Journal of Hospital Infection 78 (2011) 50–53

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Changes in the incidence of candidaemia during 2000–2008 in a tertiary medical centre in northern Taiwan

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ARTICLE INFO

Article history:
Received 25 July 2010
Accepted 14 December 2010
by S.J. Dancer
Available online 12 February 2011

Keywords:
Candidaemia
Liver cirrhosis
Mortality
Secular trend

SUMMARY

Candidaemia is associated with high mortality and high healthcare costs. The incidence of candidaemia in Taiwan rose markedly during the period 1980–2000. We conducted this hospital-based surveillance study in order to explore the secular trend in incidence of candidaemia during the period 2000 to 2008. In our study, *Candida* spp. were the fourth most common cause of bloodstream infections, with a 30-day crude mortality rate of 36.7%. *Candida albicans* was the most common species identified, although mortality rate did not differ significantly among species. The incidence of candidaemia began to decrease in 2004. Risk factors related to higher mortality included longer hospital stay before onset of candidaemia, liver cirrhosis, malignancy, end-stage renal disease requiring renal dialysis, dependence on mechanical ventilation and urinary catheterisation.

Introduction

Invasive fungal infections in hospitalised patients are associated with significant morbidity and mortality.[1] The mortality rate associated with invasive candidiasis has been reported to be as high as 40–50%.[2,3] *Candida* spp. are the most common cause of invasive fungal infections, accounting for about 15% of total hospital-acquired infections and more than 72% of nosocomial fungal infections.[1,4] Moreover, candidaemia has become the fourth most common cause of nosocomial bloodstream infections (BSIs) in the USA and in much of the developed world.[1,5]

The rising incidence of candida infections has been described in several epidemiological studies since the 1980s.[5–8] The rising incidence of candida infections has been shown to be associated with the increased use of broad-spectrum antibacterial agents, central venous catheters (CVCs), implantable prosthetic devices, parenteral nutrition, renal replacement therapy, and immunosuppressive agents.[5,9–12]

The secular trends in incidence and species distribution differ not only between geographic regions but also between institutions.[6,8,13] Although more recent studies have suggested that the incidence of candidaemia has stabilised or even decreased, the secular trend in incidence in Taiwan increased between 1981 and 2000.[2,12–14] It was suspected that this increase would continue because of the increase in number of invasive procedures.

The aim of this study was to analyse the secular trend in incidence and species distribution of candidaemia during a nine-year period at a tertiary medical centre in northern Taiwan and to compare it with the overall rate of BSIs during the same period. We also analysed the risk factors related to 30-day crude mortality.

Methods

Data collection

This retrospective cohort study examined all patients at a 2900-bed tertiary medical centre in whom candidaemia was diagnosed during the period 1 January 2000 to 31 December 2008. Infection control nurses reviewed the medical records of the patients concerned. The culture result was considered true candidaemia only when at least one positive blood culture had been sampled via a peripheral vessel in a patient with symptoms and signs compatible with systemic inflammatory response syndrome. Patient characteristics and information on comorbid diseases, number and types of invasive procedures, types of immunosuppressive agents, including

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doi:10.1016/j.jhin.2010.12.007

steroids at doses equivalent to prednisolone ≥20 mg per day, ward location at the onset of candidaemia, and 30-day crude mortality were collected for analysis.

Microbiological identification and antimicrobial susceptibility

In all, there were 871 episodes in 847 patients during the study period. From 2000 to 2001 we used the BACTEC® NR-660 system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD, USA) and from 2001 to 2008 the BacT/ALERT 3D system (bioMérieux, Marcy l'Etoile, France). Species identification was determined by standard biochemical testing with an ATB ID 32C kit (bioMérieux, Hazelwood, MO, USA) and the Yeast Biochemical Card (bioMérieux Vitek, Hazelwood, MO, USA).

Statistical analysis

The χ^2-test or Fisher's exact test was used for categorical comparisons of data and differences in continuous variables were analysed by the unpaired Student's *t*-test. The χ^2-test for trend was used to estimate the relationship between candidaemia and overall BSIs during the same period. $P < 0.05$ was considered statistically significant. Significant predictors in the univariate analysis were included in a logistic regression model to identify the most important risk factors. A natural logarithm scale was used to plot the incidence of all BSIs and that of candidaemia to minimise baseline differences. All analyses were performed with the Statistical Package for the Social Sciences for Windows, version 17.0 (SPSS, Inc., Chicago, IL, USA).

Results

Candida spp. accounted for 10.4% of BSIs and were the fourth most common cause of BSIs during the study period, following *Staphylococcus aureus* (18.2%), *E. coli* (11.0%) and *Klebsiella pneumoniae* (10.4%). *Candida* spp. were the eighth most common cause of BSIs isolated in 2000, but by 2007 *Candida* spp. had risen to the second most common. Relative to the incidence of non-candida BSIs, the secular trend in incidence of candidaemia increased significantly from 2000 to 2008 ($P < 0.005$) (Figure 1). The incidence of candidaemia in 2000 was 0.05 per 1000 patient-days (4.6% of BSI), but in 2008 it was 0.14 per 1000 patient-days (11.2% of BSI). The trend showed a sharp upturn in 2003 and a peak in 2004 (15.7% of BSI). The incidence of candidaemia increased more rapidly than that of BSIs caused by the three principal bacterial pathogens (Figure 2).

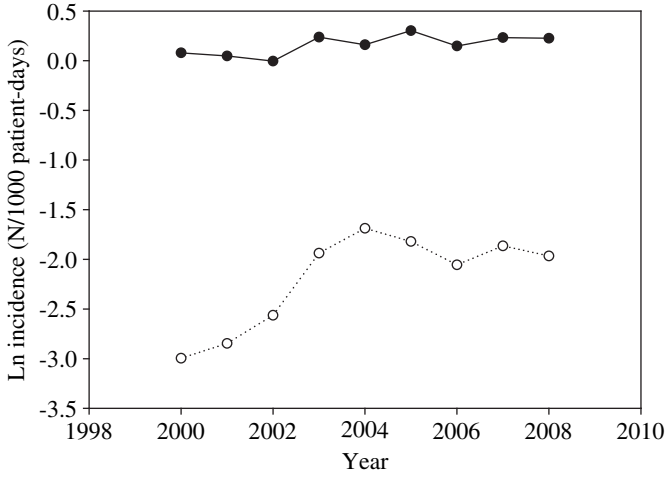

Figure 1. Secular trend of candidaemia from 2000 to 2008. ●, overall bloodstream infections; ○, candidaemia.

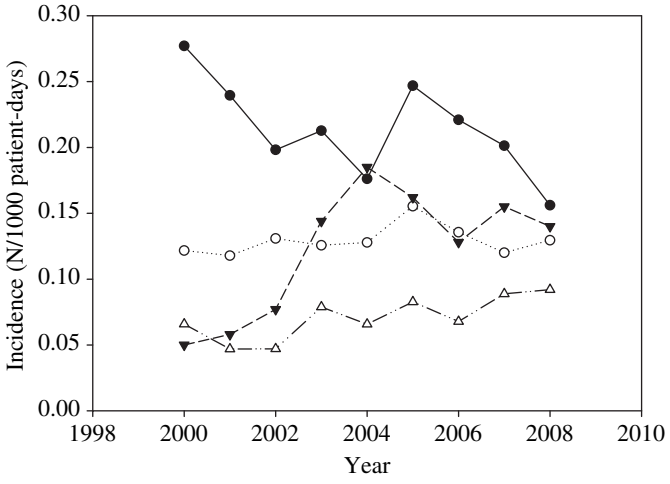

Figure 2. The incidence of the four most common pathogens of bloodstream infections. Bloodstream infection caused by: ●, *Staphylococcus aureus*; ○, *Escherichia coli*; ▼, candidaemia; △, *Klebsiella pneumoniae*.

The mean age of the patients was 64 years (range: 0–97). The mean hospital stay before the onset of candidaemia was 37 ± 30 days, and the mean total length of hospital stay was 75 ± 71 days. Other demographic data and clinical characteristics are summarised in Table I.

The most common candida isolated from blood specimens was *C. albicans* (62.1%) followed by *C. tropicalis* (15.4%) and *C. parapsilosis* (13.3%) (Figure 3). *C. glabrata* (7.2%) and *C. krusei* (0%), two candida species that are potentially resistant to fluconazole, were less frequently isolated during the period.

Table I
Demographics and clinical characteristics of patients with candidaemia

Variable	No. (%)
Age (years, mean ± SD)	64 ± 22
≤ 1	36 (4.1)
2–12 years	12 (1.4)
13–64 years	297 (34.1)
≥65 years	526 (60.4)
Male sex	580 (66.6)
Onset in ICUs	292 (33.5)
Pre-infection hospital stay (days, mean ± SD)	37 ± 30
Length of hospital stay (days, mean ± SD)	75 ± 71
30-day crude mortality	321 (36.9)
Underlying comorbidity	
Diabetes mellitus	155 (17.8)
Liver cirrhosis	15 (1.7)
Malignancy	356 (40.9)
ESRD under dialysis	88 (10.1)
Immunosuppressive therapy	149 (17.1)
Nasogastric tube usage	505 (58.0)
Endotracheal tube usage/tracheostomy	359 (41.2)
Mechanical ventilation	328 (37.7)
Peripheral lines	236 (27.1)
Non-tunnelled CVCs	
CVCs of neck	495 (56.8)
FVCs	66 (7.6)
Tunnelled CVCs	
Port-A	185 (21.2)
Total parenteral nutrition	209 (24.0)
Urinary catheterisation	429 (49.3)
Surgical drainage devices	130 (14.9)

ICU, intensive care unit; ESRD, end-stage renal disease; CVC, central venous catheter; FVC, femoral venous catheter.