Major Article

Risk factors for sepsis morbidity in a rural hospital population: A case-control study

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Background: The aim of the study was to identify risk factors for sepsis morbidity in a rural hospital population.

Methods: We used a case-control study design. Patients included adult admissions to a rural health system between January 1, 2012, and December 31, 2015. Case selection was by electronic medical record search for codes of the ICD-9-CM. Cases were validated against Quick Sequential Organ Failure Assessment criteria. Multiple logistic regression modeling was performed to determine which predefined variables were significantly associated with sepsis diagnosis.

Results: A total of 220 patients were studied (110 cases and 110 controls). Cases had an in-hospital mortality of 20% compared with 0% of the controls. Indwelling medical device use during hospitalization (adjusted odds ratio [OR], 3.02; 95% confidence interval [CI], 1.44-6.30; $P = .003$), coronary heart disease (adjusted OR, 2.59; 95% CI, 1.13-5.97; $P = .03$), and type of health insurance (adjusted OR, 2.36; 95% CI, 1.13-4.93; $P = .02$) were independently associated with sepsis diagnosis after adjusting for potential confounders.

Conclusions: This study underscores the need for implementation and maintenance of infection control measures during management of patients with indwelling medical devices at a rural hospital.

Sepsis, as currently defined by the international consensus conference criteria, is an acute organ dysfunction caused by a dysregulated host response to infection.[1] This systemic inflammatory syndrome imposes a significant burden on the U.S. health care system, constituting a major cause of morbidity and mortality in hospitalized patients.[2] Care of sepsis patients in the United States has been reported to exceed $24 billion in medical expenditures annually,[3,4] and in-hospital mortality associated with severe sepsis ranges from 20%-50% of afflicted patients.[5] Furthermore, sepsis survivors are more likely to suffer a long-term, substantial reduction in quality of life[6,7] and have a higher risk of major adverse cardiovascular events.[8]

Because of the high morbidity and mortality associated with sepsis, it is critical to examine factors that confer an increased risk of developing sepsis of any severity. Previous studies have identified various risk factors including advanced age,[9-11] male sex,[12-14] nonwhite race,[13,14] chronic medical conditions (eg, chronic lung disease, chronic renal disease, coronary artery disease, hypertension, diabetes mellitus),[10,11,14,15] alcohol dependence,[11,16,17] catheterization (eg, urinary, vascular),[18-20] immunosuppression,[11,21] and health insurance status.[22,23] However, published data on the epidemiology of sepsis in the United States have been derived predominantly from academic, tertiary, and larger community hospitals, with rural or nontertiary care hospitals in lower socioeconomic settings receiving little attention. A rare study examining demographic and socioeconomic factors influencing sepsis disparities found that U.S. community populations associated with a high incidence of sepsis mortality were more likely to cluster in the Southeastern United States and be differentiated by lower education, higher poverty, no medical insurance, and higher unemployment rates.[24] Such investigations highlight the need for continued research on sepsis epidemiology and etiology in

resource-limited settings to inform clinical management of this serious disease and improve patient care.

The objective of this case-control study was to address the paucity of epidemiologic research in this area by identifying risk factors associated with sepsis morbidity in a rural hospital population in Harnett County, North Carolina. The impetus for this research stemmed from the 2013 Harnett County Community Health Assessment, which reported that sepsis ranked 10th among the 15 leading causes of death in this rural county based on an age-adjusted mortality rate of 17.1 deaths per 100,000 population for the 5-year aggregate period of 2007-2011.[25] Moreover, the age-adjusted mortality rate for sepsis was 25.7% higher in Harnett County compared with the statewide rate, and 61.3% higher compared with the national rate,[25] highlighting regional disparities in U.S. sepsis mortality. In the study reported here, we sought to determine significant predictors of sepsis morbidity in patients who received their medical care at a rural community hospital designated a health professional shortage area. Identification of prognostic factors associated with sepsis diagnosis will be critical in developing effective prevention and early detection strategies to reduce the incidence of this serious and costly infection in a rural inpatient setting.

METHODS

Study design, data collection, and setting

This study was conducted as a case-control study in which both cases and controls were sampled from a population of hospital system patients in Harnett County, North Carolina. Patient data were collected by searching the electronic health record system. We analyzed a total of 220 patients (110 cases and 110 controls) who were admitted to the health system during the 3-year observation period (from January 1, 2012-December 31, 2015, inclusive). This sample size was calculated using OpenEpi Version 3[26] and was adequate to have power of at least 80%. This calculation took into consideration a 2-sided confidence level of 95% and prevalence of indwelling device use among hospitalized patients of 15%-25%.[27] Cases were compared with controls to determine which predefined risk factors were associated with a sepsis diagnosis. This study was reviewed and approved by the Campbell University Institutional Review Board.

The rural health system is located in Harnett County, North Carolina, and comprises 2 hospitals with a total of 151 licensed beds, including 16 licensed intensive care unit beds. The health system's service area is designated as a health professional shortage area. This designation means that the community was able to prove to the federal and state governments that there is an ongoing shortage of primary care providers available to the community (estimated population: ~131,000). The health system is limited in terms of scope and ability to care for critically ill patients because there are no board-certified intensivists on-site to acutely manage these patients. In addition, available specialty resources are limited at the health system, including limited nephrology services (no dialysis), pulmonology services, and surgery options. As a regional medical center, this rural health system will transfer patients to nearby tertiary care medical centers when a higher level of care is needed than what the facility is able to provide.

Ascertainment of cases

Eligible patients were all adults (age ≥18 years) who were admitted to the health system during the 3-year study period. Cases consisted of randomly selected patients who were hospitalized with sepsis as a primary or secondary diagnosis, as indicated by electronic health record ICD-9-CM codes associated with sepsis (995.91, 995.92, 995.93, and 995.94). Patients were randomly selected using a random number generator. Patients were screened to confirm sepsis using the history and physical report and other admission data to ensure that they met at least 2 of the 3 updated Sepsis-3 criteria defining the Quick Sequential Organ Failure Assessment (qSOFA), a bedside clinical scoring system to characterize septic patients. These qSOFA criteria were respiratory rate ≥22 breaths per minute, altered mentation, and systolic blood pressure ≤100 mm Hg. A patient was deemed to have altered mentation if documented in the history and physical report that the patient had a change in mental status from baseline, was obtunded, or was intubated and sedated, or was otherwise noted to be altered. Patients not meeting 2 of the 3 qSOFA criteria were excluded from the case population. Patients were screened until a total of 110 cases met sepsis criteria.

Ascertainment of controls

Controls consisted of randomly selected patients (age ≥18 years) who were hospitalized at the health system with a medical diagnosis other than sepsis during the same 3-year observation period as the cases.

Covariates

Study variables collected were demographic information, medical conditions, history and physical documentation, and discharge summaries. Age was dichotomized as <65 years and ≥65 years old. Body mass index was categorized as normal (<25 kg/m^2), overweight (25-29.99 kg/m^2), or obese (≥30 kg/m^2). Race was categorized as white, black, and other (American Indian/Alaskan native, Asian/Pacific Islander, or multiracial). History of or current smoking, alcohol use, and current illicit drug use were collected and dichotomized as present or absent. History of or current medical conditions, such as diabetes mellitus (type 1 or 2), coronary heart disease (CHD), congestive heart failure, myocardial infarction, stroke, and chronic obstructive pulmonary disease, were dichotomized as present or absent. Indwelling medical device used at or during hospital admission was dichotomized as present or absent. In this study, we defined an indwelling medical device as a device that was inserted for drainage, for mechanical ventilation, for intravascular access, or for patient feeding. Predefined risk factors were selected for this study based on previous literature linking them to either indwelling medical device use, sepsis, or both.

Statistical analyses

Differences between cases and controls were analyzed using Student t test for continuous variables and Pearson χ^2 test for categorical variables. Simple logistic regression was used to estimate unadjusted odds ratios (ORs) for association between sepsis and the various explanatory variables. Multiple logistic regression was used to model sepsis as a function of medical device use, adjusting for potential confounders. All analyses were performed using SAS Version 9.3 (SAS Institute, Cary, NC), at $\alpha = 0.05$.

RESULTS

A total of 220 patients were included in the study, of which 110 cases had ICD-9-CM–coded sepsis diagnosis with confirmed 2 of 3 positive qSOFA score. Demographic, comorbidity, and health behavioral characteristics of the patients in the study population are provided in Table 1. Cases were significantly older than controls with a mean age of 70.5 ± 13.8 years compared with 59.8 ± 20.4 years, respectively. Cases and controls both were composed of mostly women (n = 64 [58.2%] for each group). The clinical outcome of 22 cases (20.2%) was death in contrast with no in-hospital mortality