A Study of Acute Kidney Injury in Patients with Upper Gastrointestinal Bleeding

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Abstract: Objective: The aim of this work was to study the prevalence of acute kidney injury (AKI) in patients presenting to Tanta emergency hospital with Upper Gastrointestinal Bleeding (UGIB) from the period of 1/7/2014 and up to 6 months. **Background:** AKI is common in UGIB settings with multifactorial causes. It is associated with high rate of recurrent GI bleeding. Moreover, UGIB is the most frequent cause of bleeding after AKI. **Aim of the work:** The aim of this work is to study the prevalence of AKI in patients with UGIB. **Patients and Methods:** In a descriptive prospective study, patients with UGIB were screened for AKI during the interval from July 2014 to January 2015 using RIFLE and AKIN classification systems. All patients enrolled in the study have subjected to full history taking, through clinical examination and upper GI endoscopy to determine the cause of bleeding. **Results:** AKI was documented in 10.7% (64/600). There was no difference between RIFLE and AKIN classification systems regarding detection of AKI. 81.2% (51/64) classified as R, 17.2% (11/64) classified as I and 1.6% (1/64) classified as F. Regarding outcome of AKI, 15.6% of patients developed rebleeding during admission, 53.1% of patients developed complications (9.4% developed SBP, 9.4% developed hepatic encephalopathy, 9.4% developed pneumonia, 6.2% developed UTI, 7.8% developed septic shock,6.2% developed AF and 4.7% developed cerebral stroke) and 15.6% of patients went into multi-organ failure. Mortality was 7.8% among patients with AKI. **Conclusion:** The prevalence of AKI in UGIB is 10.7% with great impact on outcome and high mortality.
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Key Words: acute kidney injury, Upper Gastrointestinal Bleeding.

1-Introduction:

AKI is characterized by a rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte, and acid– base homoeostasis [(1)]. It is also dangerous even mild disease affects survival [(2,3,4,5)]. Mortality rates increase sharply as AKI worsens [(3,4,5,6)]. The incidence of AKI in unsegregated patients with AUGIB varies in the published literature from 1% to 11.4% [(7,8,9)]. *Moreover,* acute gastrointestinal hemorrhage, especially in the upper gastrointestinal tract, is the most frequent cause of bleeding after AKI [(10)].

Despite the high frequency and clinical importance of AKI in UGIB, few studies (***Alkhatib et al.*** [(11)] ***Ca´rdenas et al.*** [(8)] have so far been reported aimed at specifically assessing the relationship between bleeding and kidney injury. The current study was conducted to study the prevalence of AKI in patients with UGIB. The aim of the present study was to study the prevalence of AKI in patients with UGIB.

2- Methods:

This descriptive prospective study was carried out on six hundred patients presenting to Tanta emergency hospital with UGIB from the period of 1/7/2014 and up to 1/2/2015. Exclusion criteria include patients with hepatorenal syndrome, Patients on renal dialysis, Patients with nephropathy evidenced by ultrasound and diabetic patients. Based on RIFLE and AKIN classification systems, patients were categorized into: Group I: patients with no kidney injury (536 patients, 347 males and 189 females). Group II: patients with kidney injury (64 patients, 42 males and 22 females). Written consent was taken from every patient included in this study. This study was approved from the ethical committee, Faculty of medicine Tanta University. All the included patients were subjected to: (1)- Full history taking, (2)- Full clinical examination, (3)- Laboratory investigations including: Complete blood picture, clotting screen (PT, PTT and INR) kidney function testes (blood urea, serum creatinine and potassium level), (4)-Imaging study including Abdominal ultrasonography, with stress on: Liver size & echogenicity, spleen size, portal vein diameter and flow, presence or absence of ascites and hepatic focal lesions, (5)- GI endoscope to determine the cause of UGIB and (6)- Follow up and close observation for adequate homeostasis and early detection of rebleeding and to assess morbidity and mortality.

Statistical analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS version 19 (Statistical Package for Social Studies) created by

IBM, Illinois, Chicago, USA. For numerical values the range mean and standard deviations were calculated. The differences between two mean values of the two studied groups, with and without kidney injury, were used using student's t test. Differences of mean values at admission compared to that after 24 hours were tested using paired t test. For variables where the standard deviation indicated loss of normality of distribution, comparison of mean values of the two studied groups was tested suing Mann-Whitney test. On the other hand comparisons of mean value at admission and after 24 hours were performed using Wilcoxon singed ranks test. For categorical variable the number and percentage were calculated and differences between subcategories were tested by chi square (X2). When chi square was not appropriate Fisher and Monte Carlo exact testes were used. The level of significant was adopted at $p<0.05$.

3. Results:

The prevalence of AKI among studied groups was 10.7%. (Fig.1) The distribution of patients of AKI based on RIFLE classification system was Risk was 81.2%, Injury was 17.2% and Failure was 1.6%. (Fig. 2) The distribution of patients of AKI based on AKIN classification system was stage I was 81.2%, stage II was 17.2% and stage III was 1.6%. (Fig.3) there were significant differences between our studied groups regarding age (P=0.010) as a demographic data, epigastric pain (P=0.018) as a complaint, history of CLD (P=0.027), encephalopathy (P=0.032) and SBP (P=0.001) as clinical history, presence of encephalopathy (P=0.001), Fever (P=0.001), jaundice (P=0.022), dilated veins on anterior abdominal wall (P=0.001), and lower limb edema (P=0.005) during physical examination, presence of acute coronary syndrome (ACS) (*P*=0.001), chronic bronchitis (*P*=0.001) and pleural effusion (0.009) as comorbidities, history of either NSAIDS (*P*=0.006), and anticoagulants intake regularly (*P*=0.001), MAP after 24hr (*P*=0.001), degree of AKI and degree of hypovolemic shock (*P*=0.012), blood hemoglobin level after 24hrs (*P*=0.005), mean white blood corpuscles (*P*=0.001), mean PT mean PTT, mean INR (*P*=0.001),, mean blood urea on both admission and after 24hrs, mean serum creatinine on both admission and after 24hrs, mean serum potassium level (*P*=0.001) between studied groups as laboratory findings (Tab.1) (Tab.2) (Tab.3), presence of PVT,, enlarged spleen, and ascites during ultrasound examination (*P*=0.001), development of complications (P=0. 001), MOF (P=0.001) and death (0.005) during hospitalization, gastric ulcer (*P*<0.007) and gastritis (*P*<0.007) as endoscopic findings and argon plasma photo-coagulation (*P*=0.004) as a method of therapy.

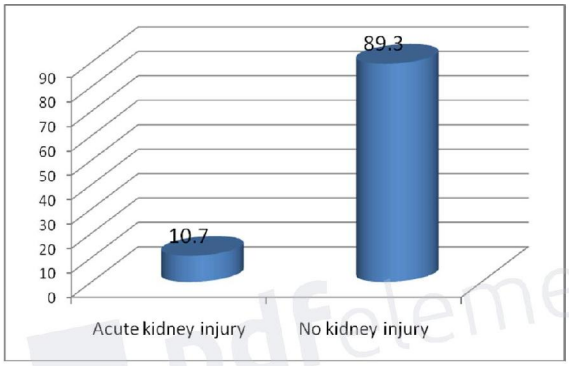
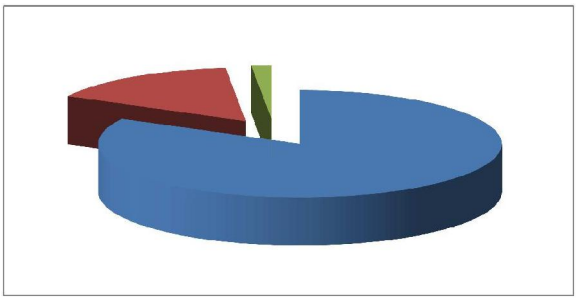


Figure (1): Prevalence of AKI among studied groups



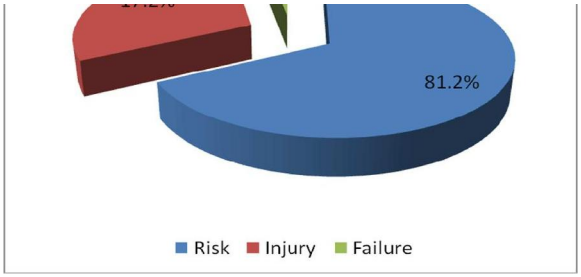


Figure (2): Distribution of patients of AKI based on RIFLE classification system

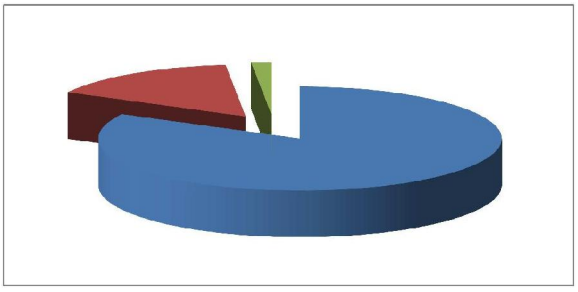


Figure (3): Distribution of patients with AKI based on AKIN classification system

Table (1); Comparison between studied groups regarding mean blood urea

Blood urea	**No kidney injury (n=536)**	**Kidney injury (n=64)**	**Z**	**p**
On admission:			11.210	0.001*
Range	0.15-220	32-220		
Mean	35.81	78.51		
SD	17.80	28.61		
After 24 hours			12.475	0.001*
Range	12-361	14-371		
Mean	40.60	140.93		
SD	22.17	58.10		
Z	9.992	6.942		
p	0.001*	0.001*		

*Significant

Table (2): Comparison between studied groups regarding mean serum creatinine

Serum creatinine	**No kidney injury (n=536)**	**Kidney injury (n=64)**	**Z**	**p**
On admission:			10.056	0.001*
Range	0.1-1.9	0.8-2.8		
Mean	0.90	1.38		
SD	0.28	0.33		
After 24 hours			12.579	0.001*
Range	0.1-3.7	0.9-4.2		
Mean	1.03	2.20		
SD	0.31	0.63		
Z	18.077	6.962		
p	0.001*	0.001*		

*Significant

Table (3): Comparison between studied groups regarding mean serum potassium level

Serum potassium level	**No kidney injury (n=536)**	**Kidney injury (n=64)**
Range	2-6	2.7-5.7
Mean	3.64	4.08
SD	0.71	0.70
t		4.742
p	0.001*	

*Significant

4. Discussion:

AKI is defined as abrupt, persisting and theoretically reversible worsening or loss of renal function associated with a decline in diuresis and increase in serum creatinine and urea. The incidence of AKI in patients with AUGIB ranged from 1% to 11.4% [12]. Results of the current study showed the prevalence of AKI was 10.7% in agree with ***Ca´rdenas* et al., (2000)** [8] they found that renal failure was developed in 11% of the bleeding episodes and disagree with retrospective study conducted by **Alkhatib et al., (2009)** [11] that showed AKI occurred in 3.5% of patients with AUGIB. **Del Olmo et al., (2000)** [7] reported an incidence of renal failure of 8%. The current study showed no difference between RIFLE and AKIN classification systems. This finding had not previously been reported in this context before, but **Alkhatib et al. (2009)** [11] found that applying the RIFLE criteria in elderly patients presenting with AUGIB helps to identify a sizeable subgroup of patients with varying degrees of renal injury, including those with subtle renal dysfunction. **As regard demographic characteristics**, the current study showed that in group I (non AKI group), the mean age was 58.57± 11.55 years, while in group II (AKI group), the mean age was 62.52 ± 11.98 years with statistically significant differences between the

studied groups (*P*=0.010), in agree with the data of **Alkhatib et al. (2009)** [11], as they demonstrated a very high prevalence of patients with some degree of AKI (48.7%) in elderly patients (≥60 years) presenting with AUGIB.

Regarding clinical history; in group I, 85.3% of patients (457/536) had history of chronic liver disease (CLD), 13.4% of patients (72/536) were admitted with encephalopathy in the past and 54 patients 10.1% of patients (54/536) were admitted with subacute bacterial peritonitis (SBP). However, in group II 95.3% of patients (61/64) had history of CLD, 23.4% of patients (15/64) were admitted with encephalopathy in the past and 25.0% of patients (16/64) were admitted with SBP. The current study demonstrated significant differences between studied groups regarding history of CLD (*P*=0.027) history of encephalopathy (*P*=0.032) and history of SBP (*P*=0.001). In a study dealing with AKI in patient with Liver cirrhosis, conducted by **Yun Jung Choi et al., (2014) based on ADQI-IAC working party proposal** [13]**,** included Six hundred and forty-three patients. Eighty-three patients (12.9%) were diagnosed with AKI. Another prospective, multi-center observational cohort study conducted by **Belcher JM et al., (2013)** [14]**,** dealing with AKI based on AKIN classification system in patient with Liver cirrhosis, include 219 patients with cirrhosis and AKI, 129 patients (67%) were have history of hepatic encephalopathy and 31patients (16%) were have history of SBP.

Regarding clinical findings on admission; in group I 16.8% (90/536) of patients were in encephalopathy. While In group II 34.4% of patients (22/64) were in encephalopathy with significant differences between studied groups (*P*=0.001). In agree with **Ca´rdenas A et al., (2000)** [8]**,** as they demonstrated significant differences between bleeding cirrhotic patients who developed renal failure and presence of encephalopathy at admission (*P*≤0001).

Regarding drug history; while in group I 24.6% of patients (132/536) were on regular NSAIDS, in group II 40.6% of patients (26/64) were on regular NSAIDS with significant differences between studied groups (*P*=0.006). In Prospective cohort study conducted with **Chiara Elia et al. (2015)** [15]**,** designed to evaluate the severity of AKI in cirrhotic patients treated with NSAIDS, Thirty patients (30/780) with cirrhosis and NSAIDs-associated AKI were identified (3.8%). In nineteen patients (19/30) AKI was transient and kidney function rapidly recovered (4±3 days) after NSAIDs withdrawal. In the remaining 11 patients (11/30) AKI was more severe and persisted during hospitalization despite drug withdrawal. They conclude that Patients with cirrhosis treated with NSAIDs may develop severe AKI which may be irreversible. In contrast to our study, **in Alkhatib et al. (2009)** [11]**,** 40 patient of 58 patients (69%) not developed acute kidney dysfunction were on NSAIDS while 29 patients of 55 patients (53%) developed acute kidney dysfunction were on NSAIDS with no significant difference between the 2 groups**.** A nested case-control study conducted by **Huerta C et al., (2005)** [16] to evaluated NSAIDS and risk of ARF in the general population and include were 386,916 patients aged 50 to 84 years. They found that NSAID users had a 3-fold greater risk for developing a first-ever diagnosis of clinical ARF compared with non-NSAID users in the general population [#1]**.** A study conducted by **Griffin MR et al. (2000)** [17], dealing with NSAIDS and acute renal failure in elderly persons. Of the 1,799 patient ≥ 65 years with acute renal failure, 18.1% were current users of prescription NSAIDs as compared with 11.3% of 9,899 randomly selected population controls. They found current NSAID use increased the risk of acute renal failure 58 percent. **Regarding vital data;** in group I while mean arterial pressure (MAP) was 94.57±16.69 mmHg during first 24hr, it was 62.40±11.45 mmHg after 24 hr. In group II MAP was 93.75± 17.02 mmHg during first 24hr and 62.09±10.77 mmHg after 24hr with significant differences between studied group regarding MAP after 24hr (*P*=0.001), in disagree with data reported by **Ca´rdenas et al., (2000)** [8] as they demonstrated significant differences regarding mean blood pressure during first 24hr (*P*<0.001). Regarding mean pulse rate (beats/minute), while in group I mean pulse rate was 94.86±15.17, In group II, it was 97.34±15.57 with no significant differences between studied groups, in agree with **Ca´rdenas et al., (2000)** [8] as they found no significant differences regarding mean pulse rate and bleeding cirrhotic patients developed renal failure. **Regarding laboratory findings,** regarding hemoglobin level**,** in group I mean hemoglobin level was 8.64±2.40 g/dl on admission and 9.75±2.00 g/dl after 24hr, in group II it was 8.01±2.19 g/dl on admission and 9.01±1.95 g/dl after 24hr. Regarding white blood corpuscles (WBCs), in group I mean WBCs was 9.09±5 X103, in group II it was 13.88±7.14 X103. Regarding blood platelets, in group I mean blood platelets was 134.08± 85.33, in group II it was 120.20± 79.52. There were significant differences between studied groups regarding mean hemoglobin level after 24hrs and mean WBCs (*P*=0.005) (*P*=0.001), in agree with **Ca´rdenas et al. (2000)** [8] as they found significant differences in bleeding cirrhotic patients developed renal failure regarding mean Leukocyte count (*P*=.001). No significant differences between studied groups regarding blood hemoglobin level during first 24hrs in agree with **Ca´rdenas et al. (2000)** [8] **and Alkhatib et al. (2009)** [11] as they found no significance

differences between studied groups regarding hemoglobin on admission. In disagree with the current study **Ca´rdenas et al. (2000)** [8] found significant differences regarding blood platelets in cirrhotic UGIB who developed renal failure (*P*=0.03). Regarding prothrombin (PT), in group I mean PT was 16.35±4.65, in group II it was 19.08±5.85. Regarding PTT, in group I the mean PTT was 51.05±14.55, in group II it was 56.28±17.08. Regarding INR, in group I the mean INR was 1.57±3.85, in group II it was 1.81±0.61. There were significant differences between studied groups regarding PT, PTT and INR (*P*=0.001), in agree with **Ca´rdenas et al., (2000)** [8] as they found significant differences between studied groups regarding PT (*P* <0.01), **Tsien et al., (2013)** [18] who found significant differences between cirrhotic ascetic patients not developed AKI and those developed AKI during fellow up after 12 month regarding INR (*P*<0.05), in disagree with **Fasolato et al., (2007)** [19] who reported no significance difference between cirrhotic patients not developed renal failure and those developed renal failure regarding PT and **Alkhatib et al. (2009)** [8] who found no significant difference between their studied groups regarding prolonged INR (≥1.5) on admission. Regarding blood urea, in group I mean blood urea was 35.81± 17.80 on admission and 40.60±22.17 after 24hrs. In group II, mean blood urea was 78.51±28.61 on admission and 140.39±58.10 after 24hrs. **Regarding serum creatinine,** in group I mean serum creatinine was 0.90±0.28 mg/dl on admission and 1.03±0.31 mg/dl after 24hr. In group II mean serum creatinine was 1.38±0.33 on admission and 2.20±0.63 after 24hrs. Regarding serum potassium, in group I mean serum potassium was 3.64±o.71 mg/dl. In group II, it was 4.08±0.70 mg/dl. There were significant differences between studied groups regarding mean blood urea, mean serum creatinine and mean serum potassium level between studied groups (*P*=0.001). In agree with our study, **Ca´rdenas et al., (2000)** [8] who found significant differences between their studied groups regarding baseline mean serum creatinine (*P*<0.001), **Fasolato et al., (2007)** [19] who reported significance differences between cirrhotic patients not developed renal failure and those developed renal failure regarding serum creatinine (*P*<0.0001), **Alkhatib et al., (2009)** [11] who found significant differences between their studied groups regarding the average serum creatinine on presentation (*P*<0.002) and **Wong et al., (2013)** [20] a study dealing with AKI in cirrhotic patients, who found significant differences regarding mean serum creatinine on admission (P<0.0001). In disagree with this study **Ca´rdenas et al., (2000)** [8] found no significant differences between their studied groups regarding baseline mean serum potassium.

Conclusion:

From results of our study we concluded that the prevalence of AKI in UGIB patients was 10.7% with great impact on outcome and high mortality. Further studies including new biomarkers and large number of patients for longer time may be useful to diagnose AKI in UGIB settings.

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No conflict of interest

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