

Review

Candidaemia in Europe: epidemiology and resistance

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Abstract

Despite the widespread use of antifungals for prophylaxis, *Candida* bloodstream infection (BSI) remains the most frequent life-threatening fungal disease. From an analysis of multi-institutional surveys of *Candida* BSIs performed in Europe, including the large prospective survey by the European Confederation of Medical Mycology (2089 episodes from seven countries), a limited role of species with decreased susceptibility to azoles in causing BSIs and a low proportion of antifungal resistance was evident. Large prospective epidemiological surveys using common databases are needed to monitor trends in incidence and changes in species distribution, to identify new at-risk patients and to evaluate the impact of the introduction into the market of new antifungal agents.

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1. Introduction

Despite the widespread use of antifungals for prophylaxis and treatment of invasive fungal infections in immunocompromised patients, candidaemia remains the most frequent life-threatening fungal disease and is associated with a prolonged hospital stay and a resulting rise in costs [1,2].

Most of our knowledge of the epidemiology of candidaemia comes from studies done in North America [3]. Up to 1996, only one survey involving more than one hospital in a European country had been published [4]. Therefore, in 1997 the European Confederation of Medical Mycology (ECMM) launched, among other epidemiological working group initiatives, a survey of candidaemia [5]. Six national societies

participated in this prospective sequential study conducted from September 1997 to December 1999: the British, French, German-speaking, Italian, Spanish and Swedish mycology societies. A total of 2089 reports were submitted from 106 participant centres selected by the national coordinator in each country [6]. Different approaches were adopted for selection: in Italy all of the institutions present in one region and equipped with a microbiology laboratory were included in the survey, whilst in other countries only teaching or large general hospitals were selected [7–12]. For each episode of candidaemia, a questionnaire regarding risk factors or predisposing diseases, diagnosis of candidaemia, intravascular catheter management, initial treatment and outcome (30 days after diagnosis) was completed [5].

2. Epidemiology of candidaemia

Table 1 summarises the multi-institutional surveys of *Candida* bloodstream infections (BSIs) performed in Europe.

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Table 1
Multi-institutional surveys of *Candida* bloodstream infections performed in Europe

Country	Period	Type of study	No. of hospitals (no. of episodes)	Reported incidence			Reference
				/1000 admissions	/10 000 patient-days	/100 000 inhabitants	
Specific patient populations							
Spain	1991–1992	Prospective	28 (46), ICU patients	2.0	–	–	[13]
France	1995–1997	Retrospective	32 (104), ICU patients	2.0	–	–	[1]
Europe	1992–1994	Prospective	30 (249), cancer patients	–	–	–	[14]
Spain	1997–1998	Prospective	27 (118), neonates	3.8	–	–	[15]
Nationwide							
Iceland	1980–1999	Retrospective	nationwide (172)	–	–	2.85	[16]
Norway	1991–1996	Prospective	nationwide (571)	0.17 (0.15–0.20)	0.26 (0.22–0.29)	2.17	[17]
Finland	1995–1999	Retrospective	nationwide (479)	0.17 (0.12–0.21)	0.4 (0.3–0.5)	1.9	[18]
Overall hospitals							
The Netherlands	1987–1995	Retrospective	5 (625)	–	0.51 (0.32–0.74)	–	[4]
Slovak Republic	1989–1998	Prospective	71 (288)	–	–	–	[19]
Switzerland	1991–2000	Retrospective	6 (774)	–	0.50 (0.38–0.58)	–	[20]
Switzerland	2000	Retrospective	18 (92)	–	0.49 (0.06–1.14)	–	[20]
Spain	1994–1997	Prospective	34 (165)	–	–	–	[21]
France	1995	Prospective	25 (156)	0.29 (0.17–0.71)	0.35 (0.17–1.16)	–	[22]
Spain	1997	Prospective	39 (143)	–	–	–	[23]
France	1998–2001	Retrospective	10 (190)	0.28	–	–	[24]
Belgium	2002	Prospective	28 (211)	–	–	–	[25]
Spain	2002–2003	Prospective	14 (345)	0.53 (0.09–0.96)	0.73 (0.14–1.50)	4.3	[26]
UK	2003	Prospective	171 (1380)	–	–	2.53	[27]
Denmark	2003–2004	Prospective	34 (303)	0.49 (0.29–1.26)	–	11.0	[28]
ECMM survey							
France	1997–1999	Prospective	25 (645)	0.20 (0.04–1.3)	–	–	[6,8]
Germany/Austria	1997–1999	Prospective	5 (231)	–	0.31 (0.12–0.49)	–	[6,7]
Italy	1997–1999	Prospective	35 (569)	0.38 (0.03–1.45)	0.44 (0.04–1.64)	–	[6,12]
Spain	1997–1999	Prospective	19 (293)	–	–	3.5	[6,11]
Sweden	1997–1999	Prospective	6 (191)	0.32 (0.1–0.4)	–	–	[6,10]
UK	1997–1999	Prospective	6 (163)	–	0.30 (0.19–0.65)	–	[6,9]

ECMM, European Confederation of Medical Mycology.

Few studies designed to estimate the incidence based on appropriate denominator data, such as admissions, patient-days or inhabitants, have been performed. In addition, in some series, data regarding candidaemia and invasive candidiasis are reported together.

Some surveys have focused on selected patient populations such as intensive care, neonate or cancer patients [1,13–15]. The reported incidence in intensive care patients is 2/1000 admissions. However, a considerable variation among units has been noted and has been attributed to the different patient populations hospitalised in the different units [1,13]. In one study, candidaemia was diagnosed in 3.8 per 1000 neonates, with a significantly higher incidence in very low birth weight infants [15].

Apart from the annual analysis of the reports submitted from laboratories in England, Wales and Northern Ireland to the Health Protection Agency's Communicable Disease Surveillance Centre [27], three nationwide surveys have been published [16–18]. They concern countries with a limited number of inhabitants: Norway and Finland with 4–5 million inhabitants and Iceland with only a quarter of a million inhabitants. The rate ranges from 1.90 to 2.85 per 100 000 inhabitants [16–18,27].

Other national surveys, involving between 5 and 71 hospitals, have found rates ranging from 0.28 to 0.53 per 1000 admissions, from 0.51 to 0.73 per 10 000 patient-days and from 2.53 to 11.00 per 100 000 inhabitants [4,19–28].

3. The ECMM survey

The countries participating in the ECMM survey reported rates of candidaemia (0.20–0.38 per 1000 admissions and 0.31–0.44 per 10 000 patient-days) comparable with those reported in other European surveys but lower than rates reported in the USA (1.5 per 10 000 patient-days) [6,29]. A similar particularly high rate (1.64 per 10 000 patient-days) was observed in a hospital in Italy that experienced a large outbreak of *Candida* BSIs during the study period [12].

In general, the rate of candidaemia increased with the hospital bed size. The larger the hospital, the broader the patient population requiring invasive diagnostic and therapeutic interventions associated with a greater risk for developing *Candida* infection.

In the ECMM survey, similarly to other reports, *Candida* BSI predominates in males (60%). Infants younger than 1

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