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Candidemia in Norway (1991 to 2003): Results from a Nationwide Study

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A long-term, nationwide prospective candidemia study has been ongoing in Norway since 1991. All medical microbiological laboratories in the country have participated. During the period 1991 to 2003 a total of 1,393 episodes of candidemia occurred in 1,348 patients. The incidence of candidemia episodes per 100,000 inhabitants increased from approximately 2 episodes in the early 1990s to 3 episodes in 2001 to 2003. The average annual incidences varied markedly between the age groups. The incidence was high in patients aged <1 year and in patients aged ≥70 years. In patients ≥80 years of age, the incidence has increased during the last 3 years from an annual average of 6.5 to 15.6 cases/100,000 inhabitants in 2003. Four *Candida* species (*C. albicans* [70%], *C. glabrata* [13%], *C. tropicalis* [7%], and *C. parapsilosis* [6%]) accounted for 95.5% of the isolates. The species distribution has been constant during the 13-year study period. The distribution of the most important species varied with the age of the patient. In patients <1 year of age, the majority of episodes were caused by *C. albicans* (91%). The occurrence of *C. glabrata* increased with age. In patients ≥80 years of age, approximately 1/3 of all episodes were due to this species. All *C. albicans* strains were susceptible to fluconazole. The percentage of yeast isolates with decreased susceptibility to fluconazole (MICs ≥ 16 μg/ml) was 10.7% during the first period of this study (1991 to 1996) and 11.7% during the second period (1997 to 2003).

Since the late 1980s, numerous candidemia studies have documented the increasing importance of invasive *Candida* infections (8, 9, 19, 23). Most epidemiological studies have, however, been performed in single hospitals (8, 19), and incidence rates are usually reported as cases per 1,000 admissions or discharges or per 10,000 patient days. Although such studies are useful, it is difficult to compare results between hospitals, since reported rates will vary with the type of hospital, patient turnover, and the definitions used for admission, patient days, etc. Active population-based surveillance studies are, on the other hand, designed to detect all candidemias in a defined population and provide accurate incidence rates in the population as a whole and in various age groups. The *Candida* isolates obtained will also provide a true picture of the species distribution and of antifungal resistance rates. Such studies are unfortunately few.

In Norway, the medical microbiological laboratories have a close connection, which has made a long-term, nationwide prospective candidemia study possible. The study started in 1991 and is the most extensive prospective population-based study ever performed. The specific objectives have been threefold: (i) to define the incidence of fungal bloodstream infections in Norway; (ii) to identify the spectrum of pathogens causing yeast bloodstream infections; and (iii) to obtain antifungal susceptibility data for Norwegian bloodstream isolates. Results for the years 1991 to 1996 have been published previously (20). This report presents the candidemia data from this study for the whole 13-year period from 1991 to 2003.

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MATERIALS AND METHODS

All medical microbiological laboratories in Norway have participated in the study. These laboratories cover the microbiology service for all hospitals in the country. Episodes of candidemia among hospitalized patients were recorded in each laboratory. For most of the 13-year study period, three automated blood culture systems have been used in Norway: Bactec (BD Diagnostic Systems, Sparks, Md.), 12 laboratories; BacT/ALERT (bioMérieux, Marcy l'Etoile, France), 7 laboratories; VITAL (bioMérieux), 3 laboratories. An episode of candidemia was defined as at least one blood culture positive for *Candida*. Episodes of candidemia in a single patient were considered distinct if they occurred at least 1 month apart.

The candidemia strains were immediately sent to the Norwegian Mycological Reference Laboratory for verification of species identification and susceptibility testing. At intervals, the laboratories have additionally been asked to examine their records for candidemia episodes not reported previously and to send such strains to the reference laboratory.

Identification. Species identification was based on germ tube production, microscopic morphology on cornmeal agar, carbohydrate fermentation and assimilation, urease activity, and ATB 32 C (bioMérieux, Marcy l'Etoile, France).

Susceptibility testing. All isolates were tested for susceptibility to amphotericin B and fluconazole. The majority of strains isolated in the period 1991 to 2001 were also tested for susceptibility to flucytosine. The susceptibility method used has varied throughout this period. From 1991 until the end of 1993, a microdilution method in broth was used for amphotericin B and flucytosine and an agar dilution method for fluconazole (21). Since 1994, a colorimetric microdilution method based on Clinical and Laboratory Standards Institute (CLSI) recommendations has been used for the majority of the isolates (20). The Etest method (AB Biodisk, Solna, Sweden) was, however, used for the isolates from 2002 and 2003. Susceptibility results were categorized according to CLSI breakpoints (15).

Yearly population data for all age groups were obtained from Statistics Norway (http://www.ssb.no).

TABLE 1. Annual incidence of candidemia by age group in Norway from 1991 to 2003

Age (yr) group	No. of episodes per 100,000 population (no. of cases)													
	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	Total
<1	20.6 (12)	6.7 (4)	0 (0)	3.4 (2)	6.7 (4)	8.3 (5)	3.3 (2)	11.7 (7)	12.0 (7)	23.6 (14)	15.2 (9)	12.3 (7)	10.8 (6)	10.3 (79)
1–9	0.6 (3)	0 (0)	0.6 (3)	0.6 (3)	0.2 (1)	1.3 (7)	0.2 (1)	0.2 (1)	0.2 (1)	1.1 (6)	0.4 (2)	0.7 (4)	0.5 (3)	0.5 (35)
10–19	0.2 (1)	0.5 (3)	0.4 (2)	0.2 (1)	0.9 (5)	0.4 (2)	0.4 (2)	0 (0)	0.4 (2)	1.1 (6)	0.5 (3)	0.4 (2)	0.5 (3)	0.4 (32)
20–29	0.9 (6)	0.4 (3)	0.7 (5)	0.1 (1)	0.9 (6)	0.5 (3)	0.3 (2)	0.9 (6)	1.0 (6)	0.7 (4)	0.8 (5)	0.7 (4)	0.9 (5)	0.7 (56)
30–39	1.3 (8)	0.6 (4)	1.4 (9)	1.1 (7)	0.8 (5)	2.0 (13)	0.6 (4)	0.9 (6)	1.6 (11)	1.5 (10)	1.5 (10)	1.6 (11)	1.3 (9)	1.3 (107)
40–49	2.1 (12)	2.4 (14)	1.7 (10)	1.8 (11)	1.3 (8)	1.3 (8)	1.3 (8)	1.5 (9)	1.1 (7)	1.3 (8)	1.1 (7)	2.7 (17)	2.0 (13)	1.7 (132)
50–59	1.3 (5)	2.9 (11)	1.8 (7)	3.7 (15)	2.1 (9)	2.4 (11)	3.4 (16)	4.2 (21)	2.1 (11)	2.6 (14)	3.6 (20)	3.3 (19)	3.6 (21)	2.9 (180)
60–69	6.7 (27)	2.8 (11)	4.7 (18)	3.5 (13)	5.2 (19)	3.6 (13)	8.0 (28)	7.4 (26)	4.6 (16)	4.0 (14)	4.8 (17)	6.2 (22)	6.1 (22)	5.2 (246)
70–79	6.4 (21)	6.4 (21)	5.1 (17)	6.3 (21)	8.6 (29)	5.1 (17)	7.2 (24)	6.6 (22)	8.9 (29)	8.9 (29)	9.5 (30)	10.9 (34)	7.2 (22)	7.4 (316)
≥80	7.5 (12)	4.3 (7)	6.0 (10)	5.9 (10)	7.5 (13)	8.5 (15)	5.5 (10)	7.6 (14)	6.9 (13)	5.3 (10)	12.2 (24)	13.9 (28)	15.6 (32)	8.4 (198)
Unknown	(0)	(3)	(5)	(3)	(0)	(1)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(12)
All groups	2.5 (107)	1.9 (81)	2.0 (86)	2.0 (87)	2.3 (99)	2.2 (95)	2.2 (97)	2.5 (112)	2.3 (103)	2.6 (115)	2.8 (127)	3.3 (148)	3.0 (136)	2.4 (1,393)

RESULTS

During the 13-year period from 1991 to 2003, a total of 1,393 episodes of candidemia in 1,348 patients occurred in Norway (Table 1). A total of 1,415 yeast strains were recovered, since 22 patients had a mixed infection with two yeast isolates. All strains except 67 (4.7%) were sent to the national reference laboratory for identification and susceptibility testing. Patient information was lacking for 12 patients. Of the 1,381 candidemia episodes with adequate patient information, 58% of the patients were male and 42% were female (Table 2). There was a male dominance in all age groups, most marked in the very young and for patients aged ≥60 years (approximately 60% of the patients in these age groups were males).

The annual number of episodes of yeast bloodstream infections has increased from 80 to 90 episodes in 1992 to 1994 to 127 to 148 episodes in 2001 to 2003 (Table 1). The incidence of candidemia episodes per 100,000 inhabitants (Table 1) showed an overall increase from approximately 2 episodes in the early 1990s (except 1991) to 3 episodes in 2001 to 2003. The average annual incidences vary markedly between the various age groups. The incidence is high in patients aged <1 year (10.3 episodes/100,000 inhabitants) and very low in the age groups 1 to 39 years (0.5 to 1.3 episodes/100,000 inhabitants). Thereafter, there is a gradual increase with age from 1.7 in patients aged 40 to 49 years to 7.4 in patients aged 70 to 79 years and 8.4 episodes/100,000 inhabitants in patients aged ≥80 years (Table 1). The incidence in the oldest age group was high for the whole 13-year period, but from 2001, there was a markedly increased incidence from an average of 6.5 for the period 1991 to 2000 to an average of 13.9 for the years 2001 to 2003 (Table 1).

TABLE 2. Gender distribution in each age group

Age (yr) group	No. (%) of patients	
	Female	Male
<1	31 (39)	48 (61)
1–9	17 (49)	18 (51)
10–19	14 (44)	18 (56)
20–29	27 (48)	29 (52)
30–39	49 (46)	58 (54)
40–49	57 (43)	75 (57)
50–59	85 (47)	95 (53)
60–69	90 (37)	156 (63)
70–79	129 (41)	187 (59)
≥80	78 (39)	120 (61)
Total	577 (42)	804 (58)

Thirty-three patients had two or more episodes of candidemia occurring at least 1 month apart. The majority (27) of these patients had two episodes of candidemia, while 6 patients had three to five episodes. In 24 patients, the new episode(s) occurred within 2 to 10 months of the first episode, and 9 patients had one or more episodes per year or more after the first candidemia episode. The same *Candida* species were isolated from all patients, except for one patient with three candidemia episodes with three different species. The *Candida* species isolated from the remaining 32 patients were *Candida albicans* (22 patients), *Candida glabrata* (4 patients), *Candida parapsilosis* (3 patients), *Candida tropicalis* (2 patients), and *Candida dubliniensis* (1 patient).

The various species isolated each year and the frequencies at which they occurred are listed in Table 3. The four most frequently isolated species were *C. albicans* (69.8%), *C. glabrata* (13.2%), *C. tropicalis* (6.7%), and *C. parapsilosis* (5.8%). These four species accounted for 95.5% of the isolates. The yearly incidence of both *C. albicans* (range, 61.5 to 74.7%) and *C. glabrata* (range, 9.8 to 16.7%) varied somewhat throughout the study period, but no significant increase or decrease was noted (Table 3). The *C. albicans* incidence was above 70% for the whole period 1997 to 2003, except for the year 2002.

Nearly all candidemia episodes were caused by a single *Candida* species; only 22 (1.5%) episodes were caused by two species. In 20 of these patients, *C. albicans* was isolated in combination with *C. glabrata* (9 patients), *C. tropicalis* (4 patients), *C. parapsilosis* (4 patients), *Candida norvegensis* (2 patients), or *C. dubliniensis* (1 patient). The remaining two patients had *C. tropicalis* in combination with *Candida guilliermondii* (1 patient) or *Candida kefyr* (1 patient).

The distribution of the two most important *Candida* species, *C. albicans* and *C. glabrata*, varied with the age of the patient (Table 4). In patients <1 year of age, nearly all episodes were caused by *C. albicans* (91%) and *C. parapsilosis* (8%). The *C. albicans* proportion varied between 66 and 77% for the age groups 1 to 79 years but decreased to 57% for patients aged ≥80 years. *C. glabrata* showed a gradual increase with age. In patients aged ≥80 years, nearly one-third of all episodes were

TABLE 3. Yeast species isolated from blood cultures in Norway from 1991 to 2003

Species	No. of isolates isolated in yr:													Total (%)
	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	
C. albicans	76	52	58	65	67	59	72	81	78	88	92	100	99	987 (69.8)
C. glabrata	16	8	9	10	13	16	13	12	16	13	20	19	22	187 (13.2)
C. tropicalis	3	6	10	4	4	9	5	13	7	8	9	16	1	95 (6.7)
C. parapsilosis	10	11	6	5	6	6	5	1	2	10	5	6	9	82 (5.8)
C. krusei		1	2	1	5	2	2	1	1	1	1	4	1	22 (1.6)
C. dubliniensis								1		2	1		4	8 (0.6)
C. guilliermondii	1	2	1			2						1	1	8 (0.6)
C. norvegensis					1	1		1	1		1	2	1	8 (0.6)
C. kefyr					2	1	1	2				1		7 (0.5)
Other *Candida* spp.[a]	2		1	1	1							2		7 (0.5)
Yeast not identified		2		1			1							4 (0.3)
Total	108	82	87	87	99	96	102	113	106	122	130	151	138	1,415

[a] Other *Candida* spp. are as follows: *Candida blankii* (1 isolate), *Candida inconspicua* (1 isolate), *Candida lusitaniae* (2 isolates), *Candida sake* (2 isolates), *Candida sphaerica* (1 isolate).

due to *C. glabrata* (Table 4). The *C. glabrata* proportion has been high in this age group during the whole study period (range, 14.3% to 50%; median, 30.8%).

The two most commonly used blood culture systems in Norway during the period of this study were Bactec and BacT/ALERT. The routine aerobic medium used for Bactec is the Plus Aerobic/F medium. In addition, a few laboratories have used the Mycosis IC/F medium when a fungal infection was suspected. A total of 1,059 *Candida* isolates were recovered using these two blood culture systems. The remaining isolates were recovered by other blood cultures systems used in the beginning of the study or by the 3 laboratories using the Vital blood culture system. The percent recovery of *C. glabrata* varied from 0% to 19.4% (mean, 9.0%) for Bactec users and from 14.5% to 22.5% (mean, 18.1%) for the laboratories using BacT/ALERT. The proportion of old patients did, however, differ somewhat between the two groups of laboratories (Bactec users, 31% >69 years, 12% >79 years; BacT/ALERT users, 43% >69 years, 17% >79 years).

A total of 1,348 (95.3%) strains were tested for susceptibility to amphotericin B and fluconazole and 1,065 (75%) were tested for susceptibility to flucytosine (Table 5). Nearly all strains (99.5%) were susceptible to amphotericin B (MIC $\leq$ 1 μg/ml). Most strains (95.8%) were also susceptible to flucytosine. Only 16 (2.2%) *C. albicans*, 4 (2.9%) *C. glabrata*, and 2 (2.5%) *C. tropicalis* isolates had decreased flucytosine susceptibility with MICs of $\geq$8 μg/ml.

All 934 *C. albicans* strains and nearly all *C. tropicalis* and *C. parapsilosis* isolates were susceptible to fluconazole (Table 5). Only one (1.3%) *C. parapsilosis* and three (3.2%) *C. tropicalis* strains had decreased susceptibility, with MICs of $\geq$16 μg/ml. All *Candida krusei* strains had MICs of $\geq$32 μg/ml, and the majority of *C. glabrata* strains (68.7%) had MICs of $\geq$16 μg/ml. The percentage of yeast isolates with decreased susceptibility to fluconazole (MICs $\geq$ 16 μg/ml) was 10.7% during the first period of this study (1991 to 1996) and 11.7% during the second period (1997 to 2003).

DISCUSSION

The average annual candidemia incidence in Norway during the 13-year study period was 2.4 episodes per 100,000 population and 3.0 for the last 3-year period (2001 to 2003). Three population-based studies from the United States all report a two- to three-times-higher incidence than Norway. The average annual incidence in Atlanta and San Francisco for the years 1992 to 1993 was 8.7 and 7.1 per 100,000 population, respectively (12). In a study from Iowa for the years 1998 to 2001, the mean annual incidence was estimated to be 6.0 per 100,000 population (7). Another study performed in the same period (1998 to 2000) reported a very high incidence in Baltimore (24 cases per 100,000), while the incidence in Connecticut (7 cases per 100,000) was similar to the other U.S. studies (10).

The candidemia incidence in Norway is also lower than what has been reported from most other European studies. The only

TABLE 4. Distribution of the most important *Candida* species in various age groups

Species	No. (%) of isolates found in age (yr) group:									
	<1	1–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	≥80
C. albicans	72 (91)	25 (71)	22 (69)	43 (75)	83 (77)	90 (66)	129 (71)	179 (71)	221 (68)	114 (57)
C. glabrata			1 (3)	3 (5)	7 (7)	12 (9)	22 (12)	27 (11)	52 (16)	62 (31)
C. tropicalis		1 (3)	1 (3)		9 (8)	9 (7)	14 (8)	24 (19)	27 (8)	9 (5)
C. parapsilosis	6 (8)	7 (20)	3 (9)	5 (9)	8 (7)	13 (10)	10 (6)	12 (5)	12 (4)	6 (3)
Total no. of isolates in each group	79	35	32	57	108	136	182	251	324	199

TABLE 5. In vitro activity of amphotericin B, fluconazole, and flucytosine against Norwegian candidemia isolates

Species	Antifungal agent (no. of isolates)	MIC range (μg/ml)	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)
C. albicans	Amphotericin B (934)	0.06–2	0.5	1
	Fluconazole (934)	0.25–4	0.5	1
	Flucytosine (734)	0.06–64	0.125	0.5
C. glabrata	Amphotericin B (180)	0.06–2	0.5	1
	Fluconazole (180)	1–64	16	64
	Flucytosine (138)	0.06–32	0.125	0.25
C. tropicalis	Amphotericin B (93)	0.06–1	0.5	1
	Fluconazole (93)	0.5–64	1	4
	Flucytosine (81)	0.06–64	0.125	0.5
C. parapsilosis	Amphotericin B (82)	0.06–1	0.5	1
	Fluconazole (82)	0.25–16	1	2
	Flucytosine (69)	0.125–1	0.125	0.25
C. krusei	Amphotericin B (22)	0.25–2	1	2
	Fluconazole (22)	32–64	64	64
	Flucytosine (17)	16–32	16	32
Other[a]	Amphotericin B (37)	0.06–1	0.5	1
	Fluconazole (37)	0.25–64	0.5	64
	Flucytosine (26)	0.06–64	0.25	16
All isolates	Amphotericin B (1,348)	0.06–2	0.5	1
	Fluconazole (1,348)	0.25–64	0.5	16
	Flucytosine (1,065)	0.06–64	0.125	0.5

[a] Other species include *C. blankii*, *C. dubliniensis*, *C. guilliermondii*, *C. kefyr*, *C. lusitaniae*, *C. norvegensis*, *C. sake*, and *C. sphaerica*.

exception is a nationwide study from Finland for the years 1995 to 1999 (yearly average, 1.9 cases/100,000 population) (18). The other European studies all show higher incidences. Two studies, one from Iceland for the period 1995 to 1999 (3) and the other from Barcelona, Spain, for the years 2002 to 2003 (1), reported a similar incidence of 4.9 cases per 100,000 population. A recent seminational study from Denmark (May 2003 to April 2004) reported a high estimated annual fungemia incidence of 11 cases/100,000 population (2).

The low candidemia incidence in Norway and Finland compared to other countries is interesting. The level of medicine is probably equally advanced in all countries, but there might be differences, e.g., in antibiotic use patterns. The antibiotic use policies in Denmark and Norway are, however, usually regarded to be quite similar and equally restrictive (5). The reason for the high candidemia incidence in Denmark compared to Norway must therefore be explained by other factors.

Many studies have shown a higher fungemia incidence in old people. Differences in age distribution in a population might therefore be one reason for differences in candidemia incidences between countries. However, this does not explain the different candidemia incidence in Denmark and Norway since the age distribution in these two countries were quite similar in 2003; 34.2% of the population in Denmark and 32% in Norway were aged ≥50 years and 10.6% and 11.2% were aged ≥70 years in Denmark (http://www.dst.dk) and Norway (http://www.ssb.no), respectively.

Most population-based studies report annual incidences for 2 to 3 years. It is therefore not possible to study long-term trends. The only studies covering a more prolonged period are the three studies from the Nordic countries (3, 18). Our study from Norway showed an increase in the average annual candidemia incidence from 2.1 cases/100,000 population for the first 5 years of the study to 2.9 for the last 4 years. Most of the increased incidence in the last part of the study is explained by a markedly increased incidence for patients aged ≥80 years. In this age group, the annual incidence increased from an average of 6.5 cases/100,000 population for the years 1991 to 2000 to 13.9 for the years 2001 to 2003. The reason for this change is not known.

Surprisingly, many patients (2.4%) in our study were found to have recurrent candidemia episodes with the same *Candida* species. Approximately half of these recurrences occurred within 2 to 6 months, while 9 patients had new episodes a year or more after the first episode. In one recent study, five patients with recurrent candidemia were described (6), but otherwise, this problem has not attracted much attention. These cases might be difficult to recognize, since patients may be admitted to different hospitals, as was the case with seven of our patients, and also due to the fact that the recurrent episode(s) might occur quite a long time after the first episode. Investigations are currently ongoing to characterize the *Candida* strains and also to obtain clinical information for these patients.

It is interesting that the species distribution has remained approximately equal for all the years in the study (Table 4). It seems that the impact of an increased use of fluconazole (0.022 defined daily doses [DDD]/1,000 inhabitants/day in 1991 [20] to 0.094 DDD/1,000 inhabitants/day in 2003 [http://www.legemiddelforbruk.no]) during this period has been limited. In 2003, *C. albicans* and *C. glabrata* accounted for 72% and 16%, respectively, of the Norwegian blood culture isolates. The *C. glabrata* incidence increased with age. In patients aged ≥80 years, nearly one-third of all episodes were due to *C. glabrata* (Table 4). Similar results have been demonstrated in other studies previously (13, 17). The fluconazole-resistant species, *C. norvegensis*, is isolated quite regularly in Norway (22) and accounts for 0.6% of the candidemia isolates. This species is seldom reported from other countries (16, 19). The reason for this is unknown.

The species distribution in Norway is somewhat different from Denmark, which is 63% *C. albicans* and 20% *C. glabrata* (2). Some of this difference may be explained by a marked difference between Denmark and Norway in the use of antimycotics for systemic use (ATCC group J02A). In 2003, the total consumption of fluconazole and itraconazole was 0.4 DDD/1,000 inhabitants/day in Denmark and 0.1 in Norway. This high level of fluconazole and itraconazole use in Denmark compared to Norway may explain the difference in species distribution between the two countries. It might also be the reason why decreased azole susceptibility in *Candida* species that are normally susceptible (e.g., *C. albicans*) to fluconazole occur more frequently in Denmark (2) than in Norway. In the 1-year study from Denmark, 11 isolates with decreased azole susceptibility (MIC ≥ 16 μg/ml) were recovered (6 *C. albicans*, 1 *C. tropicalis*, 2 *C. parapsilosis*, and 2 *C. guilliermondii* isolates) (2), while we only detected seven such strains for the whole 13-year study period in Norway.

It is usually regarded that yeasts grow well in commercially available blood culture broths and do not need special handling (4). The results from our study and also from other studies do, however, indicate that the *C. glabrata* recovery rate might vary between routine aerobic media. In this study, the

average *C. glabrata* isolation rate was 9% for hospitals using the Bactec blood culture system and 18.1% for the BacT/ALERT users. Our study was not designed to study differences between blood culture systems. The findings must therefore be interpreted with caution. There is, however, some additional evidence supporting the finding from our study. Horvath et al. have shown that the aerobic Bactec medium (Plus Aerobic/F) only detected 6 of 10 *C. glabrata* isolates in a simulated candidemia study (11). A large clinical study comparing the aerobic Bactec medium (Plus Aerobic/F medium), which is the routine medium used by most laboratories, with the Bactec fungal medium (Mycosis IC/F medium) showed a much higher *C. glabrata* detection rate using the latter medium (14). The findings from these studies indicate that the detection of *C. glabrata* is inadequate using the aerobic (Plus Aerobic/F medium) Bactec blood culture medium.

The results of this study provide important information regarding overall long-term candidemia trends and antifungal resistance in Norway. These data should be helpful to physicians and antibiotic use committees in establishing guidelines for the appropriate use of antifungal agents in Norwegian hospitals. Equally important, the results raise some new questions that should be subjected to further studies. The quite marked difference in candidemia incidence between the neighboring countries Denmark and Norway is interesting. It is also important to elucidate the reason why some patients have recurrent candidemia and the increase in candidemia incidence among elderly patients in Norway in recent years.

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