RISK, PREDICTORS, AND OUTCOMES OF ACUTE KIDNEY INJURY IN PATIENTS ADMITTED TO INTENSIVE CARE UNITS IN EGYPT

Samar Abd ElHafeez DrPH*[1, 2]; Giovanni Tripepi* PhD[3]; Robert Quinn MD, PhD, FRCPC[2]; Yasmine Naga MD, PhD[4]; Sherif Abdelmonem MD, PhD[5]; Mohamed AbdelHady MD, PhD[6]; Ping Liu PhD[2]; Matthew James MD, PhD[7]; Carmine Zoccali FASN, FNKF, FERA[3]; Pietro Ravani* MD, PhD, FERA[2]

[1] Epidemiology Department, High Institute of Public health, Alexandria University, Alexandria, Egypt.
[2] Departments of Medicine and Community Health Sciences, University of Calgary, Calgary, Canada.
[3] CNR-IFC Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension Unit, Ospedali Riuniti, Reggio Calabria, Italy.
[4] Internal Medicine Department (Nephrology Unit), Faculty of Medicine, Alexandria University, Alexandria, Egypt.
[5] Critical Care Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
[6] Anesthesia and Surgical ICUs Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
[7] Departments of Medicine and Community Health Sciences, Libin Cardiovascular Institute of Alberta, O'Brien Institute for Public Health, University of Calgary, Calgary, Canada.

#GT and PR co-supervised SA (post-doctoral fellow)

Correspondence:
Name: Dr. Samar Abd ElHafeez
Address: High Institute of Public Health, Alexandria University, 165 ElHorreya Avenue, ElHadara, Alexandria, Egypt
Telephone: +201005052416
Email: samarabdelhafeez.epid@gmail.com
Word count: 3362
Abstract: 199

Running title: AKI in ICUs in Egypt

Table S1: Baseline characteristics of AKI patients at ICU admission

Baseline characteristics	No AKI at ICU admission	AKI at ICU admission	P value
Number of patients	321 (60.3)	211 (39.7)	
Age (years)	40 (28-75)	53 (32-67)	<0.001
Male (%)	134 (41.7)	88 (41.7)	0.99
Ex-smokers (%)	36 (11.2)	28 (13.3)	0.48
Current smokers (%)	39 (12.1)	22 (10.4)	0.54
Marital status			
Single (%)	54 (16.8)	17 (8.1)	
Married (%)	256 (79.8)	180 (85.3)	0.10
Divorced (%)	4 (1.2)	0	0.10
Widowed (%)	7 (1.2)	14 (6.6)	0.01
Education			
Received some forms of education	232 (72.3)	118 (55.9)	<0.001
Residence			
Urban	163 (50.8)	110 (52.1)	0.95
Rural	158 (49.2)	101(47.9)	
Type of ICU unit			
Surgical	217 (67.6)	93 (44.1)	<0.001
Medical	104 (32.4)	118 (55.9)	
Co- morbidities			
Diabetics	58 (18.1)	65 (30.8)	<0.001
Cancer	48 (15)	17 (8.1)	0.02
Liver disease	24 (7.5)	30 (14.2)	0.01
CVD	116 (36.1)	119 (56.4)	<0.001
Pre-existing CKD	0	60 (28.4)	<0.001
COPD	19 (3)	7 (3)	0.17
History of sepsis at hospital admission	44 (13.7)	72 (34.1)	<0.001
Severity of sepsis			
Severe sepsis	29(65.9)	31(43.1)	
Septic shock	9(20.5)	35(48.6)	
Reason for ICU admission			
Pulmonary	32 (10)	43 (20.4)	0.001
GIT	36 (11.2)	24 (11.2)	0.96
CVD	24 (7.5)	31 (14.7)	0.009
Malignancies	49 (15.3)	5 (2.4)	<0.001
Infection	4 (1.2)	20 (9.5)	<0.001
Neurologic	50 (15.6)	26 (12.3)	0.29
Trauma	57 (17.8)	18 (8.5)	0.003
Obstetric/gynecological disorders	36 (11.2)	28 (13.3)	0.50
Others	33 (10.3)	16 (7.6)	0.29
Previous use of vasopressors	40 (12.5)	71 (33.6)	<0.001
Previous use of diuretics	27 (8.4)	47 (22.3)	<0.001

Previous use of Ca channel blockers	14 (4.4)	22 (10.4)	0.008
Previous use of ACEI	38 (11.4)	30 (14.8)	0.42
Previous use of ARB	5 (1.6)	10 (4.7)	0.03
Previous use of NSAIDs	97 (30.2)	51 (24.2)	0.13
BMI (Kg/m^2)	28.42±11.16	29.33±9.90	0.88
Length of ICU stay in days	7 (3-12)	6 (3-11)	0.51

AKI: Acute kidney injury, CVD: Cardiovascular diseases, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, GIT; Gastrointestinal tract, ACEI: Angiotensin converting enzyme inhibitors, ARB: Angiotensin receptor blockade, NSAIDs: Non-steroidal anti-inflammatory drugs, BMI: Body mass index, ICU: Intensive care units

*Previous use refers to the use at the time of ICU admission

Table S2: Clinical characteristics of AKI at ICU admission (study entry; N=211)

Clinical characteristics	Frequencies
AKI stages	
Stage 1	47 (22.2)
Stage 2	105 (49.8)
Stage 3	59 (28)
Mechanical ventilation	119 (56.4%)
FiO2 (%)	40 (21-60)
PaO2	80 (67-98)
Vaosactive therapy	71 (33.6)
Glasgow coma score	12 (8-15)
APACHE II	20.67±8.46
Platelets ($x10^3$/µl)	188 (130-257)
Urine output(ml/kg/hr)	0.49 (0.28-1.05)
ALT (U/L)	29 (19-84)
AST (U/L)	40 (23-84)
Serum creatinine at ICU admission (mg/dl)	1.84 (1.25-3.80)
Serum creatinine at ICU discharge (mg/dl)	0.82 (0.65-1.20)
Na(mmol/l)	137±7.72
K(mmol/l)	4.1±0.85
Blood urea (mmol/l)	4.34 (2.67-7.18)

AKI: Acute kidney injury, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, APACHE II: Acute Physiology and Chronic Health Evaluation

*Use of mechanical ventiation during the whole ICU stay

Table S3: Baseline characteristics for AKI after ICU admission

Baseline characteristics	AKI free	AKI after ICU admission	P value
Number of patients	201 (62.6)	120 (37.4)	
Age (years)	38 (27-54)	46 (34-62)	0.01
Male (%)	74 (36.8)	60 (50)	0.02
Ex-smokers (%)	14 (7)	22 (18.3)	0.002
Current smokers (%)	27 (13.4)	12 (10.1)	0.36
Marital status			
Single (%)	36 (17.8)	18 (15.1)	
Married (%)	159 (79.1)	97 (80.8)	0.71
Divorced (%)	2 (1)	2 (1.7)	0.60
Widowed (%)	4 (2)	3 (2.5)	0.76
Education			
Received some forms of education	147 (73.1)	85 (70.6)	0.66
Residence			
Urban	97 (48.3)	66 (55)	0.24
Rural	104 (51.7)	54 (45)	
Type of ICU unit			
Surgical	146 (72.6)	71 (59.2)	0.01
Medical	55 (27.4)	50 (40.8)	
Co- morbidities			
Diabetics	32 (15.9)	26 (21.7)	0.20
Cancer	31 (15.4)	17 (14.2)	0.76
Liver disease	11 (5.5)	13 (10.8)	0.08
CVD	63 (31.3)	53 (44.2)	0.02
COPD	10 (5)	9 (8)	0.35
History of sepsis at hospital admission	23 (11.4)	21 (17.5)	0.13
Severity of sepsis			
Severe sepsis	16 (69.6)	13 (61.9)	
Septic shock	3 (13)	6 (28.6)	
Reason for ICU admission			
Pulmonary	17 (8.5)	15 (12.5)	0.24
GIT	24 (11.9)	12 (10.0)	0.59
CVD	11 (5.5)	13 (10.8)	0.08
Malignancies	31 (15.4)	18 (15.0)	0.92
Infection	2 (1)	2 (1.7)	0.60
Neurologic	29 (14.4)	21 (17.5)	0.46
Trauma	38 (18.9)	19 (15.8)	0.49
Obstetric/ gynecological disorders	28 (13.9)	8 (6.7)	0.04
Others	21 (10.4)	12 (10.1)	0.90
Previous use of vasopressors	18 (9)	22 (18.3)	0.01
Previous use of diuretics	11 (5.5)	16 (13.3)	0.01
Previous use of Ca channel	6 (3)	8 (6.7)	0.12

blockers			
Previous use of ACEI	21 (10.4)	17 (14.2)	0.32
Previous use of ARB	5 (2.5)	0 (0)	0.08
Previous use of NSAIDs	55 (27.4)	42 (35)	0.15
BMI (Kg/m^2)	28.29±12.70	28.66±7.21	0.78
APACHE II	12.23±5.66	15.46±5.54	<0.001
Length of ICU stay in days	5 (2-10)	9 (5-15)	<0.001

CVD: Cardiovascular diseases, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, ACEI: Angiotensin converting enzyme inhibitors, ARB: Angiotensin receptor blockade, NSAIDs: Non-steroidal anti-inflammatory drugs, BMI: Body mass index, APACHE II: Acute Physiology and Chronic Health Evaluation

*Previous use refers to the use at the time of ICU admission

Table S4: Clinical characteristics of AKI after ICU admission (N=120)

Clinical characteristics	Frequencies
AKI stages	
Stage 1	89 (74.2)
Stage 2	19 (15.8)
Stage 3	12 (10)
Mechanical ventilation	78 (65.5)
FiO2 (%)	40 (38-53)
PaO2	93 (82-93)
Vaosactive therapy	44 (30.6)
Glasgow coma score	11 (9-15)
APACHE II	15.39±5.21
Platelets ($x10^3$/µl)	208 (148-287)
Urine output (ml/kg/hr)	0.49 (0.68-1.33)
ALT (U/L)	32 (21-60)
AST (U/L)	41 (33-60)
Serum creatinine at ICU admission (mg/dl)	0.80 (0.65-1.00)
Serum creatinine at ICU discharge (mg/dl)	0.82 (0.65-1.20)
Na (mmol/l)	137±7.72
K (mmol/l)	4.1±0.85
Blood urea (mmol/l)	4.34 (2.67-7.18)

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, APACHE II: Acute Physiology and Chronic Health Evaluation

*Use of mechanical ventiation during the whole ICU stay

Table S5: Predictors of mortality in sensitivity analysis

Variables	Hazard ratio	95% confidence interval
AKI at ICU admission	2.29	(1.09-4.82)
AKI after ICU admission	2.89	(1.53-5.48)
Age (years)	1.00	(0.98-1.01)
Sex	0.91	(0.62-1.33)
History of CKD	1.20	(0.71-2.004)
History of diabetes mellitus	1.45	(0.96-2.19)
History of cardiovascular disease	1.22	(0.81-1.86)
AKI stage 2[$]	0.87	(0.49-1.56)
AKI stage 3[$]	0.99	(0.80-1.21)
APACHE II	1.04	(1.01-1.07)

AKI: Acute kidney injury, ICU: Intensive care unit, CKD: Chronic kidney disease, APACHE II: Acute Physiology and Chronic Health Evaluation

[$] AKI stage 1 is the reference group

*In the model of mortality, both AKI and APACHE II maintained similar association with the outcome

Table S6: KDIGO definition and staging of AKI

AKI is diagnosed in the presence of: • Increase in serum creatinine by ≥ 0.3 mg/dl within 48 hours; or • Increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or • Urine volume < 0.5 ml/kg/h for 6 hours.		
Stage	**Serum creatinine**	**Urine output**
1	1.5–1.9 times baseline, or ≥ 0.3 mg/dl increase	< 0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline, or increase in creatinine to ≥ 4.0 mg/dl, or initiation of renal replacement therapy	< 0.3 ml/kg/h for ≥ 24 hours OR anuria for ≥ 12 hours

KDIGO: Kidney Disease Improving Global Outcome[43]