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NEUROCRITICAL CARE SOCIETY

ORIGINAL WORK

Health Care-Associated Infections in a Neurocritical Care Unit of a Developing Country

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Abstract

Background: Health care-associated infections (HAIs) in intensive care units (ICUs) specialized for neurocritical care (neurocritical care units [NCCUs]) are serious yet preventable complications that contribute significantly to morbidity and mortality worldwide. However, reliable data are scarcely available from the developing world. We aimed to analyze the incidence, epidemiology, microbial etiology, and outcomes of HAIs in an NCCU of a tertiary care teaching hospital in a high-income, developing country.

Methods: In this 3-year retrospective cohort study, all patients admitted to the NCCU at the Ibn Sina Hospital in Kuwait for ≥ 2 calendar days were included. Patient demographics, hospitalization, and details of ICU-acquired infections were evaluated. Patient-related outcomes included hospital and ICU length of stay (LOS) and in-hospital mortality.

Results: Among 913 patients with a total of 4921 ICU days, 79 patients had 109 episodes of HAIs. The overall incidence rate and incidence density of HAIs were 11.9/100 patients and 22.1/1000 ICU days, respectively. Multiple episodes of infection were documented in 29% of patients. The most prevalent infections were urinary tract infections (UTIs; 40/109 [37%]), bloodstream infections (30/109 [28%]), and pneumonia (16/109 [15%]). Seventy-six percent of infections were device-associated infections. A total of 158 pathogens were isolated, of which 109 were Gram-negative bacteria. Of the 40 Gram-positive bacteria, 22 were staphylococci. Seven infections were due to *Clostridium difficile*. There were 15 *Staphylococcus aureus* isolates, 47% of which were methicillin resistant. Two episodes of UTIs were due to *Candida* species. There were 84 Enterobacteriaceae isolates, 24% of which were extended-spectrum β-lactamase producers. All *Pseudomonas aeruginosa* isolates were susceptible to aminoglycosides and carbapenems. *Klebsiella* species were the most common pathogen (45/158 [28%]), causing pneumonia (11/33 isolates [33%]), bloodstream infections (12/37 isolates [32%]), and UTIs (16/52 isolates [31%]). One episode of bloodstream infection was due to multidrug resistant *Acinetobacter baumanii* which was susceptible only to colistin. Only pneumonia was independently associated with mortality, while all HAIs that occurred were significantly associated with a prolonged ICU LOS.

Conclusions: This is the first HAI surveillance study in an NCCU in Kuwait, and our results demonstrate the burden of HAIs on the neurologically injured patient, regardless of the site of infection. The high prevalence and resistant profile of HAIs in an NCCU in a developing country relative to a developed country has important implications for patient safety and emphasizes the need to strengthen collaboration between NCCU teams and infection control teams to prevent serious complications in this setting.

Keywords: Critical care, Nosocomial infections, Pneumonia, Ventilator-associated pneumonia, Urinary tract infections, Ventriculostomy-associated infections

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Introduction

Health care-associated infections (HAIs) acquired in intensive care units (ICUs) are a serious issue and a major cause of patient-related morbidity and mortality. This is of pronounced significance among neurologically injured patients, as prolonged use of multiple invasive catheters is common, and patients tend to require extended ICU care, which increases their risk for nosocomial infections [1–3]. In addition, such patients may be at increased risk of developing an HAI given that they are more likely to have altered mental status, aspiration, immunosuppression, and concomitant trauma [2, 4, 5]. However, the epidemiology of HAIs in specialized ICUs for neurocritical care (neurocritical care units [NCCUs]) is scarcely addressed in the literature, especially in developing countries. Reported incidence rates of HAIs in NCCUs in both developing and developed countries have ranged between 3.7 and 88.9 per 100 patients, although there were differences in the definitions and surveillance methods used among the countries [6–10]. The resulting burden of HAIs on hospitalization and patient-related outcomes in the neurocritical care setting is not known, especially in regions outside of Europe and North America [11–13]. Studies using data from neurology ICUs in developing countries report higher infection rates and higher risk of infections when compared to developed countries, emphasizing the need for further research in order to identify solutions to relieve this burden [14–16].

Surveillance of HAIs is recommended as part of an effective infection control program and is considered a metric for evaluating the quality of health care in hospitals [17]. To ensure uniformity of reported data worldwide, many international hospitals have adopted the US Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) definitions for HAIs and device-associated infections (DAIs) [15, 18, 19]. Kuwait, which is considered to be a high-income, developing country, has implemented prospective national surveillance programs aimed at monitoring HAIs using these definitions [20]. A prospective surveillance study in 7 adult, pediatric, and neonatal ICUs in Kuwait found that DAI rates were higher than CDC/NHSN rates [20]. Thus, data collected by HAI surveillance programs represent valuable sources of information that can provide insights into the impact of HAIs on patients and the health care system in a particular region or clinical setting.

This study is the first to evaluate HAI surveillance data from an NCCU in Kuwait, a region that remains underrepresented in the medical literature. The aim of this study was to analyze the epidemiology, incidence rates, microbial etiology, and patient-related outcomes of all ICU-acquired HAIs in a neurocritical care patient population from a single center in a high-income, developing country.

Methods

Study Design and Setting

In 2014, a prospective, year-round surveillance program was established to identify and report all HAIs at Ibn Sina Hospital (a tertiary care teaching hospital in Kuwait), including the specialized ICUs. This retrospective cohort study reviewed the prospectively collected surveillance dataset and reported the 3-year cumulated data of all ICU-acquired HAIs in the NCCU, including patient-related outcomes. All patient admissions of ≥ 2 calendar days to the dedicated neurocritical care beds between January 1, 2015, and December 31, 2017, were included in the study.

The NCCU was one of the specialized ICUs in a 514-bed center with 120 ward beds dedicated to neurosurgical and neurological patients. Intensive medical care was also provided in 2 other specialized adult ICUs and 1 neonatal ICU. This setup is unique as there are no other NCCUs in the country. The center received transfers from all hospital emergency rooms and ICUs in the country, covering a population of 4.3 million. The ICU had 13 active beds of which 7 (3 beds in single-patient rooms and 4 ward beds) were dedicated to neurocritical care patients. The analysis was conducted on patients admitted to the 7 dedicated neurocritical care beds. Infrequently, other medical patients were admitted to the dedicated neurocritical care beds.

The NCCU was staffed by a trained neurointensivist and anesthetists and allowed for management of a mixed neurosurgical and neurological critical care patient population in which both the NCCU team and the admitting service team collaborated on daily rounds and management plans. As an ICU policy, all patients receive stress ulcer prophylaxis on admission in the form of a proton pump inhibitor or H2 blockers. Invasive procedures, including insertion of central lines, external ventriculostomy drains (EVDs), and Foley catheters, were performed by ICU staff, neurosurgeons, and nursing staff, respectively. EVDs were only inserted in operating rooms.

For simplicity and accordance with commonly used terms for outcomes, the NCCU will herein be referred to as the *ICU*.

Patient Characteristics and Outcomes

Collected variables per admission included patient demographics, principle diagnosis on discharge, the administration of prophylactic antibiotics, and primary interventions during the ICU stay. Based on existing ICU databases and radiology records, and in line with other studies [10], admissions were retrospectively categorized by a single investigator into one of the following diagnostic categories: central nervous system (CNS) neoplasm, CNS infections, intracerebral/intraventricular hemorrhage, ischemic stroke, medical complications, neurological readmissions, neuromuscular/demyelinating/motor neuron diseases, postoperative/post-neuroendovascular intervention, seizure/status epilepticus, spinal cord disease, subarachnoid hemorrhage (SAH), subdural hematoma, traumatic brain injury, or other neurovascular diseases/surgeries.

Collected variables for each episode of HAI included the type of infection, related devices and catheters, and associated pathogens and their antimicrobial susceptibility.

The primary outcome was all-cause in-hospital mortality censored at 30 days from an episode of infection. Secondary outcomes were ICU length of stay (LOS), hospital LOS, and in-hospital mortality.

Surveillance Program

ICU-acquired HAI surveillance definitions were adapted from the 2015 CDC/NHSN definitions [19, 21], and data were collected using mandated Kuwait National Healthcare-Associated Infections Surveillance System forms (see supplemental methods for surveillance definitions). Each patient's entire ICU stay up to 48 h after ICU discharge was assessed daily using the following data sources: medical and nursing case records; ICU case sheets; imaging and microbiology reports, including antimicrobial susceptibility profiles; and, where necessary, discussion with clinical staff and direct clinical observation.

Additionally, records for specific infection signs and symptoms were completed by trained infection control nurses. Clinical clues of infections included fever, diarrhea, urinary or respiratory symptoms, wound discharge, and non-prophylactic antibiotic prescription. Charts, laboratory results, and imaging for any patients identified by these methods were reviewed and validated by the infection control consultant to identify site-specific infection criteria using the CDC/NHSN definitions. An ICU-acquired HAI was defined as an infection arising ≥ 48 h after admission to the ICU that was neither present nor incubated on ICU admission. Rigorous quality assurance of data was retrospectively undertaken to ensure that recorded HAIs met one of the case definitions. HAIs occurring at more than one site in the same patient were reported as separate episodes.

Device-specific denominator data, including patient days and device days, were collected daily by trained health care personnel [18]. The device utilization (DU) ratio, which measures the intensity of the device used in the ICU, was calculated as the ratio of device days to patient days [22].

Microbial Identification and Antimicrobial Susceptibility Testing

Microbial identification and antimicrobial susceptibility testing were performed using VITEK® 2 system (bioMerieux, France). Additionally, ETEST® reagent strips (bioMerieux, France) were used for confirmation of some antimicrobial susceptibility results.

Infection Control Strategies

Patient hygiene measures consisted of washing with soap and water. Chlorhexidine baths were only performed preoperatively and if the patient was colonized with methicillin-resistant *Staphylococcus aureus* (MRSA). Bundles-of-care for ventilator-associated pneumonia (VAP) prevention and central line-associated bloodstream infection (CLABSI) were utilized throughout the study period. The VAP prevention bundle included the following elements: (1) elevation of the head off the bed between 30° and 45°, (2) daily sedation windows and assessment for readiness to extubation, (3) peptic ulcer disease prophylaxis, (4) deep vein thrombosis prophylaxis, and (5) daily oral care using chlorhexidine. The CLABSI bundle included the following elements: (1) hand hygiene, (2) maximum barrier protections upon insertion, (3) chlorhexidine skin antisepsis preparation, (4) optimal catheter site selection (with avoidance of the femoral vein for central venous access in adult patients), and (5) daily review of line necessity with prompt removal of unnecessary lines. Central line maintenance included hand hygiene before all line manipulation, aseptic dressing change using chlorhexidine gluconate intravenous securement dressing (gel pad containing 2% chlorhexidine gluconate) which is routinely changed every 5–7 days or earlier if compromised, injection caps alcohol swab 15 s wipe before access, and ensuring patency of the catheter lines. When a central line is deemed infected, it is removed and if necessary, a replacement line is inserted in a different location. Training on aseptic techniques for urinary catheter insertion

was part of health care staff training throughout the study period.

All admissions were screened for MRSA. Patients were under contact precautions and isolated only when MRSA screening was positive. Nasal MRSA screening was performed using the Xpert® MRSA NxG system (Cepheid, USA). If MRSA screening was positive, conventional cultures were analyzed for antimicrobial susceptibility. After a decolonization protocol, the nasal screening was repeated, and the contact precaution was discontinued if the culture was negative for MRSA. Patients who developed a *Clostridium difficile* infection or an extended-spectrum beta-lactamase producing infection were transferred to an isolation room and treated under contact precautions until results become negative.

Statistical Analysis

Descriptive statistics were calculated using frequencies, means, medians, and interquartile ranges (IQRs). We used Kaplan–Meier curves and Cox regression analyses to estimate the risk of developing an HAI in each diagnostic category compared to CNS neoplasm as a reference (which is IDH-wild type) after adjusting for age and sex. In this study, there were 21 recurrent infections; these recurrent time-to-events were analyzed by the Andersen–Gill method [23], which generalizes the Cox regression model by formulating increments in the number of events along the timeline. We also studied the effect of the type of HAI on hospital LOS and ICU LOS using multivariate linear regression models. In addition, we studied the excess mortality attributable to each type of HAI using Cox regression models after adjusting for age and sex. A separate time-dependent variable was classified as infected for 30 days after the onset of infection. A significance level of 0.05 was used.

Compliance with Ethical Standards

The institutional research ethics board and Kuwait University Health Sciences Center Ethical Committee approved this study. This study was purely observational. For this type of study, formal consent was not required as data extracted were derived from medical records and existing databases.

Results

Overall Population

During the 3-year study period, 985 patients were admitted to the NCCU of which 913 stayed ≥ 2 calendar days, for a total of 4921 ICU days. Fifty-eight percent of patients were men and 42% were women. The median age of patients was 47 years (IQR, 36–57); only 29 (3%) admissions were of patients younger than 18 years of age. There was an average of 140 ± 57 patients in each ICU bed (83 ± 11 patients in the single-patient room bed and 183 ± 24 in the ward bed). Seventy percent of patients (640/913) received prophylactic antibiotics (64 before an EVD insertion and 576 before a surgical intervention). The mean ICU LOS was 5.4 ± 7.8 days. ICU admissions and LOS for each diagnostic category are presented in Table 1. In this study, missing data were sporadic and

Table 1 ICU admissions and LOS based on principle diagnostic category

Diagnostic category	ICU admissions		ICU LOS (days)			HAIs	
	Total	%	Total	%	Median (IQR)	Total	Rate[a]
CNS neoplasm	453	49.6	1360	27.6	1 (1–2)	20	14.7
SAH	213	23.3	2663	54.1	11 (4–17)	71	26.7
Postoperative/post-neuroendovascular intervention	110	12.0	161	3.3	1 (1–1)	0	–
Medical complications	25	2.7	67	1.4	1 (1–3)	0	–
Intracerebral/intraventricular hemorrhage	22	2.4	143	2.9	4 (2–12)	3	21.0
Neurological readmissions	18	2.0	106	2.2	3 (2–7)	3	28.3
Spinal cord disease	18	2.0	42	0.9	1 (1–2)	1	23.8
CNS infections	16	1.8	33	0.7	1 (1–2)	1	30.3
Subdural hematoma	10	1.1	60	1.2	4 (1–11)	1	16.7
Neuromuscular/demyelinating/motor neuron diseases	9	1.0	111	2.3	4 (1–14)	5	45.0
Ischemic stroke	7	0.8	82	1.7	3 (2–5)	1	12.2
Other neurovascular diseases/surgeries	6	0.7	78	1.6	10 (3–22)	3	38.5
Seizure/status epilepticus	5	0.5	13	0.3	1 (1–4)	0	–
Traumatic brain injury	1	0.1	2	0.0	2 (2–2)	0	–
Total	913		4921			109	22.1

CNS central nervous system, *ICU* intensive care unit, *IQR* interquartile range, *LOS* length of stay, *SAH* subarachnoid hemorrhage, *HAI* health care-associated infection

[a] Rate per 1000 ICU days. Percentages may not total 100 because of rounding

seldom (< 2% of all variables); hence, we did not perform any interpolations.

Health care-Associated Infections

A total of 109 ICU-acquired HAIs in 79 patients were detected during the study period, translating to an incidence rate of 11.9/100 patients and an incidence density of 22.1/1000 ICU days. During the same ICU admission, the majority of patients developed one episode of HAIs (56/79 [71%]), while multiple episodes were documented in 29% of patients (two episodes in 16/79 [20%]) and three episodes in 7/79 [9%]). Urinary tract infections (UTIs) were the most common type of HAI (40/109 [37%]), followed by bloodstream infections (30/109 [28%]), pneumonia (16/109 [15%], 12 late-onset pneumonia [> 4 days from ICU admission] and 4 early-onset pneumonia), and ventriculostomy-associated infections (VAIs; 8/109 [7%]). All 40 UTIs were catheter-associated urinary tract infections (CAUTIs). The bloodstream infections included 3 primary bacteremia, 20 CLABSIs, and 7 secondary bacteremia (4 UTIs, 2 skin and soft tissue infections [SSTIs], and 1 VAP). There were 8 VAIs, 5 (63%) of which were associated with SAH.

Of the 109 HAIs, 83 (76%) were DAIs, the most common of which were episodes of CAUTIs (40/83 [48%]), CLABSIs (20/83 [24%]), and VAP (12/83 [14%]). Ten (83%) of the 12 cases of VAP occurred ≥ 4 days after admission (late-onset pneumonia). Annual trends for these DAIs over the 3-year study period are listed in Table 2. Details of those DAIs, the DU ratio, and number of days from device insertion to infection were as follows: 4585 indwelling urinary catheter days resulted in a mean rate of 8.7 CAUTI episodes/1000 catheter days (DU, 0.95) with a median of 7 days from device insertion to infection; 1548 ventilator days resulted in a mean rate of 7.8 VAP episodes/1000 ventilator days (DU, 0.32) with a median of 5 days from device insertion to infection; and 3235 central line days resulted in a mean rate of 6.2 CLABSI episodes/1000 central line days (DU, 0.67) with a median of 8 days from device insertion to infection.

Table 3 presents hazard ratios (HRs) of acquiring a nosocomial infection associated with different diagnostic categories. Except for subdural hematoma, risk of developing an infection was high among all studied diagnostic categories relative to the reference category; however, none of these associations were statistically significant. While validating these relations with conventional Cox regression (considering only time to the first episode), there was an indication that patients admitted with neuromuscular/demyelinating/motor neuron diseases may have had an increased risk of developing a nosocomial infection (HR = 1.78; 95% confidence interval [CI] = 0.95–3.34). From the Kaplan–Meier curves for the diagnostic categories with the highest risk of infection (SAH, spinal cord disease, and neuromuscular/demyelination/motor neuron diseases), the probability of infection increased with the length of ICU stay (Fig. 1). At one week after ICU admission, 22% (2/9) of patients admitted with neuromuscular/demyelinating/motor neuron

Table 2 DAI incidence rates by year for CAUTI, VAP, and CLABSI

Type of DAI	Year	Number of episodes	Number of patient days	Number of device days	Rate per 1000 device days	DU ratio	Days from devise insertion to infection, median (IQR)
CAUTI							
	2015	13	1514	1420	9.2	0.94	5 (4–11)
	2016	13	1461	1376	9.4	0.94	6 (4–11)
	2017	14	1874	1789	7.8	0.95	8 (6–15)
	Total	40	4849	4585	8.7	0.95	7 (4–11)
VAP							
	2015	6	1514	542	11.1	0.36	5 (3–5)
	2016	2	1461	348	5.7	0.24	8 (6–9)
	2017	4	1874	658	6.1	0.35	6 (4–9)
	Total	12	4849	1548	7.8	0.32	5 (4–9)
CLABSI							
	2015	6	1514	1043	5.8	0.69	5 (4–11)
	2016	5	1461	870	5.7	0.60	11 (7–12)
	2017	9	1874	1322	6.8	0.71	8 (5–16)
	Total	20	4849	3235	6.2	0.67	8 (5–14)

CAUTI catheter-associated urinary tract infection, *CLABSI* central line-associated bloodstream infection, *DAI* device-associated infection, *DU* device utilization, *IQR* interquartile range, *VAP* ventilator-associated pneumonia

Table 3 HR comparing the risk of developing episodes of HAIs with the reference category (CNS neoplasm) for each diagnostic category using the Andersen–Gill method after adjusting for age and sex

Diagnostic category	HR	95% CI	*P* value
CNS infections	3.35	0.44–25.49	0.24
Neuromuscular/demyelinating/motor neuron diseases	2.53	0.93–6.87	0.07
Neurological readmissions	1.67	0.49–5.66	0.41
Spinal cord disease	1.48	0.19–11.32	0.71
Intracerebral/intraventricular hemorrhage	1.28	0.37–4.37	0.70
SAH	1.23	0.73–2.06	0.44
Subdural hematoma	0.64	0.08–4.92	0.66
Others	1.47	0.33–6.53	0.61

CI confidence interval, *CNS* central nervous system, *HAI* health care-associated infection, *HR* hazard ratio, *SAH* subarachnoid hemorrhage

disease developed an HAI, 16% (35/213) of patients with SAH, and 6% of patients with spinal cord disease.

Microbiology Profile and Antimicrobial Resistance

Table 4 summarizes the distribution of pathogens responsible for the 109 HAIs, stratified by site of infection. A total of 158 pathogens were isolated. Some infections were polymicrobial (18/109 [17%]). Most of those were from respiratory (28%) and wound infections (28%). All patients with polymicrobial infections were symptomatic. Out of 158 pathogens isolated, 109 (69%) were Gram-negative bacteria, 40 (25%) were Gram-positive bacteria, 2 (1%) were *Candida* species, and 7 (4%) were *Clostridium difficile*.

Of the 109 Gram-negative bacteria isolated, 84 were Enterobacteriaceae, 24% of which were extended-spectrum β-lactamase (ESBL) producers. Fifteen of the 109 Gram-negative pathogens were *P aeruginosa,* and all were susceptible to aminoglycosides and carbapenems.

Of the 40 Gram-positive bacteria isolated, 11 (28%) were *Enterococcus faecalis,* and none were vancomycin resistant. Seven of the 15 *Staphylococcus aureus* isolates (47%) were MRSA, and all were susceptible to both vancomycin and linezolid.

ICU-acquired pneumonia episodes, of which (12/16 [75%]) were ventilator associated, were mainly caused by Gram-negative organisms (27/33 [82%]). *Klebsiella species* was the most common pathogen (45/158 [28%]), causing pneumonia (11/33 isolates [33%]), bloodstream infections (12/37 isolates [32%]), and UTIs (16/52 isolates [31%]). Pneumonia cultures were isolated from 10 endotracheal suction, 3 sputum cultures, 1 bronchoscopy lavage, and 1 blood culture. VAIs were mainly caused by *Staphylococcus* (4/10 [40%]), predominantly coagulase-negative staphylococci. There was only 1 bloodstream infection caused by multidrug-resistant *Acinetobacter baumanii*, which was resistant to cephalosporins, quinolones, piperacillin/tazobactam, and carbapenems; the isolate was susceptible only to colistin.

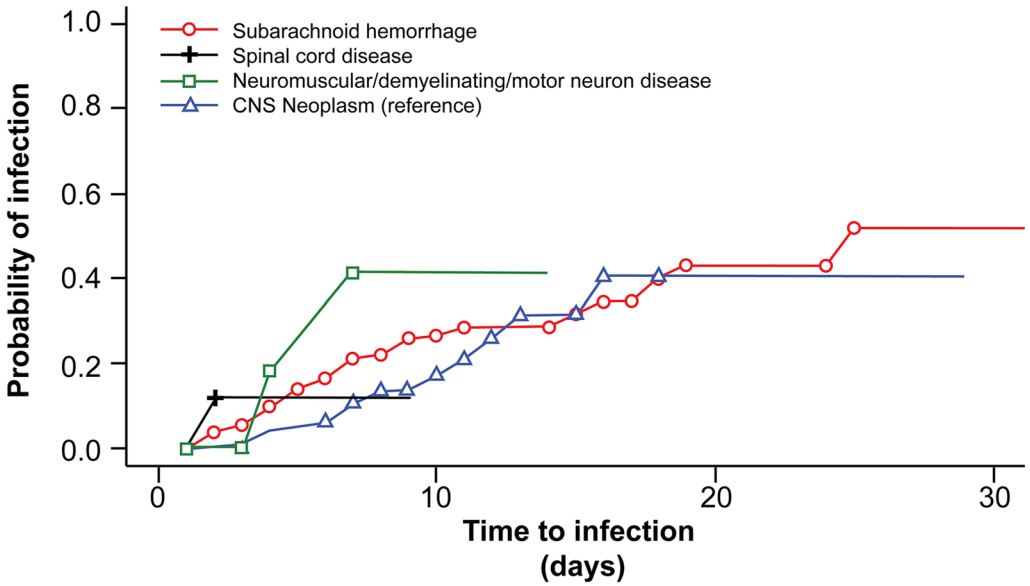

Fig. 1 Kaplan–Meier plot depicting the probability of developing a nosocomial infection in diagnostic categories with the highest risk. *CNS*, central nervous system

Table 4 Pathogen distribution across the types of HAIs

Pathogen (gram stain)	UTI (*N* = 40)	Pneumonia (*N* = 16)	VAI (*N* = 8)	Bloodstream infection (*n* = 30)		Other HAIs[b] (*N* = 15)	Overall
				Primary and CLABSIs (*N* = 23)	Secondary[a] (*N* = 7)		
Klebsiella species (−)	16	11	2	9	3	4	45
Escherichia coli (−)	13	4	0	0	3	2	22
Pseudomonas aeruginosa (−)	7	4	0	2	0	2	15
Enterobacter (−)	1	5	1	3	0	1	11
Enterococcus faecalis (+)	7	0	0	1	0	3	11
Staphylococcus aureus (+)	1	5	1	0	0	1	8
MRSA (+)	1	1	0	3	0	2	7
Acinetobacter baumanii (−)	0	1	1	2	0	2	6
Stenotrophomonas maltophilia (−)	0	1	0	3	0	0	4
Staphylococcus epidermidis (+)	0	0	2	2	0	0	4
Serratia marcescens (−)	1	0	0	1	0	1	3
Other Enterobacteriaceae (−)	1	1	0	0	0	1	3
Staphylococcus hemolyticus (+)	2	0	1	0	0	0	3
Streptococcus mitis (+)	0	0	1	1	1	0	3
Other Gram-positives (+)	0	0	1	3	0	0	4
Candida spp.	2	0	0	0	0	0	2
Clostridium difficile	–	–	–	–	–	–	7
Total isolates	52	33	10	30	7	19	158

CLABSI central line-associated bloodstream infection, *HAI* health care-associated infection, *MRSA* methicillin-drug resistant *Staphylococcus aureus*, *N* number of episodes, *SSTI* skin and soft tissue infection, *UTI* urinary tract infection, *VAI* ventriculostomy-associated infection

[a] Secondary bacteremia isolates are derived from pathogens detected in blood cultures and are not isolated from the primary source of infection

[b] The 15 other HAIs included 8 surgical site infections and 7 SSTIs

Outcomes

Ten percent of patients with an ICU-acquired HAI died within 30 days of infection during their hospitalization, while the in-hospital mortality rate of patients admitted to the NCCU ≥ 2 days was 6.3% (51/815). The median hospital LOS was 18 days (IQR, 10–32). Twenty-four patients (3%) remained in the hospital for more than 6 months, of which 8 remained in hospital during data analysis, accounting for 39 ICU admissions. Those 8 patients who remained in hospital at the end of the observation period were censored during data analysis.

Table 5 shows the association between ICU and hospital LOS with the various diagnostic categories and HAIs. SAH, ischemic stroke, neuromuscular/demyelinating/motor neuron diseases, and most of the HAIs were associated with an increase in ICU LOS. Similarly, hospital LOS was increased for patients admitted with CNS infection, neuromuscular/demyelinating/motor neuron diseases, and patients complicated with bloodstream infections and *C difficile* infections.

Table 5 also shows the estimated risk of in-hospital mortality associated with the various HAIs after adjusting for age and sex. Despite the higher observed risks for some HAIs, only ICU-acquired pneumonia was associated with an excessive risk of in-hospital mortality. Though the CIs are dispersed widely (HR = 72.73; 95% CI: 11.30–468.3; $p = < .0001$), this strong association may be a result of the small number of infections documented (n = 16).

Discussion

We conducted a large 3-year surveillance study of ICU-acquired HAIs in all patients admitted to an NCCU for ≥ 2 calendar days in Kuwait. The main findings of our study were that (1) the overall incidence rate and incidence density of HAIs were 11.9/100 patients and 22.1/1000 ICU days, respectively; (2) the most prevalent infections were UTIs, bloodstream infections, and pneumonia; (3) all HAIs were associated with prolonged ICU LOS; (4) the probability of nosocomial infection increased for high-risk diagnostic categories, with variable probabilities, 1 week following ICU admission; and (5) ICU-acquired pneumonia was independently associated with an increased risk of in-hospital mortality.

Despite implementing evidence-based infection control strategies, HAIs remain a serious complication and a major threat to the safety of patients. Therefore, HAIs deserve meticulous attention for both prevention and

Table 5 Estimated increase in ICU and hospital LOS and risk of in-hospital mortality for each diagnostic category and type of HAI

Characteristics	ICU LOS (*N* = 913)		Hospital LOS (*N* = 839)		In-hospital mortality (*N* = 800)	
	Estimated increase	95% CI	Estimated increase	95% CI	Hazard ratio	95% CI
Diagnostic category						
SAH	**6.77**	**5.85 to 7.68**	− 10.57	− 26.02 to 4.88	**2.65**	**1.22–5.77**
Ischemic stroke	**6.36**	**2.39 to 10.33**	− 8.82	− 74.46 to 56.82	–	–
Neuromuscular/demyelinating/motor neuron diseases	**5.35**	**1.81 to 8.88**	**130.58**	**68.60 to 192.55**	2.80	0.52–15.11
Subdural hematoma	1.77	− 1.61 to 5.16	− 34.41	− 96.74 to 27.92	–	–
Intracerebral/intraventricular hemorrhage	1.76	− 0.52 to 4.05	− 13.05	− 50.92 to 24.82	0.42	0.03–5.25
Neurological readmissions	0.69	− 1.84 to 3.21	− 31.09	− 202.02 to 139.85	–	–
Seizure/status epilepticus	0.22	− 4.45 to 4.90	46.06	− 39.88 to 132.00	–	–
Traumatic brain injury	− 0.01	− 10.42 to 10.39	18.87	− 152.43 to 190.17	–	–
Medical complications of neurological/neurosurgical patients	− 0.15	− 2.31 to 2.01	− 23.97	− 61.92 to 13.98	**13.57**	**3.95–46.69**
Spinal cord disease	− 1.17	− 3.69 to 1.35	− 13.16	− 55.86 to 29.55	1.62	0.21–12.65
Postoperative/post-neuroendovascular intervention	− 1.17	− 2.28 to − 0.07	− 2.93	− 21.66 to 15.79	0.31	0.04–2.35
CNS infections	− 1.50	− 4.16 to 1.15	**117.03**	**70.49 to 163.7**	0.91	0.12–7.10
Others	4.06	− 0.33 to 8.45	**126.29**	**52.34 to 200.24**	–	–
Type of HAI						
Pneumonia	**18.53**	**15.77 to 21.29**	59.28	0.23 to 118.33	**72.73**	**11.30–468.3**
VAI	**18.27**	**14.26 to 22.29**	57.12	− 20.01 to 134.26	–	–
Bloodstream infection	**13.43**	**10.46 to 16.40**	**102.63**	**49.65 to 155.60**	2.92	0.37–23.02
C difficile infection	**12.54**	**8.23 to 16.86**	**135.31**	**64.12 to 206.50**	–	–
UTI	**9.99**	**8.03 to 11.95**	25.64	− 6.45 to 57.72	1.50	0.42–5.29
Other HAIs	**20.37**	**16.02 to 24.72**	− 6.16	− 74.85 to 62.54	3.85	0.43–34.10

CI confidence interval, *CNS* central nervous system, *HAI* health care-associated infections, *ICU* intensive care unit, *LOS* length of stay, *SAH* subarachnoid hemorrhage, *UTI* urinary tract infection, *VAI* ventriculostomy-associated infection. Bold denotes statistical significance ($p < 0.05$)

management, particularly in ICUs. Compared with other studies conducted in other countries, we found similar rates of overall ICU-acquired infections in our patient population (9.6 compared with 3.7–25.0 per 100 patients) [7–10]. When analyzing the various DAIs, our study found that DAI rates per 1000 device days were comparable to frequencies reported by other neurology and neurosurgery ICUs, including rates for CAUTI (8.7 compared with 3.0–17.17 per 1000 catheter days), VAP (7.8 compared with 2.1–19.2 per 1000 ventilator days), and CLABSI (6.2 compared with 0.6–10.14 per 1000 central line days) [9, 10, 13, 14, 18, 22, 24, 25]. The highest rates were reported in neurology ICUs in developing countries [14], thus emphasizing the marked prevalence of this complication in this setting.

Several studies have highlighted the significantly higher risk of infection and how this translates into a major burden in developing countries when compared to developed countries [15, 16]. A 14-month study from a Turkish 6-bed neurological ICU (surveillance period between 1999 and 2000) reported a strikingly high nosocomial infection incidence rate of 88.9/100 patients and an overall mortality rate of 60% [6]. By comparison, data from a German 10-bed neurological ICU derived from the same surveillance period reported an infection incidence rate of 24.2/100 patients (mortality data were not presented) [7]. More recently, a large 6-year Canadian study from a mixed neurosurgical/neurological ICU estimated that the infection incidence rate was 3.7/100 patients [10]. Similar frequency rates were also recently found in a 5-year study analyzing data from a Turkish neurosurgery ICU [8].

In our study, a greater proportion of patients affected with pneumonia died compared to patients without these infections. Although the large Canadian study failed to find a significant association between pneumonia and mortality [10], we confirmed pneumonia as a robust and independent predictor of mortality, after adjusting for diagnostic category, age, and sex. This difference may

be explained by the fact that pneumonia episodes from our cohort were predominantly caused by Gram-negative bacteria, while the majority of pneumonia episodes from the Canadian study were caused by Gram-positive bacteria.

Pneumonia and bloodstream infections have been shown to be an independent predictor of death after acute ischemic stroke and SAH, after adjusting for the severity of the disease [2, 26]. We did not find a statistically significant association between bloodstream infections and in-hospital mortality (HR = 2.92; 95% CI: 0.37–23.02; $p = 0.3084$). This may be due to underpowering, although interestingly the large Canadian study also found that statistical significance was not reached for this association, despite an HR of 1.59 (95% CI: 0.39–6.44) [10].

In our study, bloodstream infections were predominantly device associated. Compared with other benchmark studies from developed and developing countries, which included critically ill neurosurgery and neurology populations, central line utilization in our study was higher (DU ratio of 0.67 compared with 0.28–0.54) [14, 18, 22, 25]. This may be partly reflected in the strikingly high CLABSI rate we observed, as duration of catheterization tends to be prolonged in certain diagnostic categories, namely SAH. However, our incidence density rate for CLABSI is in line with those reported by other developing countries [14], yet it is 6 times higher than those reported by the US CDC/NHSH in similar settings [18, 22, 24, 25]. Efforts are needed to successfully eliminate this issue in developing countries. Several studies have demonstrated that CLABSI rates may be sustainably reduced and that CLABSI might even be preventable [27, 28]. Recommendations to reduce the frequency of CLABSI in general ICUs have included bundles-of-care with the following elements: placement and maintenance of central lines using rigorous sterile technique, chlorhexidine skin preparation, avoidance of femoral central lines, use of three-way stopcock, sterile dressing in good condition, administration set replacement every 3 to 4 days, and early discontinuation of central lines [29–31]. These recommendations are generalizable to neurosurgical and neurological ICUs, including those in developing countries.

Very few studies have included data about antimicrobial resistance in the neurocritical care population. This existing paucity of information on antimicrobial resistance highlights the caution needed when interpreting findings. In our study, the rate of MRSA isolated from different infections was 47% compared to only 3% in the large Canadian study [10]. The incidence of multidrug-resistant bacteria was high in our study as 24% of Enterobacteriaceae were ESBL compared to less than 6% in the Canadian study [10]. The antimicrobial susceptibility of *P aeruginosa* was comparable in both studies. This may indicate that antimicrobial resistance is more prevalent in ICUs in developing countries [20]. Further studies reporting data on resistance patterns among neurologically critical patients are needed.

This study has several limitations. First, data were collected from a single-center, specialized NCCU with a defined neurocritical care patient population, which limits its generalizability to other settings. However, our study allows for benchmarking comparative data from emerging specialized units in developing countries. Second, the confounding effects of patient-specific risk factors for HAIs, such as comorbidities, level of consciousness on admission, and concomitant immunosuppression, were not analyzed. Third, all-cause mortality censored at 30 days from infection might have caused detection bias and likely underestimated this outcome; however, it was selected to ensure consistency with other studies [10, 32]. Fourth, this is a retrospective cohort study which comes with the inherent weaknesses of this method; however, HAI surveillance and microbiology data were prospectively collected and validated. Fifth, despite utilizing preset definitions of nosocomial infections, central fever is prevalent in certain diagnostic categories among neurocritical care patients and prompts collection of cultures [33] and might have produced an overestimate of certain infection rates, namely CAUTI. Finally, the study was purely observational, and we did not implement any new infection control measures to prevent the various HAIs; however, our aim was to report current practice and not explore efficacy of various infection control strategies.

Conclusions

ICU-acquired HAIs have a serious impact on patient outcomes, especially among neurologically ill patients. We found that frequencies and resistance of infections to antibiotic treatments remained high in an NCCU in a developing country when compared to NCCUs in developed countries using similar surveillance definitions and methodology. In our study, ICU-acquired pneumonia independently predicted in-hospital mortality, and all infections were associated with a prolonged ICU LOS. The DAI rates reported highlight that central line management needs improvement and should be prioritized to include focused infection control measures tailored to this patient cohort, with the ultimate goal of eliminating CLABSIs. Finally, as the first HAI surveillance study in an NCCU in Kuwait, our data provide regional benchmarking from an NCCU in a developing country, thereby allowing for useful comparison for similar specialized units.

Electronic supplementary material
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Authors Contributions
Drs. YBA, MAR, and EMM contributed to study concept and design. Drs. YBA, SAS, MAR, and WY contributed to data acquisition. Drs. YBA, AAA, SAS, and EMM contributed to analysis and interpretation of data. Drs. YBA, AAA, MAR, and EMM contributed to drafting the manuscript. All authors revised the manuscript and approved the final version to be published.

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Conflict of interest
The authors declare that they have no conflict of interest.

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