

## ORIGINAL ARTICLE

## DIAGNOSTIC VALUE OF SERUM UREA, CREATININE, SODIUM AND POTASSIUM FOR COMPLICATED APPENDICITIS - A ONE YEAR RETROSPECTIVE STUDY

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**Background:** Acute appendicitis is a common surgical emergency and if complicated, manifesting as abscess, perforation, suppurative or gangrenous appendicitis, carries significant morbidity and mortality. Its early preoperative diagnosis can improve outcome in patients and reduce incidence of negative appendectomies. It, however, mandates identification of new diagnostic parameters for it. This retrospective study evaluates diagnostic accuracy of serum urea, creatinine, sodium and potassium for complicated appendicitis. **Methods:** Sixty patients with suspected appendicitis were grouped into complicated and uncomplicated appendicitis based on histological reports. Preoperative laboratory results for serum urea, creatinine, sodium and potassium levels were obtained from hospital records. Diagnostic strength of these markers was calculated as specificity, sensitivity and area under curve. ROC curve analysis was used for their diagnostic accuracy. **Results:** The levels of serum urea, creatinine and K were not significantly different in uncomplicated and complicated appendicitis. However, sodium was significantly higher in complicated appendicitis. ROC curve analysis showed AUC values for all the studied variables to be greater than 0.5. However, none of the markers had good capability to differentiate complicated appendicitis from uncomplicated appendicitis. **Conclusion:** Serum urea, creatinine, sodium and potassium levels have shown a tendency to be predictive of complicated appendicitis but a strong association could not have been established. Hence, further investigation is warranted.

**Keywords:** Appendicitis; Creatinine; Urea; Sodium; Potassium

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## INTRODUCTION

Acute appendicitis is a common surgical emergency.<sup>1</sup> It has a lifetime risk of 6.7% in females and 8.6% in males.<sup>2</sup> Its peak incidence is between 10 and 30 years of age.<sup>3</sup> One-third of patients with appendicitis present with complicated appendicitis, which manifests as abscess, hyperplastic appendix, gangrenous, perforated and suppurative appendicitis.<sup>3,4</sup> Incidence of perforation ranges from 16-40%, and has higher occurrence in females and in patients older than 50 years.<sup>3</sup> Complicated appendicitis is linked to higher morbidity and mortality risk than non-complicated appendicitis. The risk in acute non-gangrenous appendicitis is less than 0.1%, which increases to 0.6% in gangrenous, and around 5% in perforated appendicitis.<sup>3</sup> Limited definitive diagnostic parameter has been confirmed to help diagnose complicated appendicitis preoperatively. Despite the progress made in the medical profession, appendicitis still remains a significantly morbid condition.<sup>4,5</sup> The clinical diagnosis of acute appendicitis and subsequent decision to operate continues to be based on a combination of history, laboratory, clinical and radiological findings. Evaluation based on history and clinical parameters alone leads to high percentages of negative appendectomies ranging from 9.2-35%.<sup>1</sup> Neutrophil to Lymphocyte ratio (NLR)

has been proven to not only diagnose acute appendicitis from normal appendix with sensitivity and specificity of 88.89% and 90.91% (AUC of 0.96), but it can also diagnose complicated appendicitis from non-CA with sensitivity and specificity of 76.92 and 100% respectively.<sup>13</sup> Due to atypical findings, many well experienced surgeons carry out negative appendectomies or miss out complicated appendicitis. Many convenient scoring systems and investigative tests have been designed to aid in predicting complicated appendicitis, but none have been widely acknowledged and applied.<sup>4</sup>

Association of right hydronephrosis with complicated appendicitis has been well documented. It has been suggested that spread of peri appendiceal inflammation may cause it.<sup>6</sup> Based on this, we assume serum urea, creatinine, sodium and potassium level to fluctuate in acute appendicitis as it may alter kidney function. Studies have shown delay in surgery, male gender, appendicoliths, and diabetes mellitus to have significant association with appendiceal perforation and post-operative complications. These studies were based on CT imaging scan, which has low sensitivity in identifying complicated appendicitis.<sup>4</sup> However recent studies have contraindicated these associations.<sup>4,6</sup> So far, intraoperative diagnosis is the most efficient method of identifying complicated appendicitis. Limited local

evidence is available on association of complicated appendicitis with derangement of biochemical profile. Devising preoperative diagnostic tools with high sensitivity and specificity remains a challenge. The objective of our research is to ascertain diagnostic accuracy of deranged serum urea, creatinine, sodium and potassium level for complicated appendicitis. This shall enable the surgeons with even limited experience to make timely and accurate diagnosis of complicated appendicitis and subsequently prioritize patients with complicated appendicitis for urgent operative intervention. The eventual outcome will be a decrease in the frequency of negative appendectomies and their associated complications.

## MATERIAL AND METHODS

This retrospective cohort study was conducted on patients who underwent emergency open appendectomies from January to December 2019, at Pakistan Institute of Medical Sciences, Islamabad. A cohort of 60 patients, who fulfilled inclusion and exclusion criteria was recruited for analysis. Patients with pain in lower abdomen, having a positive history and clinical findings for appendicitis, with Alvarado score of 6 or more, between 18–60 years and with no comorbidities were included in this study. The exclusion criteria included patients who underwent elective appendectomy and those who had history of any kind of renal disease. Data on demographic details, presenting symptoms and signs and preoperative blood test results of serum levels of creatinine, urea, sodium and potassium were obtained from hospital computer records. Preoperative blood tests are defined as those blood results available within 24 hours prior to surgical intervention. Informed consent was taken from all subjects after detailed explanation of study objectives. Approval from the Institute's ethics committee was obtained prior to retrieval of records.

Histopathology reports were taken as the gold standard for diagnosis. Depending on the outcome of the final histopathology report, patients were grouped as complicated appendicitis and uncomplicated appendicitis. Perforated, suppurative and gangrenous appendicitis with or without abscess was counted as complicated appendicitis. For inference statistics, t-test and one-way ANOVA were used to analyse continuous data and chi-square test was used to analyse categorical data. Sensitivity and specificity were calculated for each test individually to predict diagnostic value. Diagnostic accuracy at the optimal cut-off threshold scores was derived from the receiver operating curve (ROC). The level of statistical significance was set at 0.05. Statistical analysis was performed using SPSS v.23.

## RESULTS

Based on inclusion and exclusion criteria, this study enrolled 60 patients with suspected appendicitis. There

was a male predominance with appendicitis in this study (60.0%, n=36). The mean age was 25.2±10.03 years and the majority of the cases were in younger age groups, especially between 21 and 40 years of age (50.0%), with very few cases above 41 years. (Table-1)

The majority of cases had acute uncomplicated appendicitis 37 (61.6%) while 18 (30.0%) had suppurative appendicitis. A few patients presented with other complications of appendix. (Table-1)

56.7% (n=34) of the patients reported generalized abdominal pain. 80% (n=48) presented with vomiting while 95% (n=57) had abdominal tenderness. Only 41.7 (n=25) patients with suspected appendicitis had elevated temperature. 75% (n=45) showed raised WBC count (> 11,000/uL) while only 60% (n=36) were found to have leukocyte left shift. Mean Alvarado score was 7.22 with standard deviation of 1.76.

Serum urea level ranged from 10 mg/dL to 47 mg/dL with a mean of 25.24 mg/dL±8.341. Mean creatinine level was found to be 0.928 mg/dL ±0.44 with a range from 0.3 mg/dL to 2.3 mg/dL. Serum Na and K level were 135.8±11.95 and 4.00±0.83 mEq/L respectively. In Table-3, it is shown that no significant variation was observed for studied variables, except potassium, between different appendicitis groups according to ANOVA test, however, some parameters varied slightly across the types. Serum level of sodium was higher in suppurative appendicitis (141.06±15.46 versus 133.14±9.82) as compared to uncomplicated appendicitis. Serum potassium level varied significantly across appendicitis groups with highest level in appendicitis with hyperplasia (4.83±1) followed by suppurative appendicitis (4.31±0.89). Overall, it was witnessed that the serum urea, creatinine, sodium and potassium levels were greater in patients with suppurative appendicitis.

When the serum levels of serological markers were compared between uncomplicated appendicitis and other types combined, a statistically significant association was observed in Potassium levels ( $p=0.027$ ). Overall, the levels of other parameters were found similar between uncomplicated appendicitis and all three types of complicated appendicitis categories. (Table-4) The ROC curve analysis was done to measure sensitivity, specificity and AUC for serum urea, creatinine, sodium and potassium for detecting complicated appendicitis patients. All the serum markers have AUC greater than 0.5 showing average level of detection strength for complicated appendicitis. All of these parameters were found to have above average to fair level of sensitivity to detect a positive case of appendicitis. However, the specificity was below average in most parameters. Amongst all the studied markers, Na was found to have maximum AUC. (Table-5)

**Table-1: Descriptive characteristics of patients (n=60)**

	Variable	Number of cases (%)
Gender	Male	36 (60.0%)
	Female	24 (40.0%)
Age categories (years)	Up to 20	23 (38.3%)
	21 to 40	30 (50.0%)
	41 or above	7 (11.7%)
Appendicitis type	Uncomplicated appendicitis	37 (61.7%)
	Suppurative appendicitis	18 (30.0%)
	Perforated appendicitis	2 (3.3%)
	Appendicitis with Hyperplasia	3 (5.0%)

**Table-2: Mean levels of serum urea, creatinine, Na and K of all the subjects**

	Mean	Standard Deviation	SEM (Standard Error of Mean)
Urea (mg/dL)	25.24	8.341	1.077
Creatinine (mg/dL)	0.928	0.44	0.057
Na (mEq/L)	135.8	11.95	1.542
K (mEq/L)	4.00	0.83	0.108

**Table-3: Comparison of mean level of urea, creatinine, sodium and potassium within different appendicitis types**

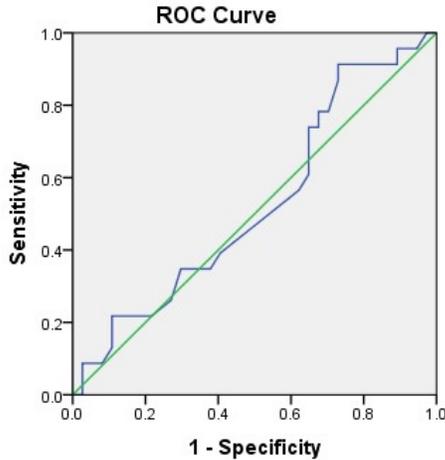
Variable	Uncomplicated appendicitis (n=37)	Suppurative appendicitis (n=18)	Perforated/gangrenous appendicitis (n=2)	Appendicitis with hyperplasia (n=3)	p- value
Urea	24.93±8.57	25.74±6.67	29.0±11.31	23.67±16.25	0.895
Creatinine	0.903±0.39	1.03±0.56	0.75±0.21	0.70±0.26	0.519
Na	133.14±9.82	141.06±15.46	137.0±8.48	136.33±4.72	0.147
K	3.85±0.72	4.31±0.89	3.25±0.35	4.83±1.00	0.04

**Table-4: Comparison of mean level of urea, creatinine, sodium and potassium between uncomplicated and complicated appendicitis group**

	Uncomplicated appendicitis (n=37) Mean±SD	Complicated appendicitis (n=23) Mean±SD	p-value
Urea (mg/dL)	24.93±8.58	25.75±8.11	0.713
Creatinine (mg/dL)	0.903±0.39	0.97±0.52	0.578
Na (mEq/L)	133.1±9.8	140.1±14.0	0.027
K (mEq/L)	3.85±0.72	4.28±0.96	0.053

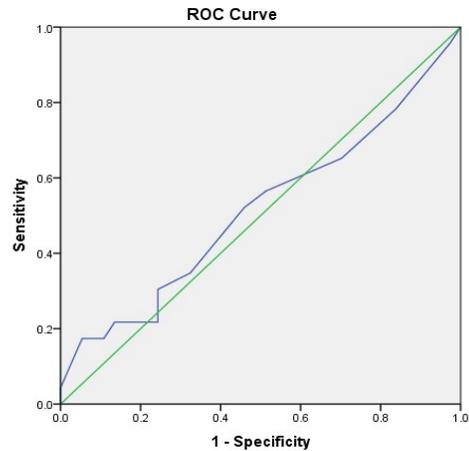
**Table-5: Sensitivity and specificity of serum urea, creatinine, Na and K in detecting complicated appendicitis (n=60)**

Variable (cut off value)	Sensitivity (%)	Specificity (%)	AUC
Urea ( $\geq 21.5$ mg/dL)	65.2	35.1	0.526
Creatinine ( $\geq 0.65$ mg/dL)	65.2	30.0	0.515
Na ( $\geq 134.5$ mEq/L)	73.9	51.4	0.690
K ( $\geq 3.45$ mEq/L)	78.3	27.0	0.607



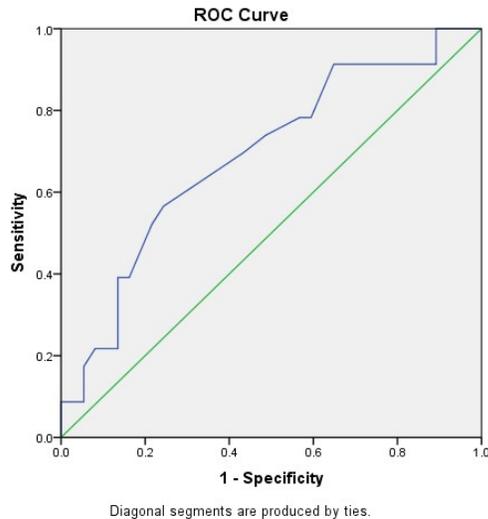
Diagonal segments are produced by ties.

**Figure-1: ROC curve for urea**

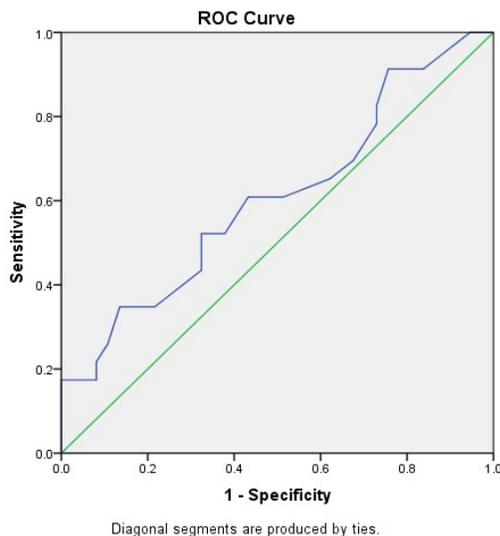


Diagonal segments are produced by ties.

**Figure-2: ROC curve for creatinine**



**Figure-3: ROC curve for Sodium**



**Figure-4: ROC curve for Potassium**

## DISCUSSION

This study has been carried out on 60 patients, with a male predominance in the study sample, in agreement with similar studies on appendicitis patients.<sup>5,7</sup> A previous study has proved male gender to be a significant predictor of acute and complicated appendicitis.<sup>5</sup> However, our study showed no such association. Majority of patients with appendicitis were young, between 21–30 years of age. While other studies have shown that with advancement of age, incidence of complicated appendicitis increased, our study revealed no such trend.<sup>5</sup>

Our study has shown that serum urea, creatinine, sodium and potassium are all generally elevated in suppurative appendicitis as compared to other forms of appendicitis. (Table-3) However, no

significant association between the aforementioned parameters and complicated appendicitis could be established in our study except sodium. The AUC of ROC curves of all serum markers were around 0.5, which shows their low capability of precisely diagnosing complicated appendicitis. None of the studied serological markers was found to have the power to discriminate complicated appendicitis from uncomplicated appendicitis. This is contrary to the findings of previous studies that have shown significant rise of blood urea nitrogen and creatinine in patients with perforated appendicitis.<sup>7,8</sup>

International literature reports a strong diagnostic association of hyponatremia with acute appendicitis in children. A study with the largest sample size proved hyponatremia's association with perforated or gangrenous appendicitis.<sup>9</sup> Another study also proved a strong association between hyponatremia and complicated appendicitis while in our study, hypernatremia with cut off value of 135 mEq/L was found to be significantly higher in patients with histologically proven complicated appendicitis.<sup>10</sup> An old study, conducted in Pakistan has also shown that the serum levels of urea, creatinine and electrolytes stayed within normal ranges in acute appendicitis patients.<sup>11</sup>

A significant association between complicated appendicitis with right hydronephrosis with OR of 4.90 and specificity of 99.3% has been reported<sup>12</sup>, and as hydronephrosis alters kidney function, it may lead to deranged serum urea, creatinine, Na and K levels as well. However, our study could not establish the role of appendicitis in altered levels of above serum markers to label them as preoperative diagnostic parameters.

## CONCLUSION

Serum urea, creatinine, sodium and potassium levels show a tendency to be predictive of complicated appendicitis but a strong association could not be established. Further studies on these parameters are encouraged to assess their diagnostic accuracy for complicated appendicitis.

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## AUTHORS' CONTRIBUTION

MM: Conception of study, designing, planning, manuscript writing, study conduction, analysis, interpretation, discussion. FK: Conception of study, designing, planning, manuscript writing, study conduction, analysis, interpretation, discussion. AM: Conception of study, designing, planning, manuscript writing, study conduction, analysis, interpretation,

discussion. SA: Critical review, interpretation, discussion, facilitated for reagents/material analysis. MH: Critical review, interpretation, discussion, facilitated for reagents/material analysis. MA: Critical review, interpretation, discussion, facilitated for reagents/material analysis

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