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Research Article

Prevalence and Incidence of Infections and Sepsis in Critical Care Units at Two Tertiary Referral Hospitals in Kenya

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Summary

Background: *Sepsis is a major global challenge affecting millions of individuals annually. The incidence of sepsis is 535 per 100000 person-years however, this varies by geographical region. In Critical care units, sepsis accounts for 29% of Critical care unit (CCU) admissions with an estimated mortality of 25%. Common causes of sepsis are respiratory tract infections, intra-abdominal infections, and urosepsis. Nosocomial infections are frequent causes of sepsis in Critical care Units, with patients having an increased risk of developing nosocomial infections as compared to the general hospital population. The prevalence of multi-drug resistant infections is also significantly higher with Multidrug-Resistant Organisms (MDROs) such as Pseudomonas and Acinetobacter being responsible for a large portion of nosocomial infections.*

Objectives: *To determine three-month period prevalence and incidence rates of infections, sepsis and septic shock in adult patients admitted to CCU's at tertiary care hospitals in Nairobi. We aimed to document primary infection foci, causative organisms, and their antibiotic susceptibility patterns. We also aimed to determine the 28-day case fatality rates in patients with infections, sepsis, and septic shock.*

Study Design: *Hospital-based prospective observational study among patients admitted to the adult Critical Care Units at the Kenyatta National Hospital and the M.P Shah Hospital carried out between December 2020 and March 2021*

Study Site and Subjects: *The Kenyatta National Hospital (KNH) is a national tertiary referral hospital with an 1800 bed capacity, two medical Critical Care Units (CCU's)with six beds each as well as a multidisciplinary CCU with 20 beds. The M.P. Shah Hospital is a 200-bed private tertiary level facility with a 16 bed CCU. All consecutive patients admitted to these adult CCU's meeting the inclusion criteria were eligible to participate in the study.*

Methods: *All patients admitted to the Critical Care Units were evaluated on admission using the International Sepsis Forum (ISF) Consensus definitions for presence of infection(s). The Sequential Organ Failure Assessment (SOFA) score was applied to all patients to identify those with sepsis. A patient case report form was used to collect data and patients were followed up from admission to discharge from the CCU. Patients were assessed for development of incident infections, sepsis and septic shock. Microbiologic culture reports were documented to determine antibiotic susceptibility patterns. Vital status for all subjects at 28 days was assessed via either direct follow up or via telephone contact. The primary investigator and research assistants were not involved in patient care or management.*

Statistical Analysis: *Proportions and 95% confidence intervals were calculated as the number with the event of interest (infection, sepsis) divided by the total sample size. Case fatality rates were calculated for the CCU's as well as for patients with sepsis and septic shock. The analysis was done for the combined sample size and further stratified by hospitals (KNH and MP Shah). Prevalence, incidence and mortality rates for KNH and MP Shah were compared using a chi-squared test.*

Results: *A total 160 subjects were recruited (108 from KNH and 52 from MPSH. The prevalence of infection, sepsis and septic shock on admission were 52.5% (95% CI: 44.5-60.4), 35% (95% CI: 27.6- 42.9) and 13% (95% CI: 8.8-20.1) respectively. The incidence of infections, sepsis and septic shock were 41.3% (95% CI: 33.5-49.3), 31.8% (95% CI: 20.9-44.4) and 27.2% (95% CI: 17.0-39.6). The 28-day case fatality rate (CFR) for the sample cohort was 38.8% (95% CI: 31.2- 46.8). Among patients with sepsis and septic shock, the CFRs were 46.8% (95% CI: 35.3-58.5) and 59.1% (95% CI: 36.4-79.3) respectively. Foci of prevalent infection were mainly respiratory and intra-abdominal while foci of incident infection were mainly Catheter associated urinary tract infections and ventilator associated pneumonia. The most common organisms isolated were Gram- negative bacilli.*

Conclusion: *Our study demonstrated high prevalence rates and incidence rates of infections, sepsis and septic shock among critical care patients at KNH and MPSH with higher-than-average case fatality rates in all sample cohorts. Incident infections were primarily related to invasive devices such as urinary catheters, endotracheal tubes and intravascular catheters.*

Key words: *Critical Care Unit (CCU), International Sepsis Forum (ISF), Sequential Organ Failure Assesment Score (SOFA)*

Introduction

Sepsis is defined as a "syndrome of physiologic, biologic and pathologic abnormalities induced by infection"(1) In the critical care population, sepsis accounts for more than a quarter of all admissions and is associated with an increase in mortality rates (2). There is increasing data that demonstrates that patients who have suffered from sepsis develop significant long term complications(3). Although several studies have provided epidemiological data on sepsis in high income countries, there is a sizeable deficit of data regarding the burden of sepsis in lower income countries and Sub Saharan Africa (4).

Sepsis accounts for 29.5% of all diagnoses amongst critical patients worldwide (2). The general prevalence rate of sepsis is estimated at 535 cases per 100,000 person-years with an analysis of 27 studies illustrating more than 30 million incident cases of sepsis and more than 19 million incident cases of severe sepsis occur worldwide (5).

Patients with sepsis have an elevated mortality rate of 25% as compared to 16% for patients in the Intensive Care Unit (ICU) admitted without sepsis (2). These numbers vary according to geographical region with mortality rates in the United States at 19% as compared to 27% in Uganda (6), (7).

This difference has been attributed to differences in populations, availability of care, and aetiogenesis. The ICON audit showed that ICU patients from low-income countries had a higher mortality as compared to upper- and middle-income countries. Currently, there is limited epidemiological data on sepsis in developing countries where the prevalence and incidence rates are higher.

Septic shock is a more severe subset of sepsis in which profound metabolic abnormalities result in cardiovascular instability. Septic shock carries a mortality rate of approximately 60%.(8)

Hospital-acquired infections contribute significantly to mortality and morbidity and are a significant cause of sepsis in ICU patients. Critical care units suffer from an increased burden of nosocomial infections that is 2-5 times higher than general inpatient populations as critically ill patients are commonly immunosuppressed and often require invasive procedures. (9).

The INDICAPS study demonstrated an incidence of infections in the ICU of 12.2% with a mortality of 28% (10). A point prevalence study done in multiple Intensive care units (ICU) in Turkey showed that 57% of ICU patients had infections. Out of these, 54% were nosocomial infections (11).

Multidrug-resistant organisms pose an emergent problem in-hospital care. A study in 2006 at the KNH, ICU isolated *Pseudomonas aeruginosa, Klebsiella, Citrobacter, Staphylococcus Aureus, and Streptococcus Pneumoniae* as common pathogens. (12) A similar surveillance study in South Africa in 2018 isolated *Klebsiella Pneumoniae* as the most common cause of healthcare-associated infections with over half of the isolated bacteria demonstrating resistance to penicillin(13). Approximately, 74.8% of Acinetobacter species, 39.0% of Klebsiella species and 26.5% of Pseudomonas species isolates were resistant to carbapenem antibiotics (11). Additionally, a surveillance study in Kenya published a Methicillin Resistant Staphylococcus Aureus (MRSA) prevalence of 54% at Kenyatta National Hospital (14). Data regarding the prevalence and incidence of sepsis as well as the types of infections, pathogens isolated, and antibiotic susceptibility patterns would be invaluable in quantifying the burden of sepsis in Intensive care units while knowledge of causative organisms and local antibiotic susceptibility patterns is essential in guiding antibiotic selection and empiric treatment.

Materials and Methods

This was a prospective cohort observational study carried out over a total of four months between December 2020 and March 2021. Three months were used for patient recruitment with a 28 day follow up period to assess mortality. The study was carried out at Kenyatta National Hospital multidisciplinary CCU and medical CCU's as well as the M.P. Shah Hospital CCU. All patients over the age of 18 admitted to the CCU's were recruited into the study. Covid-19 positive patients were excluded from the study. Patients admitted to the CCU's were consecutively recruited on a daily basis by the primary investigator and research assistants within 24 hours of admission. Data was collected from all recruited patients who met the inclusion criteria and provided informed consent.

Admission data included diagnoses, biodata, co-morbidities, vital signs and laboratory data needed to compute the SOFA score. Patients were evaluated for infections using the ISF case definitions and those with infections were subsequently screened for sepsis using the SOFA score. Patients were then stratified into the following categories:

No infection: These patients did not have evidence of infection. A baseline SOFA score was calculated on admission to assess for pre- existing organ dysfunction.

Infection but no sepsis: These patients met the ISF definitions for infection but had a SOFA score of less than 2 on admission Primary foci of infection were categorized according to the ISF case definitions

Sepsis: Presence of an infection as per the ISF definitions and a SOFA score >2, or an increase in SOFA score by 2 points from a previous baseline.

Septic shock: Sepsis and a mean arterial pressure less than 65mmHg necessitating use of norepinephrine >0.1mcg/kg/min despite a 30ml/kg fluid bolus.

After admission to CCU's, all study subjects were then followed up during their CCU stay on day 2, 4, 7, 10, 14, 21 and 28 to assess for development of incident infection(s), sepsis and septic shock. All positive microbial culture reports were documented and analyzed and 28-day vital status was recorded.

Recurrent infections were not considered in this study and only Index CCU admissions were included.

Frequencies (percentages) were used to compute the prevalence and incidence of infection and sepsis. Incidence densities for episodes of infection and incidence rates at specific time intervals for infections, sepsis and septic shock were also calculated. Prevalence rates were calculated as the number with the event of interest (infection, sepsis) divided by the total sample size. Incidence rates were computed as the proportion of patients who developed the outcome of interest. Case fatality rates were calculated as the number of patients who died divided by the population. This was done for patient populations with no infection, patients with sepsis and patients with septic shock.

Wald 95% confidence intervals around the prevalence, incidence, and mortality rates were also calculated.

Foci of infection were tabulated using frequency distribution tables and presented using bar charts. The analysis was stratified by the hospitals (KNH and MP Shah) and chi-squared tests were used to determine statistically significant differences in prevalence, incidence and mortality rates. Analysis was also done for the combined sample population.

The antimicrobial culture data was analyzed as a combined data set for each type of culture specimen to determine common causative organisms. Antibiotic susceptibility and resistance patterns were then tabulated.

Results

Between the months of December 2021 and February 2021, a total of 172 critical care admissions from KNH and MP SHAH Hospital (MPSH) CCU's were sequentially screened for eligibility. Of these, 8 subjects were excluded as they were under the age of

18 and 4 subjects declined to provide informed consent. A total of 160 subjects (108 from KNH and 52 from MPSH) were recruited into the study and subsequently screened using the ISF consensus definitions and SOFA scores for infection, sepsis and septic shock.

Patient demographic

Among subjects in the combined sample, 61.2% of subjects were male, 38.8% were female. The mean age was 45.8 years and the range was between 18 and 93 years. The median age was 44.5 years with an interquartile range (IQR) of 30-59 years.

Among subjects in the KNH sample, 63.9% of subjects were male and 36.1% were female. The mean age at KNH was 40 years, the range was between 18 and 86 years and the median age was 38 years with an IQR of 28-49.5 years.

Among subjects in the MPSH sample, 56% of subjects were male and 44% female. The mean age at MPSH was 56.9 years and the range was between 21 and 93 years. The median age was 58 years with an IQR of 46.5-72.5 years. When the two sample populations were compared, the average and median ages among the KNH cohort were significantly lower than the MPSH cohort. ($p<0.001$)

Among the KNH sample, 52.8% of admissions were in-hospital ward transfers, 36.1% were admitted from home as de-novo admissions and 11.1% were external transfers from a peripheral health facility. At MPSH, 15.4% of subjects were in-hospital ward transfers, 80.8% were admitted from home as de-novo admissions, and 3.8% were external transfers from a peripheral health facility. A significantly larger proportion of patients in the KNH cohort compared to the MPSH cohort were admitted either directly from home or transferred from another hospital ward. ($p<0.001$)

The average CCU length of stay (LOS) in the combined sample was 8.3 days. The LOS in the KNH cohort (9.3 days) was significantly longer than the LOS in the MPSH cohort (6.3 days) ($p<0.001$) (Table 1)

Table 1: CCU Patient Demographic

		Sites		P value
Variables	**Combined** % (n=160)	**KNH** % (n=108)	**MPSH** % (n=52)	
Sex				
Male	61.2% (98)	63.9% (69)	55.8%(29)	0.3234
Female	38.8% (62)	36.1% (39)	44.2%(23)	0.3234
Average Age (years)	45.8(SD:18.9)	40.4(SD:16.2)	56.9(SD: 19.3)	< 0.001
Median Age (years)	44.5	38	58	< 0.001
Interquartile Age range (years)	30-59	28-49.5	46.5-72.5	
Source of admission:				
Home	50.6% (81)	36.1% (39)	80.8%(42)	< 0.001
In hospital Transfer	40.6 % (65)	52.8 % (57)	15.4 % (8)	< 0.001
External transfers	8.8 % (14)	11.1 % (12)	3.8 % (2)	0.1277
Average Length of ICU stay (days)	8.3 (SD:8.4)	9.3 (SD: 9)	6.3 (SD:6.8)	< 0.001

P value: Computed to compare the KNH versus MPSH sample cohorts.

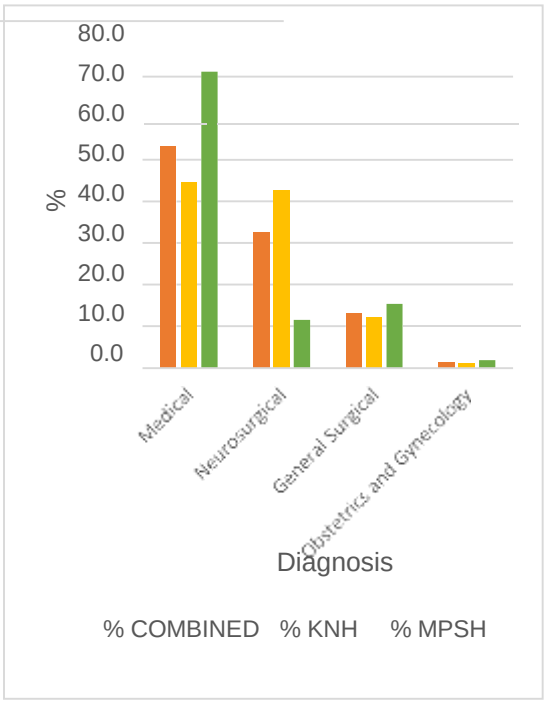
Admission Diagnosis and Co-morbidities

In the combined sample, 53.1% of CCU admission diagnoses were medical, 32.5% were neurosurgical, and 13.1% were general surgical. In the KNH sample, 44.4% of subjects were medical, 42.6% were neurosurgical and 12% admitted with a general surgical diagnosis. In the MPSH sample, 71.2% of subjects were medical diagnosis, 11.5% were neurosurgical and 15.4% had a general surgical diagnosis.

The KNH cohort had a significantly smaller proportion of medical admissions (44.7% vs 71.2%) (p=0.0015) and a significantly larger proportion of neurosurgical admissions (42.6% vs 11.5%) (p=0.0001).

61.9% of all critical care admissions had one or more co-morbidities. Among subjects with co-morbidities in the combined sample, diabetes (insulin and non-insulin dependent) accounted for 31% followed by hypertension at 30%, malignancies at 15% and retroviral disease infection at 14%.

FIGURE 1: Admitting diagnosis amongst CCU patients at KNH and MPSH



Prevalence of Infections, Sepsis and Septic Shock

In the combined sample, the prevalence of infection on admission to CCU was 52.5% (n =84; 95% CI: 44.5-60.4). The prevalence of sepsis was 35% (n=56; 95% CI: 27.3-43.3) and the prevalence of septic shock was 18% (n= 22; 95%CI: 9.0-20.3). Only 3.8% (n=6 95% CI: 1.5-8.3) of subjects with infection did not have sepsis. At KNH, the prevalence of infection was 55.6% (n=60; 95% CI 45.9- 65.1). All infected subjects had sepsis and the prevalence of sepsis was 38.9% (n= 42, 95%CI: 29.9-48.8) while the prevalence of septic shock was 16.7% (n=18; 95%CI 10.4- 25.3).

At MPSH, the prevalence of infection was 46.2%(n=24, 95%CI 32.3-60.5). The prevalence of sepsis was 26.9% (n= 14; 95%CI 16.0-41.3) and the prevalence of septic shock was 7.7% (n=4; 95%CI 2.5- 19.4). Among the MPSH sample 11.5% (n=6; 95% CI 4.8-24.1) had infection without sepsis. The prevalence of subjects with infection (no sepsis) was significantly higher at MPSH (11.5%) compared to KNH (0%), (p=0.0003)

Table 2: Prevalence of infections, sepsis and septic shock on admission.

Category	**Combined n-160 % (n) (95% CI)**	**KNH n- 108 %(n) (95% CI)**	**MPSH n- 52 % (n) (95% CI)**	**P**
All Infections	52.5% (84) (44.5-60.4)	55.6% (60) (45.7-65.0)	46.2% (24) (32.5-60.54)	0.343
Infection (no sepsis)	3.8% (6) (1.5-8.3)	0%	11.5% (6) (4.8-24.1)	0.004
Sepsis	35% (56) (27.7-43.0)	38.9% (42) (29.8-48.8)	26.9% (14) (16.0-41.3)	0.190
Septic Shock	13.8% (22) (9.0-20.3)	16.7% (18) (10.4-25.3)	7.7% (4) (2.5-19.4)	0.194

P value: Computed to compare the KNH versus MPSH sample cohorts.

Incidence of infections, sepsis and septic shock

Among the subjects in the combined sample, the incidence of infection was 41.3% (n=66; 95% CI 33.5-49.3). Among these subjects, 57.6% (n=38) had a prevalent infection on admission. The incidence of sepsis and septic shock were 25.6% (n=21; 95%CI 16.6-36.4) and 11.6% (n=18; 95%CI 7.9-19.8) respectively.

Among the KNH sample, the incidence of infection was 50% (n=54; 95% CI: 40.2-59.8). Among these subjects 57% (n=31) had a prevalent infection at admission. The incidence of sepsis and septic shock was 37.5% (n=18; 95%CI 23.9-52.6) and 17.8% (n=16; 95%CI 10.5-27.3) respectively.

Among the MPSH sample, the incidence of infection was 23.1% (n=12; 95% CI 12.5-36.8). Among these subjects, 58% (n=7) had a prevalent infection on admission. The incidence of sepsis and septic shock was 8.9% (n=3; 95%CI 1.9- 23.7) and 4% (n= 2; 95% CI 0.4-13.7) respectively

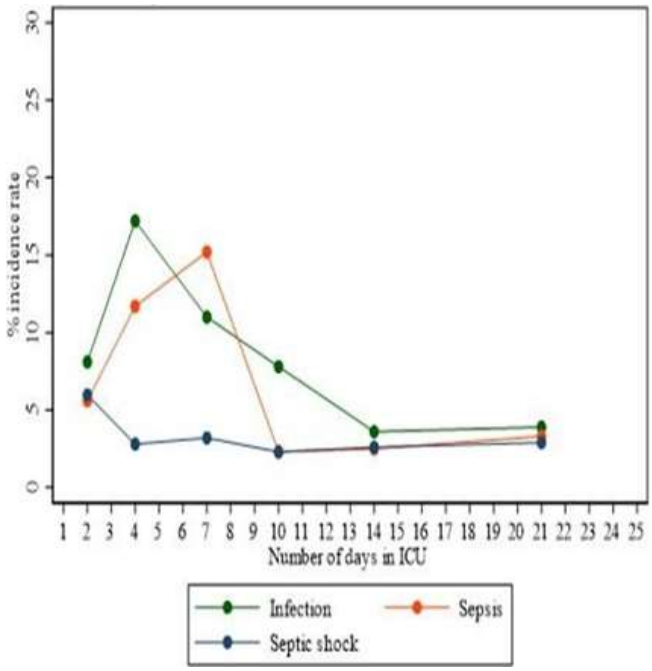
When the two samples were compared, the incidence of infections at KNH (50%) was significantly higher than MPSH (23.1%) (p=0.0012). The incidence of sepsis and septic shock at KNH (37.5%), (17.8%) was significantly higher than MPSH (8.9%), (4%), (p=0.0034), (p= 0.02) respectively. (Table 3)

To demonstrate the time period during which incident episodes of infection, sepsis and septic shock occurred, incidence rates for infections, sepsis and septic shock were computed for the days at which subjects were screened for these events (Day 2, 4,7, 10, 14, 21, 28). (Figure 2)

Table 3: Incidence of Infections, Sepsis and Septic Shock

Category (patients)	**Combined % (n) (95% CI)**	**KNH % (n) (95% CI)**	**MPSH % (n) (95% CI)**	**p- value**
Infection (1 or more)	41.3% (66) (33.5 –49.3)	50% (54) (CI 40.2- 59.8)	23.1% (12) (12.5-36.8)	0.0012
Sepsis	25.6% (21) (16.6-36.4)	37.5% (18) (23.9-52.6)	8.9% (3) (1.9-23.7)	0.0034
Septic shock	13.0% (18)(7.9-19.8)	17.8%(16) (10.5-27.3)	4% (2) (0.4-13.7)	0.02

Figure 2: Incidence rates of infections, sepsis and septic shock at KNH and MPSH CCU's.



Case Fatality Rates

The Case fatality rate (CFR) for the combined sample population was 38.8% (n=62; 95% CI: 31.2-46.8).

The CFR for the KNH sample cohort was 46.3% (n=50; 95% CI 36.7-56.2), compared to 23.1% in the MP Shah cohort (n=12; 95% CI 12.5-36.9). The CFR in the KNH cohort was significantly higher compared to MPSH (p=0.0048).

Among subjects without any incident or prevalent infection, the combined CFR was 27.1% (n=13; 95% CI 15.3-41.9). The CFR among the KNH cohort was 44% (n=11; 95% CI 24.4-65.1),

whereas the CFR among the MP Shah cohort was 8.7% (n=2 95% CI 1.1-28.0).

The CFR in subjects without infection at KNH was significantly higher compared to MPSH (p=0.0060).

. Among subjects with sepsis (either incident or prevalent), the combined CFR was 46.8% (n=36; 95% CI 35.3-58.5) The CFR among the KNH cohort was 46.7% (n=28; 95% CI: 33.7-60.0),

whereas the CFR among the MPSH cohort was 47.1% (n=8; 95% CI: 23.0-72.2).

Among subjects with septic shock (either incident or prevalent), the combined CFR was 59.1% (n=13; 95% CI 36.4-79.3%. The CFR among the KNH cohort was 61.1% (n=11; 95%CI: 35.8-82.7), whereas the CFR among the MPSH cohort was 50% (n=2; 95%CI: 6.8-93.2).

There was no statistically significant difference between KNH and MPSH in the CFRs for patients with sepsis and septic shock. (Table 4)

Table 4: Case fatality rates for subjects at KNH and MPSH CCU's.

	COMB INED % (95% CI)	**KNH % (95% CI)**	**MP SHAH % (95% CI)**	**p-value**
ALL STUDY Subjects	38.8%(31.2-46.8)	46.3%(36.7-56.2)	23.1% (12.5-36.9)	0.0048
NO INFECTION	27.1% (15.3- 41.9)	44% (24.4- 65.1)	8.7% (1.1-28.0)	0.0060
SEPSIS	46.8% (35.3-58.5)	46.7% (33.7-60.0)	47.1% (23.0-72.2)	0.9
SEPTIC SHOCK	59.1% (36.4-79.3)	61.1% (35.8-82.7)	50% (6.8-93.2)	0.7

Foci of prevalent and incident infections

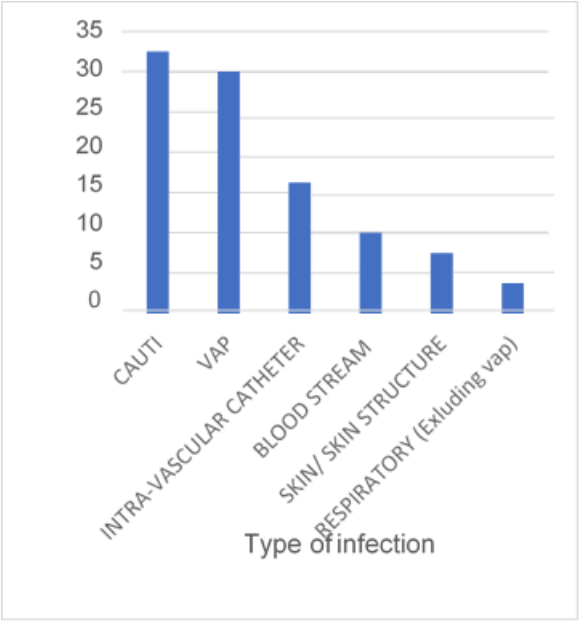
The ISF definitions of infections were used to classify infections according to foci which were tabulated and expressed as proportions.

On admission, among subjects in the combined sample, a total of 84 subjects had one or more prevalent infections. Among these 84 patients, 77.3% (n=65) had a single focus of infectionwhile 22.7% (n=19) had multiple foci. Therefore,a total of 103 foci of infection were computed. Foci of prevalent infection were respiratory (48.6%), intra-abdominal (14.6%), central nervous system (13.6%), skin and skin structure (11.7%) and uro-sepsis (8.7%).

Subjects were screened using the ISF definitionsfor development of incident infections. Among subjects in the combined sample, 66 subjectsdeveloped one or more infections. Among these subjects, 79%(n=52) had a singular focus of infection and 21% (n=14) had multiple foci computing a total of 80 foci of infection.

Foci of infection among incident infections acquired in the critical care units were CAUTI (33%), VAP (30%), intravascular catheter infections (16%), bloodstream infections (10%), skin and skin structure infections (8%) and non- ventilator respiratory infections (4%).

Figure 3: Foci of CCU acquired infections in thecombined sample population.



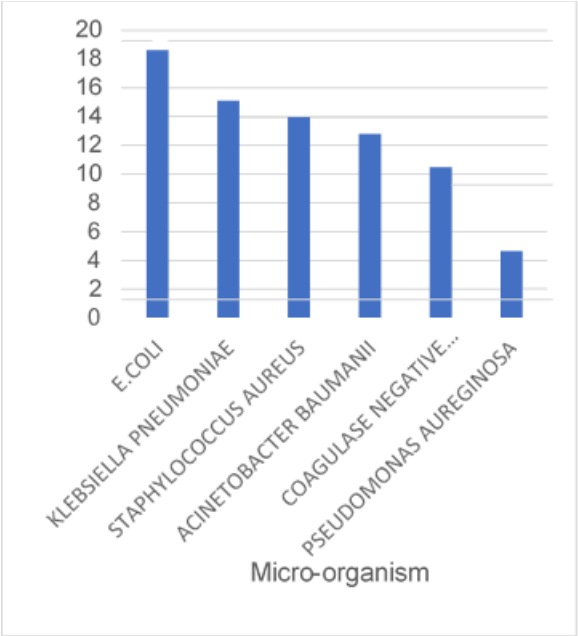
Organisms Isolated and Antimicrobial susceptibility patterns

A total of 321 specimen cultures were analyzed from both hospitals, 62% from KNH and 38.0% from MP shah. The culture positivity rate (all culture specimens) was 33.7% (n=67; 95%CI: 27.1-40.7) at KNH and 15.6% (n=19; 95%CI: 9.6-23.2) at MP.

Shah.

Analysis of antimicrobial sensitivity patterns was done from the combined set of culture reports. Organisms isolated from all culture samples include *E. coli* at 19%, *K. Pneumoniae* at 15%, *S. Aureus* at 14% and *A. Baumanii* at 13%. (Figure 4)

Figure 4: Common organisms isolated from microbial culture specimens.



Sensitivity and resistance patterns were analyzed for the micro-organisms with more than 10 isolates namely E. coli, K. pneumoniae, S. aureus and A. baumanii.

From isolates of E. coli, fifteen were sensitive to Amikacin, twelve to Meropenem, nine to piperacillin/tazobactam and levofloxacin whereas eight of the isolates were resistant to Ceftazidime, six to Ceftriaxone, six toAoxicillin/Clavulanic acid and five to Piperacillin/Tazobactam.

From isolates of K. pneumoniae, ten were sensitive to Meropenem and Amikacin, seven were sensitive to Cipro/Levofloxacin and six to Amoxicillin/Clavulanic acid. Ten of the isolates were resistant to Ampicillin, eight to Cefepime and Ceftazidime, and five to Piperacillin/Tazobactam.

From isolates of S. aureus, all eleven were sensitive to teicoplanin, nine were sensitive to linezolid, eight to levofloxacin and seven to clindamycin whereas eight of the isolates were resistant to benzylpenicillin, six to erythromycin and four to clindamycin.

From isolates of A. baumani, eight were sensitive to colistin, four to ciprofloxacin, and three to meropenem whereas ten isolates were resistant to cefepime and ceftazidime, nine isolates were resistant to piperacillin/tazobactam and meropenem.

Discussion

We set out to primarily determine the magnitude of infections and sepsis among CCU patients, determine 28-day Case fatality rates and characterize the microbial profile of infections.

In this study, we observed a high prevalence of infection whereby over fifty percent of all CCU patients had one or more prevalent infections, thirty five percent had sepsis and thirteen percent met the criteria for septic shock. Foci of prevalent infections were mainly respiratory, intra-abdominal and central nervous system infections.

The proportion of patients who developed one or more CCU acquired infections was as high as 41% whereas 25% and 13% developed sepsis and septic shock respectively. A significantly larger proportion of patients admitted to the parastatal hospital developed infections, sepsis and shock as compared to the private hospital. The incidence density for infections was as high as 18.1 per 100 person days with the highest peak occurring on day 4 of admission whereas the peaks for sepsis and septic shock occurred on day 7 and 2 respectively. Foci of incident infections were mainly CAUTI's, VAP, and intravascular catheter related infections.

The global prevalence rate of infections in critical care patients is approximately 51% while in Africa, the prevalence is estimated at 46% (15). Prevalence rates of sepsis globally are approximately 29%, whereas a Nigerian study demonstrated a prevalence as high as 66%.(16) Globally, the prevalence rate of septic shock is estimated at approximately 13.75%(17). According to data from the EPIC study, the foci of prevalent infections globally are mainly respiratory, intra- abdominal and bloodstream.(15)

Our study demonstrated prevalence rates of infections that were in line with global averages, however our prevalence rates of sepsis were significantly higher than global average. In comparison with the EPIC study, our study found higher rates of CNS infections namely meningitis and encephalitis.

This data highlights a higher burden of sepsis and septic shock in Kenyan CCU's compared to CCU's worldwide. Factors that contribute to this included a large proportion of patients that were referrals from primary centers after clinical deterioration for higher level care especially in the KNH cohort, as well as a large proportion of retroviral disease co- infected patients.

Critical care patients have the highest incidence of infections among hospitalized patients with incidence rates of 21% globally whereas in Africa the incidence is as high as 35%. (17,18) The incidence of sepsis and septic shock worldwide is estimated at 11% and 5.8% respectively. Common foci of incident infections according to a large European audit were CAUTI's and VAP's. (19)

Our study demonstrated higher than average incidence rates of infections, sepsis and septic shock which can be attributed to high rates of invasive device related infections such as CAUTI's, VAP's and intravascular

catheter associated infections that accounted for the bulk of incident infections. A high incidence of infections observed early on day 4 can be attributed to the presence of incubating infections among patients transferred from the ward. Development of new invasive device associated infections that were inserted on admission to the critical care units led to the peak incidence of sepsis on day 7.

High numbers of CAUTI's have been linked to prolonged catheter stay with the risk increasing to almost 100% in 30 days.(8) Similarly prolonged periods of mechanical ventilation and poor endotracheal tube care have been directly associated with increased risk of VAP. (20). High rates of intravascular catheter infections have been linked to prolonged catheter use, poor septic techniques during fixation and use of multiple intravascular devices (21).

Our study found that case fatality rates among patients in the entire sample cohort were as high as 46% (significantly higher in the parastatal hospital) with CFS's in patients without infections, sepsis and septic shock at 27%, 47% and 59% respectively.

Patients in critical care units suffer from an average mortality of up to 9% in North American CCU's and 16% in African CCU's according to a recent audit. (5). Furthermore, patients with sepsis and septic shock suffer from even higher mortality rates of up to 35% and 40% respectively. According to prevalence studies, mortality rates for sepsis was 55% in Brazilian CCU's, and 64% in Indian CCU's. Mortality rates for septic shock were as high as 82% in Tunisia. (11)

Our study demonstrated a critical care unit CFR that was higher than global averages but in line with average CFRs from other lower income countries. Similarly, the CFRs among all patient subsets (no infections, sepsis and septic shock) were significantly higher than the global average but in line with data from other Lower income countries.

High mortality rates in our setting can be explained by a high prevalence of sepsis and septic shock on admission, as well as a high incidence of rates of CCU acquired infections which has been found to be an independent predictor of CCU mortality. (17).

In our setting, although we had a relatively younger patient demographic, a large proportion of our patients had one or more co-morbidities which may have contributed to the high mortality rate observed. A high CFR in our patient population can also be explained by the large proportion of neurosurgical patients in the KNH cohort among which severe head injury accounted for more than one third.

Our study also aimed to identify common causative organisms isolated. We discovered a high prevalence of Gram-negative bacteria namely E. coli, K. pneumoniae and A. baumanii. The most common Gram-positive isolate was S. Aureus.

According to large global studies. gram negative bacteria account for 62% of isolates in ICU's followed by Gram positive bacteria (47%) and fungal isolates (19%). (11,15) A study in Uganda isolated K. Pneumoniae, Acinetobacter and S. aureus as the most frequently isolated bacteria.

In keeping with global data highlighted above, isolates in our study were predominantly gram-negative bacteria. High prevalence rates of Acinetobacter are particularly significant as it is known to contaminate hospital water supplies. CCU practices such as flushing of nasogastric tubes with tap water and poor cleaning of ventilator circuits can lead to increased rates of Acinetobacter infection. (22)

Conclusion

The results from this study demonstrated higher than average prevalence rates of infections and sepsis among a relatively young critical care population with high rates of CCU acquired infections resulting in unacceptably high fatality rates. The data from this study sheds light on the current burden of infections and sepsis in critical care units, and highlights areas for potential interventions that aim to reduce the current morbidity and mortality rates.

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