# In-hospital acute kidney injury

Ahmed M. Alkhunaizi<sup>1</sup>, Munifah Al Shammary<sup>1</sup>

<sup>1</sup>Johns Hopkins Aramco Healthcare Dhahran, Eastern Province, Saudi Arabia (Correspondence: Ahmed M. Alkhunaizi: aalkhunaizi@gmail.com).

### Abstract

**Background:** Hospital-acquired acute kidney injury (AKI) is associated with increased mortality and has major public health implications. The incidence of in-hospital AKI in Eastern Saudi Arabia is not known.

**Aims:** This study aimed to determine the incidence of in-hospital AKI in eastern Saudi Arabia.

**Methods:** A single centre, retrospective cohort study was performed at a major community hospital between July 2015 and July 2017.

**Results:** A total of 26 383 patients were hospitalized and 293 (1.11%) were diagnosed with AKI. Drug-induced AKI was diagnosed in 38 (13%) patients, while 255 (87%) patients had AKI not attributed to drugs. Full recovery of renal function was observed in 39% and 44% in the drug induced and non-drug induced AKI groups, respectively.

**Conclusions:** AKI is a serious complication in hospitalized patients. Full recovery of renal function was observed in a minority of patients.

**Keywords:** acute kidney injury, adverse drug effect, community hospital, kidney function, Saudi Arabia

Citation: Alkhunaizi AM; Al Shammary M. In-hospital acute kidney injury. East Mediterr

Health J. 20xx;xx(x):xxx-xxx. https://doi.org/10.26719/emhj.19.100

Received: 16/11/18; accepted: 26/02/19

Copyright © World Health Organization (WHO) 2019. Some rights reserved. This work is available under the CC BY-NC-SA 3.0 IGO license

(https://creativecommons.org/licenses/by-nc-sa/3.0/igo)

# Introduction

Acute kidney injury (AKI) is a major public health concern and is associated with high morbidity, mortality and healthcare costs. The incidence of AKI has increased recently, both in hospital and community settings (1,2). It is estimated that > 13 million people are affected by AKI annually worldwide, with wide geographic variations according to

countries, regions and economies (1,2). In the developed world, AKI manifests mainly in older patients and in the intensive care unit, while in developing countries, adults and women are more commonly affected (3,4). Despite all the advances in the field, mortality of AKI remains high; estimated at 24% in adults and 14% in children (2). In addition to the high mortality, hospital-acquired AKI is associated with high resource utilization, prolonged hospitalization, prolonged mechanical ventilation, and development of chronic kidney disease (CKD) (5). Recovery from AKI is not always, as previously thought, complete and many patients progress to develop CKD, end-stage renal disease (ESRD) or worsening of pre-existing CKD later in life (6-8). The objective of this study was to determine the incidence of in-hospital AKI in Eastern Saudi Arabia and to assess the recovery of renal function following AKI.

## Methods

This was a single-centre retrospective cohort study at Johns Hopkins Aramco Healthcare (JHAH), a large community hospital in Eastern Saudi Arabia, between July 2015 and July 2017. We included 26 383 adult patients aged ≥ 18 years. Cases of AKI were obtained from hospital discharge records and coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Etiology of AKI was classified into drug induced (DI) and non-drug induced (NDI). DI AKI was considered when a nephrotoxic agent was administered, and other factors that are known to cause AKI such as sepsis, hypovolaemia, hypotension, urinary obstruction, major surgery, and administration of intravenous contrast agents were excluded. Preadmission creatinine clearance (Cr Cl) was considered as the baseline value. Cr Cl was calculated from serum creatinine, age, ideal body weight and sex, using the Cockcroft–Gault formula (9). Patients with advanced CKD with a baseline Cr Cl < 10 ml/min were excluded. Recovery of renal function was classified into full, partial or no recovery if follow-up Cr Cl was > 90%, 50-90% or < 50 % of the baseline, respectively. Follow-up Cr Cl was calculated from serum creatinine at the first post-hospitalization encounter or, if not available, the last recorded value.

Baseline and clinical demographics were reported as mean (standard deviation), or median and interquartile ranges. Categorical variables were reported as numbers and proportions. Comparison of the mean values was performed using Student's t test while median values were compared using the Mann–Whitney U test. Population proportions were compared using the Z test. Sex ratios were compared using the  $\chi^2$  test. P < 0.05 was considered significant. Microsoft Excel 2013 was used for statistical calculations. Approval for the study was obtained from the Institutional Review Board at JHAH.

#### Results

A total of 26 383 patients were admitted to the hospital over the study period, and AKI was diagnosed in 293 (1.11%). The mean age of affected patients was 68 (14.7) years (range 19–95 years) and the median baseline Cr Cl was 43 (27–63) ml/min. DI and NDI AKI were diagnosed in 38 (13%) and 255 (87%) cases, respectively. The demographics of patients with DI and NDI AKI are summarized in Table 1. Full, partial and no recovery was observed in 39, 37 and 24% in the DI AKI group compared to 44, 33 and 23% in the NDI AKI group; P = 0.56, 0.63, 0.89 for full, partial and no recovery, respectively. Nonsteroidal ant-inflammatory drugs (NSAIDs) were the most common agents leading to AKI (32%) followed by antibiotics (24%) and diuretics (18%).

## Discussion

The aim of this study was to determine the incidence of AKI among hospitalized patients at a major community hospital in Eastern Saudi Arabia. This is the first study to address the issue in this region. Despite all the improvement in hospital care, a decline in renal function among hospitalized patients remains a significant event and is associated with high mortality, prolonged hospitalization and high cost (10–12). The reported incidence of AKI among hospitalized patients is variable and depends on multiple factors including study design, population characteristics, definition of AKI, time of reporting and geographical location. In our cohort, the diagnosis of AKI was made in 1.11% of hospitalized patients. We have used the ICD-9-CM coding to identify cases of AKI. ICD-9-CM is specific but not sensitive in identifying cases of AKI as has been shown in earlier studies (13). Thus, the result of our study may underestimate the true magnitude of AKI encountered in hospital settings.

In the United States of America, using the National Hospital Discharge Survey database, the incidence of AKI was reported at 1.9% in 2001 (12). In an earlier study, Hou et al. reported an AKI incidence of 4.9% in 2200 medical and surgical inpatients whose medical records were reviewed (11). A higher incidence of 7% was reported in a tertiary referral centre (10). Unlike community hospitals, academic tertiary medical centres provide care to patients with greater severity of illness and in whom AKI is more likely to develop. Other studies from other countries have reported an AKI incidence varying between 0.37% in Spain to 7% in China (14,15).

Age is an important factor that predisposes to the development of AKI. In our cohort, the mean age of the patients who developed AKI was 68 years. Similarly, the median Cr Cl was 43 ml/min, reflecting the susceptibility of older individuals and those with CKD to renal injury. Age, pre-existing renal insufficiency and severity of CKD are risk factors for

developing AKI (10,16,17). A number of meta-analyses have shown how AKI risk, ESRD and mortality are independently determined by severity of CKD (17,18).

Drugs were the cause of AKI in 13% of the cases, and 87% of patients developed AKI due to other causes. An earlier report from Southern Saudi Arabia implicated drugs in 7% of all cases of AKI (19). In our cohort, NSAIDs were the most common drugs causing AKI, which is not surprising due to their extensive use and over-the-counter availability (20,21). We have not individually studied other factors that typically cause AKI such as sepsis, administration of intravenous contrast agents and major surgery. It is well known that sepsis is a leading cause of AKI among patients admitted to the intensive care unit, affecting > 50% of patients (22). Similarly, major surgery is associated with AKI. We previously found that AKI affected 29% of patients who underwent cardiac surgery at our institution (23).

The group who developed DI AKI was younger than the NDI AKI group. The cause for this is not clear, and may be related to the fact that older individuals are more likely to have comorbidities that predispose them to AKI, as compared to the healthier and younger population. Similarly, the baseline Cr Cl of the DI AKI group was higher than that of the NDI AKI group; most likely reflecting the younger age of the DI AKI group. Recovery of renal function was poor as < 50% of the patients had full recovery and around 25% had no recovery. AKI is a known cause of CKD and multiple studies have shown that patients with AKI are at high risk of progression to advanced-stage CKD and death following hospital discharge. In a meta-analysis of 13 cohort studies comparing the risk of CKD, ESRD and death in patients with and without AKI, the pooled incidence of CKD and ESRD in patients with AKI was 25.8 and 8.6 per 100 person-years, respectively (8). Patients with AKI had higher risks of developing CKD, ESRD and mortality than patients without AKI (8).

This study had several limitations related to the retrospective nature of the design. First, we used ICD-9-CM codes to ascertain the diagnosis of AKI. There is a potential for misclassification when administrative coding that depends on accurate documentation by healthcare professionals and hospital coders is used. Second, we did not look at other factors besides age and baseline renal function that predispose to the development of AKI. Third, we did not report the impact of AKI on length of hospital stay and there was no follow-up to evaluate long-term outcome and mortality. Finally, there was no cost analysis to assess the financial impact of AKI.

Despite the limitations, this study sheds light on the magnitude of AKI in the hospital setting and should help to implement standards for prevention, early recognition, and

intervention. Future research should focus on more-accurate estimates of AKI and better describe the relative contribution of AKI to the utilization of healthcare resources in this region.

# Acknowledgements

The authors acknowledge the use of Johns Hopkins Aramco Healthcare (JHAH) facilities for research data used in this article. Opinions expressed in this article are those of the authors and not necessarily of JHAH.

Funding: None.

**Conflict of interest:** None declared.

### References

- Mehta RL, Cerda J, Burdmann EA, Tonelli M, Garcia-Garcia G, Jha V, et al. International Society of Nephrology's Oby25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology. Lancet. 2015 Jun 27;385(9987):2616–43. http://dx.doi.org/10.1016/S0140-6736(15)60126-X PMID:25777661
- Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, et al. World incidence of AKI: a meta-analysis. Clin J Am Soc Nephrol. 2013 Sep;8(9):1482–93. http://dx.doi.org/10.2215/CJN.00710113 PMID:23744003
- 3. Cerda J, Bagga A, Kher V, Chakravarthi RM. The contrasting characteristics of acute kidney injury in developed and developing countries. Nat Clin Pract Nephrol. 2008 Mar;4(3):138–53. http://dx.doi.org/10.1038/ncpneph0722 PMID:18212780
- 4. Jha V, Parameswaran S. Community-acquired acute kidney injury in tropical countries. Nat Rev Nephrol. 2013 May;9(5):278–90. http://dx.doi.org/10.1038/nrneph.2013.36 PMID:23458924
- Zeng X, McMahon GM, Brunelli SM, Bates DW, Waikar SS. Incidence, outcomes, and comparisons across definitions of AKI in hospitalized individuals. Clin J Am Soc Nephrol. 2014 Jan;9(1):12–20. http://dx.doi.org/10.2215/CJN.02730313 PMID:24178971
- Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med. 2014 Jul 3;371(1):58–66. http://dx.doi.org/10.1056/NEJMra1214243 PMID:24988558

- 7. Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, et al. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol. 2009 Jan;20(1):223–8. http://dx.doi.org/10.1681/ASN.2007080837 PMID:19020007
- 8. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int. 2012 Mar;81(5):442–8. http://dx.doi.org/10.1038/ki.2011.379 PMID:22113526
- 9. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31–41. http://dx.doi.org/10.1159/000180580 PMID:1244564
- 10. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis. 2002 May;39(5):930–6. http://dx.doi.org/10.1053/ajkd.2002.32766 PMID:11979336
- 11. Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: a prospective study. Am J Med. 1983 Feb;74(2):243–8. http://dx.doi.org/10.1016/0002-9343(83)90618-6 PMID:6824004
- Liangos O, Wald R, O'Bell JW, Price L, Pereira BJ, Jaber BL. Epidemiology and outcomes of acute renal failure in hospitalized patients: a national survey. Clin J Am Soc Nephrol. 2006 Jan;1(1):43–51. http://dx.doi.org/10.2215/CJN.00220605 PMID:17699189
- Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayer WC, Liangos O, et al. Validity of International Classification of Diseases, Ninth Revision, Clinical Modification Codes for Acute Renal Failure. J Am Soc Nephrol. 2006 Jun;17(6):1688–94. http://dx.doi.org/10.1681/ASN.2006010073 PMID:16641149
- 14. Liano F, Pascual J. Epidemiology of acute renal failure: a prospective, multicenter, community-based study. Madrid Acute Renal Failure Study Group. Kidney Int. 1996 Sep;50(3):811–8. http://dx.doi.org/10.1038/ki.1996.380 PMID:8872955
- Yang L, Xing G, Wang L, Wu Y, Li S, Xu G, et al. Acute kidney injury in China: a cross-sectional survey. Lancet. 2015 Oct 10;386(10002):1465–71. http://dx.doi.org/10.1016/S0140-6736(15)00344-X PMID:26466051
- 16. Hsu CY, Ordonez JD, Chertow GM, Fan D, McCulloch CE, Go AS. The risk of acute renal failure in patients with chronic kidney disease. Kidney Int. 2008 Jul;74(1):101–7. http://dx.doi.org/10.1038/ki.2008.107 PMID:18385668
- 17. Gansevoort RT, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, et al. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts. Kidney Int. 2011 Jul;80(1):93–104. http://dx.doi.org/10.1038/ki.2010.531 PMID:21289597

- Astor BC, Matsushita K, Gansevoort RT, van der Velde M, Woodward M, Levey AS, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int. 2011 Jun;79(12):1331–40. http://dx.doi.org/10.1038/ki.2010.550 PMID:21289598
- 19. Al-Homrany M. Epidemiology of acute renal failure in hospitalized patients: experience from southern Saudi Arabia. East Mediterr Health J. 2003 Sep-Nov;9(5–6):1061–7. PMID:16450538
- 20. Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. Am J Med. 1999 May 31;106(5b):13s–24s. http://dx.doi.org/10.1016/s0002-9343(99)00113-8 PMID:10390124
- 21. Green GA. Understanding NSAIDs: from aspirin to COX-2. Clin Cornerstone. 2001;3(5):50–60. http://dx.doi.org/10.1016/s1098-3597(01)90069-9 PMID:11464731
- 22. Hoste EA, Bagshaw SM, Bellomo R, Cely CM, Colman R, Cruz DN, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015 Aug;41(8):1411–23. http://dx.doi.org/10.1007/s00134-015-3934-7 PMID:26162677
- 23. Alkhunaizi AM, Shah SS, Wesslen US, Al Sadah ZA, Antony A. Acute kidney injury after cardiac surgery in eastern Saudi Arabia. East Mediterr Health J. 2011
  Jun;17(6):495–500. PMID:21796967

**Table 1.** Characteristics of patients with drug induced and non-drug-induced AKI.

	Drug-induced AKI	Non-drug-induced AKI	Р
Number (%)	38 (13)	255 (87)	
% Female	47	44	0.10
% Male	53	56	0.18
Mean age (SD) (range), yr	63 (14.8) (21–87)	68 (14.5) (19–95)	0.02
Median Cr Cl (IQR) ml/min	53 (34–67)	42 (27–62 )	0.049

AKI = acute kidney injury; Cr Cl = creatinine clearance; IQR = interquartile range; SD = standard deviation.