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Epidemiology and microbiology of sepsis in mainland China in the first decade of the 21st century

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SUMMARY

Objectives: This study describes the epidemiological and microbiological profile of sepsis during the first decade of the 21st century in mainland China.
Methods: The sepsis-related mortality data from 2003 and 2007 were retrieved from the China Health Statistical Yearbook. The microbiology data were retrieved and selected from a literature search of the China Academic Journal Database between 2001 and 2009. A meta-analysis was performed to synthesize the available data on the proportion of positive blood cultures in septic patients and the microorganism distribution.
Results: The sepsis mortality in small and medium-sized cities and rural areas declined obviously over time. The mortality of the subpopulations aged 1–54 years tended to be lower than the national averages. In contrast, the sepsis mortality among neonates and the elderly (≥75 years) was obviously higher than national averages. While the mortality in the elderly declined between 2003 and 2007, the neonate sepsis mortality increased dramatically, especially among male neonates. The overall positivity of blood culture were 17.0%, 13.3% and 10.6% among neonatal, pediatric and adult patients with suspected sepsis, respectively; this proportion tended to decrease over time. Among identified microorganisms, the proportions of Gram (+) and (−) bacteria were similar (47.2% vs. 44.5%) among adult patients, while Gram (+) bacteria was predominant among neonatal (77.4%) and pediatric (73.2%) patients and increased in prevalence over time. The positivity of blood cultures and proportions of microorganisms varied by geographical region across mainland China. Sepsis with fungus was rare but was more prevalent in adult sepsis patients (6.4%) than in neonatal patients (0.8%).
Conclusions: The difference in sepsis mortality between urban and rural areas decreased over time. Males, the elderly, and neonates were found to be high-risk subpopulations. Gram (+) bacteria were predominant among neonates with sepsis, but the proportion of patients with Gram (+) or Gram (−) bacteria was similar among adults with sepsis.

1. Introduction

Sepsis is a significant cause of mortality worldwide, and its cost is a significant burden to the healthcare system.[1,2] The incidence of sepsis is increasing globally according to certain estimates.[1,3] In 2003, management guidelines for severe sepsis and septic shock were developed under the auspices of the Surviving Sepsis Campaign.[4] The campaign is an international effort to increase awareness and improve the outcomes for patients with sepsis; the guidelines were updated in 2008 and 2013.[5] In a study from Finland, the incidence of severe sepsis in the intensive care units was as high as 0.38/1,000 adult patients.[6] Esteban et al. reported a hospital mortality of 12.8%, 20.7% and 45.7% for patients with sepsis, severe sepsis and septic shock, respectively.[7] The decision to use empirically prescribed antimicrobials for managing sepsis depends highly on epidemiological factors.[8] Since 1987, Gram (+) bacteria have become the most common organisms associated

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with the development of sepsis.[9,10] However, the predominant microorganism associated with sepsis varies by region. Baharoon et al. reported Gram (–) bacteria were the most frequently isolated microorganisms among sepsis patients in Saudi Arabia.[11] Jaramillo-Bustamante et al. also reported Gram (–) bacteria were the most frequent etiological agent for sepsis among pediatric patients in Colombia.[12] In addition, the incidence of fungal organisms associated with sepsis has increased rapidly in recent years.[10] Nevertheless, few studies have addressed the overall mortality from sepsis and the relevant microorganism distribution in mainland China. In this study, we aimed to observe the ecological, epidemiological and microbiological changes of sepsis over time during the first decade of the 21st century in mainland China.

2. Materials and Methods

2.1. Mortality data

For the ecological analysis, the crude sepsis mortality rates were retrieved from the China Health Statistical Yearbook issued by the Ministry of Health of China.[13] Mortality data were available from the Yearbook for 2003 and 2007. The sepsis mortality rates were stratified by gender, age group, and region (classified as major city, small and medium-sized city, and rural areas).

2.2. Microbiology data

The China Academic Journal Full-text Database (CAJ) updated by the China National Knowledge Infrastructure (CNKI) central servers was searched for articles published between 2001 and 2009. CAJ is currently the most comprehensive database of Chinese journals.[14] The search terms utilized were "sepsis"[MeSH] AND "blood culture"[MeSH]. The titles and abstracts of 420 citations were initially identified, and irrelevant citations were excluded. Secondly, the full texts were retrieved to identify eligible studies. Hospital-based cross-sectional studies on blood culture examination for patients with suspected sepsis in mainland China were eligible for the analysis. The only exclusion criterion was an observation duration of less than 1 year. Finally, 84 adult and 77 neonatal-pediatric patient studies were included in the analysis. The positivity of a blood culture examination was defined as the percentage of positive microorganisms identified in the blood specimens from hospitalized patients with suspected sepsis. Additionally, the proportions of Gram (+) bacteria, Gram (−) bacteria, and fungus among all identified microorganisms were extracted. The data on adult or neonatal-pediatric patients were retrieved and extracted separately. The eastern, central and western regions of China have different economic conditions and healthcare accessibility.[15] Therefore, the epidemiological differences among these three regions of China were analyzed. Due to possible changes in the epidemiology of sepsis related to advances in healthcare accessibility in mainland China over time, the included studies were categorized into three periods: 1990–1999, 2000–2004 and 2005–2009. If the observation duration of a study covered two periods, the period containing the majority of the observation duration was chosen.

2.3. Statistical analyses

The 2003 and 2007 mortality rates by age group were initially compared by the Friedman test for multiple subpopulations. The Wilcoxon signed ranks test was used to compare the mortality of two related subpopulations.

The positivity of the blood culture examinations among tested specimens from patients with suspected sepsis was estimated by meta-analysis to combine eligible studies. Likewise, the proportions of Gram (+) bacteria, Gram (−) bacteria, and fungus among all identified microorganisms from positive blood culture were estimated by meta-analysis using the same approach. All meta-analyses were performed using a random effect model. Subgroup analysis was performed among different regions of China, as well as among different time periods. Additional subgroup analysis was performed among neonatal or pediatric patients. The relative ratios (RRs) and 95% confidence intervals (CIs) of the synthesized positivity of blood cultures or proportion of microorganisms between different subgroups were calculated based on the estimated percentage and the sample size of each subgroup.

Nonparametric tests were conducted with SPSS 13.0 software (Chicago, U.S.). The meta-analyses were conducted with the statistical software Comprehensive Meta-Analysis 2.0 (Biostat, Englewood NJ, USA). RR and 95% CI was calculated using Microsoft Excel 2010, with the formulas for 95% CI of RR = exp(ln(p1/p2) ± 1.96 * sqrt(1 / (p1 * N1) + 1 / (p2 * N2) – 1 / N1 – 1 / N2)), and p value = 2 * (1 – normsdist(abs(p1 – p2) / sqrt(p1 * (1 – p1) / N1 + p2 * (1 – p2) / N2))). All statistical tests were two sided using an α level of 0.05.

3. Results

3.1. Nationwide sepsis mortality

In the 2003, the crude sepsis mortality gradually increased from major cities to small and medium-sized cities and then to rural areas (Figure 1). Among subgroups, the highest mortality was 0.83 per 100,000 persons among the male population in rural areas. Interestingly, in the 2007, the crude mortality was dramatically decreased in small and medium-sized cities and rural areas. The differences between rural areas and major cities became smaller. In contrast, compared to 2003, the 2007 mortality in the major cities increased among both males and females. Among all subgroups, males had higher sepsis mortality than females, with the only exception being in the 2003 in major cities.

3.2. Mortality stratified by age group, gender and region

The age-specific mortality curves had two peaks in the neonatal-pediatric and the older subpopulations (Figure 2). A sharp decline after one year of age and a sharp rise after 70 years of age could be observed in both the 2003 and the 2007 periods. Between 2003 and 2007, the sepsis mortality among the elderly decreased by approximately half in 2007, but in the <1 year of age subgroup it increased by up to 5 fold (Figure 2). The Friedman test showed significant differences between major cities, small and medium-sized cities, and rural areas in both 2003 ($p<0.001$) and 2007 ($p=0.008$).

In Figure 3, those aged between 1 and 54 years mostly had lower mortality rates than the national average. There were no significant differences between males and females ($p>0.05$) between any region or time period. Between 2003 and 2007, the sepsis related death decreased significantly in rural males ($p=0.033$) and females ($p=0.005$), as well as in males in the small and medium-sized cities ($p=0.039$), but no significant changes were found in major cities ($p>0.05$). Interestingly, the dramatic improvement in small and medium-sized cities exceeded the improvements observed in both the rural males ($p=0.012$) and females ($p=0.017$).

3.3. Sepsis among adult patients

The overall positivity of blood culture examination was 10.6% based on 71 studies in adult patients (Table 1). Compared to