ΕΘΝΙΚΟΝ & ΚΑΠΟΔΙΣΤΡΙΑΚΟΝ
ΠΑΝΕΠΙΣΤΗΜΙΟΝ ΑΘΗΝΩΝ

NATIONAL & KAPODISTRIAN
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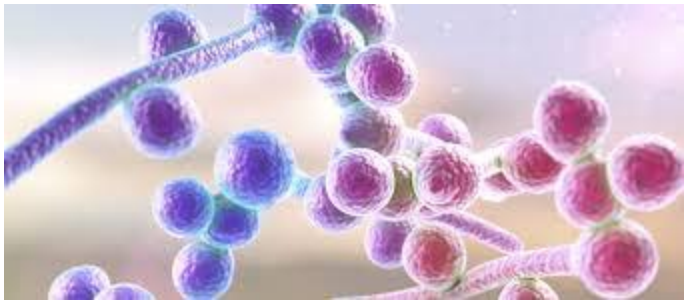
Candidaemia in Greece: epidemiological data



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Μετεκπαιδευτικό Σεμινάριο Λοιμώξεων 10-11/5/2019

Annual incidence of severe fungal infections; global estimates

~ 3.000.000 cases chronic pulmonary aspergillosis

~1.000.000 fungal keratitis

~700.000 invasive candidiasis

~500.000 *Pneumocystis jirovecii* pneumonia

~250.000 invasive aspergillosis

~223.100 cryptococcal meningitis in HIV/AIDS

~100,000 disseminated histoplasmosis

Bongomin F. *et al*., J. Fungi 2017

Invasive candidiasis

- *Candida*: Although part of the GI and genital system flora, it causes serious infections in vulnerable patients.
- Among the top four nosocomial bloodstream pathogens, especially in the setting of ICUs.
- Invasive candidiasis is not limited to candidaemia, referring instead to a variety of disease states caused by *Candida* spp., but the majority of the research on invasive candidiasis concentrates on candidaemia.

Laoth *et al*. J Antimicrob Chemother 2018

Incidence of invasive candidiasis

- The worldwide incidence of candidaemia is difficult to ascertain, in part because there are no set criteria for an incidence denominator.

  -a few countries perform population-based surveillance and use census population data as a denominator,

  -smaller studies use patient days, patient discharges, hospital admissions or ICU admissions as a denominator →

  comparisons between studies challenging.

Candidaemia epidemiology

Country	Years covered	Number of candidaemia episodes	Annual incidence rate	Proportion *C. albicans*/ non-*albicans*	Rate of azole resistance	30 day mortality rate	Reference
USA	2008–11	2675	13.3–26.2/100000 population	37/63	7%	28%–29%	7
USA	2013	515	9.5–14.4/100000 population	35/65	5%–7%	NA	8
Canada	2003–05	453	3.0/100000 population	62/38	4%	NA	143
Norway	2004–12	1677	3.9/100000 population	68/32	7%	NA	11
Finland	2004–07	603	2.9/100000 population	67/33	NA	35%	144
Iceland	2000–11	208	5.7/100000 population	56/44	3%	30%	145
Denmark	2004–09	2649	8.6/100000 population	58/42	NA	NA	13
France	2001–10	15 570	3.6/100000 population	NA	NA	NA	146
Spain	2010–11	773	8.1/100000 population	45/55	21%	31%	14
Belgium	2013–14	338	0.4/1000 admissions	50/50	8%	NA	28
Scotland	2007	242	4.8/100000 population	50/50	2%	NA	29
Australia	2001–04	1095	1.8/100000 population	47/53	NA	28%	147
Australia	2014–15	527	2.4/100000 population	44/56	6%	NA	10
Brazil	2007–10	137	NA	34/66	9%	72%	30
Peru	2013–15	157	2.0/1000 admissions	28/72	3%	40%	148
Latin America	2008–10	672	0.3–2.0/1000 admissions	38/62	3%	41%	31
South Africa	2009–10	2172	NA	46/54	18%	NA	33
Asia-Pacific	2010–11	1601	0.3–2.9/1000 discharges	41/59	NA	NA	20
India	2011–12	1400	6.5/1000 admissions[a]	21/79	12%	45%	35

Criteria for resistance, 30 day mortality and incidence may vary between the studies and may not directly correlate.
NA, not available.
[a]ICU admissions only.

Lamoth *et al*. J Antimicrob Chemother 2018

April 12, 2019

Figure 2: Candidemia incidence rates per 100,000 person-years, by age group, 2009–2017

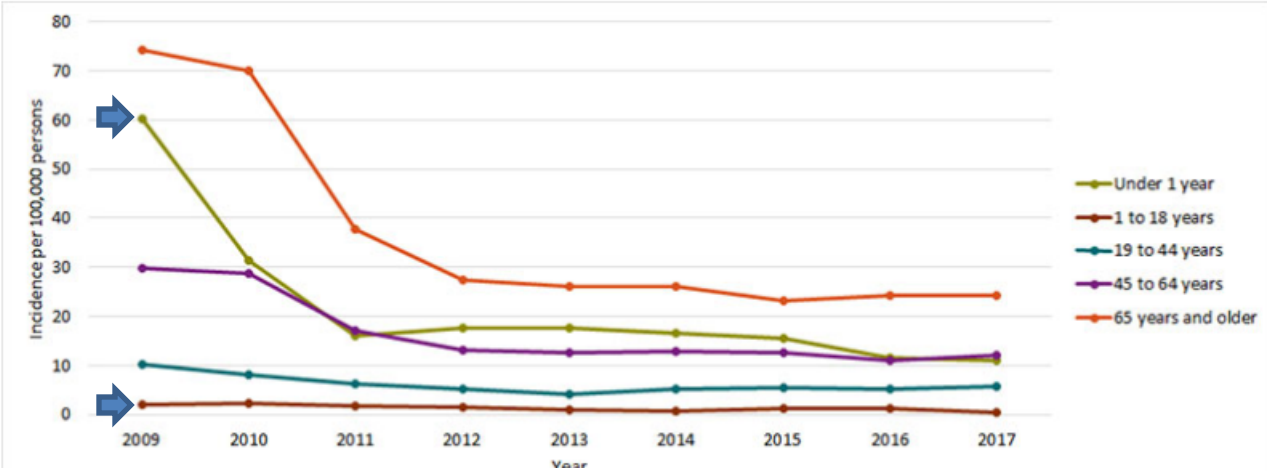
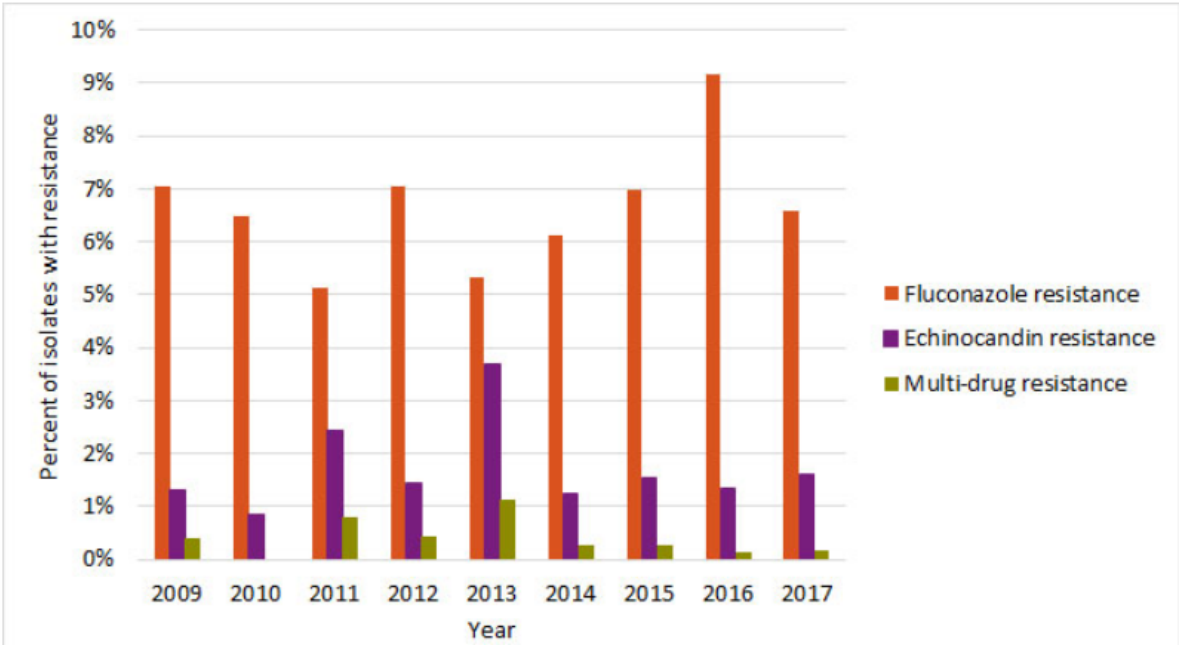


Figure 4: Antifungal resistant *Candida* spp. isolates by year, 2009–2017



https://www.cdc.gov/fungal/diseases/candidiasis/invasive/statistics.html

Distribution trends towards non-*albicans* *Candida* species

- The distribution of Candida species has been changing over the last decade, with a decrease in the proportion of *C. albicans* and an increase in C. *glabrata* and *C. parapsilosis*.
- the overall species distribution is dependent upon geographical location and patient population.

Antifungal resistance in *Candida* spp.

- The majority of *Candida* species exhibit high *in vitro* susceptibility to antifungal agents:
- in the USA, *C. albicans*, *C. tropicalis* and *C. parapsilosis* have low incidences of fluconazole resistance, at **2%**, **5%** and **4%**, respectively.
- These proportions are similar to those observed in Norway and Switzerland. The same species exhibit resistance to the echinocandins in **1%** of isolates in the USA.

Candidaemia in Greece

- There are no published Greek studies of candidaemia in the general population.
- There are studies in specific patient populations:
  - in children
  - in ICUs
  - In haematological patients
- There are conference presentations.

Since 2018, a Hellenic Society of Medical Mycology initiative :

the **"Candi" Study (ongoing)**

Nationwide retrospective survey on candidaemia cases during the years 2007-2017.

Focused on mycological data: **species distribution, antifungal resistance**.

>25 Clinical Microbiology hospital departments participating.

Co-ordinator: As. Prof. G. Vrioni

Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-016-2642-8

ORIGINAL ARTICLE

An estimate of the burden of serious fungal diseases in Greece

M. N. Gamaletsou [1,3] · M. Drogari-Apiranthitou [2] · D. W. Denning [1] · N. V. Sipsas [3]

"There are two studies from Greece assessing its frequency (candidaemia) in specific populations.

prospective study, 24 cases of candidemia among 1,627 admitted patients in a 25-bed, medical–surgical ICU over a 2-year period (2000–2002) [**Dimopoulos G, Karabinis A, Samonis G, Falagas ME, Eur J Clin Microbiol Infect Dis, 2007**].

•In a similar ICU study, 33 cases among 855 patients [**Pratikaki M, Platsouka E, Sotiropoulou C, Douka E, Paramythiotou E, Kaltsas P et al., Mycoses 2011**]. "

Incidence estimate

In another population-based, prospective, multicentre study of patients ≥ 18 years admitted to haematology and/or haematopoietic stem cell transplantation units of nine tertiary care Greek hospitals from January 2009 through to February 2012, candidaemia was detected in 40 of 27,864 patients with haematological malignancies (HM), vs 967 of 1,158,018 non-haematology patients (non-HM). The incidence was:

1.4 cases/1000 admissions (HM), vs

0.83 cases/1000 admissions (non-HM).

[**Gamaletsou MN, Walsh T, Zaoutis T, Pagoni M, Kotsopoulou M, Voulgarelis M et al., Clin Microbiol Infect, 2014**].

"…the above-mentioned figures allow us to assume that the rate of candidaemia in Greece is similar to that reported in other countries (**5.0/100,000 population**);
therefore, we calculated 541 cases of candidemia
— 379 in immunocompromised patients and 162 in ICU and surgery patients."

Gamaletsou MN et al..Eur J Clin Microbiol Infect Dis 2016

Presented studies from Greece

	Authors	Period	Hospital	Cases (N)	incidence	*C. albicans* %	*C. parapsilosis* %	*C. tropicalis* %	*C. glabrata* %	other	Mortality
	Orfanidou et al.	2004-2006	Gennimatas	71	2.7% pos	40.8	21.1	9.8	18.3	9.4	
	Orfanidou et al.	2012-2014	Gennimatas	152	4.5% pos	34.9	41.4	3.3	9.2	10.8	
	Bakossi et al.	2007-2013	Nikaia	278		35	49	7	6	2	
	Giannopoulou et al.	2011-2012	Thriasio	48		42	21	4	6	26	37.5
	Perivolioti et al.	2011-2015	Evangelismos	521	6.9% pos	47	44 (ICU)				
	Priavali et al.	2011-15	ioannina	89		56.1	20.9		9.9	13.1	49.4
	Tsiggra et al.	2010-17	Ippokrateion	364	0.3/1000 adm	30.8	46.4	5.5		14.3	
	Siopi et al.	2009-17	Attikon	376	0.8/1000 adm	41	37	11	7	4	
✓	Spiliopoulou et al.	1998–2008	Patras	255		64	13.7	7.4	9.8	5.1	
✓	Papadimitriou-Olivgeris et al.	2009-2017	Patras	505	1.5/1000 adm.*	39.6	36.6	9.9	11.1	<1	
P	Drogari-Apiranthitou et al.	2006-2010	Laiko	142		36.2	30.5	4.3	15.6	6.2	32.8
	(unpublished)	2012-2015	Laiko	153		51	26.1	12.4	9.1	1.2	
	* (1.1-1.9)					**35-64%**	**14-46%**	**4-12%**	**9-18%**	**1-14%**	**33-50%**

All retrospective studies, except Drogari-Apiranthitou, I. Anyfantis et al., 2011

✓ = published

Evolution of Candidemia during a decade in a tertiary Hospital In Greece

Maria Orfanidou, Vassilis Kitinos, Maria Moutzouri-Sidiri, Paraskevi Mantzana, Nikolaos Kantas, Lida Paraskevi Drosopoulou, Georgios Gkanteris, Eleni Vagiakou
Microbiology Department of General Hospital of Athens „G. Gennimatas“

Comparison 2 periods

- Increased incidence in medical wards, stable in ICU, decreased in surgical dep.
- Increased *C. parapsilosis infections*
- Resistance:

  No significant differences

Introduction

Candidemia is defined as bloodstream infection (BSI) caused by *Candida* species. *Candida* in a blood culture should never be considered as a contaminant.[1] The incidence of candidemia seems to vary a lot in different regions and countries, with some authors claiming increase of the i[illegible] decrease.[2, 3] However, *Candida*, undoubtfully, remains one of the most common pathogens isolated from blood cultures, fourth in the row in the USA and among the [illegible] isolated pathogens in Europe. [4, 5] One of the major threats of candidemia is the high mortality of the infection which [illegible] estimated approximately 30-40%, with a [illegible] high as 50-60%.[6, 7]
C. albicans is still accounted for the majority [illegible] due to non-*albicans* species are, constantly, increasing.[8, 9] This [illegible] consists an additional problem, as the non-*albicans* species present resistance to some antifungal agents [illegible] *glabrata* and *C. krusei*, fluconazole resistance has also been revealed in *C. tropicalis* and *C. parapsilosis* and echinocandine resistance has started to occur, possibly, due to their broad clinical use.[10]

Objectives

The aim of this study is to compare the isolated *Candida* strains from blood cultures and their susceptibility in a tertiary hospital in Greece, during two periods each, Period 1 (P1): 01/01/2004-12/31/2006 and Period 2 (P2): 01/01/2012-12/31/2014.

Materials and Methods

During the study periods P1 and P2, blood culture vials from 15,723 and 20,626 patients were sent to the laboratory respectively. BACTEC 9240 (BD) and BacT/ALERT 3D (bioMerieux) automated systems were used for the incubation of the vials. The positive samples were cultured on McConkey blood and chocolate agar when the positive vial was an aerobic one and on blood and anaerobic blood agar when it was an anaerobic one, with the addition of Sabouraud dextrose agar when yeasts were present from the Gram stain of the positive vial. The strains were identified by API-ID32C and/or VITEK II automated system (bioMerieux). Susceptibility testing was performed by VITEK II sytem and/or on RPMI agar by E-test method (bioMerieux), according to CLSI instructions.

Results

During P1 2,605 blood cultures out of a total of 15,723 (16.6%), from equal number of patients, were found positive and during P2 3,406 blood cultures out of 20,626 (16.5%) were found positive. *Candida* strains were isolated in [illegible] out of 2,605 (2.7%) positive cultures for P1 and in 152 out of 3,406 (4.5%) positive cultures for P2. Candidemia in both study periods was the eighth most common cause of BSIs in our hospital. The [illegible] Figure 1 [illegible] incidence of *Candida* species is shown on Table 1 and the changes in both origin and species incidence is shown on Table 2. The susceptibility [illegible] studied in five antifungal agents: amphotericin B, flucytosine, fluconazole, [illegible] amphotericin B and caspofungin all strains were susceptible, as it is shown in Figure 2.

Figure 1. Origin of *Candida* strains (%) during the two study periods [illegible]

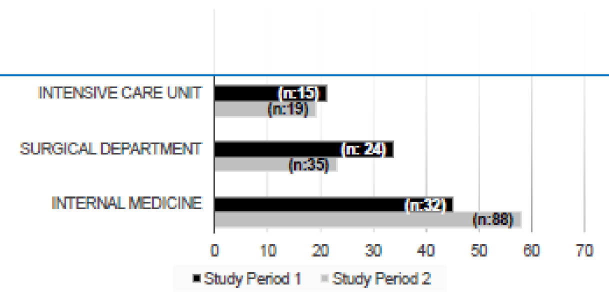


Figure 2. Resistance of *C. albicans* and non-*albicans* Candida (NAC) strains in antifungal agents during the two study periods [Period 1 (SP1) and Period 2 (SP2)] (%)

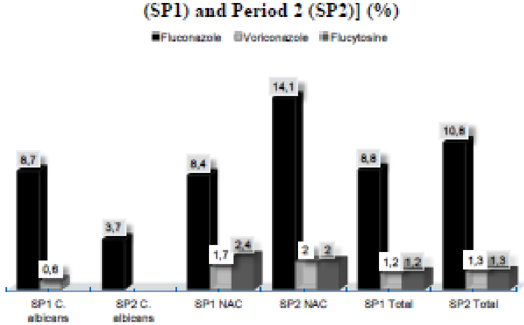


Table 1. Incidence of species of *Candida* strains during the two study periods (Period 1: 1/1/2004-31/12/2006 and Period 2: 1/1/2012-31/12/2014)

Species	Study Period 1 n:71 (%)	Study Period 2 n: 152 (%)
C. albicans	29 (40.8)	53 (34.9)
C. parapsilosis	15 (21.1)	63 (41.4)
C. glabrata	13 (18.3)	14 (9.2)
C. tropicalis	7 (9.8)	5 (3.3)
C. famata	2 (2.8)	9 (5.9)
C. lusitaniae	1 (1.4)	
C. krusei	1 (1.4)	2 (1.3)
C. dubliniensis	1 (1.4)	1 (0.6)
C. guilliermondii		1 (0.6)
C. lipolytica	1 (1.4)	
C. kefyr		1 (0.6)
C. pelliculosa		1 (0.6)
C. rugosa		1 (0.6)
C. sphaerical		1 (0.6)
Candida spp	1 (1.4)	

Table 2. Changes in the origin and in the incidence of Candida species during the two study periods [Period 1 (P1): 1/1/2004-31/12/2006 and Period 2 (P2): 1/1/2012-31/12/2014]

Species	Internal Medicine		Surgical Department		ICU	
	P1 (n:32)	P2 (n: 88)	P1 (n:24)	P2 (n:35)	P1 (n:15)	P2 (n:29)
C. albicans	14	27	9	12	6	14
C. parapsilosis	7	39	5	15	3	9
C. glabrata	6	9	4	4	3	1
C. tropicalis	4	3	2	1	1	1
C. famata	1	5		1	1	3
C. lusitaniae			1			
C. krusei		1	1	1		
C. dubliniensis		1			1	
C. guilliermondii		1				
C. lipolytica			1			
C. kefyr						1
C. pelliculosa				1		
C. rugosa		1	1			
C. sphaerical		1				

Conclusions

In the two study periods a significant increase, approximately, double, in the incidence of candidemia was observed (p: 0.0258)
Candidemia revealed increase in Internal Medicine Wards, while in ICU prevalence was similar and in Surgical Department decrease was observed
Noticeable, was the predominance of C. parapsilosis in P2 (p: 0.0014), unlike with the predominance of C. albicans in P1
No significant differences were observed in the reistance rate in the two periods, which concerned fluconazole, flucytosine and voriconazole
Echinocandins and amphotericin B seems to be the most effective treatment in our hospital
Taking under consideration, the different response of Candida spp in antifungal drugs in vivo, identification of Candida strains in species level and their susceptibility seems to be a necessity

Serious fungal infection in Northwestern Greece, during a five year period.

E. Priavali, P. Karagianni, C. Gartzonika, D. Papamichail, E. Nita, H. Sakkas, A. Miari, A. Veneti, S. Levidiotou
Department of Microbiology, Medical School, University of Ioannina

BACKGROUND

- The incidence of **severe fungal infections** has increased worldwide and represents a serious threat, especially
  - ✓ among **immunocompromised and critically ill patients.**
- The **aim of this study** was
  - ✓ to asses *candidaemia rates*,
  - ✓ species involved and sensitivity profile to antifungals as well as
  - ✓ the *incidence of other yeasts of clinical importance*, during the last 5 years (2011-2015).
- The results regarding **candidaemia**, were also compared with those of a previous retrospective analysis (decade 2001-2010).

MATERIALS/METHODS I

A retrospective study of

- *Candida blood stream episodes*
- *cryptococcal infections* and
- *invasive aspergillosis*
  - collected from the microbiology database of the **750-bed University Hospital of Ioannina,** including 5 intensive care units (ICUs), 25 medical and 16 surgical wards, over a 5-year period,

factors

MATERIALS/METHODS II

- **Isolation and identification** of the respective etiological agents was achieved using
  - ✓ the standard microbiological techniques,
  - ✓ BacT/Alert automated system, Vitek 2 system and
  - ✓ API32C (bioMerieux, France).
- **Antifungal susceptibility** of *Candida* strains was determined using Vitek 2 system complemented with E-test (bioMerieux), according to CLSI criteria.
- **Detection of galactomannan antigen** was performed using the Platelia Aspergillus enzyme immunoassay (Bio-Rad, Hercules, CA).

- *C. albicans* commonest species
- 100% susceptibility to AmB
- *C. parapsilosis* resistance:
  - CAS 47%
  - MIC 10,5

RESULTS II

- ...was the commonest species representing **56.1%** of all isolates (51/91), followed by *C. parapsilosis* (20.9%-19/91), *C. glabrata* (9.9%-9/91), *C. lusitaniae* (7.7%-7/91) as well as other non-albicans species (5.5%-5/91) (figure 2).
- The overall mortality was **49.4%** (44/89 episodes), caused mainly by *C. albicans* (61.4%-27/44 deaths).

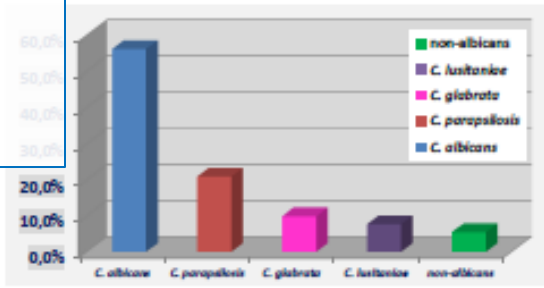


Figure 2. Distribution of *Candida* isolates by species

RESULTS III

- In terms of **in vitro susceptibility**, all isolates were **susceptible to amphotericin B,** except primary resistant strains of *C. lusitaniae*.
- Four strains **(44%)** ***C. glabrata*** were resistant to **fluconazole** as well as 2 ***C. parapsilosis*** **(11%).**
- **Resistance to caspofungin and micafungin** exhibited **47% and 10.5%** of ***C. parapsilosis*** isolates, respectively. **(Figure 3, Table 1).**

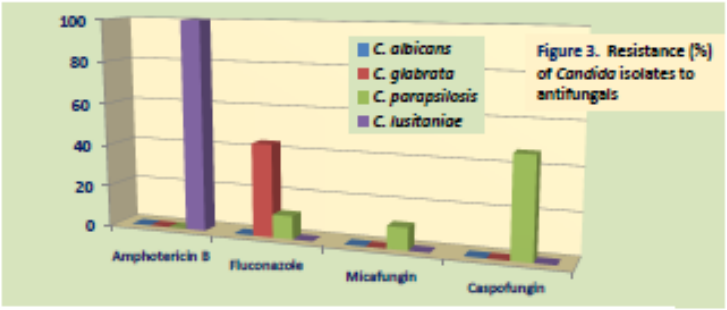


Figure 3. Resistance (%) of *Candida* isolates to antifungals

Antifungals	C. albicans	C. glabrata	C. parapsilosis	C. lusitaniae
Amphotericn B	0	0	0	100
Fluconazole	0	44	11	0
Micafungin	0	0	10,5	0
Caspofungin	0	0	47	0

Table 1. Resistance (%) of *Candida* isolates to antifungals

- The incidence of candidaemia and the distribution of species were approximately the same, in comparison with the previous study.
- There weren't remarkable changes regarding resistance.
- During the study period, 15 different cases of invasive pulmonary aspergillosis were also estimated concerning mainly patients with solid organ tumors (67%) and resulting in 2 deaths (12.5%).
- Only one episode of cryptococcal BSI and meningitis was recorded with fatal outcome and none with *P. jirovecii* pneumonia.

CONCLUSION

- *C. albicans* is still the most frequent species causing candidaemia. Amphotericin B retains a 100% sensitivity rate for *Candida* isolates.
- The incidence of other severe fungal infections remains low probably due to widespread use of antifungals for prophylaxis.
- **Continuous surveillance** is mandatory to ensure an early appropriate targeted treatment which is crucial for the successful approach to severe fungal infections.

REFERENCES

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CANDIDA BLOOD STREAM INFECTIONS IN A GREEK TERTIARY HOSPITAL: 5 YEARS SURVEY. EPIDEMIOLOGY AND IN VITRO ANTIFUNGAL SUSCEPTIBILITY PROFILES

ECCMID 26th (2016)

E. Perivolioti[1], M. Nepka[1], **E. Kraniotaki[1]**, M. Mpournia[1], E. Douka[2], V. Papastamopoulos[3], A. Skoutelis[3], K. Fountoulis[1]
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4076

INTRODUCTION AND PURPOSE

During the la... decades the rates of invasive *Candida* infections have increased dr... significant m... morbidity and mortality, monitoring of *Candida* species distribution a... among sign... their antifungal resistance is required. A retrospective study was conducted between January 2011 and N... ember 2... ...elismos General Hospital. The incidence of *Candida* species causing bloodstream infections and their suscept... bility profi... ...ated. The purpose of this study was to define the rate of *Candida* isolates among all positive blood cultures, spe... distribution between *C. albicans* and *C. non-albicans*, and ... antifungal susceptibility test among them.

- *C. albicans* commonest species in non-ICU wards
  - Resistance
  - FCZ 3%
  - VOR 1%
- *C. parapsilosis* commonest in ICU
  - Resistance
  - FCZ 3%
  - VOR 6%
- 99% susceptibility to AmB, flucytocine, VOR

METHODS

Records from the microbiology department were evaluated for the study period. All hospitalized patients who had ≥1 blood culture positive *Candida* were included in the study. Automated blood culture systems (BACTEC 9240, BD) were used. All isolates were speciated by the Vitek 2 system. Susceptibility to amphotericin B, fluconazole, voriconazole, flucytocine, micafungin and caspofungin was performed by the Vitek 2 system and to anidulafungin by the E test (AB Biodisk, Sweden). Result interpretation was according to the CLSI guidelines (revised M27-S4).

CONCLUSION

Candidemia is a significant problem especially in medical wards. Early recognition and prompt empirical treatment are essential to improve outcomes of patients at risk for developing candidemia. Improvement of surveillance is crucial to recognizing emergence of highly resistant strains.

RESULTS

- A total number of 7588 positive blood cultures were reviewed
- Fungi were cultured from 521 positive blood cultures (6,9%)
- *Candida* species were found to be the fourth most common organism causing blood stream infections (BSIs)
- Overall, *Candida* accounted for 6,9% of all BSIs - being responsible for 7,8% of BSIs in the intensive care unit and 5,7% of infections in non-ICU patients
- *C. albicans* represented the most common isolate in non-ICU wards (47%)
- *C. parapsilosis* represented the most common isolate in ICU (44%)
- All *Candida albicans* isolates were susceptible to azoles and candines (Table1)

Table1. Susceptibility profiles of *Candida* spp from 2011 to 2015

	MIC range	*Candida albicans*	*Candida parapsilosis*	*Candida glabrata*	*Candida tropicalis*
Amphotericin B	0.25-0.5	99%	98%	99%	99%
Fluconazole	1-32	97%	MIC>4=27%	MIC_{90}=8μg/l	95%
Flucytocine	1-4	99%	99%	99%	99%
Voriconazole	0.25-1	99%	94%	99%	99%
Caspofungin	Average	0.125	1	0.125	0.125
Micafungin	Average	0.125	1	0.006	0.125
Anidulafungin	Average	0.125	2	0.125	0.125

1. Bitar, D., et al. "Population-based analysis of invasive fungal infections, France, 2001-2010." *Emerging infectious diseases* 20.7 (2014): 1149-1155.
2. Poikonen, Eira, et al. "Secular trend in candidemia and the use of fluconazole in Finland, 2004-2007." *BMC infectious diseases* 10.1 (2010): 1.

29th ECCMID

Amsterdam, Netherlands
13 – 16 April 2019

The congress of ESCMID

P2155 Ten-year study on epidemiology of candidaemias and antifungal-resistance in a major Greek hospital

Athanasia Tsirigga[1], Melina Giannoula*[1], Vassiliki Skandami[1], Aikaterini Petrocheilou - Malliara[1]

[1] General Hospital of Athens, Ippokrateio, Athina

- *C. p*arapsilosis predominant pathogen during most years.
- *Candida albicans* more common in 2008, 2009 and 2012
- overall AmB resistance 1,7%, only noted in years 2013 – 2015.
  - VOR resistance 4%
  - FLZ resistance 8,8%
- Non-*C. albicans* associated with higher FLZ MICs and possibility of resistance.

29th ECCMID

Amsterdam, Netherlands
13 – 16 April 2019

The congress of ESCMID

P2235 *Candida* bloodstream infections in Greece: a 9-year survey in a tertiary care academic hospital

Maria Siopi*[1], Aikaterini Tarpatzi[1], Eleni Kalogeropoulou[1], Sofia Damianidou[1], Alexandra Vasilakopoulou[1], Spyros Pournaras[1], Joseph Meletiadis[1,2]

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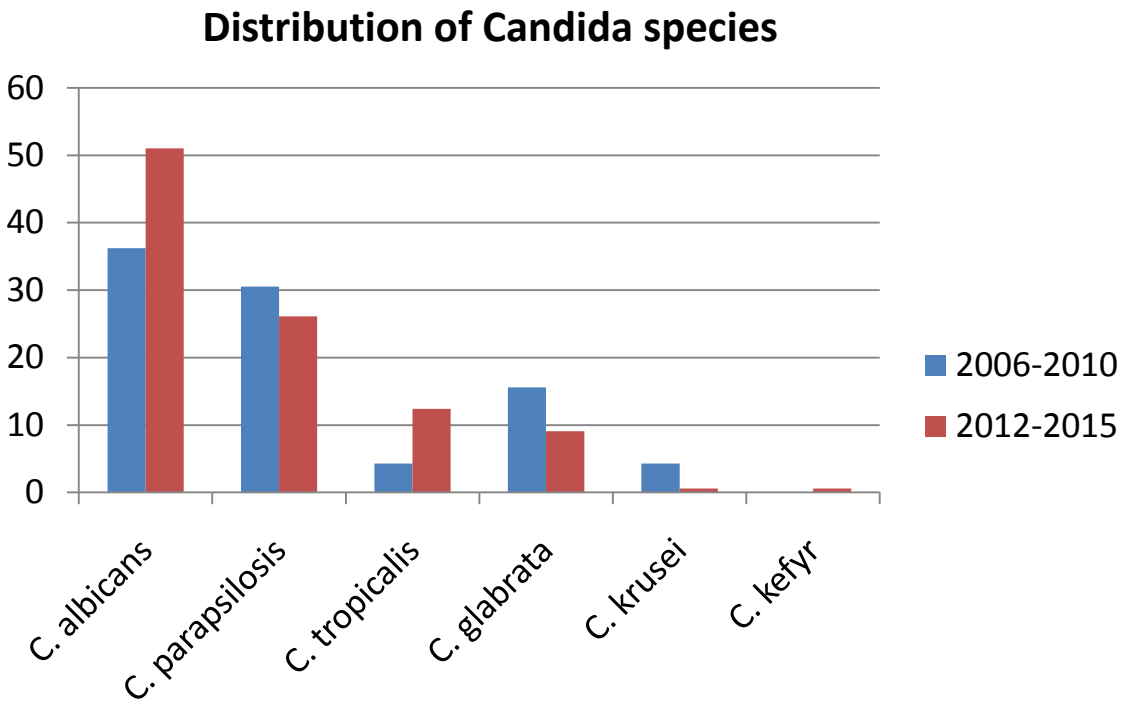
- overall incidence of candidemia remained stable over time
- the increase of fluconazole resistant *C. parapsilosis SC isolates over the last years is alarming.*

Presented and unpublished data from Laiko hospital; comparison of 2 periods

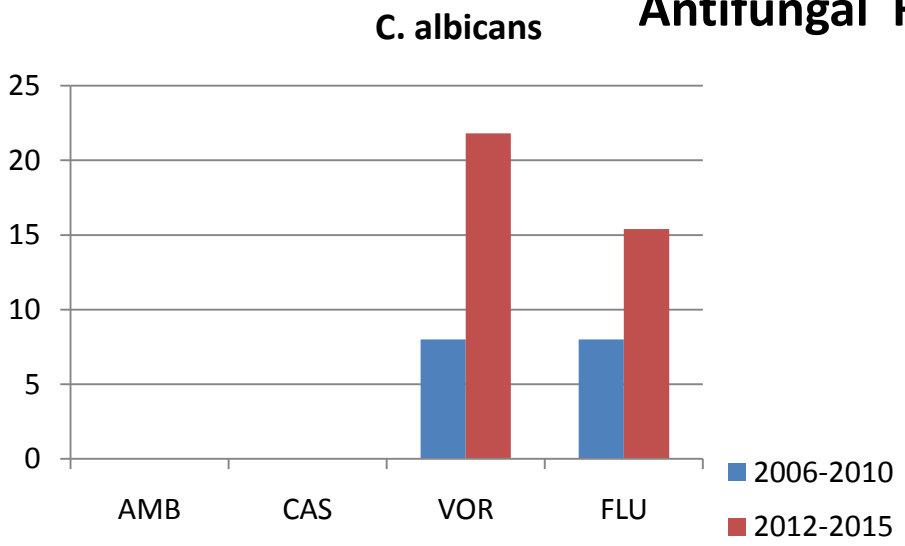


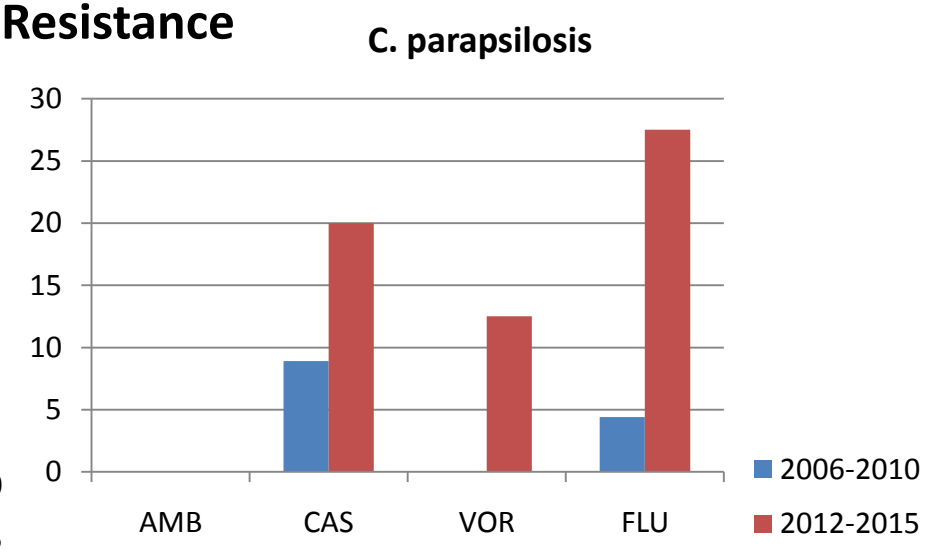
1. Drogari-Apiranthitou M, et al., 21st ECCMID 2011

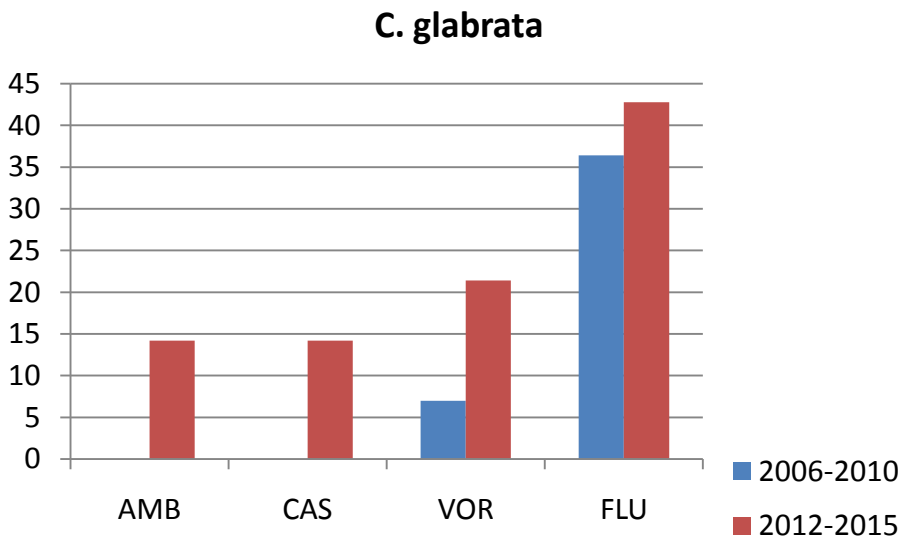
2. Laiko unpublished data

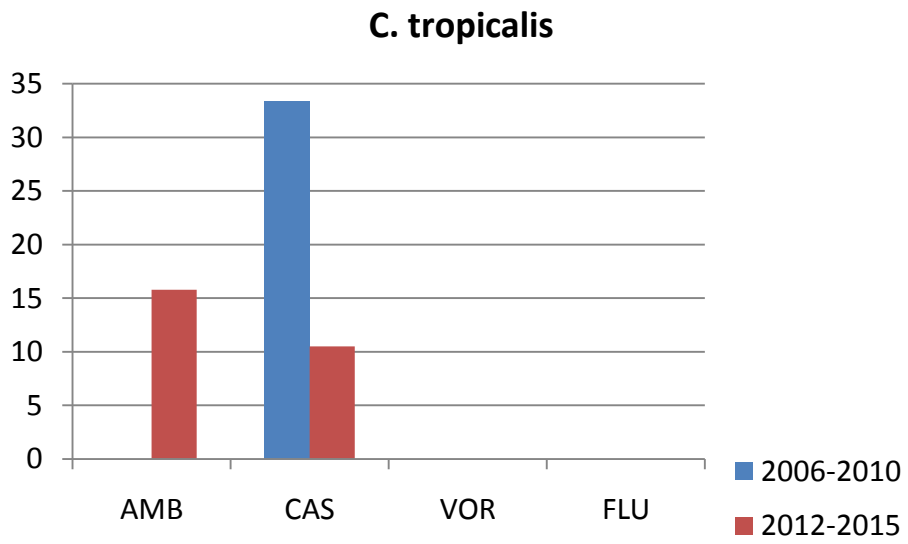
Presented and unpublished data from Laiko hospital; comparison of 2 periods

Antifungal Resistance









1. Drogari-Apiranthitou M, et al., 21st ECCMID 2011

2. Laiko unpublished data

Risk factors for isolation of fluconazole or echinocandin non-susceptible *Candida* spp. among patients hospitalized in an Intensive Care Unit

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- A high percentage of isolates were non-susceptible to FLZ and echinocandins
- Echinocandin admin. Led to isolation of non-susceptible isolates
- FLZ admin was not associated with non-susceptible isolates

Introductio

Utilization of Candida such antifu to identify fluconazole Candida sp

Methods

A retrosp conducted Intensive Hospital o catheter-tip and peritoneal fluid) from patients were tested for the presence of *Candida* spp. All yeasts were identified using Vitek 2 Advanced Expert System. Susceptibility of antifungals was assessed by Etest and was evaluated according CLSI. Antifungal consumption was calculated using the defined daily dose (DDD) per 100-patient-days.

Results

Among 2684 patients hospitalized at the ICU during the study period, 181 (6.7%) had at least one positive sample positive for *Candida* spp. Non-*albicans* species predominated (107 patients; 59.1%). *C. albicans* was the most

und that isolation of non-*albicans* P<0.001; OR 9.3, CI 3.4-25.5), f non-susceptible strain to at least one lin (*P*<0.001; OR 14.2, CI 4.6-44.3) alization during 2014-17 (*P*<0.001; CI 1.2-1.7) were associated with f fluconazole non-susceptible species. f *Candida* spp. non-susceptible to at

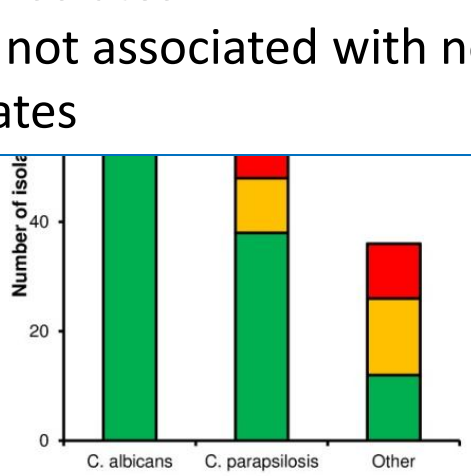

Figure 1. Susceptibility to fluconazole of *C. albicans*, *C. parapsilosis* and other Candida spp. (23 *C. tropicalis*, 17 *C. glabrata*, 2 *C. krusei*)

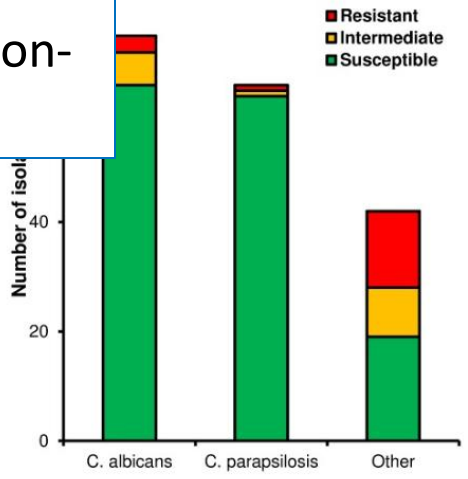

Figure 2. Susceptibility to echinocandins of *C. albicans*, *C. parapsilosis* and other Candida spp.

at least one echinocandin was independently associated with isolation of strain non-susceptible to fluconazole (*P*<0.001; OR 8.9, CI 3.4-22.9) and prior administration of the echinocandin to which the strain was non-susceptible (*P* 0.019; OR 7.3, CI 1.4-38.9). Figure 3 depicts the annual antifungal consumption.

Conclusions

A high percentage of isolates were non-susceptible to fluconazole and echinocandins. Echinocandin administration led to isolation of non-susceptible isolates, while fluconazole administration wasn't associated with isolation of fluconazole non-susceptible isolates.

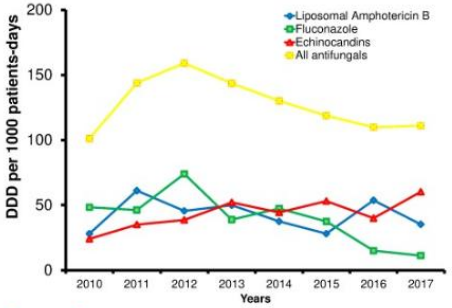

Figure 3. Annual antifungal consumption

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Journal of Fungi

MDPI

Article

Changing Epidemiology of Invasive Candidiasis in Children during a 10-Year Period

Maria Noni [1], Angeliki Stathi [2], Ilia Vaki [1], Aristea Velegraki [3], Levantia Zachariadou [2] and Athanasios Michos [1,*]

- A retrospective cohort study was performed from January 2008 to December 2017
- 178 cases of IC were recorded. The tissue distribution included blood (87.1%), cerebrospinal (7.9%), peritoneal (3.9%) and pleural fluids (1.1%).
- *Candida albicans* and *Candida parapsilosis* (*sensu lato*) were the most frequently isolated species (47.8% and 28.7% respectively).
- From period 2008⁻2012 to period 2013⁻2017, a significant **decrease in IC rates was** detected (0.21 cases/1000 hospitalization days VS 0.11 cases/1000 hospitalization days, $P = 0.040$), while median minimum inhibitory concentrations (MICs) of amphotericin B were significantly increased for both *C. albicans* and *C. parapsilosis* (*sl*) ($P = 0.037$ and $P = 0.004$ respectively).
- **The decrease in IC rates may reflect the increased awareness as well as the effective infection control initiatives and antifungal interventions.**
- However, the significant increase in the MICs for amphotericin B and echinocandins such as caspofungin, raises concerns about their common use as first-line treatment. Epidemiologic monitoring is, therefore, critically important in order to evaluate and optimize therapeutic protocols for IC in pediatric populations.

Other paediatric studies

Neonatal candidiasis: analysis of epidemiology, drug susceptibility, and molecular typing of causative isolates.

Roilides E, Farmaki E, Evdoridou J, Dotis J, Hatziioannidis E, Tsivitanidou M, Bibashi E, Filioti I, Sofianou D, Gil-Lamaignere C, Mueller FM, Kremenopoulos G.

Eur J Clin Microbiol Infect Dis. 2004 Oct;23(10):745-50.

A prospective observational study of invasive candidiasis was conducted in the neonatal intensive care unit of Aristotle University in Hippokration Hospital between **1994 and 2000**. During this period, 59 neonates developed invasive candidiasis (58 cases of candidemia and 1 case of peritonitis), resulting in an overall incidence of 1.28% that showed a decreasing trend over the study period. Eleven (18.6%) cases developed within the first week of life and the others within a mean (+/-SEM) of 13.4+/-1.7 days after birth. The three most frequent causative species were Candida albicans (65.5%), Candida parapsilosis (15.5%), and Candida tropicalis (7%). C. albicans was the predominant species between 1994 and 1998, whereas, non-albicans Candida spp., particularly C. parapsilosis, were the most frequent species during the period 1999-2000 ($P<0.001$). While the overall mortality due to candidemia was 29% (17 of 59 cases), mortality associated with C. albicans and C. parapsilosis was 39.5% and 11.1%, respectively ($P=0.032$), and that observed in the 1999-2000 period was 0% ($P=0.011$). Virtually all isolates were susceptible to amphotericin B, flucytosine, fluconazole, and itraconazole, and no increases in minimal inhibitory concentrations were observed during these years. With the exception of a limited cluster of cases due to genotypically identical isolates, no clonal relation of C. albicans isolates was found. Moreover, no clonal persistence of C. albicans and no decrease in antifungal drug susceptibility occurred over the 6-year study period. Non-albicans Candida spp., mostly C. parapsilosis, have emerged as important pathogens in neonatal intensive care units, with infected patients having better outcomes as compared to patients infected with C. albicans.

Invasive candidiasis in pediatric intensive care in Greece: a nationwide study.

Vogiatzi L, Ilia S, Sideri G, Vagelakoudi E, Vassilopoulou M, Sdougka M, Briassoulis G, Papadatos I, Kalabalikis P, Sianidou L, **Roilides E**.

Intensive Care Med. 2013 Dec;39(12):2188-95.

PURPOSE:

To record the practices for prevention and management of invasive candidiasis in the PICU and investigate the epidemiology of candidiasis and its outcome nationwide.

METHODS:

A multicenter national study among PICUs throughout Greece. A questionnaire referring to local practices of prevention and management of candidemia was filled in, and a retrospective study of episodes that occurred during 5 years was conducted in all seven Greek PICUs.

RESULTS:

Clinical practices regarding surveillance cultures, catheter replacement protocols and antibiotic use were similar, although the case mix differed. In all PICUs prophylactic antifungal treatment was administered in transplant and neutropenic oncology patients. Discrepancy existed between PICUs concerning the first-line antifungal agents and treatment duration of candidemia. Twenty-two candidemias were nationally recorded between 2005 and 2009 with a median incidence of 6.4 cases/1,000 admissions. Median age was 8.2 (0.3-16.6) years. Candida albicans was isolated in 45.4 % of episodes followed by Candida parapsilosis (22.7 %). Common findings were presence of central venous and urinary catheters as well as mechanical ventilation and administration of antibiotics with anti-anaerobic activity in almost all patients with candidemia. Total parenteral nutrition was administered to five (22.7 %) patients. Most of the patients had a chronic underlying disease; five were oncology patients, and two-thirds of those with candidemia were colonized with Candida spp. Lipid amphotericin B formulations were the predominant therapeutic choice (54.5 %). Thirty-day mortality was 18.2 %.

CONCLUSION:

This first national study adds information to the epidemiology of candidemia in critically ill children. In these special patients, candidemia has a relatively low incidence and tends toward non-albicans

Conclusions

- The incidence of candidaemia in Greece appears to be increasing
- The *C. parapsilosis* SC frequency is increasing
- The increasing resistance in antifungals especially FLZ and echinocandins is alarming
- The decrease in IC rates in children may reflect the increased awareness as well as the effective infection control initiatives and antifungal interventions.

Take-home messages

- Candidaemia epidemiology is changing
- There are geographic and local differences
- Monitoring of local epidemiology is imperative in order to decide the appropriate empirical and focused antifungal treatment
- Infection source control measures have to be enhanced
- There are still a lot of unanswered questions regarding fungal biology and antifungal susceptibility
- Need for close collaboration between clinicians and the clinical laboratory

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Thank you !