Recognition and management of acute kidney injury in the International Society of Nephrology 0by25 Global Snapshot: a multinational cross-sectional study

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Summary

Background **Epidemiological data for acute kidney injury are scarce, especially in low-income countries (LICs) and lower-middle-income countries (LMICs). We aimed to assess regional differences in acute kidney injury recognition, management, and outcomes.**

Methods **In this multinational cross-sectional study, 322 physicians from 289 centres in 72 countries collected prospective data for paediatric and adult patients with confirmed acute kidney injury in hospital and non-hospital settings who met criteria for acute kidney injury. Signs and symptoms at presentation, comorbidities, risk factors for acute kidney injury, and process-of-care data were obtained at the start of acute kidney injury, and need for dialysis, renal recovery, and mortality recorded at 7 days, and at hospital discharge or death, whichever came earlier. We classified countries into high-income countries (HICs), upper-middle-income countries (UMICs), and combined LICs and LMICs (LLMICs) according to their 2014 gross national income per person.**

Findings **Between Sept 29 and Dec 7, 2014, data were collected from 4018 patients. 2337 (58%) patients developed community-acquired acute kidney injury, with 889 (80%) of 1118 patients in LLMICs, 815 (51%) of 1594 in UMICs, and 663 (51%) of 1241 in HICs (for HICs *vs* UMICs p=0.33; p<0.0001 for all other comparisons). Hypotension (1615 [40%] patients) and dehydration (1536 [38%] patients) were the most common causes of acute kidney injury. Dehydration was the most frequent cause of acute kidney injury in LLMICs (526 [46%] of 1153 *vs* 518 [32%] of 1605 in UMICs *vs* 492 [39%] of 1260 in HICs) and hypotension in HICs (564 [45%] of 1260 *vs* 611 [38%%] of 1605 in UMICs *vs* 440 [38%] of 1153 LLMICs). Mortality at 7 days was 423 (11%) of 3855, and was higher in LLMICs (129 [12%] of 1076) than in HICs (125 [10%] of 1230) and UMICs (169 [11%] of 1549).**

Interpretation **We identified common aetiological factors across all countries, which might be amenable to a standardised approach for early recognition and treatment of acute kidney injury. Study limitations include a small number of patients from outpatient settings and LICs, potentially under-representing the true burden of acute kidney injury in these areas. Additional strategies are needed to raise awareness of acute kidney injury in community health-care settings, especially in LICs.**

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Introduction

In high-income countries (HICs), progress in acute kidney injury epidemiology (especially in the critically ill population) has translated into improved prevention, diagnosis, and treatment of acute kidney injury.[1] However, in low-income countries (LICs) and lower-middle-income countries (LMICs), epidemiology of acute kidney injury is poorly described.[2–4] In these countries, low availability of resources and inadequate health infrastructure are associated with poor recognition and treatment of acute kidney injury. In LICs and LMICs (LLMICs), the few available studies suggest that a substantial proportion of acute kidney injury cases and their adverse clinical effects could be prevented or attenuated.[2]

The International Society of Nephrology's 0by25 acute kidney injury initiative aims to prevent all avoidable deaths from acute kidney injury worldwide by 2025.[5] As an initial step, we did a Global Snapshot during a 10-week period in 2014 to assess the range of acute kidney injury seen by physicians in different settings worldwide.[6] We postulated that differences in risk factors, exposures, and resources available for non-dialytic and dialytic management and follow-up would be associated with dissimilar acute kidney injury outcomes in different settings and countries.

Methods

Study design and participants

The International Society of Nephrology Global Snapshot is a multinational, observational cross-sectional study. We recruited physicians by open invitation via the International Society of Nephrology and partnering nephrology and critical care societies, announcements at national and international meetings, a dedicated website

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For more on the **International Society of Nephrology's 0by25** see http://www.0by25.org

Research in context

Evidence before this study

Most available data for acute kidney injury epidemiology come from high-income countries (HICs), although 85% of the world's population resides in low-income and lower-middle-income countries (LLMICs). Systematic prospective studies in this population are scarce, but emerging data describe striking differences in cause, natural history, and management of acute kidney injury between HICs and LLMICs.

This study builds on our two recent meta-analyses, in which we did an extensive review of the scientific literature for the intervals 2004–12 and 2004–14, including 49 million and 77 million people worldwide, respectively. We used the following search terms: "acute renal failure", "acute kidney failure", "acute renal insufficiency", "acute kidney insufficiency", "acute tubular necrosis", "acute kidney injury", and "acute renal injury". We also used information obtained in the International Registry on acute kidney injury in intensive care unit (ICU) patients worldwide, and the EPI-AKI registry, which includes ICU patients in several countries (predominantly HICs). Before the EPI-AKI study, the largest study included 29 269 ICU patients in 2000–01 at 54 hospitals in 23 countries.

Added value of this study

Our acute kidney injury definition was a modified version of Kidney Disease: Improving Global Outcomes (KDIGO) acute kidney injury definition. KDIGO is the most recent, internationally accepted acute kidney injury definition, and enables comparison of our data with the most recent scientific literature. A standardised form allowed for cross-country comparisons with this standardised definition. Limitations are that this study is of a convenience sample and most of the participating centres were referral hospitals. Thus, data from rural settings and small urban health centres, which often have limited resources, are under-represented in this study.

Our study is the first worldwide prospective cross-sectional study designed to assess similarities and differences in recognition and management and outcomes of acute kidney injury in different health settings across six continents, including 72 countries, and with data directly obtained from HICs, UMICs, and LLMICs. Our study collected data for both community and hospital-acquired acute kidney injury. Notably, community acute kidney injury has been under-represented in past studies in LLMICs. The current study enabled us to build a network of centres where acute kidney injury initiatives can be implemented in future.

Implications of all the available evidence

Acute kidney injury is common across the world, and many cases are preventable. The causes of acute kidney injury vary by country and economic status. These data for acute kidney injury will inform the International Society of Nephrology's 0by25 initiative by providing essential baseline data that is crucial to identify modifiable elements to reduce preventable deaths associated with acute kidney injury. This study has enabled establishment of a network of researchers, who will be leveraged when initiatives are implemented, to decrease avoidable deaths associated with acute kidney injury worldwide.

for 0by25, and individual contacts between June 1 and Dec 1, 2014. We recruited 322 providers from 72 countries. Physician participation was voluntary, without financial incentive. Participating providers obtained institutional review board approval from their institutions in accordance with local ethics regulations. The International Society of Nephrology's Ethics and Patient Privacy Committee provided a Statement of Approval of the Global Snapshot Protocol. The protocol is available online.

For the **protocol** see http://www.theisn.org/images/Initiatives/Global_Snapshot_Protocol.pdf

We included adults and children (≤18 years) with confirmed acute kidney injury from hospital (tertiary, secondary, and community hospitals, and nursing homes) and non-hospital (patient clinics and health-care centres) settings, with any cause. We excluded patients with stage 5 chronic kidney disease at baseline. Informed consent was not required.

Outcomes

Outcomes were all-cause patient mortality, dialytic need, and complete and partial renal recovery. Physicians chose index days between Sept 29 and Dec 7, 2014, to screen for potential cases of acute kidney injury identified in the 3 days before, or on, the index day (appendix p 15). Each provider recorded the total number of patients under their care who were screened on the index day (acute kidney injury and non-acute kidney injury cases). We defined baseline serum creatinine as the lowest serum creatinine value closest to the time of assessment within 12 months. If no baseline serum creatinine was available within 12 months of assessment, we defined the reference serum creatinine as the first serum creatinine at patient assessment. We applied modified Kidney Disease: Improving Global Outcomes (KDIGO) acute kidney injury criteria, which defined confirmed acute kidney injury as an increase or decrease in serum creatinine of 26·5 μmol/L or greater, or an increase of 50% or more from the reference value obtained within a minimum of 3 days from index day or the known baseline value. When urine volume was available, we considered acute kidney injury confirmed if urine output was less than 400 mL/day or less than 0·5 mL/kg/h for 6 h or more. Renal recovery was determined using the last available serum creatinine measurement, and defined as complete if serum creatinine was equal to or lower than baseline or reference, partial if lower than diagnosis but not baseline or reference, and no-recovery if the serum creatinine did not decrease or if the patient remained on dialysis. Patients were classified as having

See Online for appendix

community-acquired acute kidney injury if they first presented to the hospital with acute kidney injury, and as hospital-acquired if they developed acute kidney injury after hospital admission.

History and laboratory studies at enrolment identified underlying chronic kidney disease. Patients were considered to have de-novo acute kidney injury, acute-on-chronic kidney injury, or acute kidney injury with unknown previous kidney history. Acute kidney injury stages (KDIGO criteria) were identified at diagnosis, at dialysis start, at 7 days, and at last observation. We defined patients as having an intensive care unit (ICU) admission if any portion of their hospital stay included an ICU stay.

We analysed nine geographical regions: North America, Latin America and the Caribbean, western Europe, eastern Europe, Middle East, south Asia, east and southeast Asia, Oceania, and Africa. We classified countries into three income groups in accordance with their 2014 gross national income (GNI) per person, with thresholds defined by the World Bank Atlas method:[7] LICs (GNI<US$1045), LMICs (GNI<$4035), HICs (GNI>$12 476), and upper-middle-income countries (UMICs; US$1246>GNI> US$4035). We combined data from LICs and LMICs into an LLMIC group because we had only 195 patients from LICs, more than 75% of whom were from two countries.

We collected de-identified data (51 variables) with forms that met the Health Information Portability and Accountability Act criteria. Variables included demographics, risk factors for suspecting acute kidney injury, process of care, and outcomes (appendix). We entered data into a secure platform, accessible online.

For more on **the secure platform** see http://KEEP.distributedhealthlabs.org

Statistical analysis

We present continuous variables as mean (SD) or median (IQR), as appropriate. We used the Kolmogorov-Smirnov test to check data normality. We used the Kruskal-Wallis test to compare continuous variables. Categorical variables are presented as proportions and compared with χ^2 or Fisher exact testing, as appropriate. We did multiple tests adjustment (bootstrap correction for categorical variables and Benjamini-Hochberg for continuous variables). Statistical tests were two-sided, and we considered $p<0{\cdot}05$ to show a significant difference. We did univariate and multivariate logistic regression analyses to predict mortality, assessed at 7 days or last observation if earlier. Time-to-death data were not available, so we did not do a time-to-event analysis. We included variables with $p<0{\cdot}20$ for Wald test in the multivariate regression analyses.

We built the final logistic regression model in five steps to assess the effect of inherent and aetiological risk factors, location, and process of care on mortality. Step 1 included patient characteristics and data for cause. Step 2 included process-of-care factors. In step 3, we combined results from step 2 with results from step 1 to assess the added predictive value of process-of-care factors. Step 4 included setting (eg, community *vs* hospital). In step 5, we combined results from step 4 with results from step 3 to generate the final model. We did analysis of collinearity between categorical

For the **Health Information Portability and Accountability Act criteria** see http://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations

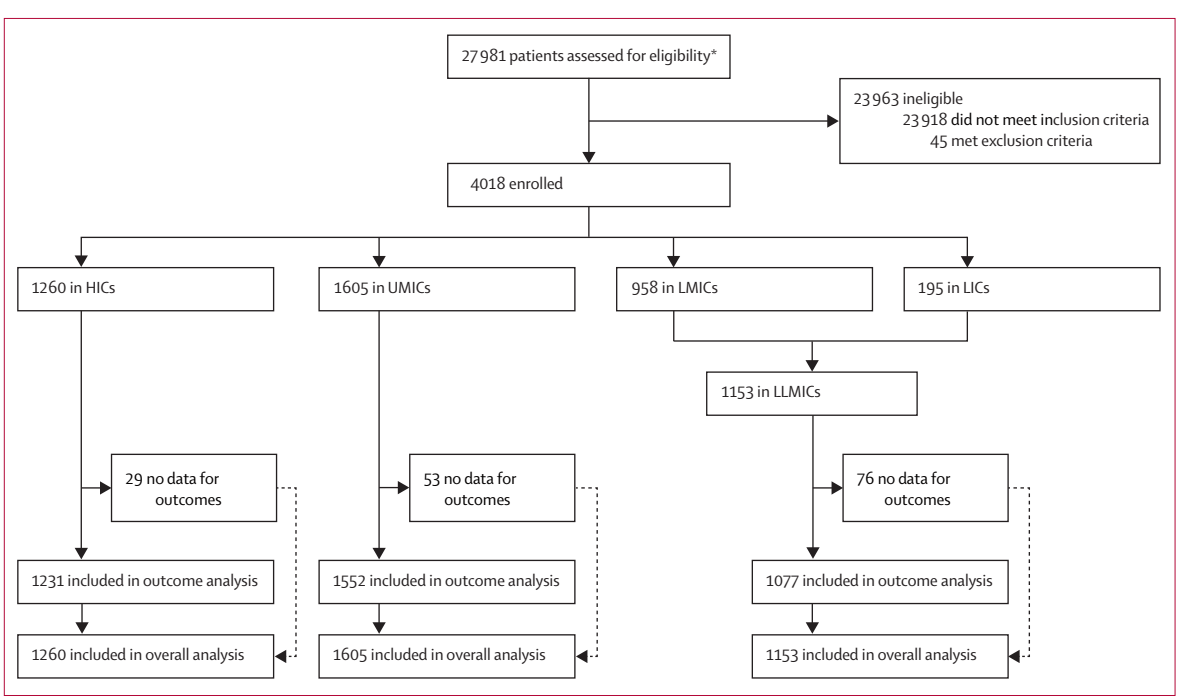

Figure: **Study profile**
HICs=high-income countries. UMICs=upper-middle-income countries. LMICs=lower-middle-income countries. LICs=low-income countries. LLMICs=LICs and LMICs.
*Patients under the care of the physician on the index day

	All (n=289)	HICs (n=132)	UMICs (n=72)	LLMICs (n=85)
Region				
Africa	44 (15%)	0*	16 (22%)†	28 (33%)‡
Eastern and central Europe	11 (4%)	6 (5%)	5 (7%)†	0
Latin America and the Caribbean	45 (16%)	16 (12%)*	22 (31%)†	7 (8%)
Middle East	14 (5%)	12 (9%)*	2 (3%)	0‡
North and east Asia	32 (11%)	18 (14%)	14 (19%)†	0‡
North America	31 (11%)	31 (23%)*	0	0‡
Oceania and southeast Asia	16 (6%)	4 (3%)*	8 (11%)	4 (5%)
Russia and CIS	17 (6%)	11 (8%)	5 (7%)	1 (1%)‡
South Asia	45 (16%)	0*	0†	45 (53%)‡
Western Europe	34 (12%)	34 (26%)*	0	0‡
Size of the cities				
<10 000	2 (1%)	0	0	2 (2%)
≥10 000 to <100 000	19 (7%)	12 (9%)	3 (4%)	4 (5%)
≥100 000 to <500 000	59 (20%)	37 (28%)*	8 (11%)	14 (16%)‡
≥500 000 to <1·5 million	68 (24%)	33 (25%)	17 (24%)	18 (21%)
≥1·5 million to <3 million	35 (12%)	16 (12%)	7 (10%)	12 (14%)
≥3 million to <5 million	33 (11%)	15 (11%)	7 (10%)	11 (13%)
≥5 million	73 (25%)	19 (14%)*	30 (42%)	24 (28%)‡
Facility type				
Institute (includes university)	124 (43%)	55 (42%)	31 (43%)	38 (45%)
Private multispecialty	45 (16%)	13 (10%)	6 (8%)†	26 (31%)‡
Private unispecialty centre	7 (2%)	2 (2%)	3 (4%)	2 (2%)
Public hospital or health-care centre	113 (39%)	62 (47%)	32 (44%)†	19 (22%)‡
Type of physician				
All physicians	322	146 (45%)	91 (28%)	85 (26%)
Nephrologist	249 (77%)	109 (75%)	76 (84%)	64 (79%)
Nephrology fellow in training	20 (6%)	7 (5%)	6 (7%)	7 (8%)
Intensivist	14 (4%)	13 (9%)*	0	1 (1%)‡
Paediatric nephrologist	26 (8%)	11 (8%)	6 (7%)	9 (11%)
Paediatrician	1 (<1%)	1 (1%)	0	0
Other	12 (4%)	5 (3%)	3 (3%)	4 (5%)

Data are n (%). HICs=high-income countries. UMICs=upper-middle-income countries. LLMICs=low-income and lower-middle-income countries. CIS=commonwealth of Independent States. Statistically significant at 5% Bootstrap correction: *compared with UMICs; †compared with LLMICs; ‡compared with HICs.

Table 1: **Characteristics of the participating centres by gross national income per person**

variables with the phi coefficient before modelling; values of greater than 0·3 suggested the need to include interaction terms in the model. Each interaction term was retained only if the c-statistic suggested that it improved model fit. We used a stepwise approach to develop the final model, including variables with p<0·10. We use odds ratios (95% CI) to report the results of logistic regression. For each step, we assessed discrimination by receiver operating characteristic curve and calibration by the Hosmer–Lemeshow goodness-of-fit test. We chose the model with the fewest variables and highest c-statistic for each step.

We analysed data with SAS, version 9.4.

Role of the funding source

The International Society of Nephrology provided funding through unrestricted grants to the 0by25 initiative, gave logistic support for this study, and holds all copyrights on the data obtained through this study. The International Society of Nephrology had no role in the study design, data collection, data analysis, interpretation, or writing of the report. The principal investigator and all authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

322 providers from 289 centres across 72 countries participated in the Global Snapshot (appendix). 27 981 patients were screened for eligibility and data were entered for 3664 adult and 354 paediatric patients with acute kidney injury (figure). 145 (45%) providers were from HICs, 91 (28%) from UMICs, and 85 (26%) from LLMICs (table 1). Data from LICs are presented separately (appendix pp 9–14). 124 (43%) of 289 participant centres were university hospitals and 249 (77%) of the 322 providers were nephrologists. 24 (28%) of 85 centres in LLMICs and 30 (42%) of 72 in UMICs were located in cities with more than 5 million people, whereas 70 (53%) of 132 centres in HICs were in smaller cities (with a population of 100 000–1·5 million). Data by geographical regions are shown in table 2. Dialysis was available in 275 (95%) participating centres. Chronic-on-acute kidney injury was more frequent than was hospital-acquired acute kidney injury, and acute kidney injury was most commonly diagnosed in the ward or stepdown unit (table 3).

Median age was 60 years (IQR 43–74), with younger patients more commonly seen in LLMICs than in other income areas (table 4). Chronic heart and liver diseases were more frequent in patients from HICs and UMICs than in patients from LLMICs, whereas anaemia was more common in patients from LLMICs than in patients from HICs and UMICs. Pre-existing chronic kidney disease was less prevalent in LLMICs than in HICs and UMICs (table 4). De-novo acute kidney injury was the most commonly reported type of acute kidney injury in all income regions.

In HICs and UMICs, hypotension or shock was the most common cause of acute kidney injury, whereas dehydration was the most frequent cause in LLMICs (table 4). 928 (60%) of 1536 dehydration episodes were associated with inadequate oral intake, and 682 (44%) were associated with vomiting. Sepsis, pregnancy-related acute kidney injury, and animal envenomation were more common in LLMICs than in other income areas. In more than half of patients, the kidneys were the only organs affected at the time of acute kidney injury diagnosis; the cardiovascular system was the most frequent non-renal system affected (table 4).

On the day of confirmation of acute kidney injury, diagnosis was made with only serum creatinine in 2839 (71%) patients and with urine output alone in 257 (6%; table 3). Higher serum creatinine at presentation and Acute Kidney Injury Network stage 3 were both more common in LLMICs than in other income areas, despite

	Number of centres	Number of patients (N=4018)	Median age (years)	ICU patients	Hospital-acquired acute kidney injury
Paediatric	89	354 (9%)	2 (0·2–11)	136 (38%)	187 (53%)
Adult	262	3661 (91%)	62 (48–75)	1102 (30%)	1429 (39%)
Region					
Africa	44	539 (13%)	53 (34·0–65·0)	103 (19%)	82 (15%)
Eastern and central Europe	11	88 (2%)	68 (56·0–78·0)	10 (11%)	17 (19%)
Latin America and the Caribbean	45	556 (14%)	60 (44·0–75·0)	178 (32%)	250 (45%)
Middle East	14	135 (3%)	60 (34·0–72·0)	31 (23%)	45 (33%)
North and east Asia	32	1105 (28%)	68 (57·0–79·0)	365 (33%)	694 (63%)
North America	31	280 (7%)	22·5 (0·3–63·0)	115 (41%)	180 (64%)
Oceania and southeast Asia	16	169 (4%)	65 (52·0–77·0)	40 (24%)	54 (32%)
Russia and CIS	17	154 (4%)	53 (34·0–66·0)	79 (51%)	65 (42%)
South Asia	45	748 (19%)	50 (34·0–63·0)	261 (35%)	134 (18%)
Western Europe	34	244 (6%)	74 (61·0–81·5)	56 (23%)	95 (39%)
GNI					
High income	132	1260 (31%)	63 (44·0–76·0)	481 (38%)	608 (48%)
Upper-middle income	72	1605 (40%)	64 (50·0–77·0)	427 (27%)	779 (49%)
Low income and lower-middle income	85	1153 (29%)	50 (33·0–64·0)	330 (29%)	229 (20%)
Lower-middle income	68	958 (24%)	50 (34·0–64·0)	278 (29%)	187 (20%)
Low income	17	195 (5%)	45 (27·0–60·0)	52 (27%)	42 (22%)

Data are n (%) or median (IQR). ICU=intensive care unit. GNI=gross national income. CIS=Commonwealth of Independent States.

Table 2: **Epidemiology and outcomes by region**

	N	All	HICs (n=1260)	UMICs (n=1605)	LLMICs (n=1153)
Community acquired	2337	58%	633 (50%)	815 (51%)†	889 (77%)‡
Location*					
Emergency room	705	18%	242 (19%)	284 (18%)	179 (16%)‡
ICU	1238	31%	481 (38%)*	427 (27%)	330 (29%)‡
Ward or step down unit	1820	45%	485 (38)*	807 (50%)†	528 (46%)‡
Outpatient clinic	190	5%	33 (3%)*	76 (5%)†	81 (7%)‡
At acute kidney injury diagnosis§					
sCr (μmol/L)	3718	221·9 (146·0–390·0)	215·0 (143·0–362·4)	203·3 (135·0–335·9)†	288·2 (176·8–512·7)‡
BUN (mmol/L)	3272	18·7 (11·4–30·7)	19·6 (12·0–31·0)*	16·0 (10·2–25·9)†	23·9 (14·3–37·1)‡
Urine output past 24 h (mL)	2329	760 (300–1500)	700 (290–1440)*	1000 (400–1655)†	500 (200–1100)‡
Criteria for acute kidney injury diagnosis*					
sCr (alone)	..	2839 (71%)	845 (67%)*	1273 (79%)†	721 (63%)‡
Oliguria (alone)	..	257 (6%)	131 (10%)*	37 (2%)†	89 (8%)‡
sCr and urine output	..	887 (22%)	277 (22%)*	291 (18%)†	319 (28%)‡
Stage at diagnosis (n=3679)					
1	..	1376 (37%)	424 (37%)*	644 (44%)†	308 (29%)‡
2	..	552 (15%)	192 (17%)	227 (15%)†	133 (13%)‡
3	..	1751 (48%)	540 (47%)*	606 (41%)†	605 (58%)‡

Data are n (%), mean (SD), or median (IQR). HICs=high-income countries. UMICs=upper-middle-income countries. LLMICs=low-income and lower-middle-income countries. ICU=intensive care unit. BUN=blood urea nitrogen. sCr=serum creatinine. Statistically significant at 5% with bootstrap correction:*compared with UMICs; †compared with LLMICs; ‡compared with HICs.

Table 3: **Acute kidney injury location and characteristics by gross national income per person**

the younger age of patients in LLMICs compared with HICs and UMICs (table 3).

Urinalysis was reported in 2903 (74%) of patients at the time of acute kidney injury diagnosis, renal ultrasound was done in 2165 (54%) patients, and renal biopsy was done in only 157 (4%) patients. Renal ultrasound and renal biopsy were more commonly done in LLMICs than in UMICs and HICs (appendix p 6).

	N	Total (n=4015)	HICs (n=1260)	UMICs (n=1605)	LLMICs (n=1153)
Age*	4015	60 (43–74)	63 (44–76)*	64 (50–77)†	50 (33–64)‡
Male sex	4015	2412 (60%)	721 (57%)*	980 (61%)	710 (62%)‡
Comorbidities					
High BMI*	2644	24·2 (21·3–27·4)	24·7 (21·4–28·4)	24·2 (21·5–27·3)	23·9 (21·3–26·7)‡
Diabetes	4018	1113 (28%)	347 (28%)	414 (26%)†	352 (31%)
Chronic liver disease	4018	282 (7%)	83 (7%)*	144 (9%)†	55 (5%)
Chronic heart disease	4018	790 (20%)	250 (20%)*	417 (26%)†	123 (11%)‡
Chronic kidney impairment	4018	864 (22%)	332 (26%)	376 (23%)†	156 (14%)‡
Creatinine, baseline (μmol/L)*	2890	97·2 (73·0–158·2)	92 (62·8–141·4)*	97·2 (75·7–151·0)†	114·9 (88·4–198·0)‡
Anaemia (haemoglobin <90 g/L)	4018	872 (22%)	267 (21%)	327 (20%)†	278 (24%)
Aetiological risk factors					
Dehydration	1536	38%	492 (39%)*	518 (32%)†	526 (46%)‡
Hypotension or shock	1615	40%	564 (45%)*	611 (38%)	440 (38%)‡
Cardiac	905	23%	306 (24%)*	448 (28%)†	151 (13%)‡
Liver	331	8%	97 (8%)	148 (9%)	86 (7%)
Acute kidney disease	488	12%	140 (11%)*	150 (9%)†	198 (17%)‡
Urinary obstruction	320	8%	99 (8%)	11 (1%)†	110 (10%)
Infection	1291	32%	363 (29%)	516 (32%)	412 (36%)‡
Pregnancy related	56	1%	5 (<1%)	15 (1%)†	36 (3%)‡
Systemic diseases	322	8%	118 (9%)	151 (9%)†	53 (5%)‡
Nephrotoxic agents	980	24%	365 (29%)*	349 (22%)	266 (23%)‡
Poisoning	73	2%	27 (2%)	23 (1%)	23 (2%)
Envenomation	35	1%	4 (<1%)	11 (1%)†	20 (2%)‡
Post-surgery	269	7%	116 (9%)*	109 (7%)†	44 (4%)‡
Sepsis	1123	28%	341 (27%)*	331 (21%)†	451 (39%)‡
Other organ failures at acute kidney injury confirmation day					
Pulmonary	657	16%	242 (19%)	275 (17%)†	140 (12%)‡
Cardiovascular	926	23%	307 (24%)	414 (26%)†	205 (18%)‡
Neurological	334	8%	95 (8%)	151 (9%)	88 (8%)
Hepatic	417	10%	119 (9%)	175 (11%)	123 (11%)
Haematological	380	9%	101 (8%)	109 (7%)†	170 (15%)‡
None	2165	54%	676 (54%)	847 (53%)	642 (56%)
Number of organ failures					
0	2165	55%	676 (54%)	847 (53%)	642 (58%)
1	1109	28%	352 (28%)	469 (29%)†	288 (26%)
2	470	12%	143 (11%)	196 (12%)	131 (12%)
3	200	5%	66 (5%)	81 (5%)	53 (5%)

Data are n (%), median (IQR), or mean (SD). HICs=high-income countries. UMICs=upper-middle-income countries. LLMICs=low-income and lower-middle-income countries. Statistically significant at 5% with bootstrap correction for categorical variables and Benjamini-Hochberg adjustment for continuous variables: *compared with UMICs; †compared with LLMICs. ‡compared with HICs.

Table 4: **Inherent and aetiological risk factors for acute kidney injury development by gross national income per person**

2930 (73%) patients received fluids as the initial acute kidney injury treatment. Crystalloid was the most common intravenous fluid used. Albumin and starch were used more often in UMICs than in other income areas (appendix p 6). Diuretics were used in half of patients in UMICs, and in fewer patients in HICs and LLMICs. Vasopressors were used in 956 (24%) patients, and 2513 (63%) were receiving antibiotics on the day of acute kidney injury diagnosis. Urinary diversion (percutaneous nephrostomy, cystectomy, or ureteral catheterisation) was done in 769 (20%) of 3942 patients (appendix p 6).

Dialysis was done in 900 (22%) patients, and was more commonly used and started at higher concentrations of serum creatinine in LLMICs than in other countries (appendix pp 7, 14). Median urine volume 24 h before dialysis initiation was 300 mL (IQR 100–600). Solute control was the reason to start dialysis in 610 (68%) patients, electrolyte or acid–base disturbances in 450 (50%), and fluid overload in 406 (45%). 516 (57%)

patients received intermittent haemodialysis. In HICs and UMICs, continuous renal replacement therapy was used in about 30% (75 [32%] of 237 patients in HICs and 67 [29%] of 230 patients in UMICs), whereas sustained low-efficiency dialysis methods were used in 70 (22%) of 323 patients in LLMICs. Peritoneal dialysis was infrequent, with a higher use in LLMICs than in HICs and UMICs (23 [7%] of 323 in LLMICs *vs* 11 [3%] of 327 in HICs *vs* 7 [3%] of 230 in UMICs; appendix pp 7, 14).

Of the 2983 non-dialysed patients, 244 (8%) had a clinical indication for renal replacement therapy but were not dialysed, with frequency similar across income category. In LLMICs, lack of resources (11 [16%] of 67) and inability to afford therapy (20 [30%] of 67), as reported by the treating physician, together accounted for almost half of these cases. Conversely, in HICs, the main reason to withhold dialysis was a perception of futility (57 [79%] of 72), which was present in 64 (61%) of 105 patients in UMICs and 22 (33%) of 67 patients in LLMICs (HICs *vs* UMICs p=0·06; HICs *vs* LLMICs p<0·0001; and UMICs *vs* LLMICs p<0·0001). Dialysis was withheld because of cultural beliefs in 35 (33%) of patients in UMICs, 14 (21%) of patients in LLMICs, and 13 (18%) of patients in HICs (appendix p 17).

Mortality at 7 days varied from 129 (12%) of 1076 patients from LLMICs to 125 (10%) of 1230 in HICs, and differed significantly in dialysed versus non-dialysed patients (17% *vs* 9%, p<0·0001; appendix p 18). Community-acquired, ICU, and paediatric mortality were significantly higher in LLMICs than in other income areas (appendix). Risk and aetiological factors associated with mortality by univariate and multivariate logistic regression are shown in table 5 and the appendix. Logistic regression showed that age, hospital-acquired acute kidney injury, higher number of organ failures, sepsis, use of antibiotics, oliguria, and dialysis were associated with increased mortality, whereas chronic kidney injury was associated with decreased mortality.

222 (23%) of 947 patients were discharged in LLMICs, 237 (17%) of 1380 in UMICs, and 153 (14%) 1105 in HICs (appendix). Of patients still in hospital, more than half were on a hospital ward, with a higher percentage of patients in the ICU in HICs compared with UMICs and LLMICs (261 [23%] in HICs *vs* 69 [7%] in LLMICs; p<0·0001).

1142 (28%) patients had complete recovery, and 1447 (36%) had partial recovery (appendix pp 8, 14). Recovery from acute kidney injury was more often complete in LLMICs than in UMICs and HICs, irrespective of whether or not dialysis was done during hospital stay. Of 900 dialysed patients, 390 (43%) were dialysis dependent after 7 days, but when only survivors were considered, 369 (50%) of 743 were still dialysis dependent on the last observation day. Non-dialysed patients had a higher proportion of complete recovery than did dialysed patients (35% *vs* 13%; p<0·0001). Scheduled follow-up for acute kidney injury was arranged in 1577 (39%) patients, with no significant difference among GNI categories (407 [32%] of 1260 in HICs, 536 [33%] of 1605 in UMICs, 634 [55%] of 1153 in LLMICs; p=0·5; data not shown).

	Univariate analysis		Multivariate analysis	
	Odds ratio estimates	95% Wald confidence limits	Odds ratio estimates	95% Wald confidence limits
Age	1·011	1·006–1·015	1·015	1·010–1·020
Hospital-acquired acute kidney injury	1·595	1·319–1·929	1·466	1·187–1·810
Number of organ failures				
1	3·941	3·044–5·103	3·213	2·459–4·199
2	7·416	5·560–9·891	4·470	3·278–6·095
3	16·944	12·001–23·923	9·542	6·573–13·851
Sepsis	3·446	2·838–4·184	1·737	1·374–2·196
Use of antibiotics	3·156	2·455–4·057	1·706	1·279–2·274
Oliguria	1·767	1·450–2·154	1·543	1·221–1·950
Chronic kidney disease	0·684	0·531–0·881	0·713	0·539–0·943
Need for dialysis	2·149	1·757–2·628	1·294	1·021–1·639
Chronic liver disease	1·713	1·246–2·355	..	..
Chronic heart failure	1·256	1·002–1·575	..	..
Anaemia	1·434	1·157–1·777	..	..
Number of inhabitants				
<10 000	1·859	0·616–5·611	..	..
≥10 000 to <100 000	0·578	0·265–1·264	..	..
≥100 000 to <500 000	1·295	0·996–1·683	..	..
≥500 000 to <1·5 million	1·207	0·912–1·599	..	..
≥1·5 million to <3 million	0·876	0·623–1·231	..	..
≥3 million to <5 million	1·334	0·926–1·922	..	..
Facility type				
Institute *vs* private multispecialty	0·918	0·692–1·219	..	..
Private university	0·293	0·090–0·956	..	..
Public	1·019	0·751–1·382	..	..
Process of care				
Diuretics	1·337	1·104–1·619	..	..
ICU	2·684	2·214–3·254	..	..
Gross national income level				
UMICs *vs* HICs	1·223	0·974–1·535	..	..
LLMICs *vs* HICs	1·117	0·869–1·436	..	..
Region				
Africa *vs* North America	2·860	1·571–5·205	..	..
Eastern and central Europe	2·717	1·184–6·236	..	..
Latin America and the Caribbean	4·414	2·477–7·866	..	..
Middle East	2·114	0·977–4·574	..	..
North and east Asia	2·435	1·380–4·299	..	..
Oceania and southeast Asia	2·395	1·166–4·918	..	..
Russia and CIS	2·526	1·206–5·290	..	..
South Asia	2·472	1·378–4·433	..	..
Western Europe	2·598	1·343–5·027	..	..

The final logistic regression model was built based on five steps to assess the effect of inherent and aetiological risk factors, location, and process of care on mortality. ICU=intensive care unit. CIS=commonwealth of Independent States.

Table 5: **Logistic regression for mortality**

Discussion

Our study is the first worldwide, prospective cross-sectional study designed to assess similarities and differences in recognition and management of acute kidney injury in different health-care settings (community, hospital, ICU, and non-ICU) across six continents. We developed this study to provide baseline evidence for the International Society of Nephrology's 0by25 initiative targeting preventable deaths from acute kidney injury.[2] In view of the paucity of information about the natural history of acute kidney injury in low-resource settings and its importance as a human rights issue,[8,9] we focused on identification of factors that would be amenable to intervention to reduce preventable deaths. We used the World Bank GNI classification system to account for differences in resources and assess the effect of economic conditions on acute kidney injury disease patterns.[10]

We used a modified KDIGO acute kidney injury definition, aiming to capture more people who truly had acute kidney injury but without serum creatinine baseline values. Although arguably more appropriate for low-resource settings, this approach might have led to incorrect classification of people with chronic kidney disease who subsequently experienced decreases in serum creatinine due to fluid expansion or muscle wasting. Use of the modified KDIGO definition might account for our finding that more than half of patients with acute kidney injury had acute-on-chronic kidney injury—including about 75% of patients from LLMICs—and why previous studies from LLMICs using other definitions of acute kidney injury have reported a much lower proportion of patients with acute-on-chronic kidney injury.[11,12] In our study, acute kidney injury was more severe on presentation in patients from LLMICs than in patients from UMICs and HICs, which might reflect delays in recognition and treatment and adversely affect outcome.[13]

Although dehydration, infections, and sepsis were important aetiological factors in all countries (and contributed to hypotension and shock as the most common cause of acute kidney injury), they probably reflect different exposures and patient factors across the different settings studied.[14] The higher incidence of cardiac failure, postoperative acute kidney injury, and nephrotoxic agents in patients in HICs and UMICs might reflect exposure to several diagnostic (eg, contrast imaging) and therapeutic interventions in patients in hospital with comorbidities and older age. By contrast, in the younger patients in LLMICs, dehydration, infections, animal envenomation, and complicated pregnancy were the most important drivers of acute kidney injury.[14]

Dialysis was more frequently used in LLMICs than in UMICs and HICs, probably because of the higher severity of acute kidney injury on presentation and the over-representation of large referral centres with dialysis facilities in LLMICs. However, access to dialysis in LLMICs is often scarce, with variations seen even in different regions of the same country or even in different areas of the same city. Unsurprisingly, scarcity of resources was a frequent reason for not providing dialysis in LLMICs. Continuous renal replacement therapy was seldom used in LLMICs, probably owing to its higher cost,[2,15–18] and peritoneal dialysis was infrequently used across all countries, despite its value in low-resource settings.[19–23] The International Society of Nephrology's Saving Young Lives Project has successfully developed and implemented programmes for teaching and providing peritoneal dialysis in several LLMIC regions, which might help to reduce mortality and morbidity related to acute kidney injury in these areas.[24,25]

The high mortality rate associated with acute kidney injury is concerning, especially in LLMICs, where almost 80% of patients had de-novo acute kidney injury, which was associated with improved outcomes in previous studies.[26,27] We confirmed the incremental risk of oliguric acute kidney injury with concurrent other organ failures, sepsis, and need for dialysis as the major determinants of mortality associated with in-hospital acute kidney injury,[11,12,28] as shown by other studies, and confirmed that less than 50% of acute kidney injury survivors had renal follow-up arranged at discharge.[29] Appropriate management of patients with incomplete kidney recovery might delay the progressive loss of kidney function[30] and improve their later quality of life. Worldwide educational campaigns, for a full range of health-care personnel, on the importance of long-term follow-up of patients with acute kidney injury need to be developed and implemented.

This study provides a convenience sample of the incidence of acute kidney injury, and summary data are unlikely to be representative of any single country. The paucity of data from LICs and outpatient settings highlights the challenges of obtaining information from low-resource sites. Additionally, most LLMIC centres were located in referral hospitals in large cities, and thus cases of acute kidney injury in rural settings and small urban centres are under-represented. Seasonal variations in acute kidney injury were not captured in the limited time available. Finally, absence of trained personnel, infrastructure issues (eg, intermittent electricity and internet connections, a heavy workload, and time constraints) are recognised factors limiting participation in studies.[2,14] We do not know to what extent these and other factors influenced the Global Snapshot Study. Our findings provide a restricted view of the true burden of acute kidney injury in outpatient settings and in LICs, and emphasise the need for new strategies to close these knowledge gaps.

The Global Snapshot is a unique prospective cross-sectional study designed to capture regional differences in recognition, management, and outcomes of acute kidney injury. The study provides novel, but limited, information about the burden of acute kidney injury worldwide, and establishes baseline information to

design interventions to raise awareness of acute kidney injury, and to develop strategies to improve outcomes. Longitudinal studies are planned, which include centres worldwide, with an emphasis on LICs. These studies will collect information from community settings, capture sequential data for acute kidney injury and its long-term outcomes, and test interventions to reduce the incidence of, and preventable deaths from, acute kidney injury.

Contributors

All authors substantially contributed to the design of the study, acquisition, analysis, and interpretation of data, drafted and revised the manuscript for important intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

Declaration of interests

RLM reports grants from International Safety Adverse Events Consortium and Thrasos, and consultant agreements from AbbVie, AM Pharma, Eli Lilly, Ardea, Astute Inc, CSL Behring, GSK, Baxter, Sova, Astellas, Sanofi-Aventis, Ferring Research, Isis Pharmaceuticals, and Fresenius-Kabi. EAB reports consultant agreements from AbbVie and Baxter Gambro. JF reports personal fees from UCB Pharma. VJ reports grants from Baxter Healthcare and GSK. GR reports personal fees from Dompé Farmaceutici SpA, and consultant agreements from AbbVie, Alexion Pharmaceuticals, Bayer Healthcare, Reata Pharmaceuticals, Novartis Pharma, Otsuka Pharmaceutical Europe, Concert Pharmaceuticals, and AstraZeneca. JC, FF, GG-G, MG, NHL, NWL, AL, RL, EM, MR, EA-S, MT, and JZ declare no competing interests.

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