Significant Risk Factors for Acute Kidney Injury- A Case Control Study

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ABSTRACT

Background: Acute Kidney injury(AKI) is one of the common diseases that's affect more than 13 million people annually. Diabetes mellitus, hypertension, upper respiratory tract infection, septic shock and nephrotoxic agents are significant risk factors for Acute Kidney Injury.

Material and Methods: This case control study was doneon 200 urinary tract infected (UTI). The inclusion criteria for cases were patients with Acute Kidney Injury age above 15 years, both genders, diagnosed urinary tract infection. Controls were similar to cases except without Acute Kidney Injury. Demographics and risk factors for Acute Kidney Injury were recorded. We use Student t test compare continuous variable. For categorical variables we used Chi-square test. Multivariate logistic regression was carried using Acute Kidney Injury as dependent variable and risk factors as independent variables. P=0.05 was considered significant. **Objectives:** To determine significant risk factors for acute kidney injury.

Results: The male were 87(43.5%) and female were 113(56.5%). The mean age of the study was 45.19 ± 16.2 years. The frequency of diabetes mellitus (P=.008), hypertension (P<.001), upper respiratory tract infection (P=.030), septic shock (P=.011) and nephrotoxic agents (P=.013) were more in cases than controls and results were statistically significant. Positive association was found for Acute Kidney Injury with increasing age (OR=1.06; 95% CI=1.017, 1.105), serum creatinine (OR=5.9; 95% CI=2.85, 12.55). There was negative association between glomerular filtration rate (GFR) and Acute Kidney Injury (OR=0.92; 95% CI=0.888, 0.953).

Conclusion: After controlling confounding factors through multivariate analysis the increasing age, serum creatinine and low GFR were significant risk factor for acute kidney injury.

Keywords: Acute kidney injury, risk factors, urinary tract infection, serum creatinine

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INTRODUCTION

The classical definition of acute kidney injury (AKI) is the abrupt and sustained decrease in function of kidney. Nevertheless, the exact cutoffs diagnosis of AKI is not agreed.^{1, 2}Worldwide the AKI is a common disease affecting more than13 million people annually, 85% of whom belonged to developing countries.¹ In developed countries the acute kidney injury is rarely a community-acquired disease; the primary source of AKI in these countries is the hospitalizations of patients. There is five-to-tenfold increase in the incidence of hospital-acquired acute kidney injury in these areas.³ Conversely, in less-developed countries the AKI frequently found in the community.⁴

One of the frequent cause of acute kidney injury is the sepsis⁵, and more than half of affected subjects by septic shock lead to acute kidney injury⁶. Acute urinary tract infection (UTI) may lead to decline in renal function, particularly in case of urinary tract obstruction. Acute kidney injury during acute care is associated with high degree

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of morbidity as well as mortality.⁷ Patients affected by severe form of AKI are at more risk for end stage renal disease and even fatality during postdischarge period from the hospital.⁸

In developing countries the etiology of acute kidney injury are; tropical infections (e.g. leptospirosis, malaria and dengue), other form of infections (gastroenteritis, pneumonia, skin infection), acute glomerular disorders, gynecological issues, pre-disposing renal diseases (kidney, cardiac problem, diabetes mellitus, etc), herbal treatment, trauma, nephrotoxic agent, environmental causes like snake bites, and hospital-acquired AKI. Surgical intervention can lead to AKI.⁹⁻¹¹

The diagnosis of acute kidney disease can be made when glomerular filtration rate (GFR) decrease by more than 50% or two fold increase in serum creatinine comparative to baseline creatinine as per the RIFLE GFR criteria.¹² Hsiao et al.¹² conducted an study to know the risk factors of AKI in having UTI patients. They reported that associated risk factors for AKI were older age, upper UTI, diabetes mellitus (DM), lower baseline eGFR and a febrile during hospitalization.

There is lack of local studies on the risk factors for AKI which can different across the population due to genetic, ethnic and environmental factors. So the objective of this study was to know the risk factors for acute kidney injury.

MATERIALAND METHODS

This case control study was done in Medical Department, of Saidu teaching hospital, Swat. A total of 200 patients (100 cases and 100 controls) were selected by consecutive sampling technique. After in depth explanation of objective and benefits of the research verbal informed consent was taken from all participants. The participants were ensured for maintaining their confidentiality.

The inclusion criteria for cases were patients with AKI, age above 15 years, both gender, diagnosed urinary tract infection cases (pain on micturition, lumbar aches or Patient is febrile and having more than 104 colony forming units/mL of bacterial isolation .Controls were similar to cases except without AKI. The operational definition of acute kidney injury was made if glomerular filtration (GFR) decrease by more than 50% or double increase of serum creatinine level from baseline as per the 'RIFLE GFR' criteria.¹² Subjects having simultaneous infections other than urinary tract infection (UTI) or receiving chronic dialysis was excluded.

Base line demographics like age, gender, and educational level were recorded. The recorded risk factors were hypertension, diabetes mellitus (DM), Hepatitis, AIDS, cardiac diseases, cerebrovascular disease, neoplasm, and medications (antihypertensive, nephrotoxic agents, and non-steroidal anti-inflammatory drugs).All the admitted patients were treated with antibiotics according to the standard protocol.

Data analysis was done in SPSS version 23. Descriptive statistics like mean and standard deviation was calculated for numerical variables like age, Systolic blood pressure (BP), Diastolic BP, Serum creatinine, and Baseline eGFR. We use chi-square test for categorical variables and for continuous variable we used student t test. Frequency was computed for categorical variable DM, hypertension, and cause of AKI etc. Multivariate logistic regression was carried using AKI as dependent variable and risk factors as independent variables. P=0.05 was considered significant.

RESULTS

The male were 87(43.5%) and female were 113(56.5%). The mean age of the study was 45.19±16.2 years. The mean systolic blood pressure (BP), diastolic BP, serum creatinine,

baseline glomerular filtration rate was 130.3 ± 15.03 mmHg, 90.3 ± 15.04 mmHg, 2.47 ± 1.19 mg/dl and 67.98 ± 20.5 mL/min/1.73 m² respectively. In overall study the nephrotoxic agents, diabetes mellitus, hypertension, upper respiratory tract infection, septic shock were found in 77(38.55), 59(29.5%), 54(27.0%), 121(60.5%), and 21(10.5%) cases respectively.

The frequency of diabetes mellitus (P=.008), hypertension (P<.001), upper respiratory tract infection (P=.030), septic shock(P=.011) and nephrotoxic agents(P=.013) were more in cases than controls and results were statistically significant. (Table 1)

The mean age in cases $(51.57\pm15.73 \text{ years})$ was higher than controls $(38.81\pm14.2 \text{ years})$ and results were very high statistically significant (P<0.001; 95% CI=8.5, 16.9). Similarly the serum creatinine and baseline eGFR was very highly statistically significantly more in cases than controls (P<0.001). However, the results for systolic and diastolic BP was not significant (P>0.05). (Table 2)

Table 3 shows the multivariate logistic decrease model for factors related to AKI using the control (patients with no AKI) as a reference category. Coronary artery disease, upper respiratory tract infection, septic shock and systolic blood pressure were not significant risk factors for AKI after adjusting with logistic regression model as covariate (P>0.05). Positive affect was found for AKI with increasing age (OR=1.06; 95%) CI=1.017, 1.105), serum creatinine (OR=5.9; 95%) CI=2.85, 12.55). There was 5.9 odds increase in serum creatinine in patients with AKI as compared to controls. There was negative association between GFR and AKI (OR=0.92; 95% CI=0.888, 0.953).

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		Acute Kidney Injury				P-Value
		No		Yes		
		N	%	Ν	%	
Condor	Male	47	54	40	46	210
Gender	Female	53	46.9	60	53.1	.310
Diabetes	Yes	21	35.6	38	64.4	000
Mellitus	No	79	56	62	44	.008
Hypertension	Yes	9	14.3	54	85.7	< 001
	No	91	66.4	46	33.6	<.001
Upper	Yes	32	40.5	47	59.5	
Respiratory tract infection	No	68	56.2	53	43.8	.030
Septic Shock	Yes	5	23.8	16	76.2	011
	No	95	53.1	84	46.9	.011
Nephrotoxic	Yes	30	39	47	61	013
agents	No	70	56.9	53	43.1	.015

^{*}chi-square test

Table 2. Comparison of continuous risk factors in patients with and without AKI

	acute kidney injury (AKI)	Mean <u>+</u> SD	P-Value [*]	95% CI	
Age	Yes	51.57 <u>+</u> 15.73	<0.001	95 160	
	No	38.81 <u>+</u> 14.2	<0.001	0.5, 10.9	
Systolic BP	Yes	131.7 <u>+</u> 16.4		1 29 6 09	
	No	128.9 <u>+</u> 13.48	.109	-1.30, 0.90	
Diastolic BP	Yes	91.7 <u>+</u> 16.4	170	1 37 6 00	
	No	88.9 <u>+</u> 13.48	.179	-1.37, 0.99	
Serum	Yes	3.21 <u>+</u> 0.951	<0.001	1 22 1 74	
creatinine	No	1.735 <u>+</u> 0.929	<0.001	1.22, 1.74	
Baseline eGFR	Yes	55.23 <u>+</u> 16.93			
(mL/min/1.73 m ²)	No	80.74 <u>+</u> 15.34	<0.001	-30.01, -21.0	

^{*}Independent t test

Table 3. Multivariate logistic regression model for factors related to 'acute kidney injury'

Covariate	β	P-value	OR (95% CI)
Coronary artery disease	0.437	0.793	1.54(0.06, 40.19)
Upper Respiratory tract infection	-0.254	0.668	0.776(0.24, 2.47)
Septic shock	-0.477	0.612	0.621(0.098, 3.92)
Hypertension	-2.823	<0.001	0.059(0.014, 0.259)
Diabetes	-1.46	0.044	0.232(0.056, 0.961)
Age	0.058	0.006	1.06(1.017, 1.105)
Systolic blood pressure	0.01	0.555	1.01(0.97, 1.045)
Serum Creatinine	1.789	<0.001	5.9(2.85,12.55)
Glomerular filtration rate	-0.084	<0.001	0.92(0.888, 0.953)
Constant	0.477	0.891	1.611

DISCUSSION

This case control study was conducted to ascertain the risk factors for 'acute kidney injury (AKI)'. Multivariate logistic regression analysis was done to control confounders in the study and to determine associated risk factors for AKI. Our findings showed that the frequency of diabetes mellitus (P=.008), hypertension (P=<.001), upper respiratory tract infection (P=.030), septic shock (P=.011) and nephrotoxic agents (P=.013) were more in cases than controls and results were statistically significant. After controlling confounders through regression analysis our results showed that increasing age (OR=1.06), serum creatinine (OR=5.9) and GFR(OR=0.92) were significant risk factor for 'acute kidney injury (AKI)'.

In this study we include the patients with UTI which can lead to sepsis and septic shock. UTI can cause 'acute kidney injury (AKI)'.¹² Earlier investigations reported that hypotension, hypovolemia, the use of nephrotoxic agents, sepsis, urinary obstruction, contrast media were risk factors in UTI affected subjects for AKI.^{13, 14} Hsiao et al.¹² conducted an investigation to assess the risk factors of Acute Kidney Injury in UTI patients. They reported that associated risk factors for AKI were older age, upper UTI, diabetes mellitus (DM), lower baseline eGFR and a febrile during hospitalization. These results are in favor of our study except a febrile during hospitalization.

Our findings showed that that increasing age (OR=1.06) was significant risk factor for 'acute kidney injury (AKI)'. Hsiao et al.¹² reported that an odd ratio of 1.20 for increasing age with AKI in their multivariate logistic regression. These results are in consistent with our study. The reason for this association can due to the fact that in elderly there is high prevalence of UTI as compared younger population.¹⁵ In addition, age-related decrease in glomerular filtration rate may cause elder populations at more risk for AKI.¹⁶

Our findings showed that increase in serum creatinine was associated with 5.9 time increase risk for AKI (OR=5.9). Serum creatinine level is normally used in clinical practice to assess the renal function. The value of serum creatinine above one shows the dysfunction of kidney. This showed that renal dysfunction is major cause of 'acute kidney injury (AKI)'. Serum creatinine is also used directly for diagnosing AKI. ¹² Similarly

results were reported by Hsiao et al.¹²

The current study showed that less GFR was protective for 'acute kidney injury (AKI)' with odd ratio of 0.92. This shows that in 'acute kidney injury (AKI)' the GFR value become higher. Similar results were found by Hsiao et al¹². Hsu et al.¹⁷ conducted a study on chronic kidney disease patients having hospital acquired acute kidney injury managed with and without dialysis, and they reported that if eGFR is less than 60 ml/minutes/1.73m², there is higher risk of AKI. Our findings showed that renal dysfunction (high GFR) have a predictive role for 'acute kidney injury (AKI)' in urinary tract infected patients.

CONCLUSION

Based on our results it can be concluded that diabetes mellitus, hypertension, upper respiratory tract infection, septic shock and nephrotoxic agents are significant risk factors for AKI. However, after controlling confounding factors through multivariate analysis the increasing age, serum creatinine and low GFR were significant risk factor for 'acute kidney injury (AKI)'.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

 Samiullah, Ayub M: Concept and design of study, Collection of data, statistical analysis
Saeed M, Aminullah: Writing of manuscript, critical review of manuscript
Rashieed AU: Analysis and interpretation of data, statistical analysis
Raheem S: Data collection, bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.