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COLLEGE OF MEDICINE AND HEALTH SCIENCES, SCHOOL OF MEDICINE AND PHARMACY, ANESTHESIA, CRITICAL CARE AND EMERGENCY MEDECINE

QUALITY OF SPSIS MANAGEMENT AND ITS IMPACT ON MORTALITY AT ACCIDENT AND EMERGENCY KIGALI UNIVERSITY TEACHING HOSPITAL (CHUK)

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DECLARATION

I, NTEGEREJUWAMPAYE Angelique, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled "**QUALITY OF SEPSIS MANAGEMENT AND ITS IMPACT ON IN MORTALITY AT ACCIDENT AND EMERGENCY, KIGALI UNIVERSITY TEACHING HOSPITAL**." is entirely my original work and it has never been presented or submitted in a whole or in part to any other university.

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DEDICATION

To Almighty God

To my beloved family

To my sisters

To my Friends and Relatives

To my classmates and other people who contributed to my studies

To UR staff and all my lectures

I dedicate this work “God Bless you”

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NTEGEREJUWAMPAYE Angelique

ACRONYMS

CHUK: Centre Hospitalier Universitaire de Kigali

CHUB: Centre Hospitalier Universitaire de Butare

CMHS: College of Medicine and Health Sciences

WHO: World Health Organization

WBCs: white blood cells

ED: Emergency Department

MAP: Mean Arterial Pressure

SBP: Systolic Blood Pressure ICU:
Intensive Care Unit
LICs: Low-Income Countries

SIRS: Systemic Inflammatory Response Syndrome

QSOFA: Quick Sequential Organ Failure Assessment

SOFA: Sequential Organ Failure Assessment

MRSA: Methicillin Resistance Staph Aureus

HTN: Hypertension

HIV: Human Immunodeficiency Virus

DM: Diabetes mellitus

RR: Respiratory Rate

$SPO_{2:}$ Oxygen saturation

IQR: Interquartile Range

ABSTRACT

Background: Sepsis is a time-sensitive medical situation requiring immediate intervention focusing on decreasing the period of time between suspected diagnosis and effective treatment. The goal of this research was to evaluate the quality of sepsis management according to the first hour bundle as proposed in the Surviving Sepsis Campaign of 2018 and its impact on patients' in-hospital mortality(1).

Methods: This is a prospective cohort study design for patients who presented in sepsis condition on admission as hospital diagnosis by physicians at the emergency department of the CHUK from November 2021 until April 2022. Data were collected on patients' demographics, site of infection, compliance with management of sepsis according to the first hour bundle (oxygen management if saturation<94%, intravenous fluid resuscitation (30ml/kg), crystalloid if SBP <90 mmHg, continuous urine monitoring, lactate levels measurement , blood sampling before antibiotics administration, and antibiotics administration within 1 hour of admission), and patients' outcomes including mortality, length of hospital stay , requiring of mechanical ventilation, dialysis and vasopressors.

RESULTS: A sum total of 385 patients over 4,742 admissions throughout the study period presented with sepsis at the emergency department of the CHUK. The median age of the subjects was 42 years (IQR 27 to 65). Most patients were male (58.2%), and lower respiratory tract was the predominant source of sepsis (55.1%). Overall, in-hospital mortality rate was 68.3 %, the median length of stay was 6 days (IQR 1 to 20). Compliance with all 6 components was not observed in any patient, compliance with a least 4 components was seen in only 14.3% cases whereas compliance with only 3 components was remarked in 58.4% of recruited patients. From the data analysis, I found that there were no significant correlation between mortality and first hour bundle compliance (OR=1.42; 95%CI :0.74-2.72; p =0.285). The independent predictors of mortality were age ≥65 (AOR =3.19; 95% CI:1.48-6.88; p=0.003); presence of comorbidity [AOR= 3.24; 95%CI:1.54-6.78; p=0.002]. Patients with sepsis secondary to or from community-acquired pneumonia were more likely to die than that sepsis come intra-abdominal infections [OR=0.19; 95% CI: 0.11-0.31; p<0.001]. Participants who did not receive intravenous fluid resuscitation(30ml/kg) crystalloid if SBP <90 mmHg within the first hour of admission were 3.2 times more plausibly to die than those who received intravenous fluid resuscitation

(at least 30ml/kg) crystalloid if SBP <90 mmHg within first hour of admission [OR=3.26; 95%CI: 1.49-7.12; p=0.003].

Conclusion: There is a low compliance rate with the first hour bundle. There were no significant associations between mortality and first hour bundle compliance. More studies are necessary to investigate the quality of management of septic patients in more departments and hospitals in Rwanda and other Low-Income Countries (LICs)

Key words: sepsis bundle, compliance, low-resource, outcome

CHAPTERI.INTRODUCTION

I.1.BACKGROUND

Sepsis is organ dysfunction due to overactive host response to infections (2). Globally in 2017 , approximated 48.9 million incident cases of sepsis were reported worldwide with 11million of sepsis related deaths, contributing to 19.7% of all global deaths (3). In United State sepsis is approximated to 1.9 million adult cases occur every year and 265,000 deaths each year(4). Sepsis is major problem in UK with 100,000 of cases per year(5). In the UK, the death rate for people who present with sepsis is reported to range from 28% to 50%, approximated 37,000 patient deaths and an additional 65,000 individuals suffering from long-term complications (5).

Low and middle income countries has different situations in regard to sepsis specifically a research conducted in Malawi revealed a prevalence of sepsis in emergency department of 1772 per 100.000person years with mortality rate of 23.7% (6). According to a Rwandan study, 82.7% of patients with septic shock and 51.4% patients with sepsis died in hospitals(7).

In sub-Saharan African , sepsis is a main cause of mortality in adults patients(8). Adults patients with sepsis from high resource settings have improved survival rate with standardized care measure (8). In fact, sepsis is a time-sensitive medical emergency that necessitates efficient response with a goal of minimizing the time between a possible diagnosis and a successful course of therapy(9). In 2018 Surviving sepsis campaign published first hour bundle from the combination of 3 hour and 6 hours bundle in order to achieve improvement in management of sepsis(9). The benefit mainly depend on the compliance with sepsis bundle(10).

An investigation conducted in the UK revealed that sepsis six (first hour bundle) was reduced mortality compared to those of individuals who did not get sepsis six (first hour bundle) (11). The components of first hour bundle are oxygen delivery to keep SpO2(94-96%) take sample for blood cultures before administering of antibiotics, administer empiric intravenous antibiotic ,measure lactate, start intravenous fluid resuscitation(30ml/kg) crystalloid if SBP <90 mmHg, and monitoring of urine output(11). According to a Chinese study, adherence to the first-hour bundle for the surviving sepsis campaign was high in tertiary hospital compared to secondary and private hospital (12). Implementation of surviving sepsis campaign guideline by emergency physician are often hindered by doctors awareness and attitude (12). According to a Spanish

study, highlighted that use of the first hour bundle to handle sepsis and septic shock significantly improved the quality of acute emergency care(9).

There is no study done in CHUK to evaluate quality of management of sepsis especially the compliance with sepsis first hour bundle and its impact on patients' outcome at accident and emergency and impact on mortality. Therefore, our study aims to evaluate quality of management of sepsis and impact on mortality in the university teaching hospital of Kigali (CHUK).

1.2. RATIONALE

Even if the first hour bundle has been effective in reducing mortality, the benefit mainly depend on the compliance with sepsis bundle, there is no study done in Rwanda to evaluate compliance with that bundle. Therefore, the researcher evaluated that compliance with first hour bundle to help the recognition of areas to be improved during management of sepsis.

1.3. RESEARCH QUESTION

Does first hour bundle compliance have an impact on patients' outcomes (mortality rate, length of stay in hospital, need of ventilation, need of dialysis and need of vasopressors) at accident and emergency/ CHUK?

1.4. OBJECTIVES

1.4.1. GENERAL OBJECTIVE

The primary objectives of this study was to evaluate sepsis management according to the "first hour bundle and its impact on patient's mortality in accident and emergency department.

1.4.2. SPECIFIC OBJECTIVES:

-To evaluate compliance with management of sepsis within "first hour bundle" at accident and emergency/ CHUK

-To evaluate the relationship between first hour bundle compliance and patients' outcome (mortality rate) at accident and emergency/ CHUK

CHAPTER II. LITTERATURE REVIEW

2.1. Introduction

Sepsis is a dysregulated host response to infection that results in organ failure(2)(13).Despite best effort in protocol pathway management fatality rate from septic shock remain high at nearly 35% to 40% (14).Septic shock is described as circulatory, metabolic, and cellular metabolic derangements require vasopressor support (15).

Adults patients with sepsis in high resource settings have been shown improvement in survival rate with standardized management care measures (8). Sepsis is time concerned medical situation requiring a decreasing the period of time between a suspected diagnosis and effective treatment(9). In 2018 Surviving sepsis campaign published first hour bundle from combination of 3 hour and 6 hours bundle in order to achieve improvement in management of sepsis(9). The benefit mainly depend on the compliance with sepsis bundle(10).

2.2. Clinical features of sepsis

Signs and symptoms of sepsis frequently affect several organ systems (14).Extreme release of various inflammatory mediators in the course of sepsis leads to multi-organ failure (14).

For cardiovascular arterial and vasodilatation leads to hypotension and myocardial infarction observe on 60% of septic patients(14). The exact process of septic cardiomyopathy is not clear and a slight increase in troponin is commonly noticed and may be linked to the severity of sepsis (14).

For lungs, cytokine-mediated lung damage leads to raise permeability of alveolar and capillary endothelium, resulting in non-cardiogenic pulmonary edema that compromises oxygenation and ventilation (13). Development of hypoxia and acidosis results to tachypnea and incidence of acute respiratory distress syndrome in patients with sepsis are 7% (13).

Sepsis-related to renal failure contributes significantly to the morbidity and mortality(14). Risk factors for developing acute kidney injury are advanced age, chronic renal failure, and cardiovascular disorders (14).

2.3. Diagnosis of sepsis

Sepsis1 define as inflammatory response to infection by expert in1992 (14). Two or more systemic inflammatory response syndrome (SIRS) criteria, along with a possible or established cause of infection, were used to diagnosis sepsis (14). Septic shock was ongoing hypotension despite fluid resuscitation (14).Other literature define septic shock as sepsis plus either vasopressor support or MAP<or =60mmHg(16).

Sepsis 2 refers to the 2001 revision of Sepsis 1 that added the Sequential Organ Failure Assessment (SOFA) criteria to help identify organ failure as a sign of severe Sepsis (14)

SIRS criteria, which include tachycardia, fever, leukocytosis, and hypotension, are criticized most for their emphasis on the inflammatory response, which is more typical of many serious illnesses (trauma, pancreatitis, postsurgical inflammation) (14). Additionally, 13% of patients with a comparable profile of infection, organ failure, and significantly higher mortality were missed by SIRS criteria(14)

Sepsis3: Updated definition of sepsis from 2016: life-threatening organ failure brought on by an unbalanced host response to infection(13). This was identified by a SOFA score of 2 or more points with suspicion of infection (14). In new definition of sepsis, the term severe sepsis was dropped from updated definition(14). Septic shock was described as sepsis with profound circulatory, cellular and metabolic dysregulation(14). Compared to sepsis, which has a fatality rate of 10%, septic shock has a high mortality rate of 40%(14). Clinically, septic shock is characterized by prolonged hypotension that necessitates the use of vasopressors to maintain mean arterial pressure (MAP) above 65 mm Hg and an increased blood lactate level above 2 mmol despite sufficient fluid resuscitation(14)

For fast evaluation of patients outside of the ICU, the SOFA score required laboratory results that were not easily accessible. The goal of the task forces was to discover easily accessible screening methods using qSOFA (Quick Sequential Organ Failure Assessment). The term "qSOFA" has three definitions: "altered mental status," "systolic blood pressure below 100," and "respiratory rate more than or equal to 22." (12). The mortality rate for patients outside of the ICU who met two or more qSOFA criteria was comparable to that of patients who obtained a complete SOFA score(14)

2.4. Management of sepsis

As a medical emergency, sepsis and septic shock should be handled and resuscitated right away (17). First-hour bundle initial resuscitation of patients with sepsis and sepsis shock includes measuring lactate level, obtaining blood culture before giving antibiotics, giving broad-spectrum antibiotics, starting rapid administration of 30ml/kg crystalloid for hypotension, giving rapid administration of 30ml/kg crystalloid for lactate above or equal to 4mmol/l, and giving vasopressors if hypotensive during or after fluid resuscitation to keep mean arterial pressure (17).As sepsis and septic shock are medical emergencies, we recommend immediate resuscitation and standardized (18).

Patients with sepsis or septic shock ;antimicrobials should be initiated as soon as possible within the first hour of recognition (19). The risk of progression of sepsis to septic shock increase 8% each hour before initiation of antibiotics (19).

Based on patient combination factors, suspected infection sources, hospital antibiogram, anticipated infecting organisms, common local pathogens, and local microbial resistance organisms, antimicrobial agent selection is made. The starting medications should be active against common gram-positive and gram-negative pathogenic microorganisms. For intra-abdominal infections or other conditions where anaerobes are important pathogens, anaerobic coverage should be offered. There may be a need for empiric antiviral and antifungal treatment(19).

2.5. Outcome

Each hour before antibiotics are administered, the risk of sepsis developing into septic shock increases by 8%(19). According to a study on first-hour bundle adherence conducted in Japan, patients who received care according to the first hour bundle died in hospitals at a rate of 18% while patients who received care out window of first hour bundle died at a rate of 30%(20)

CHAPTER III. METHODOLOGY

3.1. Study design

During a six-month period, a prospective cohort study of patients admitted to the accident and emergency department was conducted.

3.2. Setting

CHUK is the main public tertiary and university teaching hospital, located in Kigali city and equipped with more than 500 beds. CHUK serves more than 120 000 as OPD patients, considering admissions at A/E (CHUK) receive 11520 patients per year. In order to get care, patients are typically transported from district hospitals to CHUK.

3.3. Study population

Participants in this study was all patients presenting with sepsis on admission time in accident and emergency at CHUK.

3.4. Inclusion and exclusion criteria

3.4.1. Inclusion criteria

During the study period, all patients older than 18 who were admitted to accident and emergency rooms were included.

3.4.2. Exclusion criteria

Patients referred to other facilities simply because the researcher did not have opportunity to follow up for their outcome were excluded for the current study.

3.5. Study Limitations

Challenge for providing antibiotics as there is no guideline for antibiotherapy

Challenge of assessing multiorgan dysfunction

Limitation of ICU admission as most of time ICU bed not available

3.6. Sampling and sample size

Based to information provided by statistics departments at CHUK, Emergency admitted in a total 11520 patients were estimated in2020. The study population of the current study is still estimated due to lack of an exact number of patients with sepsis at accident and emergency unit at CHUK.

And this study considered the patients presented with sepsis and with complete inclusion criteria during six months (11November 2021 to 03May 2022)

3.7. Data variables, source of data, and data collection

Data collection process started from 11st November 2021 to 03 th May 2022.The study period was 6months. Using questionnaire principal investigator collected data from patients' documents including triage form, file, medical prescription and open clinic system. Data collection form has information on patients' demography; characteristics of patients with suspected infection; Management of sepsis with first hour bundle components, initial antibiotics provides within 1 hour from diagnosis of sepsis and patients outcome. The researcher followed the patients for a given period of time until the outcomes were produced.

3.8. Data analysis

Version 21 of Excel was used to enter the data. Then exported to SPSS for analyzing rate of sepsis, the sepsis management complied to first hour bundle, mortality rate among those with compliance to first hour bundle and those without compliance and patients' outcomes. Descriptive data are summarized and presented using frequencies and percentages in tables and charts. Fischer's exact tests were used for associations with >25% cell with count 5 and Statistical significance for associations was evaluated at P-value 0.05 in the binary logistic regression. The Chi-square test was employed to test the proportional relationships between the variables. To identify independent predictors of the desired outcome, multivariable logistic regression was used with variables that had a p-value of less than 0.10 in the univariate analysis.

3.8. Ethics considerations:

3.8.1. Ethical issues: At order to perform this data collection in its Accident and Emergency department, the primary investigator sought IRB approval, ethical approval from the University of Rwanda, College of Medicine and Health Sciences, and ethical approval from University Teaching Hospital of Kigali.

3.8.2. Data confidentiality: The data were confidential as there were not any patient's names appearing into data collected and researcher used study ID numbers. Multiple measures were taken to ensure the confidentiality by electronic password-protected documents. Hard copies will be kept

for 5 years in a locked file and after this time hard copies will be discarded. Only researchers will have access to data.

3.8.3. Specific patient benefits: Quality improvement and patient care.

3.8.4. Feedback and dissemination of results: We shall disseminate the knowledge from our research through conferences, countrywide or internationally. The paper will be published in peer-reviewed journals with free access. We will also present the paper to the CHUK staff mainly the hospital administration and accident/emergency leaders to make sure we improve current practice.

3.8.5. Collaborative partnerships: We will work with the administration board of CHUK and the leadership of accident and emergency at CHUK.

CHAPTER IV: RESULTS

Our study analyzed the information collected from 385 patients who were identified to have sepsis by hospital diagnosis on admission the median age for our patients was 42 years ranging from 18 to 92 years of age. Forty three percent of the patients aged between 31 and 64 years, twenty percent aged above 65 years. The majority of the participants were males at 58.18% and 23.64% of the participants had comorbidities with 18.96% of the total number of participants having diabetes mellitus and 1.3% having hypertension (Table 1).

Table 1: Sociodemographic details about the study's participants

Characteristics	Frequency (N=385)	%
Age [Median (IQR)	**42 (27-64) years**	
≤30	139	36.10
31-64	167	43.38
≥65 years	79	20.52
Gender		
Male	224	58.18
Female	161	41.82
Presence of comorbidities		
Yes	91	23.64
No	294	76.36
Type of comorbidity		
Diabetes mellitus	73	18.96
Hypertension	5	1.30

IQR: Interquartile Range

Considering the patients' characteristics as defined by their vital signs, the majority of patients (72.73%) scored 2 on the qSOFA scale while 14.55% had a score of 3 on qSOFA scale. Of the total number of participants, 45.19% presented in septic shock and 50.39% presented in hypotension. Considering the origin of infection/sepsis, 55.06% of the patients had community acquired pneumonia, 35.84% had intra-abdominal infections, 8.05% had urinary tract infections and 4 patients (1.04%) had their sepsis originated from a Fournier's gangrene (Table 2)

Table 2: Patients' characteristics as defined by vital signs

Characteristics	Frequency (N=385)	%
qSOFA score/level		
<2	49	12.73
2	280	72.73
3	56	14.55
Severity of sepsis		
Sepsis	211	54.81
Septic shock	174	45.19
Hypotension (SBP <90 mmHg)		
Yes	194	50.39
No	191	49.61
Source of infection		
Community-Acquired Pneumonia	212	55.06
Intra-abdominal infections	138	35.84
Urinary tract infection	31	8.05
Fournier's gangrene	4	1.04

Using **"first hour bundle" components** for assessing the compliance rate of sepsis management has performed and revealed that 16.1% patients received Oxygen with Spo2 =94-96%;8% of patient not received oxygen and Spo2 =94-96%; 8% of patient no oxygen and Spo2<94%;57.9% of patients received oxygen while Spo2 was <94%; 8% of patients no oxygen while Spo2 was >96%;23.6% of patients received oxygen while Spo2 >96% . Of 85.2% the patient receives enough fluid resuscitation (30ml/kg) within 1 hour of admission as the SPB<90mmHg at arrival while 14.85 did not. Urine output being monitored continuously for 93.2% of the patients while Lactates ordered among lab initial investigations for 8.3 percent. The first dose of antibiotic given 8.3% in 1st hour of sepsis recognition whereas 10.4% Sample for blood cultures were taken before administering of antibiotics.

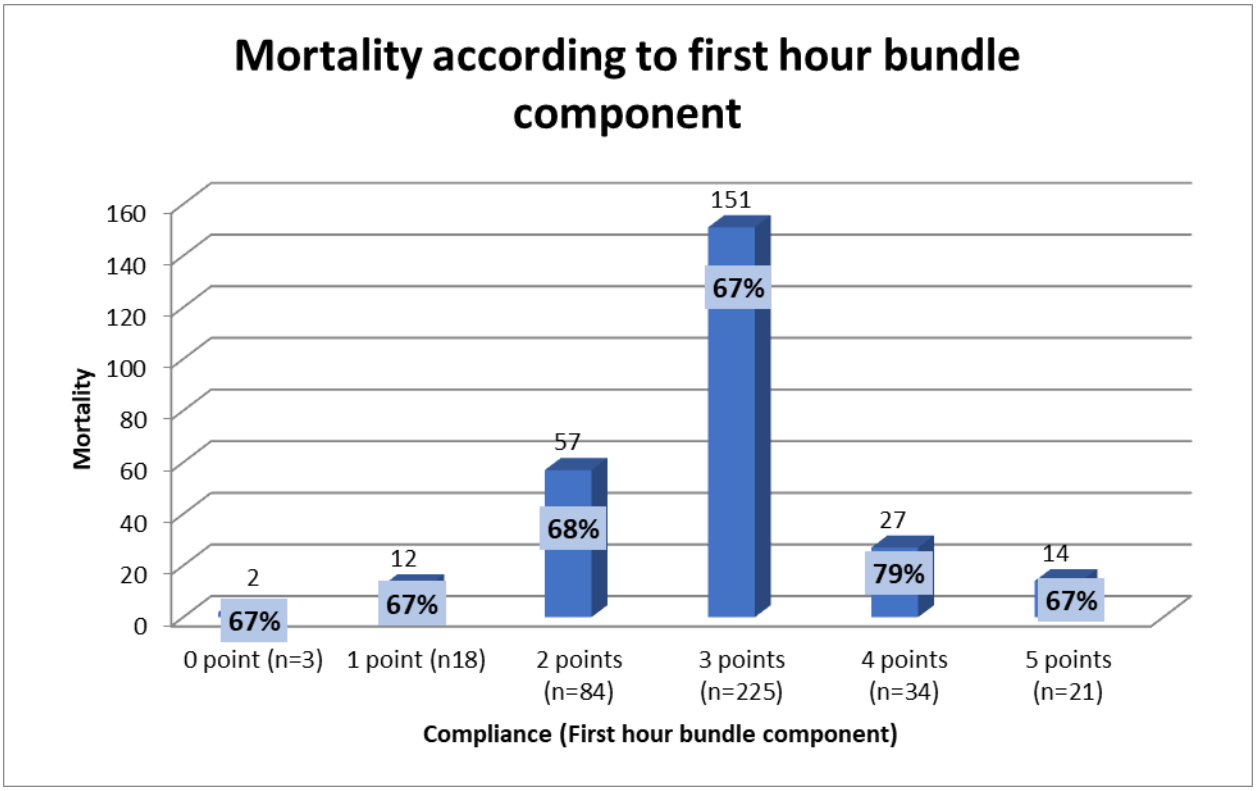
The compliance was defined by conventional compliance range whereby 6 points equals to all 6 components of first hour bundle were considered to be the maximum score and zero as minimum score. none complied with all the 6 components at a time, 5.5% complied with 5components, 8.8% complied with 4components, 58.4% complied with 3components, 21.8% complied with 2components, 4.7% complied with 1component and 0.8% complied with 0 component.(Table3)

Table 3: The rate of first hour bundle components as performed during management

Components	**Frequency**	**Percentage**
Oxygen requirement and range of SpO2 achieved		
Oxygen and SpO2<94%	223	57.9
Oxygen and SpO2>96%	91	23.6
Oxygen with SpO2=94-96%	62	16.1
No Oxygen and SpO2=94-96%	3	0.8
No oxygen and SpO2<94%	3	0.8
No Oxygen and SpO2>96%	3	0.8
intravenous fluid resuscitation(30ml/kg) crystalloid if SBP <90 mmHg,	328	85.2
Urine output being monitored continuously	359	93.2
Sample for blood cultures taken before administering of antibiotics	40	10.4
Lactates ordered among lab initial investigations	32	8.3
The first dose of antibiotic given in 1st hour of sepsis recognition	32	8.3
Resulting scores from First bundle components		
6 points	0	0
5 points	21	5.5
4 points	34	8.8
3 points	225	58.4
2 points	84	21.8
1 point	18	4.7
0 points	3	0.8

The mortality according to the first hour bundle compliance, the majority of the patients (n=225) scored 3 points in and among these 225 patients who scored 3 points, 151 patients (67.11%) died; of 84 patients who scored 2 points, 57 of them (67.86%) died; of 34 patients who scored 4 points, 27 of them (79.40%) died; of 21 patients who scored 5 points, 14 of them (66.66%) died and of 18 patients who scored 1 point, 12 of them (66.66%) died (Chart1).

Chart 1: Mortality according to first hour bundle component



The median hospital stay for our patients was 144 hours (6 days) and of the total patients, 22.86% received vasopressors, 8.57% received mechanical ventilation support and 4.16% received dialysis.

Of the total number of patients, the observed overall mortality rate among our study participants was 68.31% (Table 4).

Table 4: Outcomes of sepsis among our study participants

Outcome	Frequency	Percentage
Length of stay		
Median (IQR)	6 (1-20) days	
Organ support		
Vasopressor	88	23
Mechanical ventilation	33	9
Dialysis	16	4
Death		
Yes	263	68
No	122	32

IQR: Interquartile Range

In patients with comorbidities, the risk of death was statistically significantly higher than in patients without comorbidities (OR=2.64; 95% CI: 1.46-4.76; p=0.001). Patients with sepsis from intra-abdominal infections had a lower mortality rate than patients with sepsis from community-acquired pneumonia (OR=0.19; 95% CI: 0.11-0.31; p=0.001), and patients with sepsis from urinary tract infections had a lower mortality rate than patients with sepsis from community-acquired pneumonia (OR=0.15; 95% CI: 0.07-0.34; p=0.001). Mortality, age, and shock did not significantly correlate with first-hour bundle compliance(Table5).

Table 5: Factors associated with mortality among the study participants (binary logistic regression analysis

Predictors	Mortality rate		OR (95% CI)	P value
	Died	Survived		
First hour bundle component				
<4 points	222 (67.27%)	108 (32.73%)	Ref	
≥4 points	41 (74.55%)	14 (25.45%)	1.42(0.74-2.72)	0.285
Age				
≤30	98 (70.50%)	41 (29.50%)	Ref	
31-64	107 (64.07%)	60 (35.93%)	0.74 (0.46-1.21)	0.234
≥65 years	58 (73.42%)	21 (26.58%)	1.15 (0.62-2.14)	0.647
Comorbidities				
Yes	75 (82.42%)	16 (17.58%)	2.64 (1.46-4.76)	0.001
No	188 (63.95%)	106 (36.05%)	Ref	
Severity of infection				
Septic shock	118 (67.82%)	56 (32.18%)	0.95 (0.62-1.47)	0.849
Sepsis	145 (68.72%)	66 (31.28%)	Ref	
Site of infection				
CAP	179 (84.43%)	33 (15.57%)	Ref	
Intra-abdominal infections	70 (50.72%)	68 (49.28%)	0.19 (0.11-0.31)	<0.001
UTI	14 (45.16%)	17 (54.84%)	0.15 (0.07-0.34)	<0.001
Tissue infections	0 (0.00%)	4 (100%)		
qSOFA				
2	191 (68.21%)	89 (31.79%)	1.19 (0.65-2.17)	0.567
3	36 (64.29%)	20 (35.71%)	ref	
Gender				
Male	134 (59.82%)	90 (40.18%)	ref	
Female	129 (80.12%)	32 (19.88%)	2.71 (1.69-4.33)	<0.001

Participants who did not receive intravenous fluid resuscitation(30ml/kg) crystalloid if their SBP was over 90 mmHg within the first hour of admission had a 3.2 times higher risk of passing away than those who did (OR=3.26; 95%CI: 1.49-7.12; p=0.003). In the first hour of their arrival, patients with respiratory tract infections received more fluid at a high rate (92%) compared to patients with intra-abdominal infections (72%), with a statistically significant difference (p0.001).

All of the patients whose first dosage of antibiotics was given after sample collection passed away (X2=16.189; p0.001), and all of the patients whose blood cultures were performed before giving antibiotics passed away (X2=20.70; p0.001) [Table 6].

Table 6: Association of first hour bundle component with mortality among the study participants (binary logistic regression analysis)

Predictors	Mortality rate		OR (95% CI)	P value
	Died	Survived		
Oxygen requirement and range of SpO2 achieved				
Oxygen and SpO2<94%	152 (68.16%)	71 (31.84%)	1.02 (0.55-1.86)	0.950
Oxygen and SpO2>96%	62 (68.13%)	29 (31.87%)	1.02 (0.51-1.86)	0.950
Oxygen with SpO2=94-96%	42 (67.74%)	20 (32.26%)	ref	
No Oxygen and SpO2=94-96%	2 (66.67%)	1 (33.33%)	0.95 (0.08-11.1)	0.969
No oxygen and SpO2<94%	3 (100%)	0 (0.00%)	-	
No Oxygen and SpO2>96%	2 (66.67%)	1 (33.33%)	0.95 (0.08-11.1)	0.969
Intravenous fluid resuscitation(30ml/kg) crystalloid if SBP <90 mmHg,				
Yes	214 (65.24%)	114 (34.76%)		
No	49 (85.96%)	8 (14.04%)	3.26 (1.49-7.12)	0.003
The first dose of antibiotics administered after sample collection				
Yes	32 (100%)	0 (0.00%)	-	<0.001*
No	231 (65.44%)	122 (34.56%)		
Sample for blood cultures taken before administering of antibiotics				
Yes	40 (100%)	0 (0.00%)	-	<0.001*
No	223 (64.64%)	122 (35.36%)		
Urine output being monitored continuously				
Yes	246 (68.52%)	113 (31.48%)		
No	17 (65.38%)	9 (34.62%)	0.86 (0.37-2.01)	0.740
Lactates ordered among lab initial investigations				
Yes	24 (75.00%)	8 (25.00%)		
No	239 (67.71%)	114 (32.29%)	0.69 (0.30-1.60)	0.398

*: Fischer's exact test used

Age of participants, presence of comorbidities, source of infection, sex, first hour bundle component and receiving intravenous fluid resuscitation(30ml/kg) crystalloid if SBP <90 mmHg within 1 hour were analyzed in the multivariable logistic regression and we found that age of participants, presence of comorbidities, source of infection, sex and receiving enough fluid resuscitation within 1 hour were retained in the final model as the real predictors of mortality among our participants (Table 7).

Table 7: Multivariable logistic regression analysis of the final model of predictors of mortality among our study participants

Predictors	**AOR**	**95% CI**	Pvalue
Age			
≤30	ref		
31-64	1.05	0.57-1.89	0.884
≥65	3.19	1.48-6.88	0.003
Comorbidity			
Yes	3.24	1.54-6.78	0.002
No	ref		
Sources of Infection			
CAP	ref		
Intra-abdominal infection	0.12	0.06-0.22	<0.001
Urinary tract infection	0.14	0.06-0.33	<0.001
Sex			
Male	ref		
female	2.92	1.58-5.39	0.001
The patient receives enough fluid resuscitation within 1 hour			
Yes	ref		
No	11.26	4.46-28.42	<0.001
First hour bundle component			
<4 points	ref		
≥4 points	1.60	0.73-3.50	0.236

AOR: Adjusted Odds ratio; CI: Confidence interval; ref: reference category

CHAPTER IV: DISCUSSION

Reduce the time between a suspected diagnosis and effective treatment as early action is essential for sepsis management (9).

This was prospective analysis for 385 patients who were identified to have sepsis as hospital diagnosis on admission in emergency department. Our patients had an average age of 42 years (interquartile range: 27 to 64), with a male to female ratio of 58%.

Compliance with 6 components of the first hour bundle was rated 0%. It means that none of the patients received a complete fist hour bundle management for septic patient with in the first hour. The compliance with a least 4 components were seen in only 14.3% cases whereas compliance with only 3 components was observed in 58.4% of patients. The lack of lactate measurements within the hour was the most significant divergence from compliance. This rate is relatively similar to the study done in Turkey which show that compliance with first hour bundle in management in ICU rated 0% and most significant deviation was the absence of lactate measurement within one hour of sepsis recognition(21). This could be linked to limited resources like lack of sufficient staff nurses and doctors in ED; unavailability of arterial blood gas machine in ED, Delay in receiving adequate health care as patients are requested to pay investigations and medications before delivery and lack of awareness to some care health providers.

In our study there were no significant association between mortality and first hour bundle compliance OR 1.42(0.74-2.72; p =0.285). Similar findings were reported from a study conducted in Korea which shows that one-hour bundle achievement was not associated with improved outcomes in septic shock patient. Considering others studies ,efficient of bundle therapy in management of sepsis and septic shock is debatable(22).This could be linked with patients consult late when physiological reserve are affected.

According to our study, 65.4% of patients who did not receive antibiotics within the first hour of admission died compared to the patients who received them within that time. This is contradiction with finding from research done in Korea that showed that in-hospital mortality was decreased when broad-spectrum antibiotics were administered within an hour of sepsis detection(23). Moreover, findings from a study conducted in California revealed that each elapsed hour between emergency department registration and antibiotics administration for septic patients was associated with an increase of 9% of mortality(24). Patients with serious infections who delayed

to receive antibiotics prone to double mortality rate and even high(25). Another study done in Canada and United States showed that there was strong relationship between delay of initiation of antibiotics and in-hospital mortality (26). A study done in German showed that a delay administration of antibiotics in septic patients was associated with death among patients with a faster progression from sepsis to septic shock(27). Use of appropriate empirical antibiotics lowers 30-day mortality in septic patients with a negative culture(28). Depending on whether all cultures or solely blood cultures were examined, inadequate antibiotic delivery was linked to 20% to 40% higher odds of mortality(29). When compared to patients who were effectively treated prior to septic shock recognition, mortality was considerably higher in the patients who got initial antibiotics after shock recognition. However, mortality did not vary hourly with antibiotic therapy following the diagnosis of septic shock(30) . The high proportion of septic shock (45.2%) in our study may explain why patients in our study died despite timely administration of antibiotics.

The commonest source of sepsis in our study was the community acquired pneumonia with 55.1% followed by intra-abdominal infections 35.8%. This is not quite different to from the results of retrospective study done in Rwanda by 2020 in two tertiary hospitals, CHUK and CHUB, which show that the predominant source of infection was intra-abdominal (37.0%) followed by pulmonary at rate of (32.6%) (7). The little difference may result from the possible fact that some patients with intrabdominal sepsis may have developed the infection in postoperative period and are not reported at ED .Our results resemble those of a research conducted in California, where pneumonia was similarly the most common condition and accounted for roughly one-third of sepsis cases(31).

Patients with sepsis secondary to intra-abdominal infections were less likely to die than those with community acquired pneumonia (OR=0.19; 95% CI: 0.11-0.31; p<0.001). We discovered that patients with respiratory tract infections received more fluid in the first hour of their admission (92%) than patients with intra-abdominal infections (74%), with a statistically significant difference (p0.001). This may be related to the patients receiving insufficient IV fluids. According to certain views, resuscitating a septic patient with 30ml/kg of fluid may impair their prognosis(32).

In our study, a paradoxical finding that female patients were more likely to die than male with OR 2.71,95CI: (1.69-4.33) P <0.001 concurred with results from a study done in New York on septic

patients also showed that female were more likely to die than male (35% vs. 33%,p=0.006)(33).This finding also was showed by a study in Germany which show that female with severe sepsis were more likely to die than male(34) contrarily to another study also done in German shows that there was significantly enhanced survival of women with severe sepsis compare to men(35).

When compared with results from a retrospective analysis conducted in Rwanda in 2020, where the in-hospital mortality rate from sepsis or septic shock was 51.4%, the overall in-hospital mortality rate from sepsis and septic shock in our study was similarly quite high (68.3%)(7). Another study also done in Rwanda in two public ICU from tertiary hospitals showed an increasing mortality with worsening of the septic state. Authors found 24.6% of mortality rate from sepsis and 35.8% from septic shock(36). All patients recruited in our study from emergency department which implies that they were in critical illness mainly in septic shock compared to this retrospective study done in two tertiary hospitals they recruit all septic patients of sepsis including ward and ICU patients which was different to our study where patients are critically ill in the emergency department. Independent factors to mortality were age ≥65, the presence of comorbidity and female gender. This could be related with decreased immunity for elderly patients and patients with comorbidities

Our study's primary limitation was that it was conducted only in one in a tertiary emergency department and therefore the sample does necessary represent the conditions of other emergency department or hospital wards across the nation. Therefore, it is necessary to carry out extensive studies that will involve district hospitals expecting to have access to patients in the early stages of sepsis and evaluate the impact of the first hour bundle. It could be also interesting to explore how other tertiary hospitals comply with this guideline.

CHAPTER V: CONCLUSION AND RECOMMENDATION

5.1 Conclusion

The results of this cohort study of the quality of management of septic patients at the emergency department of the CHUK showed a low compliance rate with the first hour bundle. There were no significant associations between mortality and first hour bundle compliance for different potential reasons including the delayed admission to ED and possible the side effects of too much IV fluids in some groups of patients. More studies are needed in order to explore the quality of management of septic patients in more departments and hospitals in Rwanda and other Low-Income Countries (LICs). This will guide the implementation of appropriate interventions to improve outcomes of septic patients in LICs.

5.2 Recommendation

1. Further research should be done to explore the same variables related to the compliance of first bundle protocol at different settings including but not limited to emergency departments, may be by using a different methodology.

2. Protocol and guidelines, including the" first hour bundle" should be used as a tool to improve sepsis management during the treatment and management of emergency, urgent and critically ill patients as diagnosed as sepsis case among mothers.

3. Education is one strategy to boost sepsis bundle compliance (meeting, bedside training, etc.)

4.Avail all necessary materials like blood culture tube, ABG machine to facilitate timely decision making

5.Provide adequate human resources to decrease the waiting time

6. Encourage patients with warning signs of an infection and those at risk for early consultation to avoid subsequent problems which may lead to the complications which can cause more health problems including different outcomes for to patients.

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ANNEXES

Annex 1. Data collection tool

SECTION A. COMPLETES THE FOLLOWING ABOUT DEMOGRAPHY:

1. Study ID of the patient:☐ Age of the patient: ……. years
2. Sex of the patient: ☐ Male ☐ Female
3. Diagnosis at admission…… Date and time of admission in at A/E: ……

SECTION B. CHARACTERISTIC OF PATIENT WITH SUSPECTED INFECTION

1. **Any Comorbidity such as DMtype2** YES ☐ NO ☐ ; **HTN** YES ☐ NO ☐

Karnofsky score ☐ ; **HIV status** YES ☐ NO ☐

COVID-19 YES ☐ NO ☐ ; **Renal failure** YES ☐ NO

Liver cirrhosis YES ☐ NO ☐ ; **COPD** YES ☐ NO ☐

Heart failure YES ☐ NO

2. Vitals at admission

a). Systolic blood pressure (SBP)……. mmhg Diastolic blood pressure (DBP)……mmhg

b). Respiratory rate (RR)……**c).** Breath/min **d).** Altered mental status: GCS ……

e). Temperature (T^o)…….. degree Celsius **f).** Heart rate ……. beat/min

g). Oxygen saturation (SpO2) ……%

3. Vital sign at 6 hours post admission

a) Systolic blood pressure (SBP)……. mmhg Diastolic blood pressure (DBP)……mmhg

b). Respiratory rate (RR)……**c)** Breath/min; **d)** Altered mental status: GCS ……

e). Temperature (T^{o})……. degree Celsius; **f).** Heart rate ……. beat/min

g). Oxygen saturation (SpO2) ……%

QSOFA (point)…….

According to the above clinical features the patient has sepsis (qSOFA>=2 point confirm sepsis**) YES** ☐ **NO** ☐

SECTION C. MANAGEMENT OF SEPSIS (FIRST HOUR BUNDLE COMPONENTS)

	First hour bundle components	Yes	No
1.	If Oxygen provided, what was current SpO2? 94-96%?		
2.	Did the patient receive enough fluid resuscitation (30ml/kg) within 1 hour of admission if the SPB<90mmHg at arrival?		
3.	Was the Mean Arterial Pressure (MAP) >65mmHg within 1 hour?		
4.	If the current MAP<65mmHg, is Norepinephrine or alternative being given? Has it been started within the first hour?		
5.	Is urine output being monitored continuously?		
6.	Were lactates ordered among lab initial investigations?		

SECTION D. INITIAL ANTIBIOTIC PROVIDES WITH 1 HOUR FROM DIAGNOSIS OF SEPSIS? (Assessment of accuracy of antibiotics)

Meropenem IV 500-1g tid or bid

Ceftriaxone IV 1g bid

Metronidazole IV 500 mg tid

Ciprofloxacin IV 400mg bid

- ✓ ***The first dose of antibiotic administered after sample collection for lab analysis***

  YES ☐ ***NO*** ☐

- ✓ ***antibiotics prescribed in line with the guidelines on antimicrobial therapy according to surviving sepsis campaign YES*** ☐ ***NO*** ☐

SECTION E. OUTCOME

Interventions:

1. Admission in ICU YES ☐ NO ☐; 2.Mechanical ventilation YES ☐ NO ☐

3. Transfusion YES ☐ NO ☐; 4.Dialysis YES ☐ NO ☐

5. Vasopressors YES ☐ NO ☐ ;

7. Multi organ dysfunction YES ☐ NO ☐

Others outcomes

1. Date of discharge ……

2. Length of stay at CHUK……..…

3. Transfer YES ☐ ☐ NO

4. Death YES ☐ NO

5. Discharge at home for palliative care YES ☐ NO ☐

Thank you

Annex2.IRB approval

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 27th /August /2021

Dr Ntgerejuwampaye Angelique
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 288/CMHS IRB/2021

Your Project Title ***"Quality of Management of Sepsis at Accident and Emergency and Impact on Mortality"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
			No (Reason)	
Name of Members	**Institute**	Yes	**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 27th August 2021, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 27th August 2021

Expiration date: The 27th August 2022

Dr Stefan Jansen
Ag. Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:

- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

Annex3.CHUK approval

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

10th Nov,2021 *Ref.:EC/CHUK/124/2021*

Review Approval Notice

Dear NTEGEREJUWAMPAYE Angelique,

Your research project: ***"QUALITY OF MANAGEMENT OF SEPSIS AT ACCIDENT AND EMERGENCY AND IMPACT ON MORTALITY AT KIGALI UNIVERSITY TEACHING HOSPITAL "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 10th Nov,2021 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=450&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

Scan code to verify.

" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "