readily available in all primary healthcare settings, and their potential risks for exposure to ionizing radiation may result in increased health care costs. These concerns have led to renewed interest in clinical scoring systems and laboratory tests to better diagnose appendicitis. Many studies have been conducted to find out whether other predictive parameters could be used in diagnosing acute appendicitis. Some studies reported that abnormal urinalysis findings may exist in patients with acute appendicitis [12,13]. However, the definite correlation between urinalysis and pediatric appendicitis is quite unclear. Therefore, we analyzed 357 pediatric patients with

Table 3

The appropriate cutoff urine WBC counts and urine RBC counts in predicting patients with perforated appendicitis

Variable	Value	Sn	Sp	LR ⁺	LR ⁻	AUC (95% CI)
Urine RBC	2.0/HPF	0.56	0.78	4.67	0.56	0.620 (0.542-0.699)
Urine WBC	4.0/HPF	0.35	0.85	2.33	0.76	0.561 (0.482-0.641)

clinically suspected acute appendicitis to determine the useful urine parameters in distinguishing patients with acute appendicitis from normal appendices.

In this study, we found that urine ketone bodies, nitrate, SG, pH, RBC counts, and WBC counts appeared to be significant factors in patients with acute appendicitis, especially for perforated appendicitis. According to our analysis, children with perforated appendicitis had a higher percentage of the presentation of ketone bodies and positive nitrate, greater urine SG, lower urine pH, more urine RBC counts, and more urine WBC counts than did those with normal appendices and simple appendicitis. In addition, on the basis of the results of ROC analysis, we established the significant cutoff values of urine WBC counts and urine RBC counts in discriminating pediatric perforated appendicitis. For patients with perforated appendicitis, we identified urine RBC counts of 2.0/HPF or greater and urine WBC counts of 4.0/HPF or greater to predict perforation. Based on other investigations, irritation of the bladder or ureter by a ruptured appendix may result in the increase in urinary RBC and WBC counts in patients with perforated appendicitis [14]. Therefore, this may explain why we found abnormal RBC and WBC urinalysis findings in patients with perforated appendicitis. In addition, as we know, ketonuria could be caused by starvation; insulinoma, diabetic ketoacidosis; persistent hypoglycemia; high-fat, low-carbohydrate diets; and glycogen storage disease [15,16]. For acute appendicitis, the higher percentage of ketone bodies in urine may be associated with starvation secondary to anorexia and vomiting, which are the common symptoms of children with acute appendicitis. The urine SG ranges between 1.010 and 1.030 (higher numbers mean a higher concentration). The SG varies depending on the time of day, amount of food and liquids consumed, and the amount of recent exercise. The higher SG may result from the decreased amount of diet and liquids consumed caused by abdominal discomfort secondary to the disease. Urine pH was significantly lower in patients with acute appendicitis than that in patients with normal appendices in our study. Urine pH can be influenced by many factors including the diet, handling of the sample, and acid-base balance. Then normal pH range is between 6 and 8 for most people, depending on their diet. An alkaline pH (>7.0) is most indicative of an infectious process; a pH value below 7.1 may be considered either acidic or normal. People who eat infrequently generally have a more acidic pH; other causes include acidifying drugs, increased protein catabolism, and paradoxical aciduria associated with chloride and potassium depletion. Therefore, the lower urine pH value in patients with acute appendicitis may be associated with decreasing appetite and oral intake concomitant with the severity of appendicitis.

Simple appendicitis can progress to perforation, which is associated with much higher morbidity and mortality. Therefore, early and preoperative diagnosis of perforation is essential for clinicians. Moreover, the surgeons' choice of operative methods may depend on simple or perforated appendicitis [17–19]. Some authors have stated that nonsurgical treatment with antibiotics has recently been proposed as the first line of treatment for nonperforated appendicitis, but the immediate appendectomy approach seems to have a shorter length of stay and a lower total hospital cost compared with initial nonoperative management in perforated cases, and it could be also recommended in children with perforated appendicitis [20–23]. However, nonoperative management such as antibiotics has been proposed for the management of patients with localized

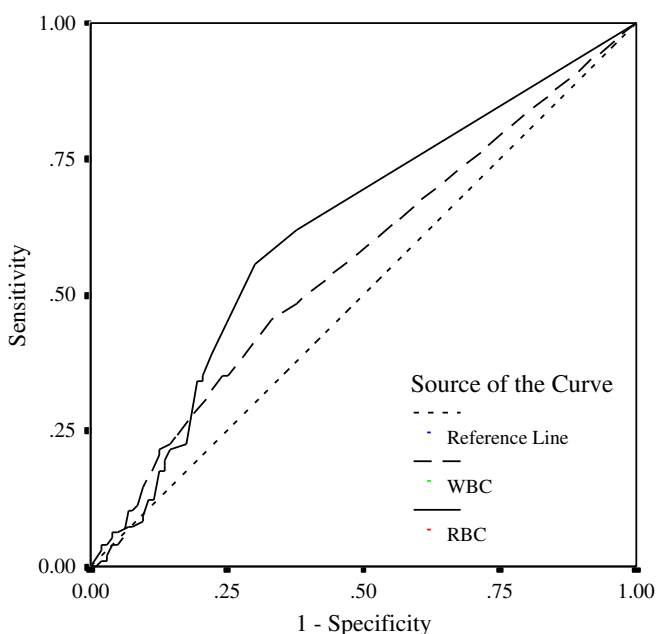


Fig. Receiver operating characteristic curves for urine WBC counts and urine RBC counts in predicting patients with perforated appendicitis.

periappendiceal abscess formation caused by perforated appendicitis [20–23]. Thus, detection of perforation may change management. Clinically, diagnosis of appendicitis is often based on clinical histories and clinical presentations. A prolonged history might lead to additional imaging to determine if an abscess is present that may require percutaneous drainage and later interval appendectomy. In this study, we have determined the cutoff urine RBC counts (≥ 2.0 /HPF) and urine WBC counts (≥ 4.0 /HPF) as an indication for additional imaging to identify appendiceal perforation or appendicitis-associated abscess formation in children with suspected acute appendicitis before proceeding to surgery.

In conclusion, routine urinalysis may serve to aid in discriminating between simple and perforated appendicitis. Clinically, we believe that these urine parameters may aid primary emergency physicians with decision making in patients with clinically suspected appendicitis.

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