NEPHROLOGY - ORIGINAL PAPER

Outcomes of hospital-acquired acute kidney injury in elderly patients: a single-centre study

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Abstract

Background HAAKI is a common clinical problem in hospitalized patients. Its incidence is high in older patients and carries worse prognosis. The presence of multiple co-morbidities, aging process, and frequent diagnostic and therapeutic interventions predispose elderly patients to HAAKI. This study aims to evaluate the spectrum, risk factors and determinants of outcome of elderly patients with HAAKI.

Methods This prospective study was conducted during January 2014 to September 2015 in the Department of nephrology, Institute of Medical Sciences, BHU, Varanasi, UP, India. First 100 HAAKI elderly (> 60 years) patients, who fulfilled the inclusion criteria were enrolled for study. HAAKI was defined as per RIFLE criteria after minimum 48 h of hospitalization. Clinical, biochemical, and radiological evaluation were done. Follow up was done till discharge or up to 30 days whichever was later.

Results Till selection and enrollment of first 100 HAAKI patients, total 23507 patients were hospitalized. 11.2% ($n = 2635$) patients were ≥ 60 years of age. Among 2635 elderly patients, 3.79% ($n = 100$) developed HAAKI. Commonest causes of HAAKI were sepsis (37%) followed by drugs like NSAID, Contrast agent, Amphotericin B, and antibiotics including amino glycosides in (24%) patents. DM and HTN were the commonest risk factors. Mortality was noted in 45% cases and rest 55% patients recovered with partial or full recovery of renal function. ICU admission, Oliguria, RIFLE-F, need of RRT, and SOFA score > 11 were independent determinants of outcome of elderly patients with HAAKI.

Conclusion HAAKI is associated with increased morbidity and mortality in elderly patients. Associated co-morbid conditions predispose elderly patients to HAAKI. ICU admission, Oliguria, severity of renal failure, requirement of RRT, and initial SOFA score were strong predictors of survival of elderly patients with HAAKI.

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Introduction

Acute kidney injury (AKI) is common in elderly individuals, as age is an important risk factor for development of AKI. It has been estimated that AKI occurs in 2–7% of all hospital admissions and at even higher rates in elderly patients [1]. The incidence of AKI in elderly is much greater than the general populations and appears to have a worse prognosis than their younger counterpart. The presence of multiple co-morbidities, decrease in age related renal reserve, requirement of frequent diagnostic and therapeutic interventions, and age related changes in systemic vasculature and immunological system predisposes these elderly patients to renal injury [2]. For the purpose of epidemiological study AKI has been categorized in two groups as Hospital Acquired AKI (HAAKI) and Community Acquired AKI (CAAKI). For a long time AKI had suffered a lack of standard defining criteria which resulted in more than 30 definition in literature. Until in 2004 KDOQI proposed a consensus definition of AKI known as RIFLE criteria [3], and in 2007 AKI has been redefined by Acute Kidney Injury Network following which outlook of AKI has changed immensely.

Hospital acquired AKI has been a major concern in hospitalized elderly population. Studies on HAAKI are done mainly in general population and in different clinical settings. There is paucity of studies on HAAKI in elderly patients using RIFLE criteria. This prospective study was conducted to evaluate the entire spectrum of HAAKI, risk factors and determinants of outcome of elderly patients with HAAKI.

Methods and materials

A prospective study was conducted during January 2014 to September 2015 in the department of Nephrology, IMS, Banaras Hindu University, Varanasi, UP, India. In study period first 100 elderly (≥ 60 years) patients of both genders who fulfilled the definition of HAAKI were enrolled in the study. Patients having age less than 60 years, pre-existing renal disease (elevated serum creatinine level at the time of admission, active urinary sediments, and radiological evidences of structural renal disease), renal transplant recipients, and patients not willing for consent were excluded from the study.

This study was approved by ethics committee of Institute of Medical Sciences, Banaras Hindu University, and Varanasi. Detail clinical evaluation, biochemical, urine microscopy and radiological investigation were done for all enrolled patients. Serial renal function test

was performed on 24 h interval for 48 h and later on as required as basis. 24 h urine output, need of RRT, and length of hospital stay of all patients were recorded.

AKI was defined as per RIFLE criteria. HAAKI was defined as "AKI as per RIFLE criteria after minimum 48 h of hospitalization". The acronym RIFLE stands for the increasing severity classes Risk, Injury, and Failure; and the two outcome classes, Loss and End-Stage Renal Disease (ESRD). The three severity grades are defined on the basis of the changes in Serum Creatinine or urine output where the worst of each criterion is used. The two outcome criteria, Loss (complete loss of renal function for > 4 weeks) and ESRD (loss of renal function > 3 months), are defined by the duration of loss of kidney function. Chronic Kidney Disease (CKD) was defined as structural and functional abnormality of kidney lasting for more than 3 months [4]. A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury. Diabetes was defined according to ADA criteria 2014 and AKI in diabetes was diagnosed in absence of proteinuria, diabetic retinopathy, neuropathy, and normal creatinine level at the time of hospitalization. Hypertension was defined as per JNC -7. Biochemical parameters were not considered as risk factors in our study. Outcomes were defined in term of either discharge from hospital or mortality. Organ failure was define by SOFA score. The sequential organ failure assessment score (SOFA score) is used to track a person's status during the stay in an intensive care unit (ICU) to determine the extent of a person's organ function or rate of failure. The score is based on six different scores, one each for the respiratory, cardiovascular, hepatic, coagulation, renal, and neurological systems. SOFA score (T0) was calculated at the time of development of HAAKI [5]. Sepsis was defined as presence of one or more of the following as a result of systemic infection; (1) Temperature (Oral) > 38 °C or < 36 °C, (2) Heart rate > 90/min, (3) Respiratory rate > 24/min, and (4) Total count > 12,000/mm^3, < 4000/mm^3, or > 10% band forms [6]. Contrast induced nephropathy was defined as development of HAAKI within 24–48 h of intravenous contrast administration [7]. Drugs induced HAAKI was considered, if patients received a drug with known nephrotoxic potential for 3 days prior to the development of HAAKI [8]. Volume depletion was evident by IVC diameter of < 1.5 cm, IVC collapsibility of > 50%, presence of orthostatic hypotension (15–20% loss of body fluid), loss of skin turgor, and loss of body weight > 5% [9]. Clinically apparent congestive heart failure and clinical shock was suspected when mean arterial pressure was less than 60 mmHg and typical clinical picture was observed [10]. Follow up was done till the last day of hospital stay or 30 days from admission whichever was later.

Table 1 Demographic characteristics of the study population

Total number of admission (during study periods)	23,507	Male	16,455 (70%)
		Female	7052 (30%)
Total numbers of elderly (> 60 years)	2635 (11.2%)	Male	2082 (79.01%)
		Female	553 (20.98%)
Age range/mean ± SD	60–96/70.97 ± 8.42		
Total numbers of HAAKI in elderly	100 (3.79%)	Male	75 (75.00%)
		Female	25 (25.00%)
Total mortality in HAAKI patients	45 (45.00%)	Male	31 (31.00%)
		Female	14 (14.00%)

Table 2 Age and sex distribution of elderly patients ($n = 2635$)

Age in years	Male (n)	Female (n)	Total (n)
60–69	1336	320	1656
70–79	464	155	619
80–89	230	55	285
> 90	52	23	75
Total	2082	553	2635

Table 3 Age and sex distribution of elderly patients with HAAKI ($n = 100$)

Age in years	Male (%)	Female (%)	Total (%)
60–69	45 (45%)	14 (14%)	59 (59%)
70–79	19 (19%)	07 (07%)	26 (26%)
80–89	08 (08%)	04 (04%)	12 (12%)
> 90	03 (03%)	00 (00%)	03 (03%)
Total	75 (75%)	25 (25%)	100 (100%)

Statistical analysis

Statistical analysis was done by using software SPSS-16 version. Calculations of statistical variable were done by using Chi-Square test, log rank test, and logistic regression analysis. Variables were considered significant if the p value is < 0.05.
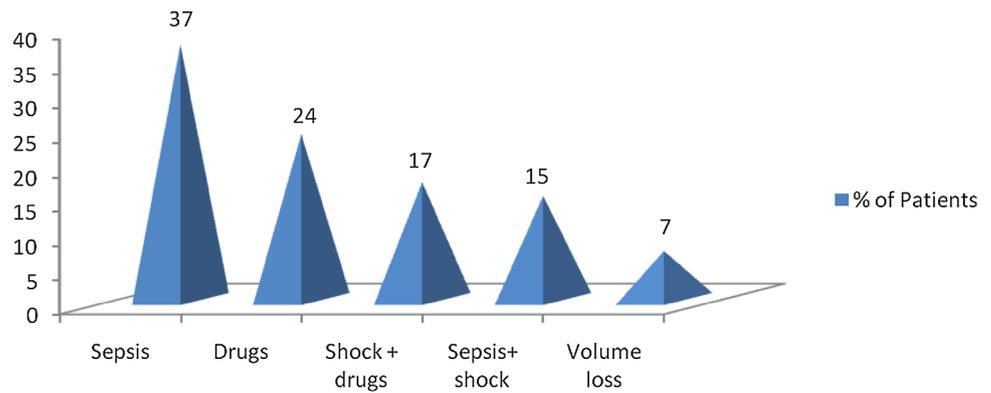
Results and observations

Till selection and enrollment of first 100 HAAKI patients, total 23,507 patients were hospitalized. 11.2% ($n = 2635$) patients were ≥ 60 years of age. The overall incidence of HAAKI was 0.42%. Among 2635 elderly patients, incidence of HAAKI was 3.79% ($n = 100$). Mortality rate was 45% (Table 1). Majority of the elderly patients were in the younger age group (Tables 2, 3). The mean hemoglobin level and total leucocytes count were 11.19 ± 1.80 gm/dl and 8907 ± 5.87/mm^3 respectively. The mean baseline, peak and discharge creatinine level were 0.97 ± 0.14, 3.33 ± 1.44, and 1.55 ± 0.83 respectively. The mean LOS and SOFA score were 13.12 days and 10.72 ± 2.86 respectively.

The most common etiology of HAAKI in our study were sepsis (37%), followed by drugs (like NSAID, Contrast agent, Amphotericin B, and antibiotics including amino glycosides) in (24%) and both were present in 17% patents (Table 4; Fig. 1). DM and HTN were the commonest risk factor associated with HAAKI in 34% and 25% patients respectively (Table 5; Fig. 2). Common class of HAAKI in our study population were RIFLE-R (47%, $n = 47$) followed by RIFLE-I (29%, $n = 29$) and RIFLE-F (24%, $n = 24$) (Table 6). It was observed that 34% ($n = 34$) patients had requirement of RRT. Mortality was noted in 45% cases and rest 55% patients recovered with partial or full recovery of renal function. The predictors of patient's poor survival in our study were ICU admission, Oliguria, RIFLE-F, requirement of RRT, and SOFA score > 11(Figs. 3, 4, 5, 6, 7 respectively).

Table 4 Etiology of HAAKI in study patients

Etiology	Male n (%)	Female n (%)	Total (%)
Sepsis	27 (27%)	10 (10%)	37 (37.00)
Drugs(NSAID, contrast agent, Amphotericin B and antibiotics including amino glycosides)	21 (21%)	03 (3%)	24 (24.00)
Shock + drugs	12 (12%)	05 (5%)	17 (17.00)
Sepsis + shock	12 (12%)	03 (3%)	15 (15.00)
Volume loss	03 (3%)	04 (4%)	07 (07.00)
Total	75 (75%)	25 (25%)	100 (100%)

Fig. 1 Bar diagram showing the etiology of HAAKI (%)

Table 5 Risk factors of HAAKI in study population

Risk factors	Male n (%)	Female (%)	Total (%)
Diabetes	27 (27%)	07 (7%)	34 (34%)
Hypertension	21 (21%)	04 (4%)	25 (25%)
DM + HTN	8 (8%)	07 (7%)	15 (15%)
Others (CAD,CLD,COPD,CVA)	19 (19%)	07 (7%)	26 (26%)
Total	75 (75%)	25 (25%)	100 (100%)
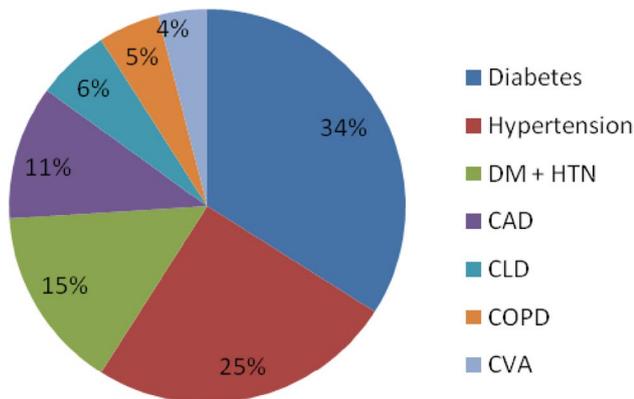
Fig. 2 Pie diagram showing the risk factors of HAAKI

Table 6 RIFLE class of study population (Z-test)

RIFLE class	ICU (n)	Non-ICU (n)	Total n (%)	p value
Risk	12	34	46 (46%)	< 0.001
Injury	15	14	29 (29%)	0.097
Failure	14	10	24 (24%)	0.105
Loss	01	–	01 (01%)	
ESRD	–	–	–	
Total	42 (42.00)	58 (58.00)	100 (100.00)	0.014

Mortality rate was highest in patients with SOFA score > 11 (85.70%) followed by patients having oliguria (80%) and ICU admission (78.57%) (Table 7). Mortality rate in RIFLE-F and RIFLE-I class was 75% ($n = 18$) and 65.51% ($n = 19$), respectively. The mortality rate was significantly high in patients who received RRT as compared to patients who didn't receive RRT (70.58 vs 34.84%; $p = 0.008$). At the time of HAAKI diagnosis, initial SOFA score < 11 and > 11 was seen in 58% ($n = 58$) and 42% ($n = 42$) patients, respectively. Mortality rate was significantly high in patients with SOFA score > 11 as compared to SOFA score < 11($p < 0.05$).

Discussion

HAAKI is a common clinical entity in hospital settings with high morbidity and mortality rate. Like other form of AKI, HAAKI is more common in elderly population. The incidence of HAAKI depends on population, clinical settings, and criteria used to define the AKI. In present study, incidence of HAAKI in elderly was 3.79%. Reported incidence of AKI in hospitalized patient varies between 5 and 7% [11, 12]. In earlier study conducted by Singh et al., at same institute using RIFLE criteria have reported 0.54% overall incidence of HAAKI in different clinical settings [13].

In various study by Nash et al., Chronopoulos et al., Pankaj et al., and Pascual et al. reported incidence of HAAKI in elderly were 5%, 8.6–10.6%, 22.72%, and 63%, respectively [5, 14–16]. In a Chinese study by Wen et al. reported 14.8% incidence of HAAKI using AKIN criteria in very old (> 80 years) Chinese patients [17]. The high incidence of HAAKI in their study is due to inclusion of both AKI and acute on chronic kidney disease. Our finding on HAAKI is also lower than the studies conducted on general population by Hon et al. [18], Abraham et al. [19] and Davidman et al. [20], where the reported incidence was 1–4.9% and this high incidence of AKI could be due to most of these studies were carried out in ICU settings and included both HAAKI and CAAKI. The lower incidence of HAAKI in our study could

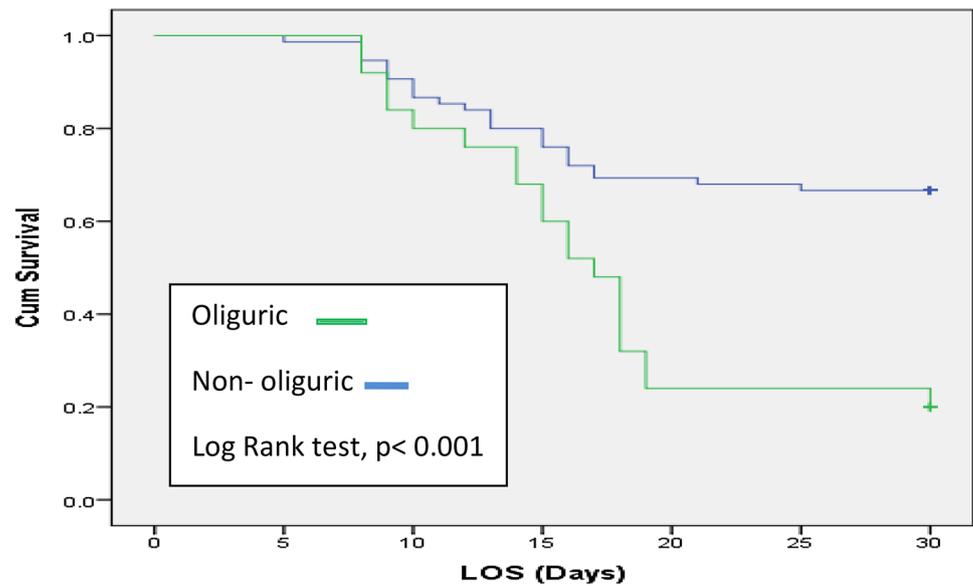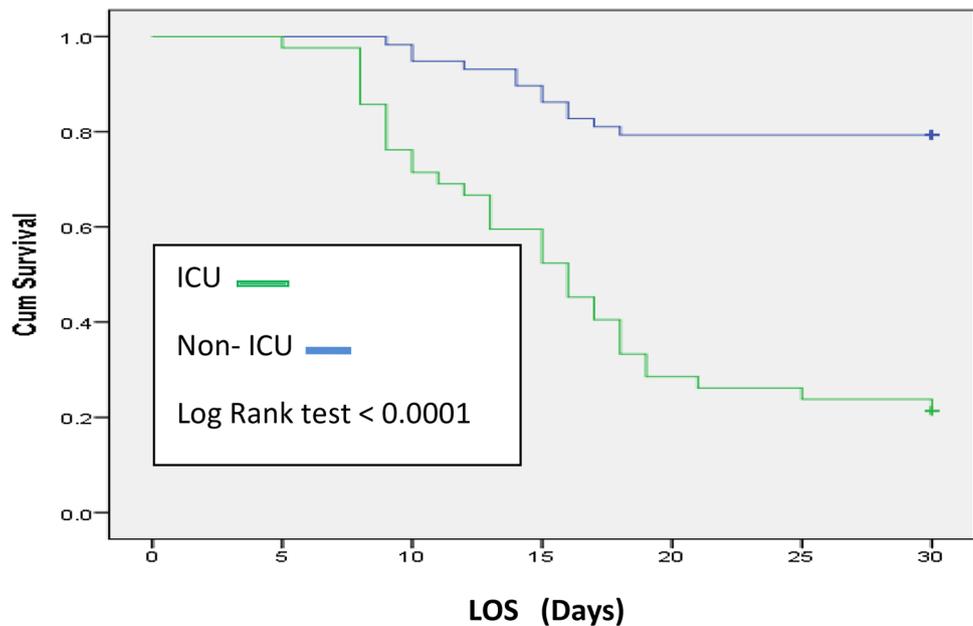**Fig. 3** Kaplan–Meier survival curve according to urine output at 30 days

Fig. 4 Kaplan–Meier survival analysis according to ICU and non-ICU admission at 30 days

be due to inclusion of patients from diverse clinical settings, cut off age for elderly as 60 years and exclusion of patients with pre-existing chronic kidney disease. The incidence of HAAKI in postoperative period ranges from 0.1 to 30%, depending on the criteria used to define AKI and the type of surgery performed [21].

It has been seen that incidence of HAAKI in elderly population is highly variable as HAAKI in general population. Thus, true incidences of HAAKI depend upon the clinical settings and population studied. Decreasing incidence of HAAKI in elderly population could be due to

better understanding of pathophysiological process, increase awareness and practice of preventive measures in managing the hospitalized elderly patients.

In our study it was observed that the most common age group affected by HAAKI was 60–69 years (59%) followed by 70–79 years age (26%). The mean age of HAAKI patients was 74.5 years. In the study by Arora et al. Lins et al. and Gong et al. in Chinese population, mean age of HAAKI patients were 67.1, 69.8 ± 14.7, and 77.8 ± 7.8 years, respectively [22–24]. Our result on mean age is consistent to above

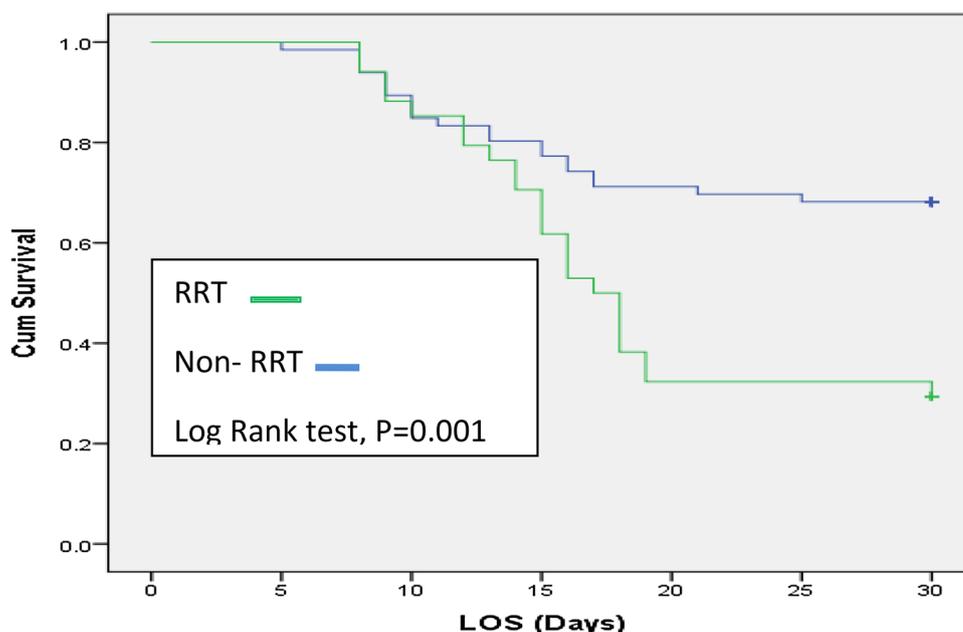**Fig. 5** Kaplan–Meier analysis of patient's survival curve according requirement of RRT
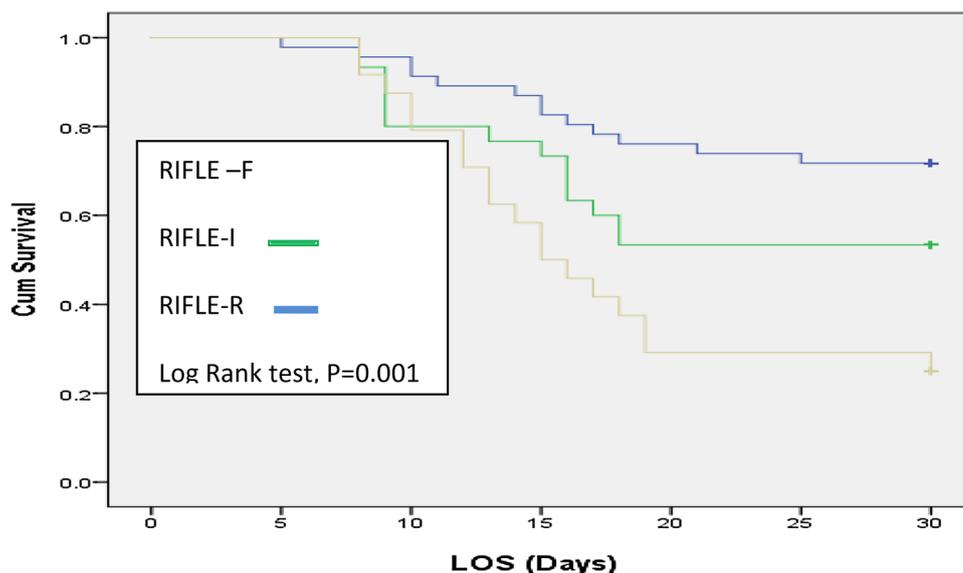

Fig. 6 Kaplan–Meier analysis of patient's survival curve according to RIFLE class


studies. Although, it depend up on the population studied and age cut off used to define elderly population in the study.

In present study Male to female ratio was 3:1. Lins et al. reported a male to female ratio of 1.49:1 [24]. This difference in the male to female ratio in present study could be a reflection of male dominant and more treatment seeking attitude of the male gender in our society.

The high incidence of HAAKI in elderly population is associated with multiple factors like age related declined in renal reserve, presence of multiple co-morbidities, high pill burden, frequent need of diagnostic and therapeutic intervention, and becoming a fastest growing population worldwide

due to increase in life expectancy in both developed and developing countries.

The most common cause of HAAKI in our study population was sepsis (37%). Habir et al. in a study on elderly found that sepsis was underlying cause in 45.7% either alone or in combination [25]. Sepsis was the most common underlying causes of HAAKI in surgical (34%) and ICU units (35.2%) in the study done by Mataloum et al. [26]. In a study by Wen et al. found that causes of HAAKI in elderly was multi-factorial and most common causes were hypovolemia, nephrotoxic drugs, and cardiac dysfunction and amongst drugs antibiotics was the commonest [17]. In our study drugs like NSAID, Contrast agent, Amphotericin

Fig. 7 Kaplan–Meier patient's survival curve according SOFA score
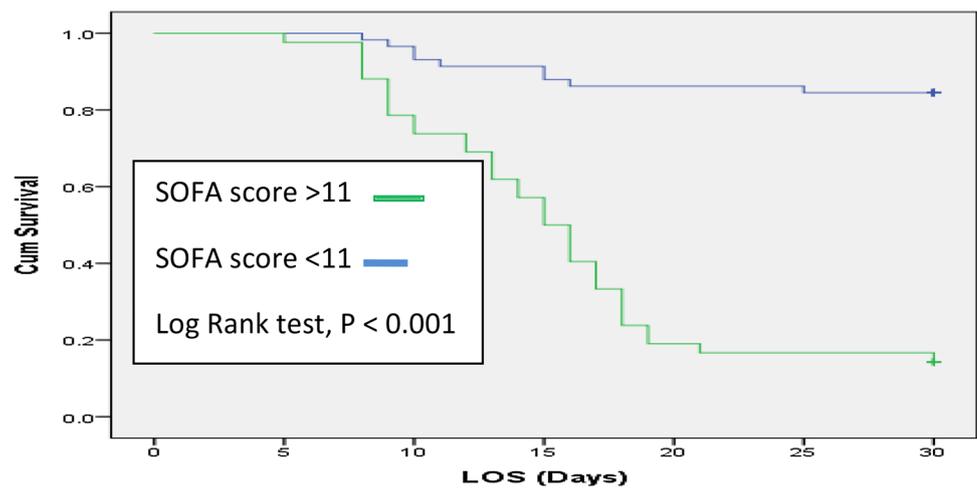
Table 7 Predictive value of various parameters for patient survival

Parameters	Died	Survive	UOR (95%CI)	p value	AOR* (95% CI)	p value
Oliguria	20 (80%)	05 (20%)	0.125 (0.042–0.372)	0.000	0.093 (0.023–0.372)	0.001
Dialysis (RRT)	24 (70.58%)	10 (29.4%)	0.194 (0.079–0.479)	0.000	0.151 (0.048–0.477)	0.001
SOFA score > 11	36 (85.70%)	6 (14.3%)	0.031 (0.010–0.094)	0.000	0.026 (0.007–0.098)	0.000
ICU admission	33 (78.57%)	09 (21.42%)	0.072 (0.027–0.188)	0.000	0.061 (0.020–0.187)	0.000
RIFLE- F	18 (75.0%)	06 (25.0%)	0.184 (0.065–0.518)	0.001	0.179 (0.055–0.583)	0.004

UOR Unadjusted odds ratio, *AOR* Adjusted odds ratio,* Adjusted with age sex, *DM* HTN and diabetes + hypertension

B, and antibiotics including amino glycosides was the second most common cause of HAAKI in 24% ($n = 24$) patients. Drugs in combination with sepsis was the cause of HAAKI in another 17% ($n = 17$) patients (Table 4). Davidman et al. found 47.7% HAAKI is due to drug, which is very high as compared to our study [20]. Lower incidence of HAAKI attributed to drug in our study may be due to increased awareness among the physician and staff involving the management of critically ill patients. In our study incidence of Contrast induced nephropathy is not evident separately because contrast was used in presence of sepsis and other drugs which is well known cause of AKI. Distinction of this entity is difficult. The effects of polypharmacy and drug toxicity exacerbate increased susceptibility of the elderly to AKI. Drugs commonly associated with AKI are often co-prescribed medication for different illness and increased used of contrast agents in diagnostic and therapeutic interventions. .

In study by Nash et al. on hospital acquired renal insufficiency, he found volume depletion as a cause of HAAKI in 89% [14]. Prakash et al. found that hypotension alone or in combination with other, was responsible for about 71.74% of HAAKI in ICU patients in the general population [27]. The causes of HAAKI in elderly patients were not different from general population as evident by our study.

The commonest risk factor associated with HAAKI were diabetes mellitus and hypertension in 34% ($n = 34$) and 25% ($n = 25$) patients respectively. Both diabetes mellitus and hypertension were present in 15% ($n = 15$). 26% ($n = 26$) patients had co-morbidity like COPD, CAD, Stroke, and chronic liver disease. Co-morbidities are common among elderly patients as evident by a study done by Anderson et al. [28]. In an analysis conducted in 1999 on a sample of 1,217,103 Medicare beneficiaries aged 65 and older living in the US, 65% of the participants were found to have 2 or more chronic conditions, 43% had 3 or more chronic conditions and 24% had 4 or more chronic conditions [29]. Our study reports on associated risk factor are almost equivocal to report of study done by previous author, though our study was conducted only on elderly HAAKI population [28, 29].

RIFLE-R (46%) was the most common class of HAAKI in our patients. RIFLE-I and RIFLE-F were present in 29% and 24% patients, respectively. Singh et al. reported an incidence of RIFLE- R in medical and surgical unit were 39.2% and 50% respectively [13]. Both this studies were conducted using RIFLE criteria in same clinical settings with different study population. Result of our study is similar to study done by Singh et al.

In our study total 45% ($n = 45$) cases expired during the hospital stay and 55% ($n = 55$) patients were discharged with partial or full recovery. RRT was given to 34% ($n = 34$)

patients. Low survival of patients was observed in group who received RRT as compared to those who didn't received RRT (AOR of 0.151; 95% CI 0.048–0.477, $p = 0.001$). Oliguria was an important outcome predictor of mortality (AOR 0.093; 95% CI 0.023–0.372; $p = 0.00$). Low survival was also seen in ICU patients with (UOR of 0.072; 95% CI 0.027–0.188, $p \leq 0.001$). Death censored Kaplan-Meire survival curve is shown in the Figs. 3, 4, 5, 6, 7 using log rank test and p values were significant. In a study by Habir et al. found an overall mortality rate of 25.4% and dialysis requirement was in 15.2% patients in their study on drug related HAAKI in elderly population. The difference in the mortality in two groups (Dialysis vs Non dialysis) was also statistically significant [25]. The need of RRT was low, in their study and could be due to study was particularly restricted to only one etio-pathological group. Another study by Biradar et al. reported a 51% mortality of HAAKI when compare to CAAKI patients and result of this on mortality was comparable to our study [30]. Nashi et al. and Chamberlin et al. in their study found requirement of dialysis were in 50% and 10% patients, respectively [11, 12, 31].

Amongst the RIFLE classes, RIFLE-F had the lowest survival with (AOR of 0.179, 95% CI 0.055–0.583) followed by RIFLE-I. Death censored Kaplan-Meire survival curve is shown in the Fig. 4, using log rank test with p value of < 0.001. One earlier study from this institution also found a similar pattern of mortality rate in their study with RIFLE-F (66.60%) in surgical unit, but their study included all adult patients (> 18 years) [23]. Mortality rate in present study is comparable with study done by others which were in ranges of 25–70% [18, 32]. In a multinational study by Uchino et al. reported a mortality rate of 60.3% in a ICU setting and Mahajan et al. found a mortality rate of 64.4% [33, 34]. In an earlier study conducted at same institute by Prakash et al. found a mortality rate of 63% in ICU setting [27]. In a cohort study of cardiac surgery Kuitunez et al. found mortality rate of 61.1% which was also equivalent to our study. Wang et al. in a Chinese study found 65.5% mortality in ICU setting [35].

The requirement of dialysis and mortality in elderly population with HAAKI varied from study to study. It seems that this is not different from that of the general population. To establish the increase mortality in elderly patient requires a large randomized control studies. Theoretically it is possible to have less hemodynamic stability during RRT in elderly. Pre-existing renal disease, multi-organ failure, infections, and lower immunity are much more common in elderly; therefore recovery from renal failure is also slower in elderly patients.

We found that initial SOFA score of < 11 and > 11 were in 58% ($n = 58$) and 42% ($n = 42$) of the patients. Survival was significantly low in patients with SOFA score of > 11 as compared to patients with SOFA score < 11 (AOR of

0.026, 95% CI 0.007–0.098, $p = 0.000$). Death censored Kaplan–Meire survival curve is shown in the Fig. 5, using log rank test, $p = 0.0001$. A study by Ferreira et al. found that an increase in SOFA score during the first 24–48 h in the ICU predicts a mortality of 90% when score was > 11 [36]. Another study conducted by Acharya et al. found that the initial SOFA score > 11 predicted a mortality of 90%. (AOR 23.72, 95%CI 2.68–209.78, $p = 0.004$) [37]. Besides initial, serial and mean SOFA score also correlates well with morality. Mortality predictability of SOFA score in our study was comparable with the studies done by Ferreira et al. and Acharya et al. [36, 37].

Conclusion

HAAKI is a common clinical entity in elderly population. Development of HAAKI is associated with overall poor survival in patients, particularly elderly. Aggressive management of sepsis, shock, and judicious use of drugs can prevent the development of HAAKI. Management of co-morbid condition should be addressed appropriately. Factors determining the survival in elderly patients are oliguria, severity of renal failure, requirement of dialysis, length of hospital stay, and initial SOFA score. Despite best available therapy, survival in elderly patient is very low; therefore preventive measures should be initiated from the very beginning to prevent HAAKI. As there is lack of studies on HAAKI using RIFLE criteria, hope present study will help in prevention and management of HAAKI.

Compliance with ethical standards

Conflict of interest The authors declare that they have not conflict of interest.

Ethical approval This study was observation study involving human subjects and participants didn't undergo any invasive procedure. This study was approved by Ethical Committee of Institute of Medical sciences, Banaras Hindu University, Varanasi, UP and India.

Informed consent Informed consent was obtained from all individual participants involved in this study.

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