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Original article

Impact of Preoperative Baseline Serum Urea and Creatinine Levels Among Patients with Perforated Peptic Ulcer Disease in Lafia, North-Central Nigeria

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ABSTRACT

Background: Perforation is the most serious surgical complication of peptic ulcer disease due to its attendant high morbidity and mortality. Hypovolemia, a consequence of gastro-duodenal perforation, is considered to be a cause of renal hypo perfusion with accompanied decreased clearance of urea and creatinine. The aim of this study was to determine the preoperative baseline serum urea and creatinine profile among patients with perforated peptic ulcer disease and the relationship of serum urea and creatinine with the outcome of care.

Methods: A retrospective study of patients who had operation for perforated peptic ulcer disease over a 5-year period at Dalhatu Araf Specialist Hospital, lafia, North-central Nigeria was conducted.

Results: Sixty-four patients were studied with a mean age of 36.6 ± 12.3 years. Majority of the patients were males, 59 (92.2%). While 38 (59.3%) patients had elevated preoperative baseline urea levels, 37 (57.8%) patients had elevated creatinine levels. Out of 29 patients who had surgical site infection, 16 (55.2%) had elevated serum urea (p = 0.535) while 19 (65.2 %) had elevated serum creatinine (p = 0.579). An overall in-hospital mortality rate of 14.1% was recorded. There was statistically significant relationship between elevated serum urea and in-hospital mortality (p = 0.007).

Conclusion: This result showed that preoperative baseline serum urea and creatinine levels were elevated in majority of the patients. In addition, the result of this study suggests that elevated baseline serum urea level has considerable relationship with in-hospital mortality.

Key words: Peptic ulcer disease, perforation, serum creatinine, serum urea, mortality

INTRODUCTION

Perforated peptic ulcer disease (PPUD) is a life-threatening complication of peptic ulcer disease. [1, 2] It is a common cause of generalized peritonitis in adults worldwide and requires emergency surgical intervention as the main stay of treatment. [3-5]

Gastroduodenal perforation may be spontaneous or traumatic. Spontaneous perforations accounts for majority of cases with non-steroidal anti-inflammatory drugs and Helicobacter pylori infection implicated as the main etiological factors. [6, 7]

Despite advances in the treatment of peptic ulcer disease and its complications, the morbidity and mortality rates are still alarming in resource-limited settings. [8-11]

Following gastroduodenal perforation, there is leakage of gastric and duodenal contents into the peritoneal cavity resulting in third space fluid loss and clinical features of peritonitis. This may result in inadequate circulatory volume, hypotension, and decreased urine output. In more severe cases, shock and multiple organ dysfunction syndrome may ensue, resulting in electrolyte derangement, elevated serum urea and creatinine levels. [9, 11] Laboratory parameters are indicators of organ dysfunction and forms part of some scoring systems. [12, 13]

Perforated peptic ulcer constitutes a significant proportion of acute abdomen in the low and middle-income countries. Clinical diagnosis may be inferred from the onset of sudden abdominal pains, tachycardia, board-like rigidity of the abdomen and peritonitis. In addition, air under the diaphragm may be detected with imaging studies. [1, 3]

Following adequate resuscitation, surgery is the main stay of treatment in majority of the cases. This could be through laparoscopic approach, open surgery, combined endoscopic and laparoscopic approaches, and combined endoscopic and interventional radiologic approaches. The surgical techniques that are commonly done includes pedicle omental patch (Cellan-jones), repair with a free (Graham's) omental patch or a simple repair. [1, 3, 10]

Despite the advances in antibiotic therapy, newer anti-ulcer medications and treatment options, post-operative complications such as surgical site infections, sepsis, wound dehiscence, leakage, prolonged ileus, pneumonia and incisional hernia's still occurs in 30% of the patients. [1, 10]

The status of PPUD patients on admission has been described as a significant prognostic indicator. [14-16]

An elevated serum urea and creatinine level is a predictor of adverse outcomes both in the general population and in varying clinical conditions. [14, 17] There are paucity of studies that addresses the preoperative baseline serum urea and creatinine profile among patients with PPUD.

The aim of this study is to determine the preoperative baseline serum urea and creatinine profile among patients with PPUD and also the relationship between the serum urea and creatinine with the outcome of care.

MATERIALS AND METHODS

Study area and design

This is a hospital-based and retrospective cross-sectional study conducted at Dalhatu Araf Specialist Hospital [DASH], Lafia, Nasarawa state, Nigeria, from July 1, 2018 to June 30, 2023. DASH Lafia is a tertiary centre with 400 beds that serves as a referral facility for primary and secondary health centre's in the state and surrounding north-central states.

Study Population

All consecutive patients who had laparotomy for perforated peptic ulcer disease within the study period and met the inclusion criteria were included in the study [**Figure 1**].

Inclusion criteria

- Patients aged 18 years and above

Exclusion criteria

- Patients with incomplete data
- Patients with pre-existing renal failure
- Patients with gastroduodenal perforation from trauma
- Patients with perforated gastric cancers

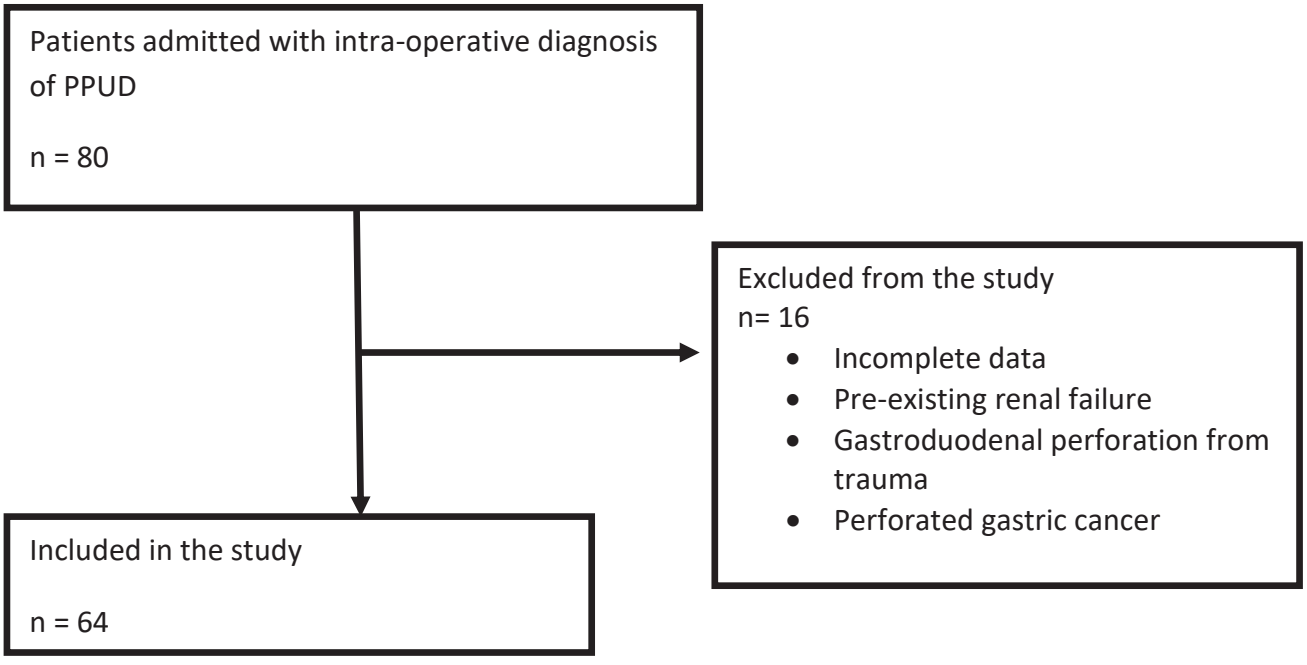

Figure 1: Flow chart showing patients' recruitment.

Data collection and analysis

In accordance with the hospitals protocol, at the emergency department, comprehensive history and physical examination were performed following adequate resuscitation. The resuscitation involved securing intravenous access with wide bore cannula with administration of isotonic fluid to correct dehydration or shock. Nasogastric tube for gastric decompression and urethral catheterization ensured for monitoring of urine output. Intravenous broad spectrum antibiotics and proton pump inhibitors were also administered. Blood transfusion and oxygen therapy were given when indicated.

Arising from the diagnosis of generalized peritonitis following perforated peptic ulcer disease, the patients were prepared and had laparotomy. Modified Graham's patch repair was performed in all the patients.

Data regarding the socio-demographic characteristics, clinical symptoms and signs, preoperative baseline serum urea and creatinine, intra-operative findings, post-operative complications such as surgical site infections (SSI), duration of hospital stay and in-hospital mortality were extracted from the patient's case notes and operation registers by trained surgical residents in the research protocol.

Data collection was supervised and the quality of data checked regularly.

Patient information was kept confidential and used only for the study.

Elevated serum urea and creatinine were defined as levels greater than 6.6 mmol/l and 126 µmol/l respectively. [18] This information was captured in a structured proforma.

The outcome measures in this study were surgical site infection, duration of hospital stay and in-hospital mortality rate.

The socio-demographic characteristics of the patients were compared using descriptive statistics. The results were presented in tables and charts. Categorical variables were summarized using frequencies and percentages. The Pearson's correlation and logistic regression were used to analyze the relationships/associations of continuous variables while non-parametric Chi-square statistical test was performed on categorical variables. A p-value of < 0.05 was considered statistically significant.

Ethical consideration

A written ethical clearance was obtained from the Dalhatu Araf Specialist Hospital [DASH] Lafia, research ethical committee [DASHREC /367].

RESULT

A total of 80 patients were operated for perforated peptic ulcer disease during the study period. However, 16 patients were excluded due to incomplete data.

The study was therefore carried out among 64 patients who met the inclusion criteria, out of which 59 (92.2%) were males. Male to female ratio was 11.8:1. Age of patients ranges between 18–70 years. Overall mean age of patients was 36.6 ± 12.3 years.

Socio-demographic characteristics

The majority of the participants were young males.

Occupationally, the study participants included individuals that were mainly engaged in farming (34.4%) [**Table 1**].

Baseline serum urea and creatinine levels on admission

The study showed an elevated serum urea and creatinine levels among 38[59.3 %] and 37[57.8 %] of the patients respectively as baseline [**Figures 2** and **3**].

Association between elevated Urea and SSI (surgical site infection)

The study revealed that out of 29 who had SSI, 16(55.2%) had elevated urea while 13(44.8%) had normal urea levels. Average urea for SSI patients was 9.3 ± 5.3 mmol/l while for patients with no SSI was 8.5 ± 4.9 mmol/l. The study showed no significant difference in the elevated urea for patients with and without SSI ($t = 0.623$, $p = 0.535$; $\chi^2 = 0.388$, $p = 0.533$) [**Table 2**].

Table 1: Socio-demographic characteristics.

Variable	Frequency (n=64)	Percent
Sex	59	92.2
Male	5	7.8
Female		
Age [years]		
<45	45	70.3
45-65	13	20.3
>65	6	9.4
Occupation		
Farming	22	34.4
Trading	14	21.9
Student	9	14.1
Artisan	7	10.9
Civil servant	5	7.8
Others	7	10.9

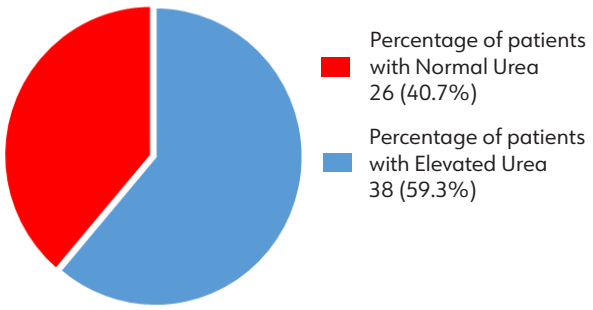

Figure 2: Percentage of patients with normal and elevated urea levels.

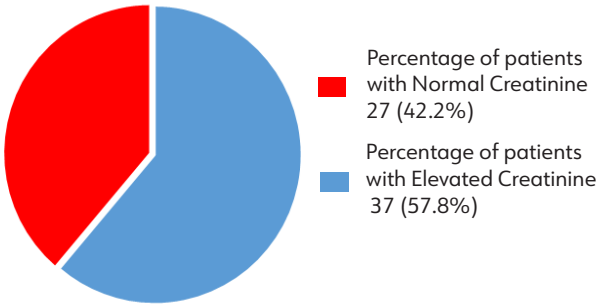

Figure 3: Percentage of patients with normal and elevated creatinine levels.

Association between elevated creatinine and SSI

The study revealed that out of 29 who had SSI, 19 (65.2%) had elevated creatinine while 10 (34.5%) had normal creatinine level. Average creatinine for SSI patients was 181.6±131.4 while for non – SSI was 164.4 ± 115.5. The study showed no significant difference in the elevated creatinine for patients with and without SSI (t = 0.558, p = 0.579; χ^2 = 1.291, p = 0.256) [**Table 3**].

Association between elevated urea and in-hospital mortality

All the 9 patients with mortality had elevated urea. This implies that mortality was significant with elevated urea (χ^2 = 7.166, p = 0.007) [**Table 4**].

Association between elevated creatinine and in-hospital mortality

It was discovered that 5(55.6%) out of 9 in-hospital mortality had elevated creatinine compared to four (4) who had normal creatinine level. However, this difference was not statistically significant (χ^2 = 0.022, p = 0.882) [**Table 5**].

Association between elevated urea and creatinine on the duration of hospital stay

The study revealed that 9(60.0%) out of 15 patients who had length of hospital stay between 1-7 days had elevated urea while 29(59.2%) who had length of stay above 7 days (one week) had normal urea. However, this difference was not statistically significant (χ^2 = 0.003, p = 0.955). In addition, 6(40.0%) out of 15 patients who had hospital length of between 1-7 days had elevated creatinine while 31(63.3%) out of 49 who had length of hospital stay above 7 days had normal creatinine. Similarly, this difference in length of hospital stay was not significant with elevated creatinine (χ^2 = 2.549, p = 0.110) [**Table 6**].

Correlations between elevated urea and creatinine on the duration of hospital stay

There was a positive but weak correlation between duration of hospital stay and elevated urea (r = 0.199) and creatinine (r = 0.124). However, this association was not statistically significant (p > 0.05) (**Table 7**).

Logistic regression – adjusting for age and sex

Serum urea levels was associated with in-hospital mortality but this relationship lost statistical significance after adjusting for age and sex [**Tables 8** and **9**].

Postoperatively, only one patient had values of serum urea and creatinine that remained elevated and for which dialysis was performed.

DISCUSSION

Despite advances made in the diagnosis and treatment of peptic ulcer disease, complications still occur in 10-20 % of patients. [19] The mean age of patients in our study was 36.6 years. This is similar to other studies from Nigeria and Ethiopia

Table 2: Association between elevated Urea and SSI (surgical site infection).

Serum Urea [mmol/l]	SSI	No SSI	Total	χ^2/t	*p*-value
Elevated urea	16(55.2)	22(62.9)	38(59.4)	0.388	0.533
Normal	13(44.8)	13(37.1)	26(40.6)		
Total	29(100.0)	35(100.0)	64(100.0)		
Mean ± SD	9.3 ± 5.3	8.5 ± 4.9	8.9 ± 5.0	0.623	0.535

Note: Min. – Max. Urea (2.6 – 26.0).

Table 3: Association between elevated creatinine and SSI.

Serum creatinine [μmol/ l]	SSI			χ^2/t	*p*-value
	SSI	No SSI	Total		
Elevated	19(65.5)	18(51.4)	37(57.8)	1.291	0.256
Normal	10(34.5)	17(48.6)	27(42.2)		
Total	29(100.0)	35(100.0)	64(100.0)	0.558	0.579
Mean ± SD	181.6 ± 131.4	164.4 ± 115.5	172.2 ± 122.3		

Note: Min. – Max. Creatinine level (24.0 – 600.0).

Table 4: Association between elevated urea and in-hospital mortality.

Serum urea [mmol/l]	Mortality			χ^2	*p*-value
	Absent	Present	Total		
Elevated	29(52.7)	9(100.0)	38(59.4)	7.166	0.007
Normal	26(47.3)	0(0.0)	26(40.6)		
Total	55(100.0)	9(100.0)	64(100.0)		

Table 5: Association between elevated creatinine and in-hospital mortality.

Serum creatinine [*μ*mol/l]	Mortality			χ^2	*p*-value
	Absent	Present	Total		
Elevated	32(58.2)	5(55.6)	37(57.8)	0.022	0.882
Normal	23(41.8)	4(44.4)	27(42.2)		
Total	55(100.0)	9(100.0)	64(100.0)		

Table 6: Association between elevated urea and creatinine on the duration of hospital stay.

Variables	Duration of hospital stay			χ^2	*p*-value
	≤ 7 days	> 7 days	Total		
Serum urea [mmol/l]					
Elevated	9((60.0)	29(59.2)	38(100.0)	0.003	0.955
Normal	6(40.0)	20(40.8)	26(40.6)		
Total	15(100.0)	49(100.0)	64(100.0)		
Serum creatinine [mol/l]					
Elevated	6(40.0)	31(63.3)	37(57.8)	2.549	0.110
Normal	9(60.0)	18(36.7)	27(42.2)		
Total	15(100.0)	49(100.0)	64(100.0)		

Table 7: Correlations between elevated urea and creatinine on the duration of hospital stay.

		Urea	Creatinine
Duration of hospital stay days	Pearson Correlation (r)	0.199	0.124
	P- value	0.115	0.329
	N	64	64

but in variance with studies in Tanzania which recorded a mean age of 28 years. [20-23] The male preponderance in our study is similar to previous reports in Nigeria and Northwestern Tanzania. [20, 23] However, this is contrary to the common depiction in western series as a disease of the elderly female. [24]

The early identification and categorization of high-risk patients prior to surgical intervention allows for enhanced and optimal decision- making process, in addition to cost-benefit strategies. This helps in better assignment of resources such as High dependency unit (HDU) and Intensive care unit (ICU) bed spaces which are limited in resource-poor settings like ours. [25]

Biomarkers such as serum urea and creatinine have the advantage of not only being objective in patient's assessment but also a routine baseline investigation in resource-limited settings. [25]

Our study demonstrated elevated baseline serum creatinine levels among 37(57.8%) of the patients. This is in variance with studies by Shashidhara et al. and Harten et al. who recorded lower levels of baseline creatinine in their studies in India and United - kingdom respectively. [11, 26]

The higher creatinine levels in our study may be attributable to worsening symptoms arising from delayed presentation which is a major problem in resource-limited countries due to financial challenges and illiteracy.

We found elevated serum creatinine levels among 65.2% of the patients that developed surgical site infection, however, it was not statistically significant (p = 0.579). Furthermore, this present study did not demonstrate any significant relationship between elevated creatinine and in-hospital mortality even though 55.6% of patients with elevated creatinine did

Table 8: Logistic Regression (Adjusting for age).

Mortality	Odds Ratio	Std Err	Z	P>/z/	95% C.I
Urea	0.917	0.061	−1.28	0.201	0.805–1.047
Age	0.977	0.03	−0.74	0.459	0.919–1.039
-Constant	33.549	47.494	2.48	0.013	2.092–537.895

Note: -Constant estimates baseline odds.

Table 9: Logistic Regression (Adjusting for Sex).

Mortality	Odds Ratio	Std Err	Z	P>/z/	95% C.I
Urea	0.916	0.062	-1.29	0.196	0.802-1.046
Sex	0.217	0.220	-1.50	0.132	0.030-1.587
-Constant	79.377	12.929	3.07	0.002	4.883-1290.292

Note: -Constant estimates baseline odds.

not survive. This is similar to the findings of Vats et al. [2] In contrast, Mulder and Co-workers in their study in South Africa found elevated serum creatinine level as the strongest single predictor of both mortality and ICU admission in patients with perforated peptic ulcer. [25] Also, in variance to our findings, Sivaram et al. and Senliku et al., both demonstrated elevated creatinine levels as a risk factor for postoperative morbidity and mortality in patients with PPUD. [14, 27] These findings may be attributable to the higher sample size of their study.

Urea as a metabolite has multiple roles in different homeostatic processes with the liver as the main urea genic organ. Until now, urea is often interpreted as a biochemical marker of renal function and its relation with other liver-specific functions and protein/nitrogen metabolism remains largely neglected.

Low urea levels are not common and are not usually a cause for concern. They can be seen in severe liver diseases or malnutrition but are not used to diagnose or monitor these conditions. Elevated urea levels should be considered not as mere biomarker of kidney damage, but an important factor in the multi-organ pathogenic interactions. [28]

Elevated levels of serum urea on admission has been reported as an independent predictor of in hospital mortality and included in some scoring systems such as Prediction of mortality in perforated peptic ulcer (POMPP) and Portsmouth physiological and operative severity score for the enumeration of mortality and morbidity (P-POSSUM). [29, 30]

In our study, elevated baseline serum urea level was found among 38(59.4%) patients. Mulder et al., in a retrospective study in South Africa similarly documented a greater proportion of their patients (55.3%) with elevated serum urea levels. [25] In contrast, Harten and co-workers reported fewer patients,66 (31.6%) with elevated serum urea levels in their study in the United Kingdom. [26] The higher numbers of patients with elevated urea levels in our study and similar studies may be a reflection of late presentation of the patients.

We found elevated baseline serum urea levels ($p = 0.007$) to be associated with in-hospital mortality. Our work confirms the few previous reports that have shown that urea is significant in predicting mortality. [14, 25, 26]

The reason for the association between elevated serum urea and mortality is not clear. [26, 28] However, both serum creatinine and urea levels are elevated with reduced renal clearance. Serum creatinine clearance is less sensitive than the clearance of urea in conditions where the urine flow rate is reduced, since the former is primarily due to glomerular filtration whereas clearance of urea is determined by both glomerular filtration and tubular reabsorption. [26, 28] In addition, during disease states, the osmotic regulations of vasopressin are over-ridden by several non-osmotic factors such as nausea, hypotension and hypovolemia which stimulates its secretion. In addition to reducing urine flow in the distal nephron, vasopressin also causes an increase in the number of urea pores in the distal nephron. Both of these effects will increase the reabsorption of urea and this may partly explain our findings that showed the association between the raised urea levels and in-hospital mortality. [26, 28]

Baseline serum urea neither demonstrated any association with surgical site infection rate nor with the length of hospital stay in our study.

Strength of the study

This study provides some useful information on the profile of baseline serum urea and creatinine levels among patients that were surgically managed for perforated peptic ulcer disease in addition to their post-operative outcome in a resource-limited setting.

Limitations

The study is limited because it has as small sample size, a single-centre and a retrospective study with some patients lacking properly registered data and incomplete investigation. Considering the geographical variations of reference ranges for abnormal values, this might have produced different results. Our results are based on a single measurement on hospital admission, and these may change prior to surgery.

CONCLUSION

In conclusion, this study showed that majority of the patients had an elevated preoperative baseline serum urea and creatinine levels. In addition, the result of our study suggest that baseline serum urea level has considerable relationship with in-hospital mortality.

AUTHORS' CONTRIBUTION

Each author has made a substantial contribution to the present work in one or more areas, including conception, study design, conduct, data collection, analysis, and interpretation. All authors have given final approval of the version to be published, agreed on the journal to which the article has been submitted, and agreed to be accountable for all aspects of the work.

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None.

CONFLICT OF INTEREST

None.

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