2022-10-29

Prevalence and Associated Factors of Acute Kidney Injury in Septic Shock Patients Admmited to Tibebe Ghion Specialized Hospital and Felegehiwot Referal Hospital Intensive Care Units

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Prevalence and Associated Factors of Acute Kidney Injury in Septic Shock Patients Admmited to Tibebe Ghion Specialized Hospital and Felegehiwot Referal Hospital Intensive Care Units

By

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A RESEARCH SUBMITTED TO BAHIR DAR UNIVERSITY COLLEGE OF MEDICINE AND HEALTH SCIENCE, DEPARTMENT OF INTERNAL MEDICINE IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE SPECIALITY CERTIFICATE IN INTERNAL MEDICINE

October 2022

BAHRDAR ETHIOPIA

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Title of research project	Prevalence and associated factors of acute kidney injury in septic shock patients admitted to TGSH and FHRH ICUs
Duration of the project	February 1/ 2022-october /2022 G.C
Study area	Tibebe Gihon Specialized Hospital and felegehiwot referral hospital
Total cost of the project	25,318.00 Ethiopian birr
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Acknowledgment

I would like to express my heartfelt gratitude to Bahir Dar University College of Medicine and Health science the department of Public Health and Internal Medicine giving me this chance and budget for preparation of a research

I would like to forward my appreciation and thanks to my advisors Dr. Alemtsehay and Dr. Nathan for their continued supports and comments for preparation of my research proposal.

I would like to say thanks to those who work in tibebeghion and felgehiwot referral hospital ICUs for availing medical records and documentation books.

Abbreviations

ACEI –angiotensin converting enzyme inhibitors

AKI – acute kidney injury

ARBS – angiotensin receptor blockers

CHF –congestive heart failure

CKD – chronic kidney disease

FHRH- felegehiwot referral hospital

Hr –hour

Scr -serum creatinine

ICU – intensive care unit

TGSH – Tibebe gion specialized hospital

UOP –urine out put

Acronym

APACHE 2 Score-acute physiologic and chronic health evaluation

KIDGO-Kidney disease improving global outcome

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Summary

Background : acute kidney injury is defined as an increase in serum creatinine by 0.3 from base line within 48 hrs or by 50% from baseline within 1 week or urine output < 0.5ml/kg/hr for 6hrs.It complicates 5–7% of acute care hospital admissions and up to 30% of admissions to the intensive care unit. It is associated with a markedly increased risk of death in hospitalized individuals, particularly in those admitted to the ICU where in-hospital mortality rates may exceed 50%. Septic shock is defined as sepsis with hypotension in which vasoactive drugs are needed to maintain a mean arterial pressure of at least 65 mm Hg and a serum lactate concentration above 2 mmol/L despite resuscitation

Methods: hospital based retrospective crossectional study was conducted from February 1/ 2022-october 30/2022 GC on patients admitted tibebeghion specialized hospital and felegehiwot referral hospital intensive care units in the past 5 years with a diagnosis of septic shock and age above 18 years to assess the prevalence of acute kidney injury in septic shock and associated factors with a calculated sample size of 161 .The study aimed to show the magnitude and associated factors to those working in the area so that the can take precautions to minimize the impact on patients.

Result: a total of 161 patients were evaluated.50.3% were males. 44.1% of them were in the age group of 40-64 years. 131 (70.2%) developed AKI.37 (23%) had KIDGO stage 1 AKI; 37 (23%) had KIDGO stage 2 AKI; and another 37 patients had KIDGO stage 3 AKI. Age group 40-64 years [P value **0.047** (AOR of 2.747 95% CI of 1.016-7.427)] and use of adrenaline [P value of **0.045** (OR of 4.58 95% CI 1.00-20.35)] were significantly associated with developing acute kidney injury.

Conclusion: In this study the prevalence of acute kidney injury is more than 70 % and the mortality was 58.4% with only 7 patients dialyzed and 1 patient having blood culture which calls for significant improvement in the management of patients with septic shock.

Key words: septic shock, acute kidney injury, prevalence, associated factors tibebegion specialized hospital felegehiwot referral hospital

1. Introduction

Background

AKI is defined as any of the following; an increase in Serum creatinine(Scr) by 0.3 mg/dl (≥26.5 lmol/l) within 48 hours; or increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume less than 0.5 ml/kg/h for 6 hours. It has three stages; stage 1: serum creatinine 1.5–1.9 times baseline or 0.3 mg/dl (26.5 mmol/l) increase from base line, stage 2 : 2.0–2.9 times increase from baseline; stage 3: 3 times baseline or increase in serum creatinine to more than 4.0 mg/dl (1)

AKI complicates 5–7% of acute care hospital admissions and up to 30% of admissions to the intensive care unit(2).Sepsis is the most common cause of acute kidney injury (AKI) in critically ill patients (3).S-AKI is a syndrome of acute functional impairment and organ damage that could be associated with long-term adverse outcomes(2, 3) .Sepsis-associated acute kidney injury (S-AKI) is a major public health condition that is associated with a significant disease burden(3) .Of particular importance is the fact that S-AKI is closely associated with poor clinical outcomes (2, 3).For instance, the mortality rate of sepsis patients with AKI complications is significantly higher than that of non-AKI patients(3)

AKI is associated with a markedly increased risk of death in hospitalized individuals, particularly in those admitted to the ICU where in-hospital mortality rates may exceed 50%(2).

The causes of AKI have traditionally been divided into three broad categories pre renal azotemia, intrinsic renal parenchymal disease, and post renal obstruction(2) .Pre renal azotemia is the a rise in SCr or blood urea nitrogen(BUN) concentration due to inadequate renal plasma flow and intraglomerular hydrostatic pressure to support normal glomerular filtration. Intrinsic AKI is due problems with in the

kidney parenchyma .The most common causes of intrinsic AKI are sepsis, ischemia, and nephrotoxins, both endogenous and exogenous. In many cases, prerenal azotemia advances to tubular injury(2). Intrinsic renal causes of AKI should be considered under the different anatomic components of the kidney (vascular supply; glomerular, tubular, and interstitial disease(4)

Sepsis induced AKI

Sepsis is a life threatening clinical syndrome characterized by organ dysfunction caused by a patient's dysregulated response to infection(5). Septic shock is a subset of sepsis with increased mortality characterized by hypotension, in which vasoactive drugs are needed to maintain a mean arterial pressure of at least 65 mm Hg and a serum lactate concentration above 2 mmol/L despite resuscitation(5).AKI complicates more than 50% of cases of severe sepsis and greatly increases the risk of death. Most cases of severe AKI typically occur in the setting of hemodynamic collapse requiring vasopressor support(2)

Despite advances in knowledge of clinical risk factors, pathobiology, response to treatment, SA AKI remains an important concern and clinical burden. Early identification of risk factors, early detection of injury, modifying clinician behavior to avoid harm, early appropriate antimicrobial therapy should be practiced to reduce morbidity and mortality The prevalence and outcomes are not well studied in resource limited areas. In this study we will identify the prevalence and associated factors of AKI in septic shock patients admitted to TGSH and FHRH ICUs.

Statement of the problem

AKI complicates 5–7% of acute care hospital admissions and up to 30% of admissions to the intensive care unit(2)

According to a study done in 22 US, Canada and Saudi ICUs of academic and community hospitals , 64.4% of patients with septic shock developed AKI; AKI patients were older, more likely female, with more co-morbid disease and greater severity of illness; . Patients with AKI were more likely to have longer delays to receiving antimicrobial therapy compared to those with no AKI; AKI was associated with significantly higher odds of death in both ICU and hospital(6)

According to a study done in china 158 hospitals Bejing the overall incidence of S-AKI was 48.1%, with 59.2% in ICU patients and 31.6% in non-ICU patients, respectively; and overall mortality rate of 55% among the S-AKI patients(7) ;Pneumonia was the most likely source of sepsis in this cohort(7)

According to a systematic review and meta-analysis done by Jiefeng Liu1 , Hebin Xie2 , Ziwei Ye etal from studies published between 2008 and 2019 and originated from 18 countries (Spain, Greece, United Kingdom, France, Netherlands, Sweden, Canada, United States, Brazil, China, Japan, Saudi Arabia, Turkey, Finland, Portugal, South Korea and Australia) on four continents (Europe, America, Asia and Oceania); the highest incidence of AKI was caused by septic shock;(8)

Based on a study done in Mulago Hospital in Uganda a sub Saharan country, among the patients admitted with AKI, 21% died while in hospital(9). Of the patients who were discharged alive, 29 (59%) had persistently elevated creatinine and 20 (41%) had resolved kidney injury(9)

Based on a study done in jimma medical center 61.2% of patients had persistent AKI ;35% patients with AKI develop systemic complications. 85% had prolonged length of hospital stay and the in hospital mortality was 6%((10)

In Ethiopia there is no comphrensive research that address such issue specifically patients with septic shock, hence showing the need to do such a research.

Significance of the study

The importance of this study is to know the prevalence and outcome of patients who was admitted to TGSH and FHRH ICU with septic shock and AKI and to know associated factors that affect outcome as well as to make action plans to decrease morbidity and mortality of patients.

This study may also serve as a pilot study to show those administrators and policy makers the burden of the problem in TGSH and FHRH ICUs so that they can plan to combat the problem, decrease mortality and cost upon the patient and the hospital

This study also will show the burden of the problem and associated factors to those working in the study area so that they can take precautions to minimize the impact on the patient as well as on the hospital and economic burden on the patient and family.

2 Literature review

Sepsis-associated acute kidney injury (S-AKI) is a major public health condition that is associated with a significant disease burden(3)

According to a systematic review and meta-analysis done by Jiefeng Liu1 , Hebin Xie2 , Ziwei Ye etal from studies published between 2008 and 2019 and originated from 18 countries (Spain, Greece, United Kingdom, France, Netherlands, Sweden, Canada, United States, Brazil, China, Japan, Saudi Arabia, Turkey, Finland, Portugal, South Korea and Australia) on four continents (Europe, America, Asia and Oceania); 66.3 % of patients with septic shock developed AKI (8)

According to a study done in 30 ICUs of 28 major hospitals in Beijing china; age, acute physiologic and chronic health related events II (APACHE II) score, duration of mechanical ventilation, duration of MAP were independent risk factors for mortality for septic AKI(7)

A study done in intensive care units of 22 academic and community hospitals in Canada, the United States and Saudi Arabia , 64.4% of patients with septic shock developed AKI(6)

According to a study done in Mulago National Referral Hospital Uganda ,the prevalence of sepsis-related AKI was 16.3%. Age >59 years ($p = 0.023$), a postural drop in systolic blood pressure of >9 mmHg ($p = 0.015$) and a white blood cell count >12,000 cells/mL ($p = 0.003$) were significantly associated with AKI(9). In-hospital mortality among patients with AKI was 21%; 59% of patients who were discharged alive or were still on the wards after 2 weeks had persistent kidney injury(9). None of the patients requiring dialysis or ICU care received either because of limited access(9)

In Ethiopia there is no compressive research that show prevalence of AKI and specifically in patients admitted to ICUs with septic shock

2.1 Risk factors for septic AKI

Analysis showed that most frequently-seen predisposing factors for sepsis-associated AKI were as follows:

Age: according to studies done in Beijing, 22 academic and community hospitals in Canada, the United States and Saudi Arabia age was significantly associated with development of septic AKI.

Hypertension: according to studies done in china, USA, Canada and Saudi Arabia and meta-analysis done by Jeifeng Liu hypertension was associated significantly with development of septic AKI

Diabetes: according to a met analysis done by Jeifeng Liu diabetes was associated with development of septic AKI (8).

Positive blood culture result, abdominal infection and pneumonia: according to studies in Beijing, met analysis done by Jeifeng Liu positive blood culture, abdominal infection and pneumonia was significantly associated with development of septic AKI (8).

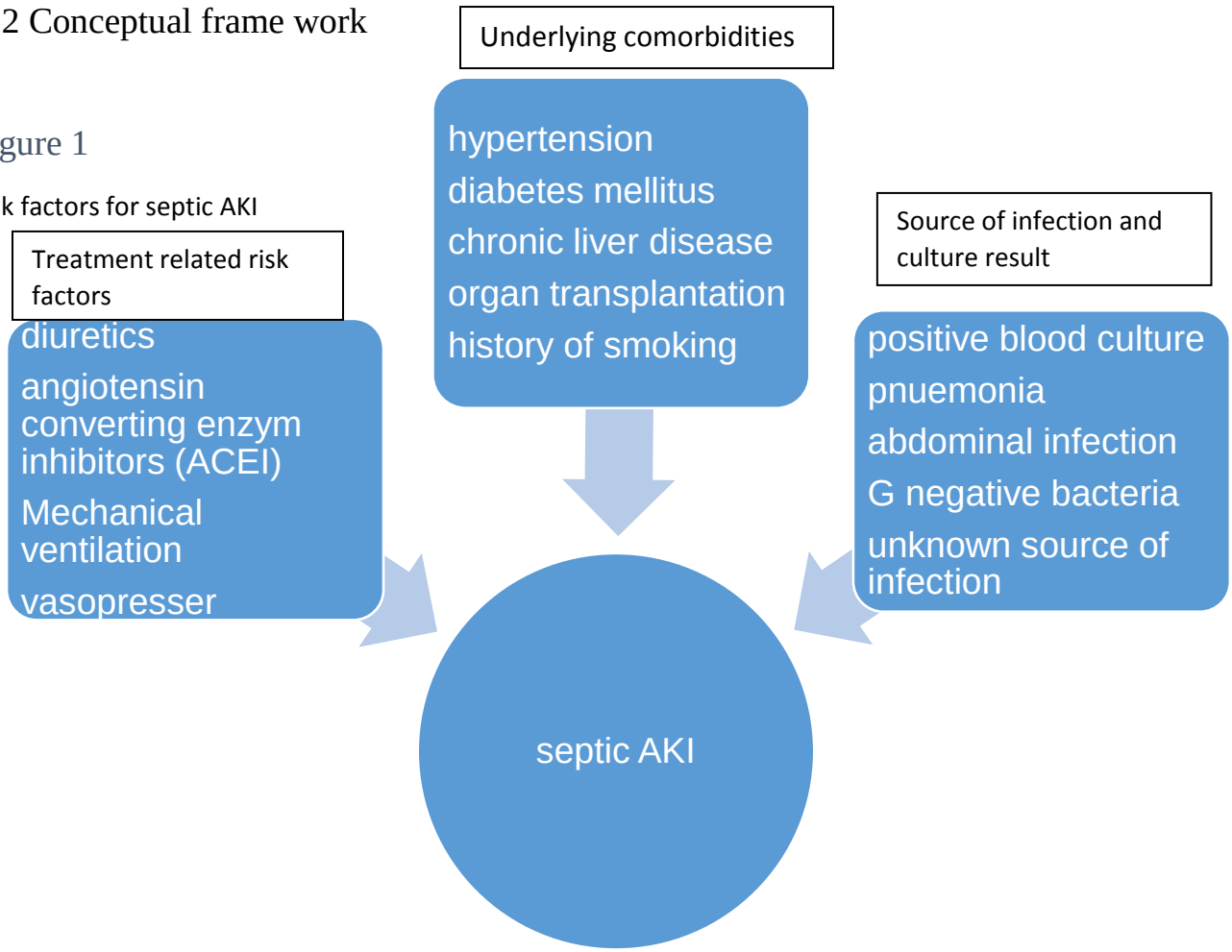
Other risk factors included cardiovascular diseases, coronary artery diseases, liver diseases, unknown infections, the administration of diuretics and ACEI/ARB, the infection caused by gram-negative bacteria, and organ transplantation(8)

Risk Factors for Mortality were age , APACHE II score , duration of mechanical ventilation , duration of MAP < 65mmHg , and progressive KIDGO stage (7)

2.2 Conceptual frame work

Figure 1

Risk factors for septic AKI



3 Objective

3.1 General objective

To assess prevalence and associated factors of AKI in septic shock patients admitted to TGSH and FHRH ICUs

3.2 Specific objectives

To assess prevalence of AKI in septic shock patients admitted to TGSH and FHRH ICUs

To assess associated factors for AKI development in septic shock patients admitted to TGSH and FHRH ICUs

4 Methodology

4.1 Study area

This study was conducted in TGSH and FHRH which is found in Amhara regional state, Bahir Dar, Ethiopia. Bahir Dar is situated on the southern shore of Lake Tana, the source of the Blue Nile (locally called Abay). Bahir Dar city (one of the ten most beautiful cities in Africa and one of the twelve UNESCO Learning Cities Awardee of 2015) .The city is located approximately 578 km (360 miles) north-northwest of Addis Ababa, and an elevation of 1,840 meters (6,036 foot) above sea level. TGSH is located about 10km south from the city center and about 7 km from the new bus station ('Addisu Meneharia') on the way to Adet District and about 23 km from the Blue Nile Falls (locally called 'Tis abay '. It is a tertiary university teaching hospital with 450 bed capacity out of which 72 are occupied by medical adult patients. It has 8 ICU beds with 450 admissions in the last 2 and half years .The hospitals receives patients who are referred from across the Amhara region and gives outpatient and inpatient services in all major departments. Both hospitals serve about 5 million catchment populations

4.2 Study period

The study was conducted in TGSH and FHRH ICUs starting from February 1st, 2022 to October 2022.

4.3 Study design

Hospital based retrospective crossectional study was held to assess the prevalence and outcome of AKI in septic shock patients admitted to TGSH and FHRH ICUs

4.4 Source population

All septic shock patients admitted to TGSH and FHRH ICUs who gets treatment and fulfill inclusion criteria was included in the study

4.5 Study population

All septic shock patients admitted to TGSH and FHRH ICUs and gets treatment from 2010 EC to 2013 EC

4.6 Inclusion criteria

Patients Age above 18yrs, with complete medical records and admission diagnosis of septic shock was included in the study

4.8 Variables

4.8.1 Dependent variables

AKI

4.8.2 Independent variables

Age

Comorbidity (hypertension, diabetes, CHF CKD)

Source of infection (focus)

KIDGO stage of AKI

Blood culture result

Medications used (ACE, ARBS, immunosuppressive drugs) and mechanical ventilation

Malignancy

HIV infection

Residency

4.9 Operational definition

Septic shock: Suspected (or documented) infection plus vasopressor therapy needed to maintain mean arterial pressure at ≥65 mmHg and serum lactate >2.0 mmol/L despite adequate fluid resuscitation

AKI: serum creatinine increment by 0.3 from base line within 48 hrs or 50% increment within 1 week or UOP < 0.5 ml/kg for 6 hrs

Septic AKI: clinical diagnosis of AKI in the presence of sepsis or septic shock

Persistent AKI: AKI for greater than 7 days

Resolving AKI: AKI with serial decreasing serum creatinine

4.10 Sample size determination

Sample was determined using EPI info7 assuming 50% prevalence 95% confidence interval and 5% margin of error with 322 source population and correction which gives us final result of 161patients.

4.11 Sampling technique

We used systematic random sampling method for sampling with k value =2

4.12 Data collection and procedures

A chart review was conducted using structured questionnaires developed in English and then it was pre-tested for validity. Data was collected by trained nurses and supervised by a resident .A format that contains study variables of interest was prepared.

4.13 Data quality assurance

Pretest was done on some records before the actual data collection started. The data collection format was checked for its completeness and any gap identified corrected.

4.14 Data processing and analysis

Data was entered using SPSS version 25 and analyzed by descriptive frequency tables, bivariate multivariate and multinomial logistic regression as applicable. The degree of association was computed using odds ratio with 95% CI taking P-value less than 0.05 as significant level for associations between dependent and independent variables

5 Ethical considerations

A written legal permission regarding the study was obtained from the Institutional Review board of the College after approval of research proposal.

6. Results of the study

6.1 socio-demographic results of

In this study 80 patients were females, 81 patients were males. The majority came from rural areas (70.8%).33.5% of patients were in the age group of 18-39; 44.1% of patients were in the age group of 40-64years.the rest were age above or equal to 65 yrs.16.8% of patients visited hospital within 24hrs of the onset of illness; 39.8% visited hospitals within 2-5 days of their illness onset and the majority43.5 visited hospital after 5 days. For 28.7% of patients the source of infection from the gastrointestinal tract; followed by the chest (27.3%) and peritoneum (19.9%).see table 1for more information.

Table 1sociodemographic characteristics of patients

		Frequency	Percent
Age	18-39	54	33.5
	40-64	71	44.1
	>/=65	36	22.4
Sex	Female	80	49.7
	Male	81	50.3
Residency	Rural	114	70.8
	Urban	47	29.2
Duration of illness before admission	Upto24 hrs	27	16.8
	2-5 days	64	39.8
	>5 days	70	43.5
Source of infection	Chest	44	27.3
	GI	46	28.6
	Peritoneum	32	19.9
	GUS	4	2.5

	CNS	4	2.5
	Skin and soft tissue	14	8.7
	Biliary	14	8.7
	Others	3	1.9

6.2: Risk factors for AKI in septic shock patients admitted to TGSH and FHRH ICUs

27 (16.85) patients had documented diabetes; 41(25.5%) patients have hypertension; 10(6.2%) patients had chronic kidney disease; 11(6.8%) patients have documented retroviral infection 47(29.2%) patients have documented negative result.12 (7.5%) patients have diagnosed cancer. 45(28%) had history of non-steroidal anti-inflammatory drug use. See table 2 for more information on risk factors for AKI in septic shock in TGSH and FHRH.

Table 2: Risk factors for AKI in septic shock in TGSH and FHRH ICUs

Diabetes	Yes	27	16.8
	No	134	83.2
HTN	Yes	41	25.5
	No	120	74.5
CKD	Yes	10	6.2
	No	151	93.8
RVI	Yes	11	6.8

	No	47	29.2
	Unknown	103	64.0
Cancer	Yes	12	7.5
	No	149	92.5
NSAIDs use	Yes	45	28.0
	No	115	71.4
ACEI/ARB use	Yes	31	19.3
	No	130	80.7
MV use	Yes	41	25.5
	No	120	74.5
Vasopressors given	Adrenaline	80	49.7
	Dopamine	69	42.9
	Dopamine + adrenaline	12	7.5

6.3: Outcome of patients admitted to TGSH and FHRH ICUs

From 161 patient admitted to TGSH and FHRH ICUs 131 (70.2%) developed AKI.37 (23%) had KIDGO stage 1 AKI; 37 (23%) had KIDGO stage 2 AKI; and another 37 patients had KIDGO stage 3 AKI according to their serum creatinine.22 patients have normal creatinine at discharge 4 patients have improve creatine when discharged and 1 patient developed ESRD.From the total admissions 26 were discharged against from hospitals while 1 patient was referred .94 (58.45) patients died in the hospital.

Table 3*: outcome of patients admitted to TGSH and FHRH ICUs with*

Septic shock	Frequency	Percent
no AKI-Discharged	12	7.5
Dead	94	58.4
ESRD	1	.6
Cr improved	4	2.5
normal Cr	22	13.7
went against	26	16.1
Referred	1	.6
discharged with the same Cr	1	.6

Factors associated with AKI in septic shock

Both binary logistic regression and multivariate logistic regression was used to identify the association of the independent variables with the dependent variable.

On bivariable logistic regression sex of the patient, DM, CKD, NSAIDs use, and mechanical ventilation were associated with development of AKI.

On multivariate logistic regression and multinomial regression was done.

On multivariate regression none the variables was associated with risk of AKI (table 4)

Table: 4 factors associated with AKI

Variables in the Equation		Sig.	AOR	95% CI	
				Lower	Upper
	Male sex	.180	1.629	.798	3.326
	DM	.130	2.015	.813	4.998
	CKD	.300	.320	.037	2.757
	NSAIDs use	.162	.543	.231	1.277
	MV use	**.047**	.374	.141	.989
	Constant	.008	.436		

a. Variable(s): male sex, Diabetes, chronic kidney disease, non-steroidal ant- inflammatory use mechanical ventilation use.

On multinomial regression age of the patient and adrenaline use were associated with development of AKI (Table 5)

Table 5 multinomial regression of variables

Variables		Sig.	AOR	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
		.187			
Duration of illness	Upto 24 hrs	.538	1.442	.450	4.619
	2-5 days	.776	.886	.385	2.040
	>5days	.	.	.	.

Source of	Chest	.414	3.053	.210	44.503
	GI	.188	6.125	.412	91.162
	Peritoneum	.182	6.842	.407	115.050
	GUS	.359	5.516	.144	211.818
	CNS	.339	5.433	.169	174.436
	Skin &soft tissue	.549	2.372	.141	40.014
	Biliary tree	.273	5.156	.274	97.024
	Others	.	.	.	.
Age group	18-39 years	.086	2.419	.882	6.639
	40-64 years	**.047**	2.747	1.016	7.429
	>64 years	.	.	.	.
Vasopressor used	Adrenaline	**.045**	4.586	1.033	20.353
	Dopamine	.275	2.279	.518	10.019
	Adrenaline +dopamine	.	.	.	.

7 Discussion

This study is intended to provide insight on prevalence of AKI in septic shock patients admitted to TGSH and FHRH ICUs and associated factors. Both clinical and laboratory data was evaluated from their charts to obtain this data.

In this study from a total of 161 patients 131 (70.2%) developed AKI. This result is higher than repots in china which is 66.3(11). This study also shows higher prevalence of AKI than a study done in 22 academic and community hospitals in Canada, the United States and Saudi Arabia, where 64.4% of patients with septic shock developed AKI(8). The possible reason for the difference might be due to the smaller sample size of the study, severity of underlying infection and delayed presentation and inappropriate medical intervention like fluid management and use of nephrotoxic medications and availability of medications and trained stuff in managing septic shock appropriately.

In this study age groups 40-64 and adrenaline use were the determinant factors associated with development of AKI in septic shock patients.

This study showed that age group 40-64 is significantly associated with development of AKI with P value of 0.047 (AOR of 2.747 95% CI of 1.016-7.427). Although there was no age grouping in other studies older age was associated with higher risk of AKI specifically age above 65 years.(12) The possible reason in our study may be the overall higher prevalence of AKI and higher percentage of patients in this age group.

Adrenaline use on the other hand showed significant association with development of septic AKI with P value of 0.045 (OR of 4.58 95% CI 1.00-20.35).This result is

similar with a met-analysis done by Liu et al which shows OR: 3.15; 95% CI: 2.00– 4.96)(8)

In this study 58.4 % of patients have died which is significantly higher than studies done in Addis Ababa which was50.9%(10).0nly 7 patients got dialysis treatment which might have increased mortality substantially. Only one patient had documented blood culture result which was negative and shows that appropriate antibiotics might not be given to patients and contributes to both higher prevalence of AKI and mortality from both septic shock and AKI.

8 Conclusion and recommendation

In this study the prevalence of AKI in septic shock patients is 70.2% which is high. Age group 40-64 and use of adrenaline was significantly associated with development of AKI. 58.4 % of patients have died. Only 7 patients received dialysis and 1 patient have blood culture available. Further study should be done to analyze the higher mortality of patients and lower utilization of dialysis and blood culture

9 Limitations of the study

Limitation may be associated with the inherent problems of retrospective study design and problems with documentation and availability and affordability of laboratory tests in which some of the results may have been changed.

10 Dissemination of results

The final result of this study will be presented for a research defense at Bahirdar University College of medicine and health science and disseminate to department of public health, Internal medicine department, Research coordinating office and Hospital Administrative and for publication of the research work and independent variable

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ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical Conduct of the research project and for provision of required progress reports as Per terms and conditions of the Research Publications Office in effect at the time of Grant is forwarded as the result of this application.

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Date. 13/03/15 E.C *Signature*

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