



MAGNITUDE OF SEPSIS AND SEPTIC SHOCK AND ASSOCIATED FACTORS IN PATIENTS ADMITTED TO CENTRAL INTENSIVE CARE UNIT OF ADAMA HOSPITAL MEDICAL COLLEGE ADAMA, ETHIOPIA

BY: BEHAYLU TESHAMARIAM (MD)

ABSTRACT

Introduction: Sepsis, a life-threatening organ dysfunction caused by a dysregulated host response to infection, and its subset, septic shock (with higher mortality and morbidity), are major health problems disproportionately affecting low- and middle-income countries. Despite the potentially high burden in low- and middle-income settings, data on prevalence and factors contributing for the development of sepsis and septic shock remains scarce.

Objectives: This study aimed to assess the prevalence of sepsis and septic shock, along with associated factors, in patients admitted to the central intensive care unit (ICU) of Adama Hospital Medical College Adama, Oromia, Ethiopia.

Methods: Cross sectional study was conducted on 298 patients admitted to the ICU. Data were collected from the patients' medical records using a checklist created by the investigator. Coded data were entered into Epi Info 7.2.5.0, transferred to Microsoft Excel, and analysed using SPSS version 25. A binary logistic regression model was employed to identify factors contributing to sepsis and septic shock.

Results: Among the 298 patients, 142 (47.7%) had sepsis, and 55 (38.7% of septic patients, 18.5% of total) developed septic shock. Pneumonia was the most common site of infection (53.9% of sepsis cases). Multivariate analysis revealed that being on mechanical ventilation (AOR 2.92, 95% CI: 1.12-7.63), higher white blood cell count (AOR 1.70, 95% CI: 1.14-2.60), lower sodium (AOR 0.91, 95% CI: 0.87-0.96), and higher chloride levels (AOR 1.11, 95% CI: 1.04-1.18) were significantly associated with sepsis. Pneumonia and intra-abdominal infections were associated with higher odds of sepsis (AOR 18.7, 95% CI: 6.1-56.0 and AOR 16.0, 95%

CI: 4.36-61.6, respectively). Male gender (AOR 0.19, 95% CI: 0.07-0.46), mSOFA score (AOR 3.25, 95% CI: 2.04-5.17), and lower lymphocyte count (AOR 0.65, 95% CI: 0.42-0.99) were associated with septic shock. Both sepsis and septic shock showed an association with low platelet count (AOR 0.99, 95% CI: 0.98-0.990 and AOR 0.98, 95% CI: 0.98-0.99, respectively).

Conclusion: This study found a higher prevalence of sepsis and septic shock compared to high-income countries, but comparable to most LMICs. Notably, the affected population was relatively younger.

Keywords: Sepsis, Septic Shock, Prevalence, Associated Factors, ICU, LMICs

1. INTRODUCTION

1.1 Background

The word sepsis is derived from the Greek word “SEPO” for “decomposition” or “decay,” and its first documented use was about 2700 years ago in Homer’s poems. It was subsequently used in the works of Hippocrates in which he characterizes sepsis by rotting flesh and festering wounds and after that multiple definitions and theories were proposed by multiple scholars (1,2).

The 1991 consensus conference (3) developed initial definitions (sepsis 1) based on sets of criteria that SIRS (systemic inflammatory response syndrome) in a patient with confirmed or suspected infection would be called sepsis and this was revised in 2001 i.e., sepsis 2, incorporating organ dysfunction to define severe sepsis, which could progress to septic shock which were defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation.

Currently sepsis defined by sepsis definition task force 2016 (sepsis 3), as dysregulated host response to infection that led to organ dysfunction. And septic shock as subset of sepsis, in which underlying circulatory, cellular and metabolic abnormalities lead to substantially increased mortality risk (2,4).

The flaw of sepsis 3 definition is that four out of the six criteria are based on laboratory result which make it difficult to apply in resource limited settings and as a solution for this a prospective observational study in a 24-bed medical, surgical, and trauma intensive care units showed that a modified sequential organ dysfunction assessment (MSOFA) predicts mortality as well as the sequential organ dysfunction assessment (SOFA) score (5).

The Institute for Health Metrics and Evaluation (IHME) on the global burden of sepsis estimate 60.2 million cases of sepsis in 1990 and 48.9 million cases of sepsis in 2017. This declining incidence was seen in nearly every location worldwide (11). In contrast to this prior systemic review and meta-analysis showed that 50% lower incidence of sepsis and increasing pattern rather than decrement (12). The intensive care over nations (ICON) audit showed that of patients admitted to ICU 29.5% was diagnosed with sepsis during their stay and including the 18% with sepsis at admission. (25).

Moreover an observational, cross-sectional, 24-hour point prevalence study done across 5 continents showed that 54% of ICU patients had suspected or proven infection and 22% had ICU acquired infection with

significant variation across different nations, ranging from 43%(Australia) to 60% (Asia and Middle east) (26).

WHO and Mayo clinic, listed older persons (over the age of 65), pregnant or recently pregnant women, neonates, hospitalized patients, chronic diseases, such as diabetes, kidney disease or COPD and condition that requires treatment with corticosteroids, which can lower immune response, like, autoimmune diseases are major risk factors for the development of sepsis. people with HIV/AIDS, with liver cirrhosis, cancer and people with no spleen as a risk group for the development of sepsis after infection (41,42)

1.2 Statement of the problem

WHO's first ever report on the global epidemiology and burden of sepsis shows on the year 2017, estimated number of 49 million individuals where affected and was related to approximately 11 million potentially avoidable deaths worldwide (10,11). As of sepsis global alliance Sepsis is a global health crisis which affects between 47 and 50 million people every year, at least 11 million die – one death every 2.8 seconds. Depending on the country, mortality varies between 15% and more than 50 % furthermore Many surviving patients suffer from the consequences of sepsis for the rest of their lives (6).

A meta-analysis done in 2020(12), endorsed by WHO, showed that significant regional differences in both the incidence of and mortality associated with ICU-treated sepsis but with very few input from LMICs and none from Africa which Conclude that urgent need for improved epidemiological sepsis surveillance in LMICs as there is significant gap and paucity of information. Regardless of the scarcity of evidence from LMICs WHO (10) estimate higher prevalence and mortality of sepsis relative to high income countries.

Furthermore, the available few evidences from LMICs are based on sepsis 2 definition which, compared to sepsis 3 definition, has inferior predictive validity for septic shock and associated mortality although it identifies similar sepsis population with 92% overlap (13).

Sepsis results when the response to infection becomes generalized and involves normal tissues remote from the site of injury or infection (7). Any infected person can potentially develop sepsis, the pathogenesis of sepsis is extremely complex, including imbalance in inflammatory response, immune dysfunction, mitochondrial damage, coagulopathy, neuroendocrine immune network abnormalities, endoplasmic reticulum stress, autophagy, and other pathophysiological processes, and ultimately leads to organ dysfunction (8)

It's uncertain why immune responses that usually remain localized, spread beyond the local environment causing sepsis. Likely multifactorial and may include the direct effects of the invading microorganisms or their toxic products, release of large quantities of proinflammatory mediators, and complement activation. In addition, some individuals may be genetically susceptible to developing sepsis (7). Progression of infection to sepsis and its treatment outcome also depends on patient and non-patient related factors including presence or absence of comorbidities like AIDS, liver diseases or cancer and other factors like site of infection and type of infection i.e. nosocomial or community acquired(14–18).

Transition of sepsis to multiple organ dysfunction could be prevented with rapid and appropriate resuscitation of shock with initiation of early goal-directed therapy (EGDT), especially if appropriate actions taken on the

critical “golden hours” of sepsis when there is abrupt transition to serious illness. Those appropriate actions being identification of high-risk patients, appropriate cultures, source control, and early administration of appropriate antibiotics, which was then followed by early hemodynamic optimization of oxygen delivery and decreasing oxygen consumption (2,9)

While general sepsis costs are high, there is considerable variability between countries regarding the costs of sepsis. With the mean total hospital costs per patient ranging between €1101(Indonesia) and €91,951(Italy). The relative amount of healthcare budget spent on sepsis was 2.65%, which equals 0.33% of the gross national product (19). Sepsis is also the most expensive healthcare problem in the United States, accounting for more than \$20 million (about 5.2% of the total hospital cost) in 2011 alone and showed increasing pattern after that (2,20). Sepsis cases not diagnosed until after admission, and those with increasing severity had a higher economic burden and mortality. Methods to improve early identification of sepsis may provide opportunities for reducing the severity and economic burden of sepsis in the (21).

Treatment outcome of patients with sepsis varies between different WHO regions and duration between onset and initiation of therapy. More than half of sepsis require ICU admission accounting for 10% of total admissions and overall mortality more than 10% and 40% for sepsis and septic shock respectively (15,16). According to WHO, approximately 20% of all-cause global deaths are due to sepsis, disproportionately affecting neonates, pregnant or recently pregnant women, and people living in low-resource settings (10). Given the change in definition with sepsis now used to refer patient who previously described as severe sepsis, mortality of sepsis in Africa is estimated to be 30-47 % (23).

Surviving sepsis is not without a consequence, sepsis survivors suffer from additional morbidities such as higher risk of readmissions, cardiovascular disease, and cognitive impairment and of death, for years following index sepsis episode. In the first year following index sepsis episode, approximately 60 % of sepsis survivors have at least one rehospitalization episode, which is most often due to infection and one in six sepsis survivors die within this time (24).

1.3 Significance of the study

Despite being one of the oldest diseases identified, little is known about the incidence, prevalence and treatment outcome of sepsis especially in a country with low and middle income. As infectious diseases are common in LMICs it's obvious that sepsis will be common and again along with many other factors delayed identification and treatment of infection will further increase the chance of sepsis following infection.

In the contrary to the higher estimation and worse prognosis of sepsis in LMIC there are limited number of studies in this subject matter especially in sub-Sahara Africa. Furthermore, most of the currently available data are timed or uses criteria before revision of sepsis definition by sepsis task force in 2016, which make those data less reliable as it might underestimate mortality of sepsis and septic shock.

This study will help hospitals and MoH in future policy making and implementing by filling the significant knowledge gap in the subject matter and as one of the few studies done regarding sepsis it will assist researchers as a foundation for further studies and as an ultimate goal this study it will help patients through improved policies

and assisting the delivery of evidence based preventive and therapeutic approaches.

2. LITERATURE REVIEW

2.1. Prevalence of sepsis and septic shock

A recent study from the Institute for Health Metrics and Evaluation (IHME) on the global burden of sepsis estimate 60.2 million cases of sepsis in 1990 and 48.9 million cases of sepsis in 2017. This change represents a decrease of 18.8% of all incident cases of sepsis in 2017. This declining incidence was seen in nearly every location worldwide (11). In contrast to this prior systemic review and meta-analysis showed that 50% lower incidence of sepsis and increasing pattern rather than decrement (12). The intensive care over nations (ICON) audit showed that of patients admitted to ICU 29.5% was diagnosed with sepsis during their stay and including the 18% with sepsis at admission. occurrence rate of sepsis varies between 13.6 to

39.6 in different regions with in ICU and in hospital mortality rates were 25.8% and 35.3%, respectively, in patients with sepsis, but it varied from 11.9% and 19.3% (Oceania) to 39.5% and 47.2% (Africa), respectively (25). Moreover, an observational, cross-sectional, 24-hour point prevalence study done across 5 continents showed that 54% of ICU patients had suspected or proven infection and 22% had ICU acquired infection with significant variation across different nations, ranging from 43%(Australia) to 60% (Asia and Middle east) (26).

A systematic review and meta-analysis by Louis Vincent et al. (27) Showed that in Europe and North America the frequency of septic shock was estimated at 10.4% in studies reporting values for patients diagnosed at ICU admission and at 8.3% in studies reporting values for patients diagnosed at any time during the ICU stay. ICU mortality was 37.3% and in hospital mortality 39.0%. Significant heterogeneity between-study was observed during this meta-analysis and was attributed to variability in defining and applying the diagnostic criteria. Another cohort done in one hundred ninety-eight ICUs, all in Europe, showed among all patients 37.4 % had sepsis (28). Other study from Turkey demonstrated that 57.4% of patients had suspected or confirmed infection among which 41.6% had sepsis (sepsis I) ,17.3% had sever sepsis and 13.5% of patents had septic shock for which, on same patient population, prevalence was 6.9% with higher mortality rate of 75.9% Vs. 70.4% when sepsis 3 criteria applied (29). Additionally, a Prospective study conducted in Caribbean showed that the 28-day mortality rates of 42% forsepsis and 47%, for septic with overall ICU mortality rate of 34% for sepsis (30).

As of global health estimate 2019, by WHO (31), communicable diseases are the leading cause of death in low income countries and the same publication shows six of the top ten causes of death are infectious diseases among which lower respiratory tract infection being the commonest and it's the second, only next to neonatal conditions. Additionally, Sepsis was reviled to be the commonest cases of critical illnesses throughout the world with south Asia and sub-Saharan Africa accounting for approximately 40% of global burden by 2004. (32) and more recent, 2019, data from WHO showed 85.0% of sepsis cases and 84.8% of sepsis related deaths occurred in low to middle income countries (LMICs) particularly in sub-Saharan Africa and South-East Asia (10).

A study done in Malawi, population incidence and mortality of sepsis in urban Africa setting, estimate that the incidence rate of emergency department–attending sepsis and severe sepsis in adults, between 2013 and 2016, was 1772 per 100 000 person-years and 303 per 100 000 person-years respectively, In-hospital mortality for patients admitted to the hospital with sepsis and severe sepsis was 23.7% and 28.1% , respectively.(33)another study from

rural areas of Rwanda found out that 14% of adult patients had sepsis at admission but this study define sepsis as quick sofa score more than 2 which currently not considered diagnostic of sepsis rather it is used only to stratify patients with infection based on risk of deterioration and mortality (22,34).

A prospective study done at four selected hospitals in Addis Ababa, ICU patients using sepsis 3 definition reported overall prevalence of sepsis and septic shock to be 26.5% with in ICU and 28 days mortality of 41.8% and 50.9 % respectively (35).

Another study from Tikur Anbessa specialized hospital septic shock is second most common form of shock with highest mortality rate (75% vs. 43.6%) (36). Contradicting to this another study from the same institution showed 28 days mortality of septic shock to be 58.3% with prevalence of 14%, although this significant difference could be attributed to the difference indefinitions used for septic shock (37).

Another study from southern Ethiopia done in three teaching hospitals showed that septic shock account for 7.7% of all ICU admissions and had 65% mortality and it accounts for 10% of all death (38). Another cross-sectional study, from Bahir Dar Felege Hiwot referral hospital, showed for all patients admitted to medical ICU infectious diseases where commonest indications for admission and sepsis account for 20% of all ICU deaths (39). Additionally, a retrospective study conducted in Jimma university specialized hospital revealed medical conditioned are the leading indication for admission and in ICU mortality, 50.4 and 53.6 respectively and septic shock accounts for 5.2% of all admissions with case fatality rate of 57.9% which, according to the study, make septic shock deadliest of all conditions in ICU (40).

2.2. Factors associated with sepsis and septic shock

2.2.1 HOST RELATED FACTORS

WHO, listed older persons, pregnant or recently pregnant women, neonates, hospitalized patients, people with HIV/AIDS, with liver cirrhosis, cancer, kidney disease, autoimmune diseases and people with no spleen as a risk group for the development of sepsis after infection (41).

As of Mayo clinic, once acquiring infection People over the age of 65, People with lower immune response, such as those being treated for cancer or HIV, chronic diseases, such as diabetes, kidney disease or COPD and condition that requires treatment with corticosteroids, which can lower immune response are major risk factors for the development of sepsis (42).

Systematic review of literatures from ICU over different countries from Europe and America, showed that old age, male gender, coma within 48 hours of admission, two or more comorbidities and emergency surgery were shown to be significantly associated with sepsis (43). Furthermore, a study from England, Wales and Northern Ireland showed that Immunocompromised state defined as AIDS, daily steroid treatment for past six months, radiotherapy or chemotherapy within past six months, metastatic disease, acute or chronic myelogenous or lymphocytic leukemia, multiple myeloma, lymphoma, or congenital humoral or cellular immune deficiency state. Respiratory comorbidity defined as shortness of breath with light activity due to pulmonary disease or using home ventilation. Cardiovascular comorbidity defined as fatigue, dyspnea or angina at rest due to myocardial or

peripheral vascular disease (New York Heart Association Functional Class IV). Liver comorbidity defined as biopsy proven cirrhosis, portal hypertension, or hepatic encephalopathy. Renal comorbidity defined as requirement for renal replacement therapy for irreversible renal disease are all associated with sepsis (44).

A meta-analysis of fifteen studies of 2800 patients from countries in sub-Saharan Africa showed that prevalence of sepsis is associated with HIV, AIDS and Tuberculosis and the median age ranged from 27 to 39 years (23). A prospective study from Gitwe district hospital, Rwanda demonstrated that male gender, history of convulsion, change in mentation as evidenced by decreased GCS, jaundice and increased qSOFA were shown to be associated with sepsis (34). Another study from Kenya showed that late referral from primary care hospitals and HIV are associated with higher prevalence of sepsis (45).

2.2.2 Infection related

Although Sepsis can originate from virtually any infecting organism (46), its more commonly associated with bacterial infection among which both gram positive and gram-negative organisms take equal share with *Staphylococcus aureus* (Gram-positive) and *Pseudomonas* species and *Escherichia coli* (Gram-negative) being the most frequently identified organisms (28).

Among the sites of infection pneumonia was showed to be the commonest and followed by abdominal infections and blood born infections(28,47) supporting this A cohort study conducted in 10 hospitals of Colombia showed , progression to sepsis and septic shock increases with intra-abdominal and respiratory sources of infection, in addition, nosocomial infection and positive culture were associated with statistically significant progression to sepsis and septic shock(48) With regard to the place of acquisition community acquired infections account for 80% of patients with sepsis while the rest had nosocomial infections(47).

2.2.3 Laboratory biomarkers

As of a paper published on 2017 by Péter Kustán et. al, more than 200 non-conventional biomarkers have been evaluated and non-had appropriate specificity to change the current practice (49). Among Elevation of serum lactate level was associated with both sepsis and septic shock, and according to sepsis 3 definition it's one of the diagnostic criteria for septic shock (4).

Low platelet counts (Thrombocytopenia) was included in the sequential organ failure assessment criteria which is used to define organ dysfunction in septic patients according to sepsis 3 definition of sepsis (4) which was formulated by a group of experts based on previous data and consensus. Leukocytosis was among the SIRS criteria which again, was diagnostic tool of sepsis before the introduction of sepsis 3 definition of sepsis and it was shown to have association with the development of sepsis (50,51).

The difference between the concentrations of chloride and sodium constitutes the major contributor to the strong ion difference (SID); which is the key pH regulator in the body, according to the physicochemical approach. Decreased sodium levels (hyponatremia) and higher chloride levels (hyperchloremia) were shown to have association with sepsis development. A retrospective cohort study in a provincial tertiary care hospital, showed presence of hyperchloremia was associated with sever disease and with the development of AKI in patient with sepsis and septic shock (52–55).

In addition to high serum nitric oxide, Plasma vasopressin level of 19 patients with septic shock was compared with 12 patients with cardiogenic shock and it was Inappropriately low in those with septic shock leading to the possible explanation for development of shock in patient with sepsis (56–58).

2.2.4 Management related

Admission to intensive care unit or longer hospital stays, Devices that go in the body, such as catheters in the vein, or breathing tubes, Treatment with antibiotics in the last 90 days where listed by Mayo clinic as treatment and interventions associated with sepsis and septic shock (42).

systematic review by M. Fathi et al. in 2019Gc (43) reported those patients with intensive care interventions like mechanical ventilation during ICU stay, urinary catheters and central venous catheters and surgery related factors including number of surgeries or procedures, urgent and emergent surgeries and abdominal surgeries were shown to have a significant association with development of sepsis and septic shock.

A study conducted in Ayder comprehensive specialized hospital showed that being on mechanical ventilator, ICU stay more than 7 days and use of central lines are associated with acquisition of nosocomial sepsis (59).



2.3 Conceptual framework of the study

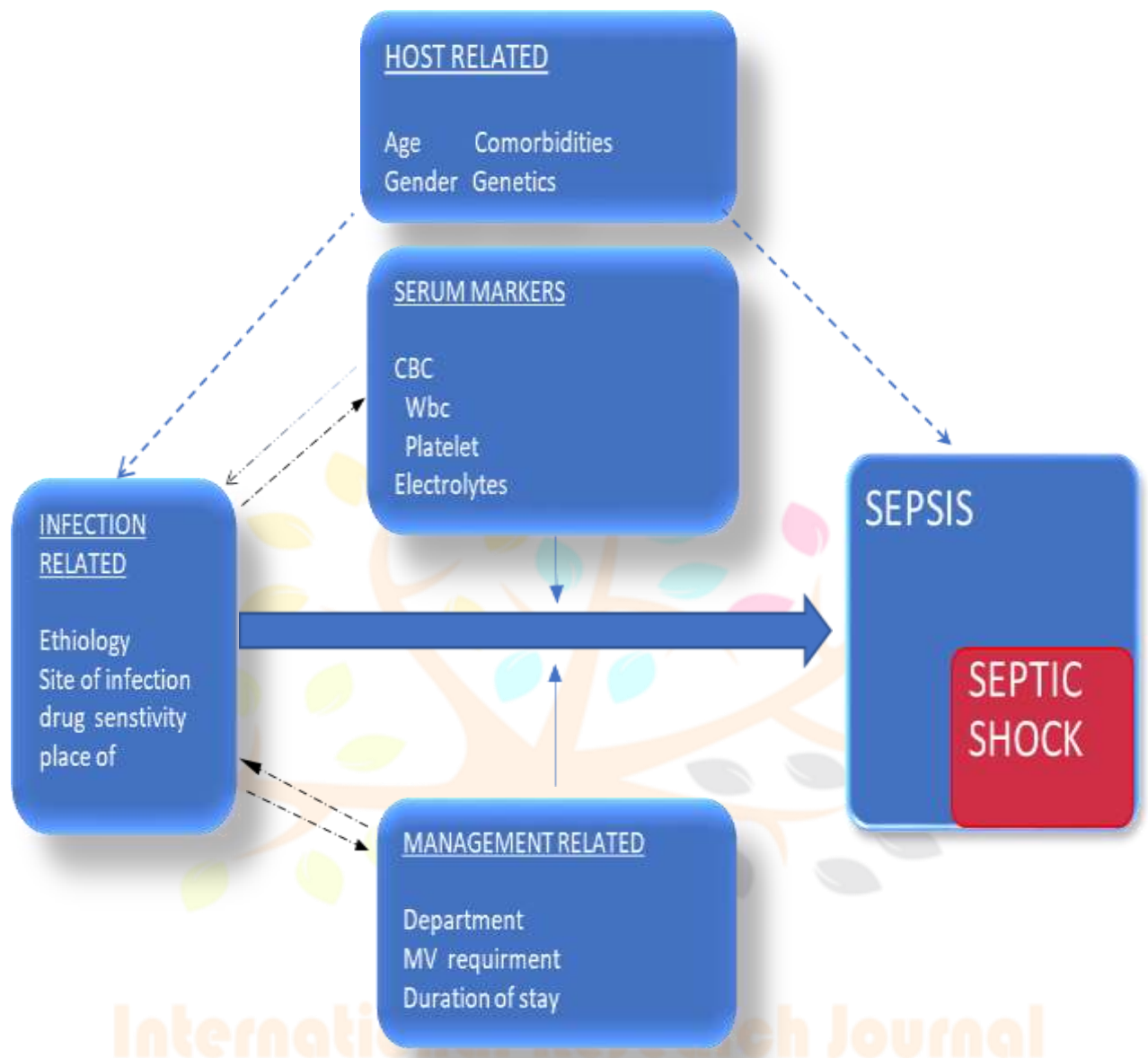


Figure 1: Conceptual framework for the study of prevalence of sepsis and septic shock and associated factors in central ICU of AHMC 2023. developed by investigator after literaturereview (2,6,28,35–40,43,52-55).

3 OBJECTIVES

3.1 General objectives

- To assess the prevalence and associated factors of sepsis and septic shock in ICU treatedpatients at AHMC during 2022/2023.

3.2 Specific objectives

- To assess the prevalence of sepsis and septic shock in ICU treated patient at AHMC during 2022/2023.
- Identify factors associated with sepsis and septic shock in ICU treated patients at AHMC during 2022/2023.

4 METHODS AND MATERIALS

4.1 Study area

The study will be conducted in Adama hospital medical college (AHMC) which is located 100 km southeast of the capital city Addis Ababa, in Oromia regional state, Adama, Ethiopia. It was established by missionaries from abroad in 1938 GC, by then it was called Haile Mariam Mamo memorial hospital later Adama referral public hospital and current name was adopted when the hospital upgraded to medical college in 2003. Currently the hospital is serving a catchment population of more than 6 million, from different region of the country. It has 232 beds capacities and serve around 1000 patents per day at six medical case teams and specialty clinics. Adama hospital medical college (AHMC) has one central ICU which serve as pediatric ICU (PICU) and adult ICU, with 12 beds and 10 mechanical ventilators. The stuff in the central ICU includes 2 anesthesiologist, one internist, 5 residents from different department and 14 nurses during the day and 10 nurses during the night shift.

4.2 Study design

Retrospective chart review (RCR) was conducted to assess the prevalence and factors associated with sepsis and septic shock among patients treated in the central intensive care unit of AHMC.

4.3 Population

4.3.1 Source Population

All medical, surgical and Gynecology/Obstetric patients admitted to the central ICU of AHMC.

4.3.2 Study Population

All ICU admitted patients who fulfil the inclusion criteria.

4.3.3 Study Unit:

All randomly selected patients chart admitted to central ICU from October 2021 through July 2023 GC.

4.4 Inclusion and Exclusion Criteria

4.4.1 Inclusion criteria

All patients with age of 15 years or above admitted to central ICU from October 2021 through July 2023 GC.

4.4.2 Exclusion criteria

Patent whose medical record number is not documented

4.5 Sample size determination and sampling procedure

4.5.1 Sample Size Determination

For determination of prevalence sample size is calculated as follow: - From prospective study (60), published on 2020Gc, which took over four selected ICU in Addis Ababa and showed prevalence of sepsis to be 26.5% which is taken as prevalence to calculate samplesize for this study using Epi info.

Where **P** = prevalence which, for our case, taken 26.5 % = 0.265 Population size = 132, Confidence limit of 5% and confidence level of 95%

With this the calculated sample size will be 244 after corrected for finite number of populations.

Sample size for the second objective which is determination of factors associated with sepsis and septic shock is determined Using double proportion formula for the following factors using online calculator. Select-statistics.co.uk

Table 1: determination of sample size for selected independent factors for the study.

Variable	Proportion 1(P ₁)	Proportion 2 (P ₂)	power	CI	Total sample
Age above 46	0.08	0.66	80%	95%	7
Male	0.33	0.52	80%	95%	103
Abdominal focus	0.014	0.086	80%	95%	140
NEED FOR MV	0.17	0.55	80%	95%	22

Taking the highest of all, which is 260 and adding 30% non-responder rate for RCR, gives the final sample result of 318.

4.5.2 SAMPLING TECHNIQUE

There were a total of 1460 patients admitted between October 2021 and July 2023 GC. After excluding 131 who were below 15 years, 9 patients who had no or incompletely documented medical record number sampling frame were generated from the remaining list of 1320 patients of which 338 were selected using systemic random sampling using sampling interval value, K

= Total population(N)/Sample size(n)=2.4 and the starting point for randomization where selected by lottery method

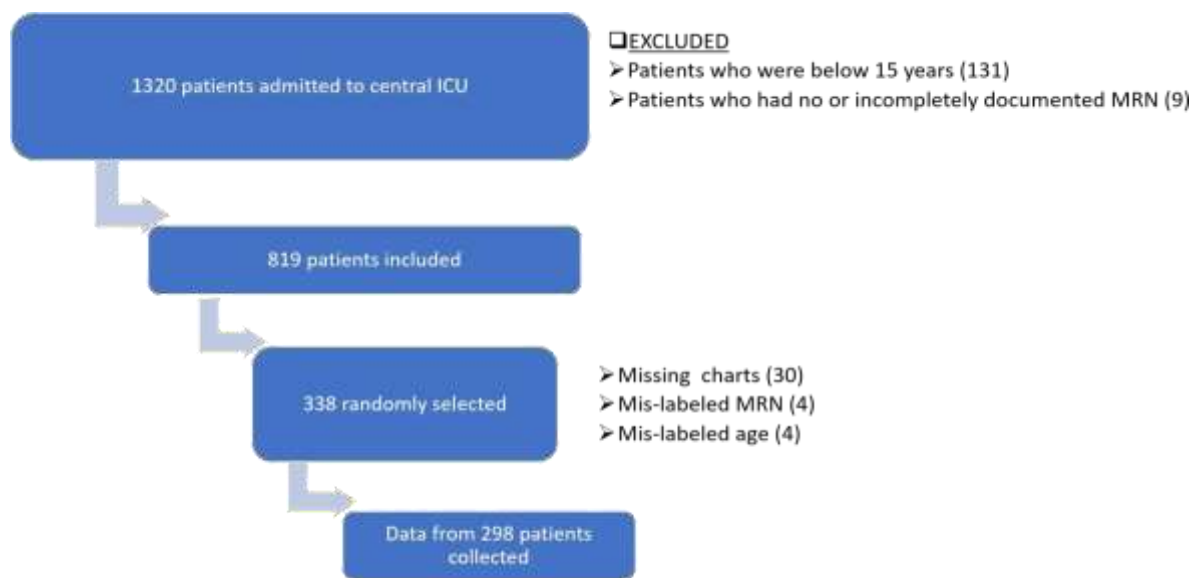


Figure 2: Schematic presentation of the sampling procedure for the study of prevalence of sepsis and septic shock and associated factors in central ICU of AHMC 2023.

4.6 Data collection

Data was collected within the hospital compound by 3 medical interns using a checklist after orientation given by the investigator

4.7 Data quality control

Pretest of the checklist was conducted on 5% of sample size on medical records after withdrawing patient chart from AHMCs store. Data collection was supervised by the investigator

4.8 Study variables

4.8.1 Dependent Variable

Sepsis

4.8.2 Independent Variable

Sociodemographic factors : - Age and sex

Comorbidities : - DM, HIV and Malignancy of any sort

Microbiological factors : - culture and sensitivity

Site of infection : -chest focus, CNS focus, GU focus, GI focus, blood stream

Acquisition of infection : -community or nosocomial

Biochemical/laboratory : - leukopenia, Anemia, thrombocytopenia,

Treatment related factors : - Need for and duration of mechanical ventilation and ICU Stay

4.9 Data analysis

The collected data was checked for completeness using Microsoft excel and was transferred to and analyzed by statistical package for social science (SPSS) version 25 then descriptive statistics was computed in order to characterize the participants and to determine proportions. Chi square test and independent sample t-tests were computed to identify significant categorical and numeric independent variables respectively. Binary logistic regression model was used for variables which was found significant in chi square and independent sample t-test in order to identify independent effect while controlling the other variables. Degree of association was computed using odd ratio with 95% confidence interval taking p-value of 0.05 or less as statically significant association between the dependent and independent variables.

4.10 Operational definition

Sepsis: should be defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Organ dysfunction: For clinical operationalization, represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more from baseline which taken as zero if previously unknown.

Infection: based on treating physician's decision and whenever conflict found between physicians the evaluation of the most senior was taken to decide presence or absence of infection.

Septic shock: septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.

MSOFA: Is a set of criteria, as shown in table 1, derived from SOFA and tested in prospective study (5) and shown to be comparable in predicting 1st and 3rd day mortality.

Table 1: Modified sequential organ failure assessment used for defining organ failure in this study.

Organ System	0	1	2	3	4
Respiratory SpO ₂ /FiO ₂	>400	400	315	235	150
Liver	No scleral icterus or jaundice			Scleral icterus or jaundice	
Cardiovascular, hypotension	No hypo- tension	MAP <70 mm Hg	dopamine 5 or dobutamine any dose	dopamine>5 epinephrine 0.1 norepinephrine 0.1	dopamine>15 epinephrine>0.1 norepinephrine>0.1
CNS, Glasgow Coma Score	15	13-14	10-12	6-9	<6
Renal, Creatinine mg/dL	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0

NOSOCOMIAL: Infection suspected/diagnosed 48 hours after hospital admission.

4.11 Ethical clearance

Ethical approval was obtained from Institutional Ethical Review Board (IERB) of adama hospital medical college (AHMC) and was submitted to department of internal medicine, and record office of AHMC.

4.12 Dissemination of the findings

The result of this study will be presented for a research defense at AHMC and disseminated for department of internal medicine and Research coordinating office and other concerned bodies. furthermore, for different journals for publication if found to be qualified.

5 RESULTS

5.1 General characteristic of the population

The overall characteristics of patients admitted to the central ICU of AHMC is summarized on the table below (**Table 2**). Among the total subjects with median age of 37 (IQR, 25-55) years and range from 15 to 85 years. Female subjects accounted for 49.3% of patients and was found to be younger with the mean age of 38.5 and median age of 34.6 which is relative to 42.2 and 41.8, respectively, for the male patients.

Table 2: summary of general characteristics of patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Variables	Median(IQR)	Variable	Count (%)
Age	37 (25-55)	Sex	
Duratio of stay	4 (2-6)	Female	147 (49.3%)
WBC count	10.9(7.4-15.6)	Male	151(50.7%)
lymphocyte	1.2(0.6-2)	Department	
Neutrophil	8.9(5.6-13.3)	GYN/OBS	20(6.7%)
Hemoglobin	12(9.5-14)	MEDICAL	164(55%)
Platelet count	210(145-293)	SURGICAL	114(38.3%)
Sodium	139(133-144)	Time from triage to admission	
Chloride	105(99-110)	Less than 48 hours	231(79.1%)
AST	62(30-11)	More than 48 hours	61(20.9%)
ALT	27(17-56)		
ALP	166(90-235)		
Bilirubin	3.4(1.25-6.35)		
Msofa score	3(1-6)		

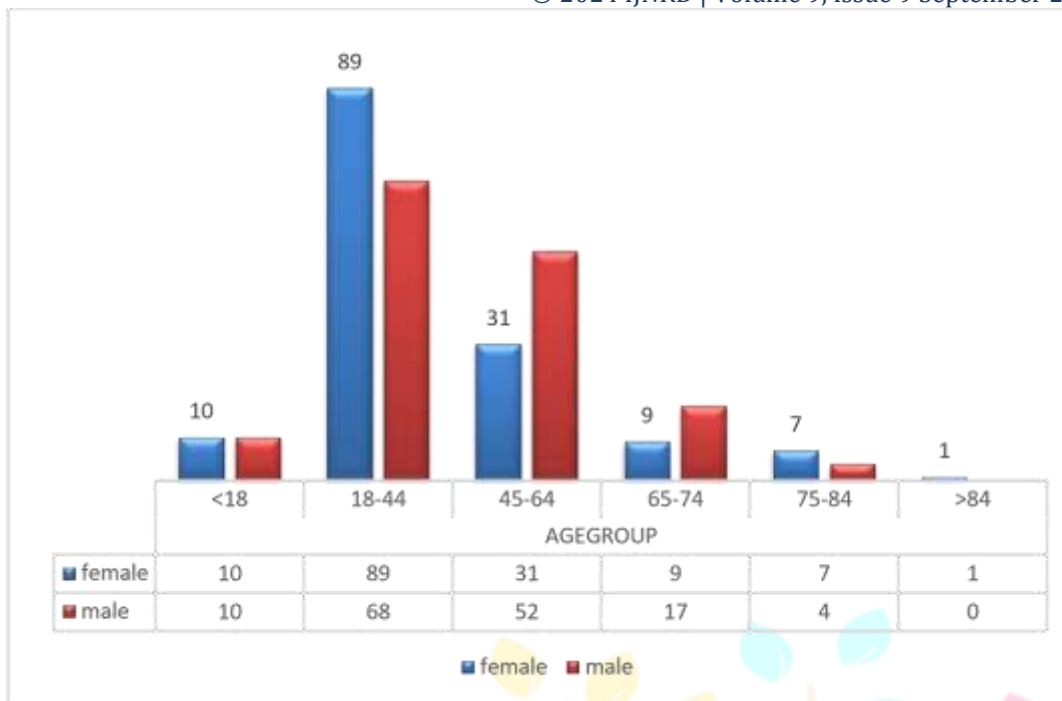


Figure 3: clustered bar chart for distribution of age group over participants sex for patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

5.2 Prevalence of infection, sepsis and septic shock

Of all the admissions 193(64.8%) of patients had suspected or confirmed infection of which pneumonia, including both community and hospital acquired, were found in 105(35.2%) accounting for more than half (54.4%) of all infections, followed by intra-abdominal infections which account for 21.8% of all. Skin and soft tissue infection is placed in the third place with 15.5% prevalence among patients with infection and it mainly occurs in the form of surgical site infections, diabetic foot ulcers, Tetanus and necrotizing fasciitis. Overall hospital acquired infections were documented in 71 patients.

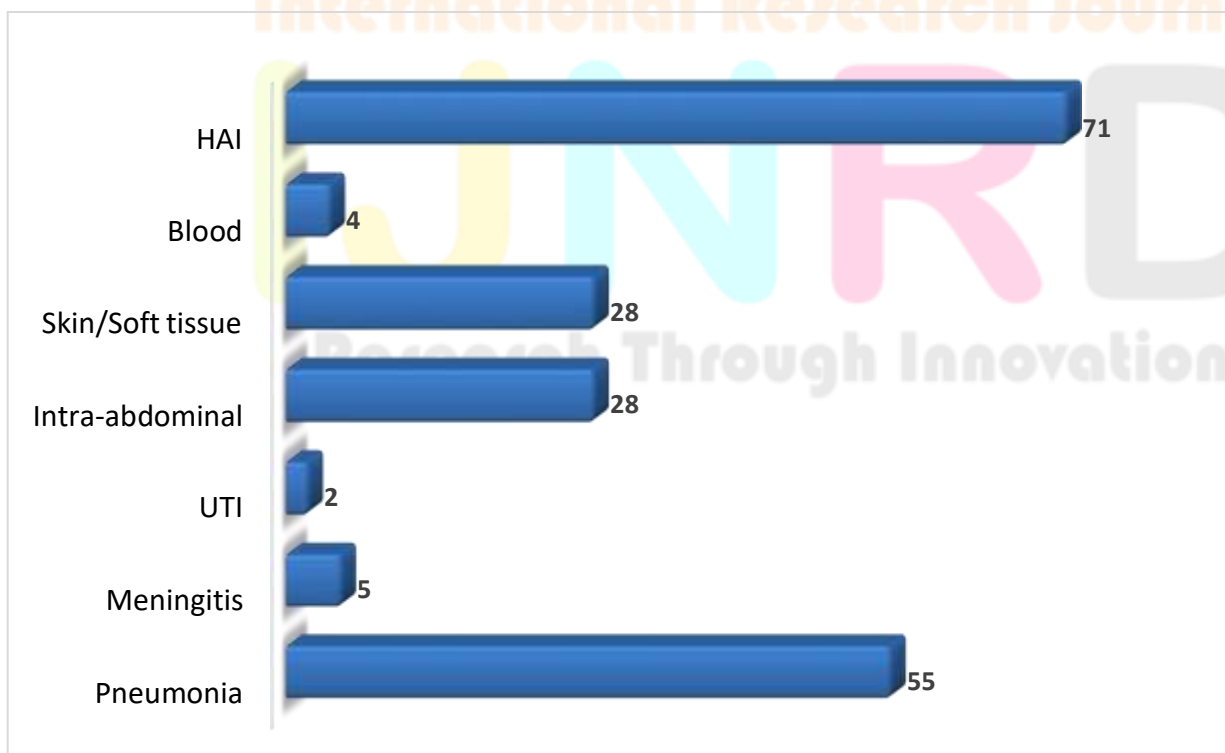


Figure 4: Bar chart showing frequency of sites of infection amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Culture was done in 31(10.7%) patients from blood, endotracheal tube aspirate and urine and among them 15(48.4) patients were reported to have positive culture result. The most commonly identified organism being *Proteus* species which was found in 7 out of the 15 positive results. *E. coli*, *Shewanella* species, *Acinetobacter Baumannii* accounts for 3,2 and 2 cases respectively. Overall Presence of positive or negative culture result were not found to be significantly associated with sepsis and septic shock based on chi square test.

Of all patients with infection (n=193), using modified sequential organ failure assessment (mSOFA), 142(73.58%) patients were found to have sepsis of which 55(38.5%) patients had septic shock. Of total admission the prevalence of sepsis was 47.7%. Among patients with infection, only 26.42% of patients had no sepsis.

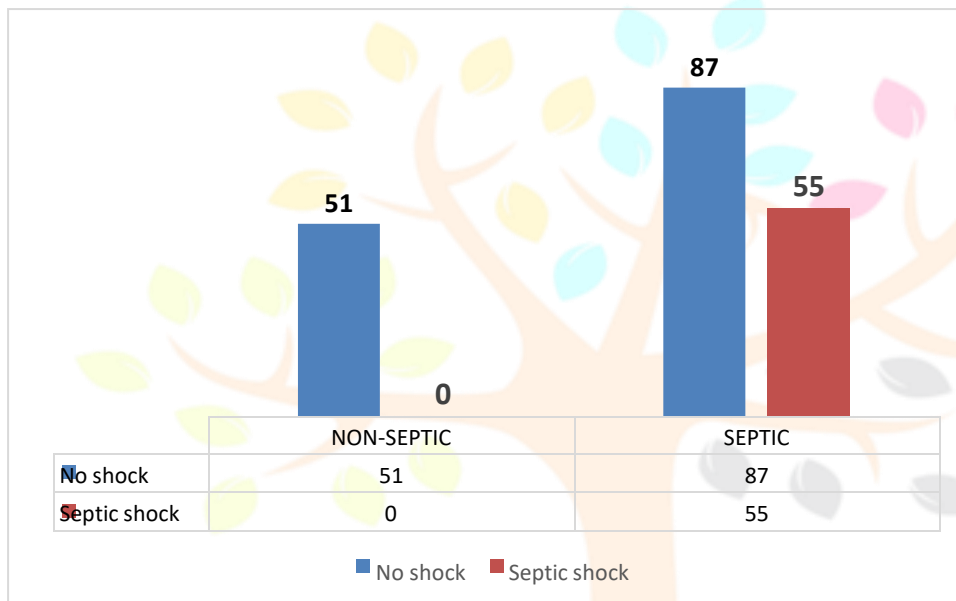


Figure 5: clustered bar chart showing frequency of sepsis and septic shock amongst patients with infection amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

5.2.1 : SOCIODEMOGRAPHIC FACTORS

Overall the median age at the diagnosis of sepsis and septic shock was 41.3 and 40.9 respectively. Patients within the age 18 through 44 was the found to be mostly affected group and account for 49.3 % of sepsis and 62.8% of septic shock and age was found to be significant ($p < 0.05$) for infection and sepsis but without significant directional measure and had not such significant association with septic shock.

As shown in Annex 2, Female patients had greater burden of infection (51.3%), sepsis (52.8%) and septic shock (68.6%) while having younger median of age at the diagnosis of both sepsis and septic shock (35 Vs 48) for sepsis and (35 Vs 40) for septic shock. Sex was found to have significant association ($p < 0.05$) with septic shock in chi square test

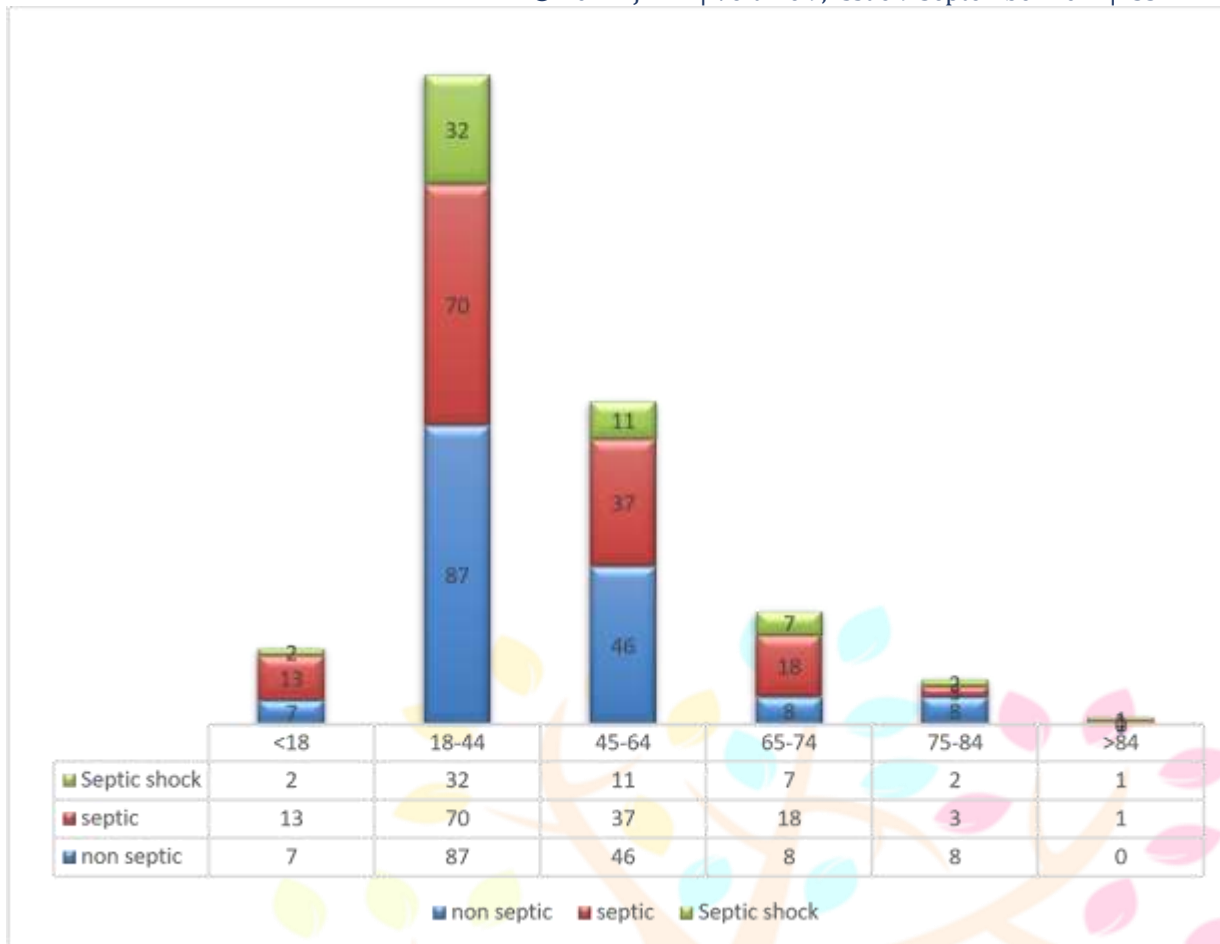


Figure 6: bar graph showing distribution of septic patients across different age groups amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC.

5.2.2 PATTERNS OF ADMISSION AND LABORATORY MARKERS

Most of admitted patients were Medical (55%) followed by Surgical patients with 38.3% and Gyn/Obs patients accounting for 6.7% of all admission. Admission diagnosis (medical, surgical or Gyn/Obs) was significantly associated with both infection and sepsis ($P < 0.05$) on chi squared test. Medical patients had 62% of all the infection across the departments while the department account for 55% of all admissions. Septic shock was not found to have significant association with admitting department or diagnosis.

Of all admissions 77.5% of patients were admitted within 48 hours of presentation to the triage while the rest was admitted after 48 hours and the duration of in hospital stay from triage to ICU admission (early Vs late) is found to be significant ($p < 0.05$) for infection, sepsis and septic shock in chi square test

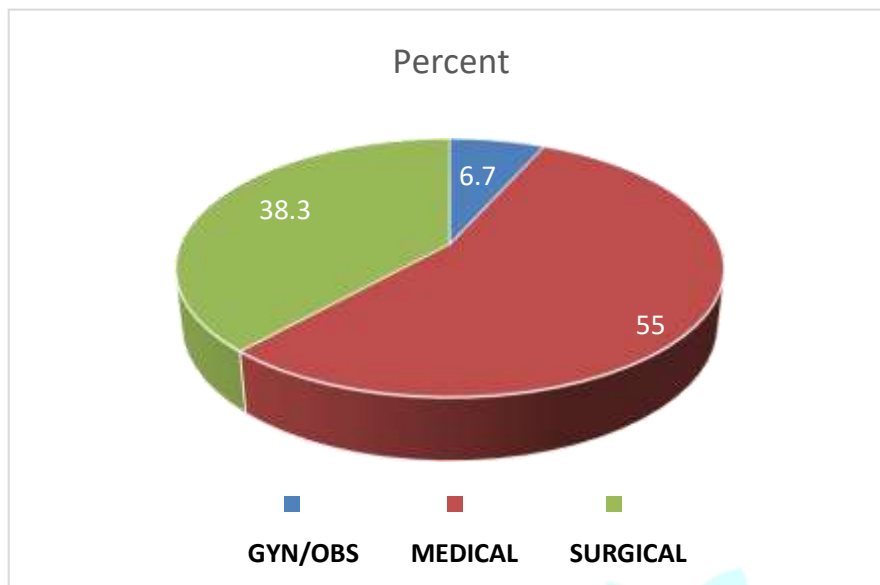


Figure7: Pie chart showing the pattern of patient admission to central ICU of AHMC from October 2021 and July 2023 GC with respect to department.

Platelets count were grouped according to sequential organ failure assessment (SOFA) criteria and was found to be significant ($p < 0.05$) for infection, sepsis and septic shock. Amongst the other laboratory investigations hemoglobin, WBC, neutrophil count, serum levels of sodium and chloride, AST and bilirubin were shown to be significant ($p < 0.05$) in independent sample t-test after checked by Leven's test for deciding whether to accept or decline the assumption of equality of variance within each continuous variable. After applying the same procedure none of the aforementioned variables along with lymphocyte count, ALT and potassium level were not found to have significant association with septic shock.

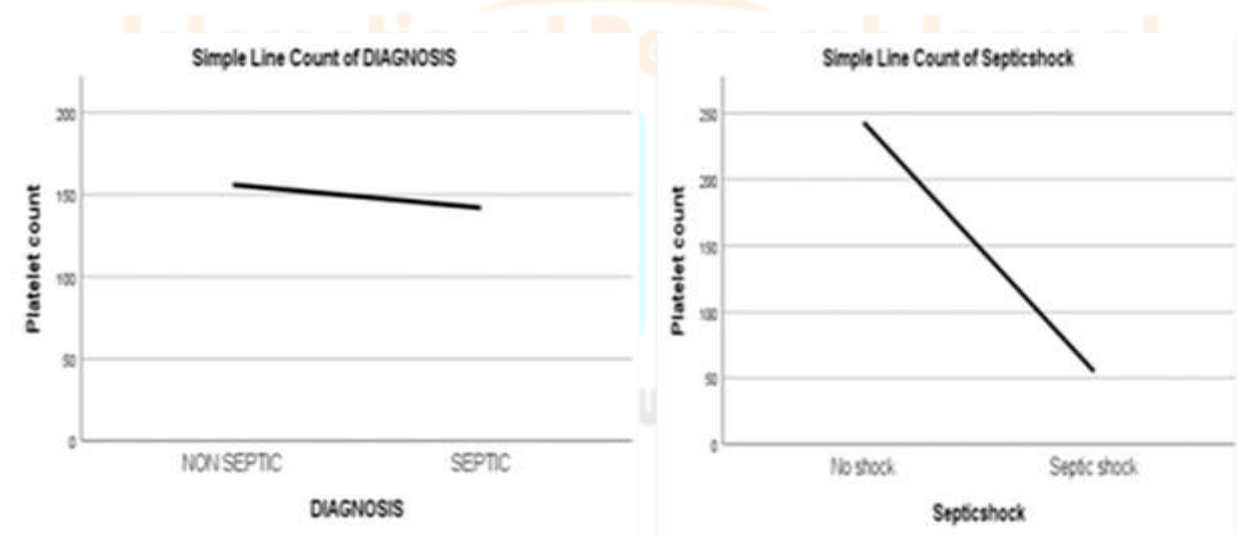


Figure 8: A- simple line graph showing distribution of platelet count over septic and non-septic patients, B- simple line graph showing distribution of platelet count over patients with and without septic shock amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Table 3: independent sample t-test result for continuous variables and sepsis amongst patientsadmitted to central ICU of AHMC from October 2021 and July 2023 GC

VARIABLE	LEVINE'S TEST	T-TEST FOR EQUALITY	DF	SIG. (2-TAILED)
PLATELET	3.097	3.899	288	0
		3.124	118.003	0.002
HEMOGLOBIN	7.686	4.423	280	0
		4.827	246.382	0
WBC	12.468	-1.837	288	0.067
		-2.196	287.71	0.029
LYMPHOCYTES	4.788	-0.789	286	0.431
		-1.061	216.879	0.29
NEUTROPHIL	6.763	-1.495	288	0.136
		-1.753	287.165	0.081
POTASSIUM	0.007	-1.152	231	0.251
		-1.101	128.016	0.273
SODIUM	5.723	-1.573	231	0.117
		-1.967	229.869	0.05
CHLORIDE	4.733	-1.672	216	0.096
		-2.201	214.567	0.029
AST	1.316	-0.971	119	0.334
		-1.187	70.165	0.239
ALT	6.188	1.137	119	0.258
		0.845	33.287	0.404
BILIRUBIN	0.802	-0.902	22	0.377
		-1.506	4.94	0.193

KEY: Shaded - Equal variances is assumed

Non-shaded - Equal variances not assumed

5.2.3 COMORBIDITIES

Among the comorbidities Hypertension was the most common with 14.1% followed by Diabetes mellitus which accounted for 12.8 % and CHF with 10.1%. Retroviral infection was present in 6 % of patients.

Among the comorbidities HIV/AIDS and hypertension was found to be significant ($p < 0.05$) for infection, sepsis and septic shock with hypertension having statistically significant negative directional measure with all the three outcomes in the chi square test. Heart failure was significantly associated with infection and sepsis($p < 0.05$) while diabetes millets and chronic liver disease was significant ($p < 0.05$) only for septic shock. Asthma, CKD and malignancy were not found to be significant in the chi square test.

Table 4: frequency and Pearson chi-square test result for comorbidities amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

COMORBIDITIES	SEPSIS			SEPTIC SHOCK		
	YES	NO	P-VALUE	YES	NO	P-VALUE
ASTHMA, N (%)						
YES	2(1.4)	2(1.3)	0.925	2(3.6)	2(0.8)	0.102
NO	140(98.6)	154(98.7)		53(96.4)	241(99.2)	
CHF, N (%)						
YES	7 (4.93)	23 (14.74)	0.005	2 (3.64)	28 (11.52)	0.079
NO	135 (95.07)	133 (85.26)		53 (96.36)	215 (88.48)	
CKD, N (%)						
YES	5(3.5)	4(2.6)	0.63	0	9(3.7)	0.147
NO	137(96.5)	152(97.4)		55(100)	234(96.3)	
CLD, N (%)						
YES	2(1.4)	1(0.6)	0.507	2(3.6)	1(0.4)	0.031
NO	140(98.6)	155(99.40)		53(96.4)	242(99.6)	
DM, N (%)						
YES	22(15.5)	16(10.3)	0.176	13(13.7)	25(10.3)	0.014
NO	120(84.5)	140(89.7)		42(76.4)	218(89.7)	
HYPERTENSION, N (%)						
YES		0.001			203	
	132 (92.96)	124 (79.49)		(96.36)	(83.54)	0.014
NO	10 (7.04)	32 (20.51)		2 (3.64)	40 (16.46)	
HIV, N (%)						
YES	14 (9.86)	4 (2.56)	0.008	47 (85.45)	233 (95.88)	0.003
NO	128 (90.14)	152 (97.44)		8 (14.55)	10 (4.12)	
MALIGNANCY, N(%)						
YES	2(1.4)	2(1.3)	0.925	2(3.6)	2(0.8)	0.102
NO	140(98.60)	154(98.7)		53(96.4)	241(99.2)	
OTHER ^A , N (%)						
YES	9(6.3)	10(6.4)	0.98	8(14.5)	14(5.8)	0.361
NO	133(93.7)	146(93.6)		47(85.5)	229(94.2)	
MORE THAN ONE, N(%)						
YES	9(6.3)	18(11.5)	0.118	4(7.3)	23(9.5)	0.609
NO	133(93.7)	138(88.5)		51(92.7)	220(90.5)	

^AHyperthyroid, pregnancy psychiatric d/o, epilepsy, atrial fibrillation.

5.2.4 TREATMENT PROVIDED AND DURATION OF STAY

Of all admissions 177 patients were on mechanical ventilator at some point of time during their ICU stay and among them 133 had infection of which 108 had sepsis with 40 patients diagnosed with septic shock, accounting for 69%, 76% and 72.8% of all infections, sepsis and septic shock respectively. Whether the patient required for mechanical ventilation or not was found to be significant ($p < 0.05$) for both infection and sepsis and septic shock.

Among the admitted patients 239 (80.2%) took at least one antibiotic and Ceftriaxone, Metronidazole, Vancomycin, and Ceftazidime were the most frequently prescribed antibiotics in specific order. As shown in figure 8, Patients with sepsis were found to be accountable for 75% of overall antibiotic prescribed. furthermore, septic patients took most of antibiotics which are not prescribed frequently including Meropenem, Chloramphenicol and iv ciprofloxacin.

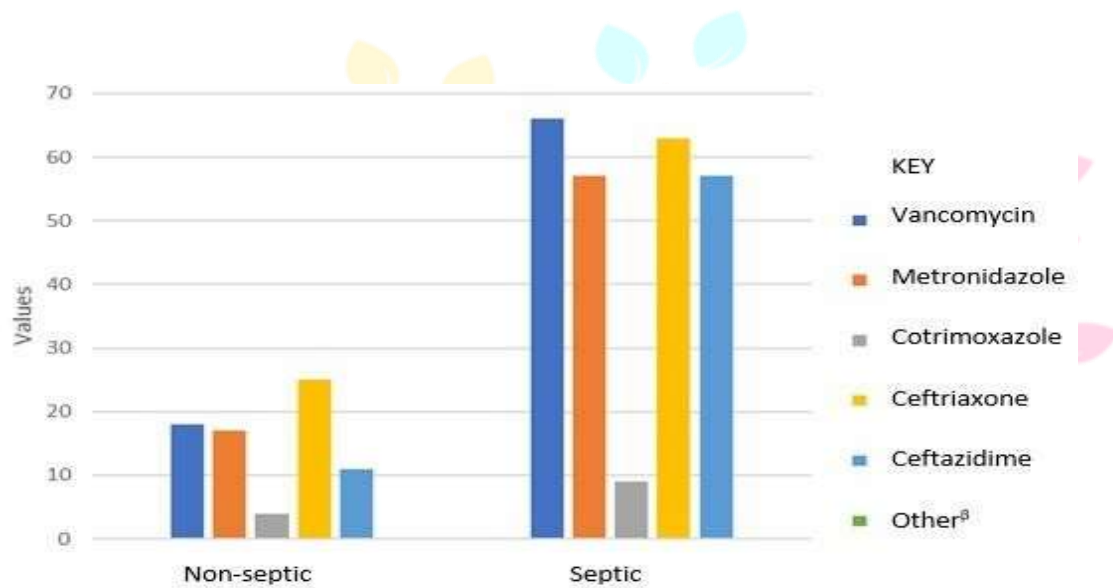


Figure 9: Pattern of antibiotic prescription among patients with suspected/confirmed infection amongst patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

The mean duration of stay was 6 days (95% CL, 5-7 days) and the longest stay was 62 days. Duration of stay was found to have significant ($p < 0.05$) association with infection in independent samples t-test, but significant association was not found for cases with sepsis and septic shock.

5.1. Binary logistic regression

5.3.1 SEPSIS

After identification of variables that have significant association with the outcome variables through chi square test and independent samples t-test, the significant variables were analyzed using binary logistic regression after going through tests to confirm absence of multicollinearity and presence of linear relationship between the logit of the dependent variable and the independent variables.

The model exhibited good overall fit, as indicated by Cox and Snell R^2 (0.50) and Nagelkerke R^2 (0.66) values. Furthermore, the Omnibus tests of model coefficients (p value 0.05) indicated that the logistic regression model significantly explained the variation in sepsis occurrence. In addition, classification table have showed high

sensitivity (86.7%) and specificity (83.4%) of the model with 85.0% overall accuracy.

The odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated to determine the strength and direction of the relationship between independent variables and the likelihood of sepsis and septic shock. The odds ratio represents the change in odds of the dependent variable for every unit change in the independent variable.

The crude and adjusted odds and p value for independent variables are shown in the **Table 4** below. Overall the findings indicate that platelet count had AOR 0.991 (95% CI: 0.980-0.998). White blood cell count AOR 1.7 (95% CI: 1.14-2.60), serum Sodium level with AOR 0.91 (95% CI: 0.87-0.96) and serum chloride levels showed AOR 1.11 (95% CI: 1.04- 1.18) all with significant p-value of <0.05. Patients with pneumonia and intra-abdominal infections had higher odds of sepsis with AOR 18.7(95% CI: 6.1-56) and AOR 16(95% CI: 4.36-61.6) respectively.

5.3.2 SEPTIC SHOCK

After going through the same procedures, binary logistic regression model with good overall fit, as indicated by Cox and Snell R^2 (0.55), Nagelkerke R^2 (0.74) values and the Omnibus tests of model coefficients (p value 0.05) with 69.8% sensitivity, 91.1% specificity with 87% overall accuracy, altogether showing that the logistic regression model significantly explained the variation in occurrence of septic shock. **Table 5** presents the Crude and adjusted ORs and pvalues for each predictor variable. Male gender showed significant negative association with AOR of 0.19 (95% CI: 0.07-0.46). mSOFA score had positive association with AOR 3.25 (95% CI: 2.04-5.17) and also on ROC it had area under curve of 0.82(95% CI: 0.76-0.88) and significant p value. Among the laboratory markers lower platelet and lymphocyte count showed significant association with AOR 0.98(95% CI: 0.98-0.99) and AOR 0.65(95% CI: 0.42-0.99) for platelet and lymphocyte count respectively. Finally, being on mechanical ventilator was found to have AOR 0.2(95% CI: 0.08-0.48).

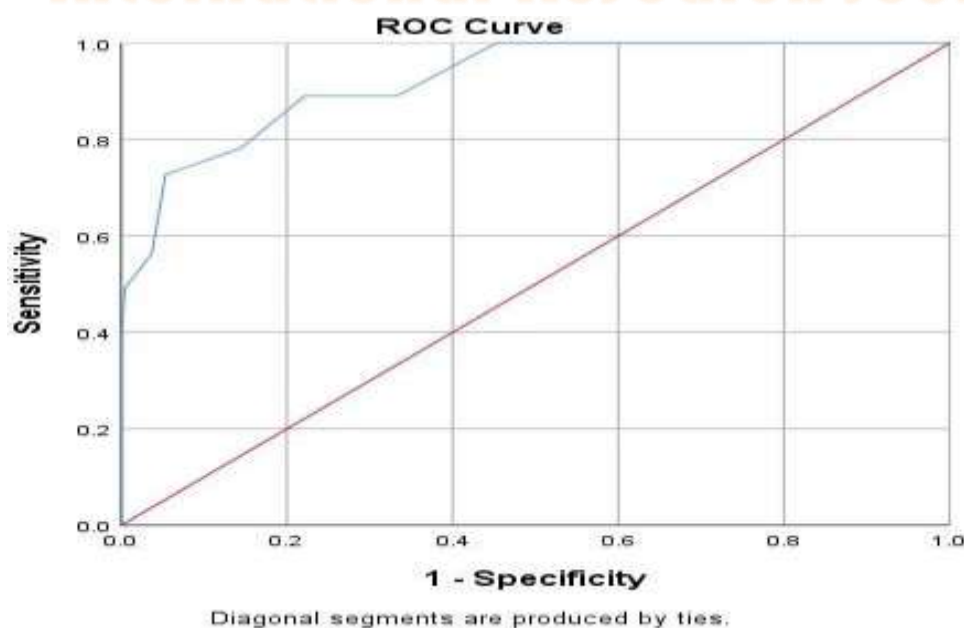


Figure 10: ROC result for MSOFA and septic shock for patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Table 5: Binary logistic regression for sepsis and selected independent variables for patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Variables		COR (95% CI)			AOR (95% CI)			P-value
COR Lower		Upper			AOR Lower Upper			
Ventilation	Mechanically ventilated	4.12	2.49	6.81	2.92	1.12	7.63	0.02
Infection	pneumonia	10.06	5.65	17.92	18.70	6.15	56.85	0.00
Intra-abdominal		3.19	1.56	6.51	16.39	4.36	61.64	0.00
Nosocomial		7.59	3.92	14.68	2.84	0.93	8.60	0.06
CBC	Hemoglobin	0.86	0.8	0.94	0.95	0.82	1.10	0.53
	WBC	1.35	1.07	1.70	1.72	1.14	2.60	0.01
Platelet		0.99	0.99	0.99	0.99	0.98	0.99	0.00
Electrolytes	Sodium	1.04	1.01	1.07	0.91	0.87	0.96	0.00
Chloride		1.06	1.03	1.09	1.11	1.04	1.18	0.00
Comorbidities	Hypertensive	0.29	0.13	0.62	0.26	0.07	1.00	0.05
	CHF	0.3	0.12	0.72	0.61	0.14	2.62	0.50
	HIV	4.15	1.33	12.94	0.55	0.08	3.74	0.54

Table 6: Binary logistic regression for septic shock and selected independent variables for patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

Variables		COR (95% CI)			AOR (95% CI)			Pvalue
		COR Lower Upper			AOR Lower Upper			
Gender	Male	0.49	0.27	0.89	0.19	0.07	0.46	0.00
Infection	Intra-abdominal	0.26	0.13	0.52	1.71	0.62	4.71	0.293
Skin/Soft tissue		0.24	0.11	0.54	3.40	0.99	11.70	0.052
CBC	Lymphocyte	0.59	0.42	0.83	0.65	0.42	0.99	0.047
	Platelet	0.99	0.99	0.99	0.98	0.98	0.991	0.00
Comorbidities	HIV	3.97	1.49	10.58	4.00	0.91	17.57	0.065
	Hypertensive	0.19	0.04	0.82	0.43	0.05	3.12	0.405
	Diabetic	2.70	1.28	5.70	3.30	0.82	13.33	0.093
Organ failure	MSOFA	26.69	10.64	66.96	3.25	2.04	5.17	0.00

6. DISCUSSION

In this retrospective chart review, it was shown that the prevalence of infection, sepsis and septic shock to be 64.8%, 47.7% and 18.5% respectively. When compared to the data from intensive care over nations (ICON) audit it was higher than the global prevalence which was 29.5% (varies between 13.6 to 39.6 in different regions) (25) and found to be comparable with that of Australia, Asia and Middle east (26).

Again, the prevalence of septic shock 18.5 % were found to be higher than that of Europe and North America which was shown to be 10.4%. (27) and it was also higher than some published local studies including Tikur Anbesa Specialized Hospital (TASH) which had prevalence of 14%. (37), 8.9 % from a study conducted in multiple ICUs in Addis Abeba (60) and 7.7% another study from southern Ethiopia done in three teaching hospitals (38).

On this study the median age at the diagnosis of sepsis was 41.3 and 40.9 years respectively, which is in contrary to the general principle which holds that sepsis is disease of elderly which is true for high income countries with mean age of ranging from 63 to 67 years on different studies, with older population disproportionately (13.1times) affected than the young(61,62).but interestingly the lower age, like in this study, seems the case in sub-SaharanAfrica as shown by a systemic review and meta-analysis of fifteen studies(23).

Generally male patients are prone to sepsis and septic shock than female patients although this is from clinical observations with low level of evidence and the incriminated factor for this observation was both social factors like risk of infection and exposure to violence and biological factors i.e. hormonal and immune system features (63). Our finding was out of what is generally expected with neither sex having significant association with sepsis and males having negative association with septic shock. There are few studies with similar finding with this finding of ours (64).

According to the finding in this study pneumonia was the most common site of infection and source of sepsis followed by intra-abdominal infection and this finding was in line with most of the studies (35,60,65,66). Unlike most studies but agreeing with our finding, the result from sub group analysis from multicenter prospective cohort FORCAST study of acutely ill patients at 59 ICU in Japan(2016-2017) showed that intra-abdominal infection was found to have significant association with septic shock and was commonest site among patients with septic shock (72%) ,while pneumonia was the most common site of infection in patients with sepsis without shock(67). in the contrary to this another retrospective, multicenter cohort study which was done in 29 ICU from Canada, USA and Saudi Arabia reported pneumonia was the most common and with significant association with septic shock (68).

According to several studies sepsis is the most expensive medical condition and among the reasons for the higher cost longer duration of stay and multiple treatment provided including antibiotics were of significant value medication alone accounting for 15-25% of the total cost (21,69,70). in this study the duration of ICU stays and number and type of antibiotics used was computed as means to compare the relative cost of sepsis and the findings was septic patients had longer duration of stay than non-septic patients, in addition septic patients were the reasonfor 75% of prescribed antibiotics, suggesting the higher cost of sepsis.

This RCR showed that being on mechanical ventilator, low platelet, higher white cell count, decreased Sodium and higher chloride levels are significant risk factors for development of sepsis and this finding are heavily supported by findings from other studies. Several studies have investigated the potential risk factors for the development of sepsis, and the findings consistently support the association between certain factors and the onset of sepsis.

the association between being on a mechanical ventilator and an increased risk of sepsis was one of the key findings in the systematic review by M. Fathi et al. in 2019Gc (43) the authors reported that patients who required mechanical ventilation had a significantly higher likelihood of developing sepsis compared to those who did not require this intervention. This result emphasizes the importance of monitoring ventilated patients closely, as they may be more susceptible to sepsis.

Moreover, low platelet counts (thrombocytopenia) were also identified as a significant risk factor for sepsis development in our study but on Receiver operating Characteristic (ROC) it showed a small area under the curve (AUC) which failed to reject the null hypothesis “AUC is equal to 0.5”, and according to this model taking the standard cut off value of 150 thousand only had 52% sensitivity and 11% specificity for sepsis. Thrombocytopenia was included in the sequential organ failure assessment criteria which is used to define organ dysfunction in septic patients according to sepsis 3 definition of sepsis which was formulated by a group of experts based on previous data and consensus (4).

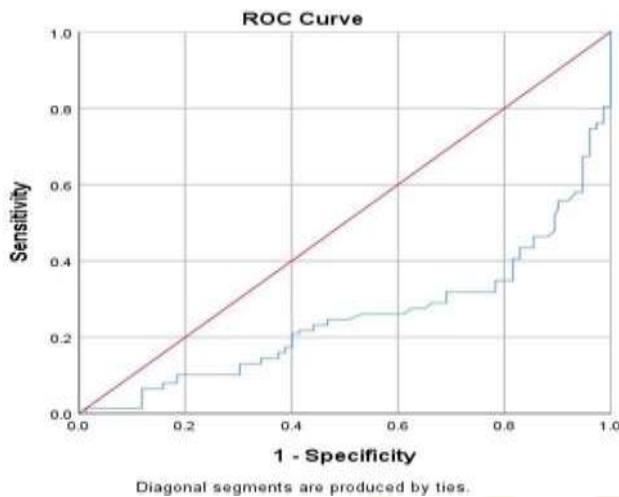


Figure 11: ROC result for platelet count and sepsis shock for patients admitted to central ICU of AHMC from October 2021 and July 2023 GC

The other hematological finding was higher white cell counts which was shown to associate with sepsis in several studies (50,51). In addition, leukocytosis was among the SIRS criteria which again, was diagnostic tool of sepsis before the introduction of sepsis 3 definition of sepsis. in our model WBC count showed AUC of 0.56 (95% CI: 0.49-0.63) and at the cut off point for leukocytosis based on our institution's laboratory i.e. 10 thousand this model showed 65% sensitivity and 45% specificity for sepsis.

Furthermore, decreased sodium levels (hyponatremia) and higher chloride levels (hyperchloremia) were shown to be significantly associated with sepsis development (52–55). These electrolyte imbalances may reflect the severity of the underlying infection and its impact on the body's homeostasis. our model had AUC OF 0.60 (95% CI: 0.50-0.71) and 0.74(95% CI:0.65-0.83) for sodium and chloride respectively.

Furthermore, mSOFA score also showed significant odd for occurrence of septic shock. The second aspect explored in the study is the association between the mSOFA score and septic shock occurrence. Since the definition of septic shock was part of the score which partly explain this finding the non-hemodynamic components of the score was computed in binary logistic regression excluding the total score and the Glasgow coma score (GCS) was found to have significant ($p < 0.05$) association with septic shock with odds ratio of 1.7 (95% CI: 1.1-1.6). an evidence going along our finding was a systematic review published in the Egyptian journal of hospital medicine (71) showed significant association between GCS and septic shock.

7. LIMITATIONS

This study has several limitations:

- **Retrospective Chart Review (RCR) and Sample Size:** The use of RCR relies on the accuracy and completeness of medical records. The relatively small sample size may limit the generalizability of the findings to other populations.
- **Limited Investigation Details:** The study was unable to comprehensively address details of investigations like cultures and sensitivities due to missing information in the medical records.
- **Model Performance:** The Area Under the Curve (AUC) for some of the predictive variables in the model was low. This could be due to several factors, including the small sample size and potential for other unmeasured variables influencing the outcome.

8 CONCLUSION AND RECOMMENDATION

8.1 Conclusion

This study highlights the higher prevalence of sepsis and septic shock in Adama Hospital Medical College's central intensive care unit compared to high-income countries. The relatively younger population affected by these conditions and when its high mortality rate in this study (69% for sepsis and 89% for septic shock) it raises a concern about the potential long-term consequences on public health and Economic effect on the country. Continued research, awareness, and targeted interventions are essential to address the growing burden of sepsis and septic shock in resource-limited settings and improve patient outcomes.

8.2 Recommendation

For health care workers

- ✦ Following appropriate infection preventive measures
- ✦ Frequent monitoring based on stratification of individual risk group and early identification of infection and initiation of timely and appropriate interventions
- ✦ Utilization of standardized evidence-based investigations including Culture and rather than using liver enzymes, to assess organ dysfunction in patients with infection its recommended to use serum bilirubin, which is of significant value as evidenced by its inclusion in SOFA score.

Researchers

- ✦ Given the significant knowledge gap, its highly recommended to have a continues researches and generation of recommendations in this highly prevailed and highly fatal entity.

For governing body of AHMC

- ✦ To have the staff members have adequate knowledge and commitment towards infection prevention and facilitate trainings when needed.

- ✦ Providing appropriate and necessary investigation and management modalities.

For Policy makers and MoH

- ✦ Making timely, appropriate and practical policy and mobilization of resources necessary to prevent and manage this significant problem.

REFERENCE

1. Majno G. w d. 1870;937–45.
2. Gyawali B, Ramakrishna K, Dhamoon AS. Sepsis : The evolution in definition , pathophysiology , and management. 2019;
3. June VINI, Supreme S, Justice C, Stewart P. editorials. Chest [Internet]. 1992;101(6):1481–3. Available from: <http://dx.doi.org/10.1378/chest.101.6.1481>
4. Opal SM, Rubenfeld GD, Poll T Van Der, Vincent J, Angus DC. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). 2016;315(8):801–10.
5. Jones J, Jephson AR, Jr JFO. NIH Public Access. 2013;
6. ABOUT US ▼ WHAT IS SEPSIS ? – DEFINITION OF SEPSIS SEPSIS - EXPLAINED IN 3 MINUTES SEPSIS - A GLOBAL HEALTH CRISIS SEPSIS - COMMON CAUSES SEPSIS - SYMPTOMS SEPSIS - RISK GROUPS POSTSEPSISSYMPTOMS (PSS) WORLD SEPSIS DAY - SEPTEMBER 13. :19.
7. Sexton DJ, Disclosures C. Pathophysiology of sepsis. 2023;
8. Huang M, Cai S, Su J. The Pathogenesis of Sepsis and Potential Therapeutic Targets.2019;20(21).
9. Ford H, Systems H, Re- CW. The Ne w E n g l a n d Jour n a l o f Me d i c i n e EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS ANDSEPTIC SHOCK. 2001;345(19):1368–77.
10. GLOBAL REPORT ON THE EPIDEMIOLOGY AND BURDEN OF SEPSIS Current evidence , identifying gaps and future directions.
11. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global , regional , and national sepsis incidence and mortality , 1990 – 2017 : analysis for the Global Burden of Disease Study. Lancet [Internet]. 2020;395(10219):200–11. Available from: [http://dx.doi.org/10.1016/S0140-6736\(19\)32989-7](http://dx.doi.org/10.1016/S0140-6736(19)32989-7)
12. Struzek CF, Mellhammar L, Rose N, Cassini A, Rudd KE, Schlattmann P, et al. Incidence and mortality of hospital - and ICU - treated sepsis : results from an updated and expanded systematic review and meta - analysis. Intensive Care Med [Internet]. 2020;46(8):1552–62. Available from: <https://doi.org/10.1007/s00134-020-06151-x>

13. Harrison DA, Rubenfeld GD, Rowan K, Thomas S, Foundation NHS, Offices ICUS, et al. Epidemiology of sepsis and septic shock in critical care units : comparison between sepsis-2 and sepsis-3 populations using a national critical care database. BJA [Internet]. 2017;119(4):626–36. Available from: <http://dx.doi.org/10.1093/bja/aex234>
14. Peres Bota D, Lopes Ferreira F, Mélot C, Vincent JL. Body temperature alterations in the critically ill. Intensive Care Med. 2004 May;30(5):811–6.
15. Kreger BE, Craven DE, McCabe WR. Gram-negative bacteremia. IV. Re-evaluation of clinical features and treatment in 612 patients. Am J Med. 1980 Mar;68(3):344–55.
16. Thiery-Antier N, Biquet C, Vinault S, Meziani F, Boisramé-Helms J, Quenot J-P. Is Thrombocytopenia an Early Prognostic Marker in Septic Shock? Crit Care Med. 2016 Apr;44(4):764–72.
17. van Vught LA, Wiewel MA, Klein Klouwenberg PMC, Hoogendijk AJ, Scicluna BP, Ong DSY, et al. Admission Hyperglycemia in Critically Ill Sepsis Patients: Association With Outcome and Host Response. Crit Care Med. 2016 Jul;44(7):1338–46.
18. Krieger JN, Kaiser DL, Wenzel RP. Urinary Tract Etiology of Bloodstream Infections in Hospitalized Patients. J Infect Dis [Internet]. 1983 Jul 1;148(1):57–62. Available from: <https://doi.org/10.1093/infdis/148.1.57>
19. Berg M Van Den, Beuningen FE Van, Maaten JC, Bouma HR. Hospital-related costs of sepsis around the world : A systematic review exploring the economic burden of sepsis. J Crit Care [Internet]. 2022;71:154096. Available from: <https://doi.org/10.1016/j.jcrc.2022.154096>
20. Buchman TG, Simpson SQ, Sciarretta KL, Finne KP, Sowers N, Collier M, et al. Sepsis Among Medicare Beneficiaries: 1. The Burdens of Sepsis, 2012–2018*. 2020;48(3):2012–8.
21. Paoli CJ, Reynolds MA, Sinha M, Gitlin M, Crouser E. Epidemiology and Costs of Sepsis in the United States—An Analysis Based on Timing of Diagnosis and Severity Level*. 2013;(5):1889–97.
22. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb;315(8):801–10.
23. Lewis JM, Feasey NA, Rylance J. Aetiology and outcomes of sepsis in adults in subSaharan Africa : a systematic review and meta-analysis. 2019;1–11.
24. Shankar-hari M, Rubenfeld GD. Understanding Long-Term Outcomes Following Sepsis : Implications and Challenges. Curr Infect Dis Rep [Internet]. 2016; Available from: <http://dx.doi.org/10.1007/s11908-016-0544-7>
25. Sakr Y, Jaschinski U, Wittebole X, Szakmany T, Lipman J, Namendys-silva SA, et al. Sepsis in Intensive Care Unit Patients : Worldwide Data From the Intensive Care over Nations Audit. 2012;1–9.

26. Vincent J, Sakr Y, Angus DC. Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017 Main Outcomes and Measures Study Design. 2017;(September).
27. Vincent J, Jones G, David S, Olariu E, Cadwell KK. Frequency and mortality of septic shock in Europe and North America : a systematic review and meta-analysis. 2019;1– 11.
28. Vincent J-L, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: Results of the SOAP study*. Crit Care Med [Internet]. 2006;34(2). Available from: https://journals.lww.com/ccmjournal/Fulltext/2006/02000/Sepsis_in_European_intensive_care_units_Results.10.aspx
29. Baykara N, Akalin H, Arslantas MK, Hanci V, Caglayan C, Kahveci F, et al. Epidemiology of sepsis in turkish intensive care units: A multicenter point-prevalance study. Crit Care [Internet]. 2017;21(1 Supplement 1):1–14. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexb&NEWS=N&AN=619526449>
30. Singh K, Hariharan S, Ventour D, Chen DR, Merritt-charles LG, Sookwah M, et al. Epidemiology and Management Trends of Patients With Sepsis and Septic Shock in the Intensive Care Unit : A Prospective Trial in the Caribbean. 2020;12(10).
31. The top 10 causes of death. 2023;2023.
32. Adhikari NKJ, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet. 2010;376(9749):1339–46.
33. Lewis JM, Abouyannis M, Katha G, Nyirenda M, Chatsika G, Feasey NA, et al. Population incidence and mortality of sepsis in an urban African setting, 2013–2016.Clin Infect Dis. 2020;71(10):2547–52.
34. Kwizera A, Urayeneza O, Mujiyarugamba P, Baelani I, Meier J, Mer M, et al. Epidemiology and Outcome of Sepsis in Adults and Children in a Rural, Sub-Sahara African Setting. Crit Care Explor. 2021;3(12):e0592.
35. Mulatu HA, Bayisa T, Worku Y, Lazarus JJ, Woldeyes E, Bacha D, et al. Prevalence and outcome of sepsis and septic shock in intensive care units in Addis Ababa, Ethiopia: A prospective observational study. African J Emerg Med [Internet]. 2021;11(1):188–95. Available from: <https://doi.org/10.1016/j.afjem.2020.10.001>
36. Worku A, Sultan A, Selassie L, Shumet A, G/Selassie K, Bekele A, et al. Shock in an Ethiopian Medical Intensive Care Unit: Characteristics and Outcomes at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia. :A3692–A3692.
37. Of C, Science H. 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. 2017;
38. Mekonnen S, Assen S, Yinges M, Basu B. Survival and predictors of mortality among patients admitted to the intensive care units in southern Ethiopia : A multi-center cohort study. Ann Med Surg [Internet].

39. OUTCOMES AND ASSOCIATED FACTORS OF PATIENTS ADMITTED TO MEDICAL INTENSIVE CARE UNIT IN FELEGE HIWOT REFERRAL. 2022;
40. Smith ZA, Ayele Y, Mcdonald P. Outcomes in critical care delivery at Jimma University Specialised Hospital , Ethiopia. 2013;363–8.
41. Sepsis [Internet]. Available from: <https://www.who.int/news-room/factsheets/detail/sepsis>
42. Sepsis - Symptoms and causes - Mayo Clinic [Internet]. Available from: <https://www.mayoclinic.org/diseases-conditions/sepsis/symptoms-causes/syc20351214>
43. Fathi M, Markazi-Moghaddam N, Ramezankhani A. A systematic review on risk factors associated with sepsis in patients admitted to intensive care units. Aust Crit Care [Internet]. 2019;32(2):155–64. Available from: <https://doi.org/10.1016/j.aucc.2018.02.005>
44. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: Secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. Crit Care. 2006;10(2):1–10.
45. Merali NM. PREVALENCE AND INCIDENCE OF INFECTIONS AND SEPSIS IN CRITICAL CARE. 2021;
46. Cecconi M, Evans L, Levy M, Rhodes A. Sepsis and septic shock. Lancet [Internet]. 2018;392(10141):75–87. Available from:[http://dx.doi.org/10.1016/S01406736\(18\)30696-2](http://dx.doi.org/10.1016/S01406736(18)30696-2)
47. Karlsson S. Incidence , treatment , and outcome of severe sepsis in ICU-treated adults in Finland : the Finnsepsis study. 2007;(January):435–43.
48. León AL, Hoyos NA, Barrera LI, De La Rosa G, Dennis R, Dueñas C, et al. Clinical course of sepsis, severe sepsis, and septic shock in a cohort of infected patients from ten Colombian hospitals. BMC Infect Dis. 2013;13(1).
49. Kustán P, Horváth-szalai Z, Mühl D. Nonconventional markers of sepsis. 28:122–33.
50. Anggraini D, Hasni D, Amelia R. Pathogenesis of Sepsis. :332–9.
51. Mammen EF. The haematological manifestations of sepsis. 1998;17–24.
52. Suetrong B, Pisitsak C, Boyd JH, Russell JA, Walley KR. Hyperchloremia and moderate increase in serum chloride are associated with acute kidney injury in severe sepsis and septic shock patients. Crit Care [Internet]. 2016;1–8. Available from: <http://dx.doi.org/10.1186/s13054-016-1499-7>

53. Filis C, Vasileiadis I, Koutsoukou A. Hyperchloraemia in sepsis. *Ann Intensive Care* [Internet]. 2018; Available from: <https://doi.org/10.1186/s13613-018-0388-4>
54. Boston VE. Hyponatraemia and Intracellular Water in Sepsis: An Experimental Comparison of the Effect of Fluid Replacement With Either 0.9% Saline or 5% Dextrose. *By*. 1990;25(4):422–5.
55. Padhi R, Panda BN, Jagati S, Patra SC. Hyponatremia in critically ill patients. :83–7.
56. vasopr septic shock.
57. Ketteler M, Cetto C, Kirdorf M, Jeschke GS, Schäfer JH, Distler A. Nitric oxide in sepsis-syndrome: potential treatment of septic shock by nitric oxide synthase antagonists. *Kidney Int Suppl*. 1998 Feb;64:S27-30.
58. Vincent J, Zhang H, Szabo C, Preiser J. Clinical Commentary Effects of Nitric Oxide in Septic Shock. 2000;
59. Hospital S, Dawit TC, Mengesha RE, Ebrahim MM. Nosocomial sepsis and drug susceptibility pattern among patients admitted to adult intensive care unit of Ayder Comprehensive. *BMC Infect Dis* [Internet]. 2021;1–8. Available from: <https://doi.org/10.1186/s12879-021-06527-4>
60. Abera H, Bayisa T, Worku Y, Lazarus JJ, Woldeyes E. African Journal of Emergency Medicine Prevalence and outcome of sepsis and septic shock in intensive care units in Addis Ababa , Ethiopia : A prospective observational study. *African J Emerg Med* [Internet]. 2020;(September):0–1. Available from: <https://doi.org/10.1016/j.afjem.2020.10.001>
61. Angus DC, Linde-zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. 2001;29(7):1303–10.
62. Chen C, Cheng K, Chan K, Yu W. Age May Not Influence the Outcome of Patients with Severe Sepsis in Intensive Care Units. *q. Int J Gerontol* [Internet]. 2014;8(1):22–6. Available from: <http://dx.doi.org/10.1016/j.ijge.2013.08.004>
63. Lakbar I, Einav S, Lalev N, Martin-loeches I, Pastene B, Leone M. Interactions between Gender and Sepsis — Implications for the Future. 2023;1–16.
64. Liu N, Ren J, Yu L, Xie J. Mechanical ventilation associated with worse survival in septic patients : a retrospective analysis of MIMIC-III. 2020;
65. Klastrop V, Hvass AM, Mackenhauer J, Fuursted K, Schønheyder HC, Kirkegaard H, et al. Site of infection and mortality in patients with severe sepsis or septic shock . A cohort study of patients admitted to a Danish general intensive care unit. 2016;4235(July).
66. Zhou J, Qian C, Zhao M, Yu X, Kang Y, Ma X, et al. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in Mainland China. *PLoS One*. 2014;9(9):1–8.
67. Abe T, Ogura H, Kushimoto S, Shiraishi A, Sugiyama T. Variations in infection sites and mortality rates among patients in intensive care units with severe sepsis and septic shock in. 2019;1–9.

68. Leligdowicz A, Dodek PM, Norena M, Wong H, Kumar A, Kumar A. Association between Source of Infection and Hospital Mortality in Patients Who Have Septic Shock. 2014;189(10):1204–13.

69. Tiru B, Dinino EK, Orenstein A, Mailloux PT, Pesaturo A, Gupta A, et al. The Economic and Humanistic Burden of Severe Sepsis. Pharmacoeconomics. 2015;

70. Chalupka AN, Talmor D. The Economics of Sepsis. CCC [Internet]. 2012;28(1):57–

76. Available from: <http://dx.doi.org/10.1016/j.ccc.2011.09.003>

71. Alalawi MSM, Aljabran HAM, Alkhamri AM, Alwahbi AM, Alqarrash ZI, Iraqi HAM, et al. Glasgow Coma Scale in Anticipation of Sepsis and Septic Shock : ReviewArticle. 2017;69(October):2663–6.

ANNEX

ANNEX 1: Data collection checklist for the study (prevalence of sepsis and associated factors in the central ICU of AHMC.)

sociodemographic characteristic

1. Age 	2 sex 	3. MRN
5 DATE OF ICU ADMISSION 	4. DATE OF DISCHARGE 	6. DEPARTMET
6. SOURCE OF ADMISSION 	Admission Diagnosis 	
7. STAY BEFORE ADMISSION ☐ < 48 HOURS ☐ > / = 48 HORS		



INFECTION RELATED

1. IS THERE INFECTION

3. WAS CULTURE DONE

5. ISOLATE FROM POSITIVE CULTURE

- ☐ S.AURES
- ☐ CONS
- ☐ S.PNEUMONIAE
- ☐ STEROCOCCUS SPP
- ☐ E.COLI
- ☐ PSEUDOMONA SPP
- ☐ ACINETOBACTER BAUMANNI
- ☐ KLEBSIELLA SPP
- ☐ OTHER

2. TYPE OF INFECTION

- ☐ PNEUMONIA
- ☐ MENINGITIS
- ☐ UTI
- ☐ INTRA-ABDOMINAL
- ☐ SKIN/SOFT TISSUE
- ☐ BLOOD
- ☐ OTHER KNOWN SOURCE
- ☐ UNSPECIFIED

4. POSITIVE CULTURE RESULT

ANTIBIOTIC

MV



MODIFIED SEQUENTIAL ORGAN FAILURE ASSESSMET

1.RESPIRATORY

- ☐ 0. $SO_2/FIO_2 > 400$
- ☐ 1. $315 < SO_2/FIO_2 < 400$
- ☐ 2. $235 < SO_2/FIO_2 < 315$
- ☐ 3. $150 < SO_2/FIO_2 < 235$
- ☐ 4. $SO_2/FIO_2 < 150$

RENAL

- ☐ 0. $CR < 1.2$
- ☐ 1. $1.2 < CR < 1.9$
- ☐ 2. $2 < CR < 3.4$
- ☐ 3. $3.5 < CR < 4.9$
- ☐ 4. $CR > 5$

3. LIVER

CNS

- ☐ 0. GCS =15
- ☐ 1. GCS OF 13-14
- ☐ 2. GCS OF 9-12
- ☐ 3. GCS OF 6-9
- ☐ 4. GCS < 6

CVS

- ☐ 0. NON HYPOTESIVE
- ☐ 1. $MAP < 70$
- ☐ 2. DOBUTAMINE OR 5 DOPAMINE
- ☐ 3. $> DOPAMINE OR 0.1 NE/EPI$
- ☐ 4. $> 15 DOPAMIE OR > 0.1 NE/EPI$

septic ?

COMORBIDITIES

Conditions

- ☐ ASTMA
- ☐ COPD
- ☐ CFF
- ☐ MALIGNANCY
- ☐ CLD
- ☐ CKD
- ☐ HIV
- ☐ HTN
- ☐ DM
- ☐ OTHER

CBC

wbc

lym

hgb

neu

plt

ELECTROLYTE

potassium

calcium

sodium

chloride

COAGULATION

INR

PT

PTT

liver

AST

ALT

ALP

Bilirubin

Albumin

outcome



International Research Journal

IJNRD

Research Through Innovation

Annex 2

VARIABLES	SEPTIC	NON- SEPTIC	P- VALUE	SEPTIC SHOCK	NO SEPTIC SHOCK	P- VALUE
GENDER, N (%)						
MALE	67 (22.48)	84 (28.18)	0.251	20 (63.64)	131 (53.91)	0.019
FEMALE	75 (25.17)	72 (24.16)		35 (63.64)	112 (46.09)	
SITE OF INFECTION,N (%)						
PNEUMONIA	44 (30.99)	11 (7.05)	0.000	18 (25.45)	41 (16.87)	0.000
INTRA- ABDOMINAL	19 (13.38)	9 (5.77)		13 (23.64)	15 (6.17)	
SKIN/SOFT TISSUE	17 (11.97)	11 (7.03)		10 (18.18)	18 (7.41)	
HAI	58 (40.85)	13 (8.33)		18 (32.73)	53 (21.81)	
OTHERS*	4 (2.82)	7 (4.49)	-		11 (4.53)	
DEPARTMENT, N (%)						
GYN/ OBS	10 (7.04)	10 (6.41)	0.000	4 (7.27)	16 (6.58)	0.927
MEDICAL	94 (66.20)	70 (44.87)		29 (52.73)	135 (55.56)	
SURGERY	38 (26.76)	76 (48.72)		22 (40.00)	92 (37.86)	
WBC	14.56 ±.86	11.36 ±.41	0.000	13.68 ±1.49	12.71 ±.47	0.427
LYMPHOCYTE	2.17 ±.42	1.50 ±.07	0.111	1.23 ±.16	1.96 ±.25	0.179
NEUTROPHIL	11.88 ±.85	9.06 ±.38	0.002	12.55 ±.1.79	9.93 ±.38	0.026
PLATELET	173.59 ±.9.93	273.16 ±9.06	0.000	144.47 ±13.15	243.96 ±7.97	0.000
POTASSIUM	4.17 ±.09	3.89 ±.11	0.05	4.23 ±.18	3.99 ±.07	0.163
HEMOGLOBIN	11.06 ±.29	12 ±.21	0.001	11.05 ±.46	11.85 ±.19	0.08
SODIUM	141.32 ±1.07	136 ±.80	0.000	139.63 ±1.87	139 ±.75	0.721
CHLORIDE	107.16 ±.95	101.60 ±.86	0.000	106.85 ±1.74	104.11 ±.71	0.96

Approval format for primary and secondary advisors**Assurance of principal investigator**

We hereby certify that we have supervised, read, and evaluated this research proposal titled as “Prevalence and associated factors of sepsis and septic shock in patients admitted to central intensive care unit of ADAMA HOSPITAL MEDICAL COLLEGE” by Behaylu Tesfamaryam prepared under our guidance. We have agreed to be submitted for oral defense.

Name of the student: _____ Date. _____

Signature _____

Approval forms of advisors

Name of the primary advisor: _____ Signature _____

