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Assessment of Urinary-5-Hydroxyindolacetic Acid as A Diagnostic Parameter in Early Detection of Acute Appendicitis

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ABSTRACT

Background: *Acute appendicitis is the most common abdominal surgical emergency especially in children and young adults. The diagnosis of appendicitis is difficult because half the cases are incorrectly identified. Serotonin was defined as a good diagnostic marker for many inflammations including appendicitis and it is metabolite into 5-hydroxyindolacetic acid (5-HIAA) to be excreted in urine. 5-HIAA is suggested to be of diagnostic importance in the detection of this disease. The aim of this study was to evaluate the diagnostic importance of urinary-5-HIAA as an added parameter to Alvarado score.* ***Methods:*** *Seventy patients (35 females and 35 males) with acute appendicitis (35 were mild and 35 severe-perforated and gangrenous) were included in this study and 70 healthy individuals were taken as a control group. Urinary-5-HIAA was estimated in all patients and control group using ELISA method.* ***Results:*** *Sensitivity for the mild group is 94.2%, specificity 100% and diagnostic accuracy is 97.4%, while the sensitivity for the severe group is 37%. It was found that there is a highly significant difference between mild and control groups ($P<0.05$). The diagnostic accuracy for the mild group is 97.4% and for the severe is 68.5%.* ***Conclusion:*** *We conclude that urinary-5-HIAA is a high sensitive test for early detection of acute appendicitis.*

Keywords: Acute appendicitis, urinary-5-hydroxyindoleacetic acid, appendix

INTRODUCTION

Acute appendicitis is one of the most common abdominal emergencies. It accounts 400,000 of hospital admission every year [1]. It affects commonly people between the age of 10 to 20 years although it can affect any age group [2], males are more commonly affected than females with male: female ratio 1.4:1. The life time risk is 8.6% for male while it was 6.5% for female in united states [3]. The main stay for diagnosis of acute appendicitis is clinical diagnosis [4]. The clinical diagnosis can be achieved in most of the cases but some patients with such disease cannot be diagnosed with certainty by clinical diagnosis alone as abdominal penetration and lack of signs can make the diagnosis difficult. Perforation is one of the complications that can occur with significant increase in the mortality rate in such patients [5]. The perforation rate could be increase by 5% per 12 hours' period, 36 hours after the onset of symptoms make up expedient diagnosis and treatment mandatory [6]. Negative appendectomy could be seen in females, because this disease can stimulate different obstetrical and gynaecological conditions that can occur specially at reproductive age group which might reach 27% [7]. The delay or incorrect diagnosis can result in both clinical and economic consequences [3]. This stimulate researchers to underwent considerable researches to identify clinical, laboratory and radiological investigations aiming in diagnosis of acute appendicitis and the development of scoring system depending on clinical data, with the aid of computer to aid the clinician reaching to correct diagnosis to reduce the delay in diagnosis and reduce number of negative appendectomy. but evidence found that despite of the introduction of new tests, the diagnosis of this condition has not improved [8]. Alvarado score had been introduced as score system that can help in correct diagnosis of the cases and reduce the delay in the diagnosis and reduce the incidence of complication. In 1986 often research the most on 305 patients in Nazareth Hospital in Philadelphia in

united states for patients presented with suspected acute appendicitis. The charts of these patients were reviewed retrospectively and the sensitivity and specificity of a number of symptoms, signs and laboratory variables were assessed with those with the greatest diagnostic value being used to form a scoring system. This resulted in the formation of a simple score consisting of three symptoms, three signs and two laboratory markers of inflammation weighted as either one or two based on their importance in diagnosis (Table 1). These variables could be recalled using the pneumonic mantrels. The maximum total score achievable is, therefore, 10. A score of 5 or 6 is compatible with a diagnosis of acute appendicitis, with a score of 7 or 8 indicating probable appendicitis and a score of 9 or 10 indicating a very probable acute appendicitis. It has been suggested that score can be used as a guide to determine which patients require further observation and which patients require surgery. Those with a score of 5 or 6 required observation while those with a score of 7 or above needed to proceed to surgery as it was likely that they had appendicitis. The Alvarado score is the best performing of the clinical scoring systems in current use [8]. Previous studies have indicated that blood serotonin levels confirm the diagnosis of AA [9]. Serotonin is released by enterochromaffin cells in the lamina propria of the appendix [10]. It may act as a local as well as a mediator of inflammation. Once serotonin is secreted in the system 90% is metabolized in the liver; and the remaining in lung and kidney, 5-Hydroxyindoleacetic acid (5-HIAA) is the main metabolite of serotonin and mainly excreted in the urine [11]. The purpose of this study was to evaluate the diagnostic importance of urinary-5-HIAA as an added parameter to Alvarado score.

Table 1 Alvarado score

Symptoms	Variable	Value
Signs	Migration	1
	Anorexia-acetone	1
	Nausea-vomiting	1
	Tenderness in right lower quadrant	2
	Rebound pain	1
	Elevation of temperature >37.3°C	1
Laboratory	Leukocytosis > 10000/L	2
	Shift to the left >75%	1

METHODS

Patients and control

Seventy appendicitis patients (35 mild appendicitis their mean age ± SD=21.54 ± 8.56) and (35 severe with perforated and gangrenous appendicitis their mean age ± SD=22.54 ± 9.74) were attending our hospital during the period from September 2015 to January 2016. All patients were diagnosed by history taking and clinical examination including abdominal ultrasonography. Seventy normal persons were diagnosed as healthy control, matched for sex, their age ± SD=20.4 ± 4.979 were participated in this study.

Biochemical assay

Urinary 5-HIAA were done for all the patients and control, the urine samples were collected using a urine preservative containing tubes by adding 5ml of urine to each tube and the tubes were stored at -20°C. The kit was provided by Demedifec-Diagnosi-Germany. The procedure was done by ELISA method and the results were expressed by mg/l.

ELISA method for the quantitative determination of 5-HIAA in urine: first 5-HIAA is derivatized by methylation. The subsequent competitive ELISA uses the microtiter plate format. The antigen is bound to the solid phase of the microtiter plate. The methylated analyte in the standards, controls, and samples and the solid phase bound analyte compete for a fixed number of antibody binding sites. After system reached equilibrium, free antigen and free antigen-antibody complexes are removed by washing. The antibody bound to the solid phase is detected by an anti-rabbit IgG-peroxidase conjugate using TMB (tetramethylbenzidine) as a substrate. The reaction is monitored at 450 nm.

Quantification of unknown samples is achieved by comparing their absorbance with a standard curve prepared with known standard concentrations.

Statistical analysis

Data processing and statistical analysis were done using mini-tab V.16 processor. Data were expressed as mean ± SD. Differences in the mean between groups were evaluated using two-sample t-test ($P<0.05$) considered statistical significant.

RESULTS

Table 2 show the age distribution of the study groups. As presented in Table 3, mean of urinary 5-HIAA (expressed in mg/l) levels there was a highly significant difference between mild and severe group with (P<0.000) as shown in Table 3. The level of urinary 5-HIAA in mild appendicitis group were highly significantly (P<0.000) higher (13.94 mg/l ± 6.11 mg/l) than in control group (2.99 mg/l ± 1.35 mg/l). A significant difference (P<0.05) between severe group (none perforated (6.11 mg/l ± 6.31 mg/l) than control group (2.99 mg/l ± 1.35 mg/l), while the results of 5-HIAA in perforated and gangrenous appendicitis patients (5 patients) cannot be detected.

Table 2 Age distribution of study groups

Group	No.	Mean (year)	SD	SEM	P-value
Mild appendicitis	35	22.54	9.74	1.65	0.415*
Severe appendicitis	35	21.54	8.56	1.45	
Control	70	20.4	4.979	0.595	

*no significant difference

Table 3 Mean urinary 5-HIAA of study groups

Group	No.	Mean (mg/L)	SD	SEM	P-value
Mild appendicitis	35	13.94	4.11	0.69	0.000**
Severe appendicitis	35	6.11	2.31	1.39	0.007*
Control	70	2.995	1.35	0.161	-

*Significant difference, **Highly significant difference.

The sensitivity, diagnostic accuracy, and specificity for mild and severe (perforated and gangrenous) are shown in Table 4, the cut off value in this study is 2.995 mg/L, which is the mean value of the control group.

Table 4 Sensitivity, diagnostic accuracy, and specificity of mild and severe appendicitis patients

Patient's Group	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
Mild	94.2	100	97.4
Severe perforated gangrenous	37	100	68.5

As for Alvarado score, when the severe and mild acute appendicitis patients were separated according to their histopathological investigation, the results show that when the mean of 5-HIAA decrease (in the severe cases) Alvarado score was high, and the reveres with the mild cases, when the level of the score decrease the mean of 5-HIAA increase, as shown in Table 5.

Table 5 Alvarado score in comparison with the mean of 5-HIAA

Alvarado score	Mean of 5-HIAA (mg/L)	No. of patients	Histopathology
8-9	2.9	29	Severe
≥ 7	4.9	7	Severe
≤ 7	14.01	8	Mild
5-6	13.9	27	Mild

DISCUSSION

Our study stated the high sensitivity of U-5-HIAA in early (mild) diagnosis of appendicitis in adult (94.2%) and the low sensitivity in perforated and gangrenous (severe) patients (37%), although, the specificity is 100%. The diagnostic accuracy for mild cases is 97.4%, while in the severe cases 68.5%.

These results are in agreement with Mentes, et al. [12], Apa, et al. [13], Balandparvaz, et al. [14], and Ilkhanizadeh, et al. [11], who stated the increase in U-5-HIAA in early appendicitis.

The results are in agreement with Oruc, et al. [15], who stated the decrease level of U-5-HIAA in severe appendicitis. But the results do not agree with Rao, et al. [16] and Jangjoo, et al. [17] who found a low sensitivity of U-5-HIAA in acute appendicitis and confirm that it can't be used as a diagnostic tool in detection of appendicitis.

The differences between the results were due to the use of different technique and different suppliers for the kit of 5-HIAA by Elisa and due to different sample size.

As the results show that there is increase in 5-HIAA in patients with mild acute appendicitis with low Alvarado score which increases the score and the diagnostic accuracy of Alvarado score in early acute appendicitis as adding 5-HIAA to the Alvarado score increase the rate of detection and decrease the numbers of the missed diagnosed cases when the signs and symptoms and Alvarado score fail to detect such cases.

CONCLUSION

Urinary 5-HIAA proved to be a good diagnostic tool for early cases of acute appendicitis in adult because of its high sensitivity and specificity. The test increases the diagnostic accuracy of Alvarado score and it decrease the number of missed cases.

REFERENCES

[1] Hospital Episode Statistics [Internet]. Leeds: NHS Digital [cited 2006 Aug 28]. Available from: http://content.digital.nhs.uk/hes.

[2] Addiss, David G., et al. "The epidemiology of appendicitis and appendectomy in the United States." *American journal of epidemiology* 132.5 (1990): 910-925.

[3] Flum, David R., and Thomas Koepsell. "The clinical and economic correlates of misdiagnosed appendicitis: Nationwide analysis." *Archives of Surgery* 137.7 (2002): 799-804.

[4] Humes, D. J., and Simpson, J. "Acute appendicitis." *BMJ: British Medical Journal* 333.7567 (2006): 530.

[5] Blomqvist, Paul G., et al. "Mortality after appendectomy in Sweden, 1987-1996." *Annals of surgery* 233.4 (2001): 455-460.

[6] Bickell, Nina A., et al. "How time affects the risk of rupture in appendicitis." *Journal of the American College of Surgeons* 202.3 (2006): 401-406.

[7] Flum, David R., et al. "Has misdiagnosis of appendicitis decreased over time?: A population-based analysis." *JAMA* 286.14 (2001): 1748-1753.

[8] Ohmann, Christian, et al. "Diagnostic score for acute appendicitis." *The surgeon; Journal for all areas of surgical medication* 66.2 (1995): 135-141.

[9] Singh, S. M., et al. Concentration of serotonin in plasma: A test for appendicitis. *Clinical Chemistry* 34 (1998):2572-2574.

[10] Rode, Jurgen, Amar P. Dhillon, and Lucienne Papadaki. "Serotonin-immunoreactive cells in the lamina propria plexus of the appendix." *Human pathology* 14.5 (1983): 464-469.

[11] Ilkhanizadeh, Behrouz, et al. "Spot urine 5-hydroxy indole acetic acid and acute appendicitis." *Hepato-gastroenterology* 48.39 (2000): 609-613.

[12] Mentes, Oner, et al. "The importance of urine 5-hydroxyindoleacetic acid levels in the early diagnosis of acute appendicitis." *The American journal of emergency medicine* 27.4 (2009): 409-412.

[13] Apak, Sami, et al. "Spot urine 5-ydroxyindoleacetic acid levels in the early diagnosis of acute appendicitis." *Journal of pediatric surgery* 40.9 (2005): 1436-1439.

[14] Bolandparvaz, Shahram, et al. "Urinary 5-hydroxy indole acetic acid as a test for early diagnosis of acute appendicitis." *Clinical biochemistry* 37.11 (2004): 985-989.

[15] Oruc, M. T., et al. "The value of 5-hydroxy indole acetic acid measurement in spot urine diagnosis of acute appendicitis." *East African medical journal* 81.1 (2004): 40-41.

[16] Rao, Ahsan, et al. "Spot urinary 5-hydroxyindoleacetic acid is not an ideal diagnostic test for acute appendicitis." *The American journal of emergency medicine* 34.9 (2016): 1750-1753.

[17] Jangjoo, Ali, et al. "Is urinary 5-hydroxyindoleacetic acid helpful for early diagnosis of acute appendicitis?." *The American journal of emergency medicine* 30.4 (2012): 540-544.