ASSESSMENT OF INCIDENCE AND TREATMENT OUTCOME OF SEPTIC SHOCK AMONG PATIENTS ADMITTED TO ADULT INTENSIVE CARE UNIT OF TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

A THESIS SUBMITTED TO THE DEPARTMENT OF EMERGENCY MEDICINE AND CRITICAL CARE, COLLAGE OF HEALTH SCIENCE, ADDIS ABABA UNIVERSITY AS PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF EMERGENCY MEDICINE AND CRITICAL CARE.

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Table of Contents

ABSTRACT

Introduction

Septic shock is a major healthcare problem, affecting millions of people around the world each year, killing one in four and increasing in incidence. In most developed countries, the incidence of Septic shock has been identified as between 50 and 100 cases per 100,000 people in the population. The mortality rate from severe sepsis in the developed countries has been estimated as being between 28 and 50%, ranging from 15% in patients with sepsis and up to 40-50% in patients with septic shock with multi-organ dysfunction syndrome (MODS)

Objective

The study aims to explore the incidence and the factors associated with outcome among patients with septic shock admitted to the intensive care unit, TASH, Addis Ababa, Ethiopia.

Method

A retrospective cross-sectional study was carried out at intensive care unit of our hospital. This study included all patients with septic shock admitted to adult ICU of TASH during Jan 2014-Dec 2017. Data was collected using a structured checklist and statistical analysis was done using SPSS version 21. Regression model was applied to identify the factors contributing to the outcome of septic shock. P-value less than 0.05 were considered statistically significant.

Results

Of 820 admissions, 115 (14%) patients had septic shock. Majority (60%) was female and the mean age was 47.9$\pm$16.5 years. The most common sites of infection were the respiratory tract infection (54.8%) followed by urethral tract infection (14.8%), Gram-negative bacteria, particularly Escherichia coli (4.3%) and Klebsiella pneumonia (3%), were the major infecting micro-organisms. All patients have received antibiotic and fluid therapy. 23.5% patients started treatment within the first hr. of ICU stay and the overall 28-day mortality rate was 58.3%.

Conclusion

The study revealed that septic shock is a frequent cause of ICU admission with a high mortality rate. This can be explained by the fact that septic shock patients have more comorbidity, a worst previous state of health and requires more life support therapies. Therefore early identification of high risk population, implementation of appropriate treatment and the design of future clinical studies are crucial to improve the outcome of septic shock.

List of abbreviations

TASH	Tikur Anbessa Specialized Hospital
ICU	Intensive care unit
ED	Emergency department
SSC	Surviving sepsis campaign
EGDT	Early goal directed therapy
MODS	Multi-organ dysfunction syndrome
UTI	Urinary tract infection
COPD	Chronic obstructive pulmonary disease
ARDS	Acute respiratory distress syndrome
DM	Diabetic mellitus
HIV	Human immunodeficiency virus

List of Tables

1. INTODUCTION

1.1 BACKGROUND

Sepsis is defined as the presence or presumed presence of an infection accompanied by evidence of a systemic response called the systemic inflammatory response syndrome(1). It is one of the most common but less identified illnesses in both the developed and developing world. Even though there are advances in modern medicine, it is the primary cause of death from infection and carries long-term complications(2). Sepsis causes more deaths than prostate cancer, breast cancer and HIV/AIDS combined(3). It is the disruption of the inflammatory response due to infection. In one out of three patients sepsis develops to more severe cases of severe sepsis and septic shock which causes long-term hospitalization and death(4). Septic shock, defined as a state of acute circulatory failure characterized by persistent hypotension unexplained by other causes, despite adequate fluid resuscitation(5) is a major healthcare problems, affecting millions of people around the world each year, killing one in four (and often more), and increasing in incidence(6).

In USA an estimated 750,000 new cases of sepsis occur every year, with roughly 215,000 deaths per year. In the last decade, its incidence has increased by about 91.3% (7). The incidence increased exponentially with age which suggests an increase in number of cases in coming years as young generation grows older. Overall hospital mortality rate was 28.6%, or 215,000 deaths per year(8). Factors such as age, severity of patient's underlying disease, number of organ system dysfunction, severity of illness, hypothermia, thrombocytopenia, lactic acidosis, multiple sources of infection, positive blood stream, type of organism, and endocrine function are associated with mortality in severe sepsis and septic shock(9).

In most developed countries, the incidence of severe sepsis has been identified as between 50 and 100 cases per 100,000 people in the population(4). Although there is a high incidence rate in the developed countries, the middle- and low-income countries are the most affected part of the world. Data in those area shows that high mortality is associated with ineffective management including delayed and improper empiric antimicrobial therapy and fluid resuscitation(10).

In general, the incidence of sepsis is three to four-times higher, reflecting the relative percentage of patients who develop organ dysfunction and thus meet more severe definitions (severe sepsis

or septic shock)(4). Severe sepsis and septic shock have a mortality rate of 20 to 54% and are among the main causes of death among hospitalized patients (4, 8). Early appropriate antibiotic therapy, early goal directed therapy (EGDT), corticosteroids, recombinant human activated protein C or drotrecogin alfa (activated), tight glucose control, and lung protective strategies have been associated with survival benefits(11, 12). Past studies have shown that with appropriate resuscitation mainly IV fluid resuscitation, early broad-spectrum antibiotics and with the use of vasopressors patients show improved result. (12). For every hourly delay after onset of shock mortality increases by 7.6%(13). Same as poly-trauma, acute myocardial infarction, or stroke, the duration and appropriateness of therapy given at the initials hours of severe sepsis and septic shock most certainly affect outcome of patients(14).

The septic patient is a difficult patient most time and early recognition and diagnosis are very important for successful treatment and outcome(15) In 2004, 2008, and 2012 the Surviving Sepsis Campaign released guidelines for severe sepsis and septic shock management (16). Implementation of this guideline together with timely administration of essential therapies (e.g., fluid resuscitation, antibiotics, and source control measures) improved management and outcome(17). The SSC also suggests "sepsis bundle," which requires administration of broad-spectrum antibiotics within 3 hours from ED triage. However, achieving these goals may not be operationally feasible in some cases and previous research has shown that compliance with guidelines regarding antibiotic administration frequently is not achieved(14).

Considering the impact of septic shock and the luck of studies in our country involving severe sepsis/septic shock, the aim of this study was to determine the incidence , demographic data, clinical characteristics, treatment pattern and outcome of patients with severe sepsis/septic shock admitted to ICU department of Tikur Anbessa Specialized hospital.

1.2 STATEMENT OF THE PROBLEM

Severe sepsis and septic shock are a major complication of infection, and are triggered by a systemic inflammatory and coagulation reaction(18). Patients suffering from severe sepsis require intensive care and account for a large part of ICU resource consumption. It was demonstrated by Bakker and coworkers(19) that 52–59% of an ICU budget was allocated to sepsis and septic shock patients.

The mortality rate from severe sepsis is high and occurs in approximately 2% of all hospitalizations in developed countries. It may occur in between 6 and 30% of all intensive care unit patients. In general, more than 50% of severe sepsis and septic shock patients will require intensive care services(20). Incidence of severe sepsis and septic shock appears to be increasing by 13.7% per year ultimately increasing overall deaths(21). The mortality rate from severe sepsis in the developed countries has been estimated as being between 28 and 50%, ranging from 15% in patients with sepsis and up to 40-50% in patients with septic shock with multi-organ dysfunction syndrome (MODS)(22).

In the developing world the incidence of sepsis, severe sepsis and septic shock are less well-described (23). But some studies reported that Sepsis is responsible for 60-80% deaths in developing countries including Pakistan(24). The incidence of severe sepsis outside modern ICUs, especially in parts of the world in which ICU care is scarce, is largely unknown(25).

There are more data available on the incidence of infectious diseases, which remains a constant battle for which there are many high incidence conditions. As infectious diseases are inevitably the cause of sepsis, sepsis presumably is of similar or even greater importance in these areas of the world than in the most developed nations. Sepsis is more frequent in younger individuals in the developing world and the responsible organisms are more likely to be Gram-negative enteric pathogens and atypical pathogens such as malaria. It should also be noted that patients dying of infectious diseases inevitably die of sepsis and sepsis -related organ dysfunction(26)

Previous studies have suggested improved outcomes with the implementation of a structured resuscitation, focusing largely on IV fluid resuscitation, timely broad-spectrum antibiotics, and vasopressor therapy(12). Data shows that delays in antimicrobial therapy lead to a significantly increased risk of dying. Especially critical for septic shock, the risk of dying increases by approximately 10% for every hour of delay in receiving antibiotics(27).

1.3 SIGNIFICANCE OF THE STUDY

Sepsis is highly aggressive and may involve the progressive loss of function of several organs, but it should be considered reversible, especially if identified and treated early in its course(28). Despite advances in knowledge of pathogenesis, diagnosis, therapeutic care, and supportive care, the incidence and mortality of severe sepsis and septic shock has increased over the past decades(29).

Knowing the prevalence, the treatment pattern and outcome of severe sepsis/septic shock will help on developing or using standard guidelines and standards to diagnose and treat it. This study mainly focuses on studying the prevalence and more importantly the treatment trend and outcome in Tikur Anbessa Specialized hospital. There is a huge gap on the diagnosis and treatment protocol of severe sepsis/septic shock in our country. Therefore the results of this study will contribute to provide information that will be help full to incorporate more advanced diagnosis system and treatment guidelines regarding severe sepsis/septic shock.

2. LITRATURE

Severe sepsis and septic shock are conditions with a mortality rate approaching 50%(30). There have been a number of studies reporting the incidence, characteristics, and outcome of severe sepsis and septic shock from different regions and countries(4, 21, 31).Not surprisingly, the incidence and mortality rates widely vary throughout the world, and significant differences in the pattern of causative micro-organisms and infection sites have been observed(32). In the last decade, its incidence has increased by about 91.3%. According to the BASES study,(8) 27% of the patients referred to intensive care units in Brazil have severe sepsis, with a mortality rate of 47% at 28 days(33).

Population characteristics and prevalence of sever sepsis/septic shock

Age, sex, and race or ethnic group all influence the incidence of severe sepsis, which is higher in infants and elderly persons than in other age groups, higher in males than in females, and higher in blacks than in whites(8).

A two decade study done in the United States shows a total of approximately 750 million hospitalizations and there were 10,319,418 reported cases of sepsis (accounting for 1.3 percent of all hospitalizations). The mean age among women was 62.1 years, as compared with 56.9 years among men(4). Another study done in Australia and New Zealand in 171 ICUs from 2000-2012 shows that mean age of the population was 3.5 years with male sex accounting for 54%. During the study period, 9.7% had severe sepsis, and 15.3%were of younger age (≤44years). The overall ICU mortality was 16% and septic shock mortality was 40.3% in 2000 which decreased to 22% in 2012(34).

In a study done in Paris, France in 22 ICUs the overall frequency of septic shock was 8.2 per 100 ICU admissions (n= 8,251). The septic shock compromised older patient with mean age of 61.4 years and a greater proportion of male gender (63.3%)(35). In another prospective multicenter cohort study done in French intensive care units a total of 10,941 patients were admitted to the participating ICUs during the study period. Among these, 1,495 (13.7%) presented a septic shock and were included in the study. Median age was 68 years (range, 58-78 years); almost two-thirds were men. The majority of admissions were of medical origin (84%)(36).

Similar study done in Dutch show sepsis on 31% of all ICU admissions. In 134 (93%) cases the sepsis was severe and in 53 cases (37%) the sepsis was complicated by cardiovascular and

metabolic organ failure meeting the definition of septic shock. On average, patients with severe sepsis were 64 ± 15 years old. Of these patients, 70% were older than 60 years and 44%were older than 70 years. The ratio of males to females was 1.7(18).

A prospective observational study carried out in ICU from February 2014 to October 2015 in Peshawar shows a total of 450 patients admitted to the Medical ICU during the study whom n= 268 patients were diagnosed with sepsis. Majority 147 (54.9%) were male patients with a mean age of 54.8. The presence of septic shock was prevalent in 59.3% with average ICU stay was 5.34 days(24).

In a 2 month prospective, observational cohort study in 22 closed multi-disciplinary ICUs in Mainland China 3063 admissions were screened during the study period and 1297 patients (42.3%) were enrolled. A total of 484 patients developed severe sepsis or septic shock, including 336 males (69.4%), and their median age was 66 (interquartile range [IQR], 51–77) years(21).

Etiology and site of infection

In a study of epidemiology of septic shock in French ICU approximately two-thirds of patients presented community- acquired infection and more than half had respiratory tract infection (53.6%) as the primary site of infection at the origin of septic shock. The infectious organism was identified in 1,035 (69.5%) patients who presented septic shock, and an antibiogram was available in 967 of these patients (93%). Gram-negative bacilli were the most frequent pathogens in 48.7%, while Gram-positive cocci micro-organisms were identified in 35.9%(36).

In a study in mainland China lung (85.7%) and the abdomen (18.0%) were the most common sites of infection. One hundred and sixty-seven patients (34.5%) had two or more infection sites. Only 37 patients (7.6%) had bloodstream infection. Only half of the ICU (11/22) reported the microbiology, and 148 patients (30.6%) had microbiological documentations associated with severe sepsis and septic shock. Out of these 148 patients with microbiological results, Gram-negative bacilli were isolated in 111 patients (75.0%), and Gram-positive organisms were isolated in 32 patients (21.6%). Only six patients were diagnosed as invasive fungal infection or fungemia (4.1%). Forty-nine patients (33.1%) had polymicrobial (>2 infection agents) infections.

The most prevalent species were Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, methicillin- resistant Staphylococcus aureus, and Stenotrophomonas maltophilia.(21) Similar results were seen in Dutch ICUs, most common sites of infection were the lungs (47%) and the abdomen (34%)(18).

In ICUs of a tertiary care hospital in Peshawar Escherichia coli ESBL was the most commonly observed bacteria followed by Candida, Acinetobacter baumannii and Methicillin resistant Staphylococcus aureus. Overall, the presence of microbes were more frequent among blood samples and the most common source of sepsis was lung infections (42.2%) followed by urinary tract infections (18.7%), soft tissue infections (6.3%), abdominal infections (6%) and in 6.3% patients the source remained unknown(24).

According to a study done in University hospitals in Korea the most common primary site of infection was the respiratory system (30.2%), followed by urinary tract (2.4%), abdomen (24.2%), skin and soft tissue (8.1%) and primary bloodstream (4.4%). Men were more likely to have respiratory (39.2% vs 19.2%, $P < 0.001$), abdominal (26.8% vs 20.9%, $P = 0.017$) and skin and soft tissue infections (11.0% vs 4.7%, $P < 0.001$), compared to women. Women showed higher rates of urinary tract infections (11.4% vs 44.8%, $P < 0.001$). Clinical infections with identification of pathogens were documented in 831 (69.7%) patients. Gram negative bacteria were the predominant organisms of the isolates, accounting for 43.0% (n = 513), while gram positive bacteria accounted for 20.4% (n = 243). Polymicrobial infections accounted for 3.6%, followed by fungi (0.7%) and anaerobes (0.6%). Escherichia coli (22.1%) was the most common isolate, followed by Klebsiella species (12.6%) and Staphylococcus aureus (8.4%)(29).

In surgical ICUs in Northern Taiwan respiratory tract (38%) and abdomen (33%) were the most frequent sites of infection. Micro-organisms were identified in only half of the study population and 62 (12%) patients had polymicrobial infection. Out of 269 patients with documented microbiological results, Gram-negative bacteria, Gram-positive bacteria, and fungi were isolated in 65%, 25%, and 10% of the severe sepsis patients. The most prevalent species were Klebsiella pneumoniae (8.6%), Escherichia coli (6.0%), Acinetobacterm baumannii (5.6%), Pseudomonas aeruginosa (5.4%), and Enterococcus species (4.5%). The distribution of infecting microorganisms was not significantly different between survivors and non survivors(37).

Generally most studies in various countries show that most common source of infection for septic shock is respiratory tract infections followed by abdominal infections. UTI are the most dominant source of infection in female population. The studies also show that Gram negative bacteria are most commonly observed bacteria and the most prevalent species are Escherichia coli, Klebsiella pneumoniae and staphylococcus aureas.

Comorbidity

The incidence of sepsis is affected by a variety of patient-specific factors. It have been long recognized that age is an important component of someone's risk for developing sepsis, as are a variety of comorbid medical conditions. Perhaps most obvious are conditions like HIV, cancer and diabetes, each of which may alter the immune system. These conditions result in a significantly elevated risk for developing sepsis, and may also increase the risk of nosocomial sepsis given these individuals' frequent interactions with healthcare systems(27).

According to a study of analysis of incidence and outcome of severe sepsis in US 55.5% of patients had an underlying comorbidity. COPD accounts 12.3% followed by HIV (6.3%) and cancer (5.3%) which has a high mortality rate. Another comorbidities were liver disease, renal disease and diabetic mellitus(8). Unlike this results a study in china shows presence of ARDS(54.8%), acute kidney injury (41.5%), bloodstream infection and comorbidity of cancer were independent risk factors for hospital mortality(21).

Studies in Dutch and France show comorbidities of COPD (13%, 9.2%), malignancy (14%, 15.3%), DM (9%, 2.2) respectively and chronic liver and kidney failure, HIV and heart failure were major risk factors for mortality(18, 35).

Treatment pattern and outcome

To improve care for sepsis, the SSC and the Institute for Healthcare Improvement recommend implementing a 6-hour resuscitation bundle including lactate determination, early cultures and antibiotics, and EGDT, as well as a 24-hour management bundle including optimization of glycemic control and respiratory inspiratory plateau pressure and determination of the need for corticosteroids or drotrecogin alfa(16).

The 2012 SSC, international guideline for management of severe sepsis and septic shock recommends initial resuscitation with in the first 6 hours screening for sepsis, at least 2 sets of blood culture(both aerobic and anaerobic bottles) has to be obtained before antimicrobial therapy is started. The goal of therapy is to administer effective IV antimicrobials with in the first hours of septic shock recognition. It also recommends fluid therapy(crystalloids) be used as the initial fluid of choice in the resuscitation and vasopressor therapy is required to sustain life and maintain perfusion during life threatening hypotension(14).

In mainland china among the 484 patients included, 139 died in ICU, and 23 died during hospitalization. Twenty patients (4.1%) were still in hospital at the end of the study period and were deemed survivors. The overall ICU mortality rate was 28.7%. The median ICU length of stay was 7 days (IQR, 4– 15). About three fourths (72.3%) of patients had stayed in ICU for less than 2 weeks, while 9.5% of patients had an ICU length of stay of more than 4 weeks(21).

A prospective study in Peshawar, Pakistan shows that septic shock alone is responsible for death of 32% of the patients. The mean length of hospital stay was 5.34 ± 4.23 days. Increase in number of hospitalization was observed to be slightly associated with the outcome of therapy. In patients with positive blood culture length of hospital stay was observed to be an important factor associated with outcome. And risk of mortality was higher among patients with respiratory, kidney and CNS complications(24).

A study done in European ICUs over all ICU mortality rate was 18.5%. On admission there was 27% mortality, 20% on day 2 of admission and 28 % in patients with ICU acquired sepsis. Organ failure occurred on 71% of patients. There was direct relationship between the number of organ failure and ICU mortality(20)

3. OBJECTIVE

3.1 General objective

- To assess the incidence and treatment outcome of septic shock among patients admitted to Intensive care unit of Tikur Anbessa Specialized hospital, Addis Ababa, Ethiopia from Jan 2017-June 2017

3.2 Specific objective

- To determine the incidence of septic shock
- To identify the commonest source of infection which predispose to septic
- To assess treatment trend of septic shock
- To assess treatment outcome of patients

4. METHODOLOGY

4.1 Study area and period

A 3 year (Jan 2014-Dec 2017) study was conducted in TASH, Addis Ababa, Ethiopia from Jan 2017- June 2017. TASH is a tertiary teaching hospital. The faculty is the largest and the oldest among health training institutions in the country, staffed with the most senior specialists and subspecialists. TASH has more than 700 beds and gives service for 37,000-400,000 patients annually. Have 200 doctors, 379 nurses and 115 other health professionals. Have around 90 beds in medical ward and around 30 in intensive care unit.

4.2 Study Design

A retrospective cross sectional record based study was conducted

4.3 Source and study population

4.3.1 Source population

All patients admitted to ICU TASH during the study period were included

4.3.2 Study population

All patients with septic shock who were admitted to ICU of TASH during the study period who fulfilled the inclusion criteria

4.4 Eligibility criteria

4.4.1 Inclusion criteria

- This study included all patients with septic shock admitted to adult ICU of TASH during Jan 2014-Dec 2016
- > 14 years old patients

4.4.2 Exclusion criteria

- Patients who have incomplete card records

4.5 Variable

4.5.1 Dependent variables

- Septic shock
- Treatment outcome
- Length of hospital stay

4.5.2 Independent variables

- Age
- Gender
- Treatment pattern
- ICU admission category
- Comorbidity
- Source of infection

4.6 Sample size and sampling techniques

Non-probability (convenience) sampling method was used.

4.7 Data collection tools and techniques

Data were collected by a single experienced data collector using standardized forms. The following information was retrieved: demographics, admission category (medical, surgical and gyn/obs), systemic inflammatory response syndrome (SIRS) criteria met, and comorbidities, sites of infection, causative micro-organisms, associated organ failure and type of treatment provided. All data were collected from patient record chart after selecting their MRN from the ICU registration book.

4.8 Data quality assurance

The quality of the data was assured by doing pretest in 10% of the sample size prior to the actual data collection in AaBET Hospital. The collected data was supervised by the principal investigator daily.

4.9 Data processing and analysis, interpretation and presentation

Data was entered to Epidata and statistical analyses were performed using SPSS version 21 software program. Chi-square test or Fisher exact tests were used for categorical variables and mean and SD for continuous variables (t-test). Associated risk factors were determined using logistic regression. Confidence Interval (CI) of 95% and statistical significance of 0.05 were established.

4.10 Ethical considerations

Ethical approval was obtained from Addis Ababa University, collage of health science department of emergency and critical care. Permission was obtained from hospital administration to conduct this study and to access the medical record. All the collected data were kept confidential and no one except the members of the research team were able to access them.

4.12 Operational definition

Sepsis = presence of a confirmed infection and occurrence of at least two SIRS criteria

Severe sepsis = presence of sepsis and at least one organ failure

Septic shock = a state of acute circulatory failure characterized by persistent arterial hypotension

ICU = adult intensive care unit in which critically ill patients are treated

Comorbidity= Patients with Diabetes mellitus, chronic kidney disease, hypertension, congested heart failure and cancer

Immunosuppression= decrease in immunity of a patient like in cases of HIV/AIDS and cancer

Length of stay= the time during the patient was admitted till discharge

Treatment outcome= Patient's condition after treatment: recovered and death

5. Results

Socio-demographic characteristics

A total of 820 patients were admitted to adult ICU of TASH during the 3 year study period. Of whom 115(14%) patients were diagnosed with septic shock. Majority 69(60%) were female and the mean age of the participants was 47.99± 16.5 years within the range of 20-82 years. Sixty two (54%) patients were admitted from the wards while the remaining was directly transferred from emergency room. Most 72(2.6%) patients were medical patients followed by surgery 32(27.8%) and Gyn/Obs 11(9.6%). More than 60% of the patients have met all the SIRS criteria. The median length of ICU stay was 4 days (interquartile range 2-7 days), mean ± SD 5.8 ± 4.8 days. Majority 75.7% of the patients have less than 1 week length of ICU stay while 7% of the patients had ICU stay of more than 2 weeks.

Table 1 Demographic characteristic of patients

Socio-demographic characteristics		Total (%)	Survivals	Non-survivals	p-value
SEX	MALE	46(40%)	21(43.8%)	25(37.3%)	.556
	FEMALE	69(60%)	27(56.3%)	42(62.7%)	.488
AGE	18-40 years	40(34.8%)	18(37.5%)	22(32.8%)	.021
	41-59 years	50(43.5%)	26(54.2%)	24(35.8%)	.005
	60+ years	25(21.7%)	4(8.3%)	21(31.3%)	.002
ICU admission	Gyn/obs	11(9.6%)	0	11(16.4%)	.003
category	Medical	72(62.6%)	33(68.8%)	39(58.2%)	.249
	Surgery	32(27.8%)	15(31.3%)	17(25.4%)	.078

From the total cases, the underlying comorbidities were identified in 103(89.5%) of the patients. Comorbidities include HIV/AIDS, malignancy, CHF, Renal disease, coronary artery disease, HTN, Liver disease and others. The most common comorbidity was immunosuppression 39(33.9%) and 32(27.8%) patients have more than 2 comorbidities. Patients with COPD (34.3%), malignancies (26.9%), renal and liver disease (34.2% and 23.9% respectively) have higher mortality rates.

The most common source of infection was respiratory tract infection 63(54.8%) followed by urethral tract infection 17(14.8%), abdominal infection 12(10.4%), skin/soft tissue infection 7(6.1%), blood stream infection 4(3.5%) and in 12(10.4%) patient source remained unknown. Respiratory focus was higher in female patients 41(59.4%) than in male while urethral focus were higher in male patients.

In majority of the patients the most failed organ was the respiratory tract, the neurologic system, cardiovascular system and the renal system with an average of 2.7$\pm$ 1 failing organ. Furthermore the respiratory system failed in 99 (86%) patients, the neurologic system in 54(47%) patients and the cardiovascular in 51 (44.3%) patients. Majority of the patients 43(37.4%) had 3 failed organs, 40(34.8%) of the case had 2 failed organs, 21(18.2%) had 4 failed organs, 2 patients had 5 failed organs while 9(7.8%) of the patients had one failed organ.

Culture was done in 19(16.5%) of patients and microorganism were identified in 15(13%) patients. Gram negative organisms were identified in 8(7%) patients and *E.coli* accounts for 5 patients while 3 patients have *K.pneumoniae*, gram positive organisms in 5(4.3%) and 4 patients have *S.aureus* and one patient has *Staphylococci* and 2 patients with fungal infection were identified.

Table 2 comparison between survivors and non-survivors

Variables	Total(n=115)	Survivors(n=48)	Non-survivors(n=67)	*p* value
Comorbidities				
Diabetics	22(19)	13(27)	9(13.4)	.086
COPD	29(25)	6(12.5)	23(34.3)	.002
CHF	13(11.3)	10(20.8)	3(4.5)	.029
Coronary artery disease	24(21)	11(22.9)	13(19.4)	.359
Cancer	24(20.9)	6(12.5)	18(26.9)	.360
HTN	22(19)	16(33.3)	6(9)	.069
Renal disease	34(29.6)	11(22.9)	23(34.3)	.333
Liver disease	17(14.8)	1(2.1)	16(23.9)	.015
HIV/AIDS	15(13)	5(10.4)	10(14.9)	.999
No of comorbidities				
0	5(4.3)	1(2.1)	4(6.1)	.306
1	38(33.3)	21(31.8)	17(35.4)	.687
2	38(33.3)	22(45.8)	16(24.2)	.016
3	27(23.7)	7(14.6)	20(30.3)	.051
4	6(5.3)	1(2.1)	5(7.6)	.093
Source of infection				
Urinary tract	17(14.8)	12(25)	5(7.5)	.100*
Respiratory tract	63(54.8)	24(50)	39(58.2)	.022
Abdominal	12(10.4)	5(10.4)	7(10.4)	.126
Skin/soft tissue	7(6.1)	4(8.3)	3(4.5)	.528
Blood stream	4(3.5)	1(2.1)	3(4.5)	.121
Unknown focus	12(10.4)	2(4.2)	10(14.9)	.008
Organ failure				
Neurologic failure	54(47)	22(45.8)	32(47.8)	.171
Cardiovascular failure	51(44.3)	12(25)	39(58.2)	<0.001
Renal failure	41(35.7)	15(31.1)	26(38.8)	.381
Respiratory failure	99(86)	42(87.5)	57(85)	.470
Hematologic failure	17(14.8)	8(16.7)	9(13.4)	.929
Metabolic failure	29(25)	8(16.7)	21(31.3)	.051
Liver failure	21(18.3)	21(31.3)		.998

Intervention and outcome

All patients have received antibiotics and fluid therapy during their ICU stay. Vasopressor therapy has been given to 87(76%) and 66(57.4%) has received antifungal medications in addition to antibiotics. In 39(33.9%) patients overall therapy was initiated within 3-6 hours of ICU admission, 27(23.5%) patients started within 1-3 hours, 32(27.8%) started treatment immediately(0-1hr.) and 17(14.8%) patients started treatment after 6 hours of ICU stay. The overall ICU mortality was 67(58.3%). Medical patients had higher mortality (58.2%) than surgical (25.4%) and gyn/obs (16.4%) patients. Patients characteristics associated with higher mortality were female gender (36.5%), >50 years of age (57%), patients with immunosuppression (42%) and COPD (34.3%). More than 2 comorbidities and organ failure was also directly associated with higher mortality. Patients with respiratory infection as source and with cardiovascular organ failure have higher mortality (58.2%). The mean length of ICU stay for survivors and non-survivors was 7.5 $\pm$ 5.6 days and 4.6 $\pm$ 4 days, respectively.

Table 3. The time treatment was initiated in septic shock and its outcome

Time treatment was initiated	**Total(n=115)**	**Survivors(n=48)**	**Non-survivors(n=67)**	***p* value**
Immediately(0-1hr.)	32(27.8)	15(31.3)	17(25.4)	.703
1-3 hr.	27(23.5)	10(20.8)	17(25.4)	.784
3-6 hr.	39(33.9)	16(33.3)	23(34.3)	.992
>6 hr.	17(14.8)	7(14.6)	10(14.9)	.469

6. Discussion

The main objective of this study was to provide representative data on the characteristics and mortality of septic shock in TASH. Of the entire study population septic shock accounts for 14% of ICU admission, the most common source of infection was the respiratory and urinary tract, Gram negative bacilli were the most identified microorganisms and the overall ICU mortality was 58.3%. Patients with the presence of COPD and immunosuppression, respiratory tract source of infection and more than 3 organ failure has greater risk of death.

This study found that there is 14% septic shock incidence in ICU of TASH. The prevalence rate is comparable with the results reported in other countries Dutch (11%)(18) and French (13.7%)(36). However it is lower compared to results reported from Peshawar (35%)(24), Brazil (34%)(28)and Korea (62.1%)(29). This variation could possibly be due to the low number of study population and this study was conducted only in one study site while the others are a multicenter studies. And only patients with admission diagnosis of septic shock were included. Those who developed septic shock on ICU were not included in our study. Another possible reason could be the lack of ICU beds in our area compared to other countries.

Our patients were younger, with a mean age of 48$\pm$16.5 as compared with septic shock patients from Taiwan (64.3$\pm$15.4 years)(37), French (median age 68 years)(36) and Dutch (64$\pm$15 years)(18). This variation could be because of the low life expectancy of the population in our study. However all the studies have reported that with older age mortality was high which is similar with our finding.

The infectious organisms were identified in only 16.5% of patients in our study which is low comparing to results from other studies (20, 21, 36, 38). This could possibly be due to the delayed time interval to get the culture results from the laboratories; as a result clinicians prefer to start antibiotic therapy regardless of the results. The 2012 Surviving Sepsis Campaign; International Guidelines for Management of Severe Sepsis and Septic Shock also recommends that cultures should be obtained before antimicrobial therapy is initiated if such cultures do not cause significant delay (<45 min) in the start of antimicrobial administration(14).

Similar to other studies (24, 28, 29, 34) we found that respiratory and urinary tract were the most common source of infection. The potential implication of this finding is that, when the source of

infection remains unknown in a septic shock patient, clinicians should consider pulmonary and urinary sources.

The SSC international guidelines for the management of severe sepsis and septic shock recommend administering antibiotics within 1 hour of recognition and within 3 hours of ED triage(14). In our study 32(27.8%) of patients have received antibiotic therapy during the 1 hour of ICU stay. However our study is from the time of ICU admission not considering the time before they come to the ICU therefore we can't conclude that those patients have received antibiotics in exactly 1 hour of recognition of shock.

On comparison to the results from study done on effectiveness of treatment in Spain(39) more of our patients have received antibiotics on the first hour of admission while patients who have received antibiotics after 6 hours were almost the same number in both studies. In a same study fluid challenge was given to 91.1% of patients while in our study all patients were challenged with fluid therapy. In Uganda(10) 53% of patients have received fluid within the first hour and 14% of the patients have not received fluid during the first 6 hours, comparing to our result 28% of our patients have received fluid during the first hour which is low and 15% have not received fluid during the first 6 hours which is comparable. Mortality was higher in patients who began treatment after 6 hours and delay in initiation of treatment has shown an increase in mortality which is a similar finding to other studies (12, 39-41).

Comparing our results with studies done in Europe(20), USA(8) and Korea(29), our mortality with septic shock was high. This difference could be due to the quality of primary care here is poor and early recognition of severity of illness is often missed. And most times our patients present very late for a number of reasons including financial restrains and travelling from far away countryside. But still the difference in study design, inclusion and exclusion criteria might explain some of the differences(42). However our results (58.3%) were comparable with Peshawar (63.5%)(24) and Taiwan (61%) (37). Women had significantly higher mortality related to men in all age groups in this study, however gender and age were not significantly associated with the outcome of therapy and this is similar to results reported from other studies(24, 29).

7. Limitation of the study

The limitations of this study include the lack of pre ICU admission data like the time of onset, treatment provided before ICU may have influenced the outcome and patients who have developed septic shock in ICU might have been missed out. And the study is a single hospital survey therefore the conclusions drawn from this study might not become generalized.

8. Conclusion and recommendation

We have seen a retrospective record of patients with septic shock admitted to adult ICU of TASH. The results indicate that septic shock accounts 14% of ICU admission. Respiratory and urinary tract were the commonest source of infection and the results have also shown that a delay in the initiation of treatment increases mortality. The study also revealed that septic shock is a frequent cause of ICU admission with a high mortality rate. This can be explained by the fact that septic shock patients have more comorbidity, a worst previous state of health and requires more life support therapies.

Undoubtedly septic shock is an important public health problem and quality improvement of care to patients at risk of, or with confirmed septic shock is needed. Therefore early identification of high risk population, implementation of appropriate treatment and the design of future clinical studies are crucial to improve the outcome of septic shock.

9. Work plan

S. No.	Activities	Responsible body	Time frame							
			Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June
1.	Research title submission	PI	■							
2.	1st draft proposal submission.	PI			■					
3.	2nd draft proposal submission.	PI				■				
4.	Final proposal submission	PI				■				
5.	Proposal defense	PI				■				
6.	Research fund & support letter collection and Training of data collectors	PI + A					■			
7.	Data collection	D.C.					■			
8.	Data quality management & entry	PI					■			
9.	Data analysis	PI						■		
10.	1st draft thesis submission	PI						■		
11.	2nd draft thesis submission	PI							■	
12.	Final thesis submission	PI							■	
13.	Open thesis defense	PI								■
14.	Result dissemination	PI								■
15.	Monitoring	PI+ A	■	■	■	■	■	■	■	■

10. Budget breakdown

Budget category		**Unit cost:** Daily wage including per diem(ETB)	**Multiplying factors:** Number of staff days(number of staffs x Number of working days)	**Total cost in ETB**
1	**Personnel**			
	Data collectors	50/patient card	50 x300	15000.00
	Coffee /tea for data collectors during training	25	1x4	100.00
	Subtotal		**Personnel total**	**15100.00**
2	**Supplies and stationery**			
	Questionnaire duplication	2 /questionnaire	200 questionnaire and format	400.00
	Pen	5	10	50.00
	Flash disk	200	2	400.00
	Bag	400	2	800.00
	CD-RW	25	2	50.00
	Printing paper (pack)	200/ pack	4	800.00
	Printing(page)	1	3x80 pages	240.00
	Binding	15	3	45.00
	Subtotal		**Supplies /stationery total**	**2785.00**
3	**Grand total**			**17885.00**
	Contingency 10%			**1788.5**
4	**Total**			**19673.5**

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Annex 1 Data collection tool

Checklist to collect data on prevalence and treatment outcome of septic shock patients in TASH Addis Ababa, Ethiopia from Jan 2014-Dec 2017

Socio-demographic characteristics of the study participants.

MRN _____ Age _____ Sex _____ Date of admission _____

ICU admission category A. From ward B. Emergency Date of discharge_____

1. Surgery 2. Medical 3. Gyn/obs

Table 1 SIRS criteria during the first 24 hours of ICU admission

Central temperature <36ºC or >38ºC	**Yes / No**
Tachycardia >90 /min	**Yes / No**
Tachypnea >20 /min or $PaCO_2$ <4.3 kPa (32 mm Hg) during spontaneous breathing, **or** Need for mechanical ventilation	**Yes / No**
White cell count >12·109/L or <4·109/L, **or** >10% immature neutrophils in a differential count	**Yes / No**

Table 2 comorbidities of patients, source of infection prior to septic shock and Organ failure of patients in TASH

comorbidities	**yes**	**no**	**Site of infection**	**yes**	**no**	**Organ failure**	**yes**	**no**
DM			Lung			Neurologic failure		
COPD			Intra-abdominal infection			Cardiovascular failure		
CHF			Urethral infection			Renal failure		
CAD			CNS			Respiratory failure		
Cancer			Blood stream infection			Hematologic failure		
HTN			Skin/soft tissue infection			Metabolic failure		
Renal failure			other			Liver failure		
Liver failure								
others								

Table 3 Type of microorganism found in patients TASH Jan 2014-Dec 2017

Microorganism identification YES ☐ NO ☐

Type of microorganism								
No	Gram negative			Gram positive			Fungi	
1	*Escherichia coli*		1	Coagulase negative *staphylococcus*		1	Candida species	
2	*Acinetobacter baumanii*		2	S.aures		2	Aspergillus spp.	
3	*Pseudomonos aeruginosa*		3	Streptococcus pneumoniae		3	Pneumocystis	
4	*Klebsiella pneumoniae*		4	Enterococcus species				
5	*Enterobacter species*		5	Streptococcus species				
6	Others gram negatives			Others_____				

Table 4 Time of treatment initiated, treatment given and outcome of septic shock patients in TASH Jan 2014-Dec 2017

Time treatment was initiated	1. 0-1 hr. 2. 2. 1-3 hr. 3. 3-6hr. 4. 4. >6hr
Treatment given	1. Fluid 2. Vasopressors 3. Antibiotics 4. Antifungal 5. others
Patient outcome	1. Death 2. Recovered

ASSURANCE FORM

I, the undersigned, assert that this MSc. thesis is my original work, has not been presented for a degree in any other university and that all sources of materials used for the thesis have been accordingly acknowledged.

Msc candidate: Hiyab Teklemichael **(Bsc)** Signature: _____ Date_____

Advisor:-

Dr Tigist Zewde (**Emergency Physician**) Signature:-_____ Date_____

Sr. Heyria Hussein (**Bsc, Msc, Lecturer)** Signature:-_____ Date_____