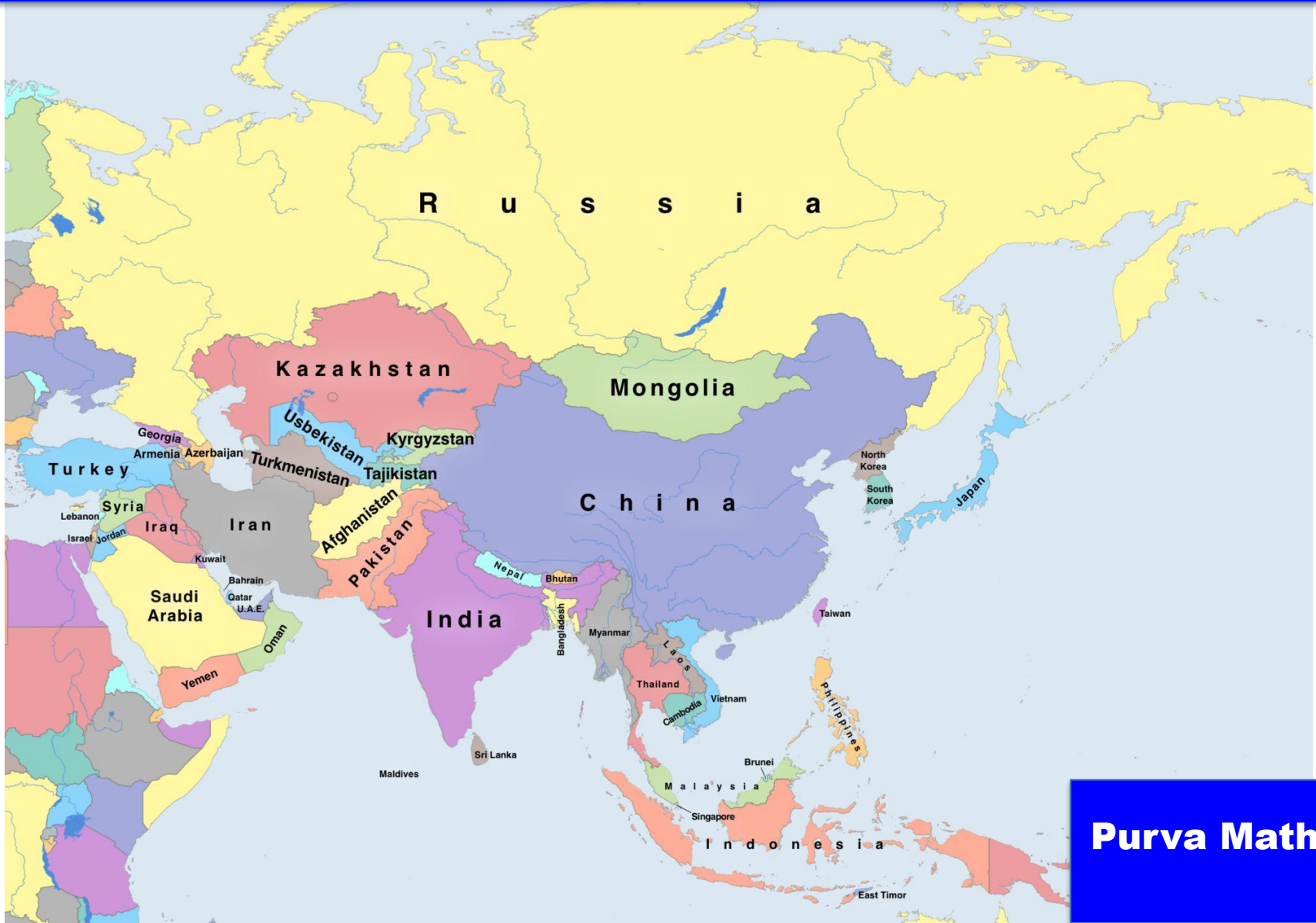


Candida Infections in ICU settings: Scenario in Asia and India



Purva Mathur

Candidemia/ Invasive candidiasis

- Important Health care associated infection (HCAI), causing high mortality, especially in critically ill patients in ICUs
- *Candida* spp. is one of the most frequent pathogens isolated in bloodstream infections (BSI)

- Past two decades, the incidence of candidemia: **doubled**
- *Candida* spp. currently ranks as the **fourth** and the **seventh** most common bloodstream pathogen in North American and European studies.
- Prevalence in Asia is much higher; studies lesser

Reasons for increasing rates

- Improved detection
- Increase in patient- population at risk
 - Invasive procedures and devices
 - Broad-spectrum antimicrobial agents
 - Advanced life-support
 - Aggressive chemotherapy

Impact

- Crude mortality rate of Candidemia is 40-75%
- Attributable mortality of 25%-38%
- Increased Length of stay (~ of 30 days)
- Increased costs of care
- Antifungal resistance

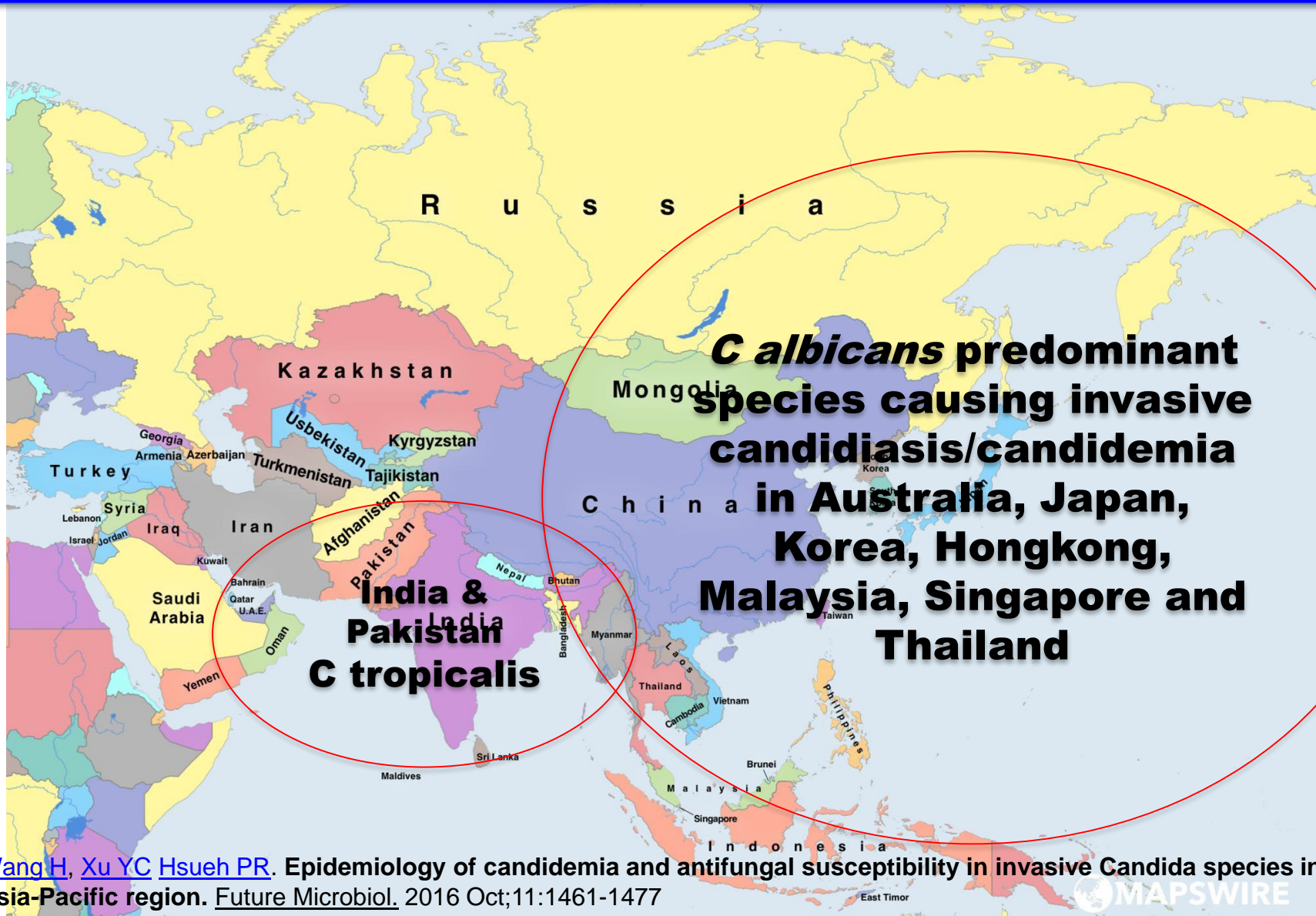
***C. albicans*/ NAC?**

- Historically, *C. albicans*: most common cause of candidemia worldwide.
- Recent years: NAC have increased
- The intrinsic and emerging resistance to azoles represents a major challenge for treatment

Epidemiology of candidemia

- Shows wide variation among countries
- E.g; Europe
 - An increasing incidence of candidemia in Iceland was reported between 2000 and 2011
 - Similarity was not observed in Switzerland, (Swiss National survey showed static rates)
- Although there are many studies from Asia, a large-scale cross-sectional study across Asia was lacking

Candida Infections in ICU settings: Scenario in Asia and India



Incidence and species distribution of candidaemia in Asia: a laboratory-based surveillance study

B. H. Tan¹, A. Chakrabarti², R. Y. Li³, A. K. Patel⁴, S. P. Watcharananan⁵, Z. Liu⁶, A. Chindamporn⁷, A. L. Tan⁸, P.-L. Sun⁹, U.-I. Wu¹⁰ and Y.-C. Chen^{11,12}, on behalf of the Asia Fungal Working Group (AFWG)

1) Department of Infectious Diseases, Singapore General Hospital, Singapore, 2) Department of Medical Microbiology, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India, 3) Department of Dermatology, Peking University First Hospital, Research Centre for Medical Mycology, Peking University, Beijing, China, 4) Department of Infectious Diseases, Sterling Hospital, Ahmedabad, India, 5) Division of Infectious Disease, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand, 6) Department of Infectious Diseases, Peking Union Medical College Hospital, Beijing, China, 7) Department of Microbiology, Faculty of Medicine, King Chulalongkorn Memorial Hospital Chulalongkorn University, Bangkok, Thailand, 8) Department of Pathology, Singapore General Hospital, Singapore, 9) Department of Dermatology, Mackay Memorial Hospital, 10) Department of Medical Research, National Taiwan University Hospital, 11) Department of Medicine, National Taiwan University Hospital and College of Medicine, Taipei and 12) National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Miaoli County, Taiwan

Future Microbiol. 2016 Oct;11:1461-1477

- 12-month, laboratory-based surveillance of candidaemia at 25 hospitals from
 - China
 - Hong Kong
 - India
 - Singapore
 - Taiwan
 - Thailand
- The incidence and species distribution of candidaemia were determined.

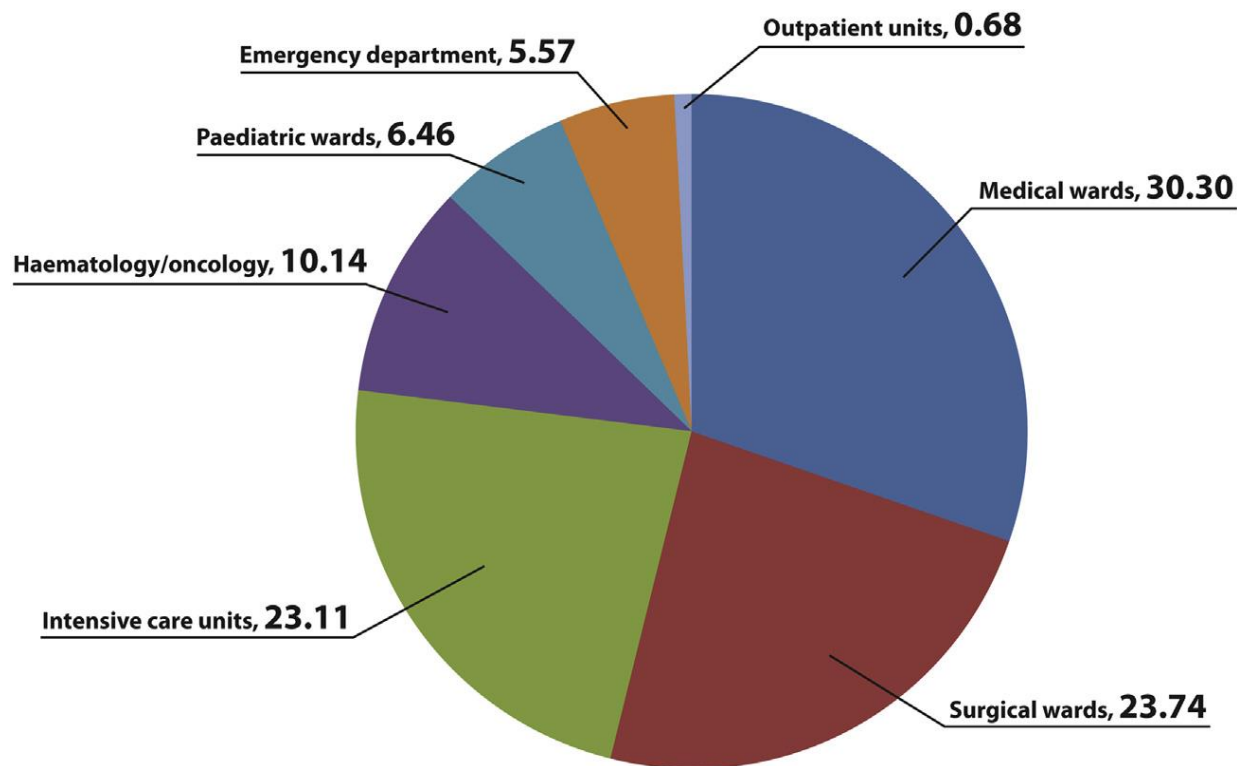


FIG. 1. Distribution of patients with candidaemia by hospital service (number denotes %).

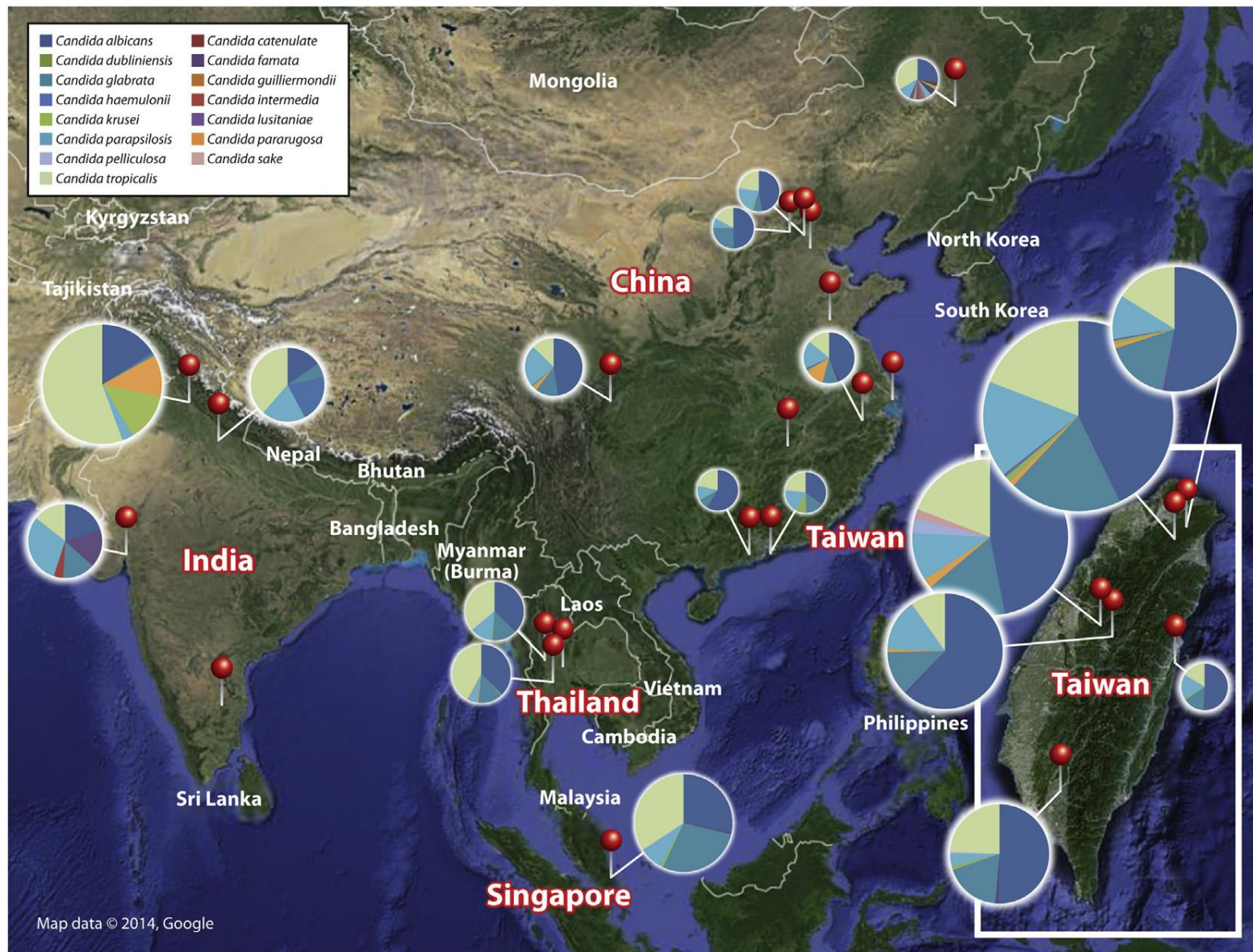


FIG. 3. Geographic locations of the 25 participating study sites. The size of the circles indicates the relative number of candidaemia episodes in each site. Only *Candida* species of 20 or more episodes at each study site are shown. The inset represents Taiwan.

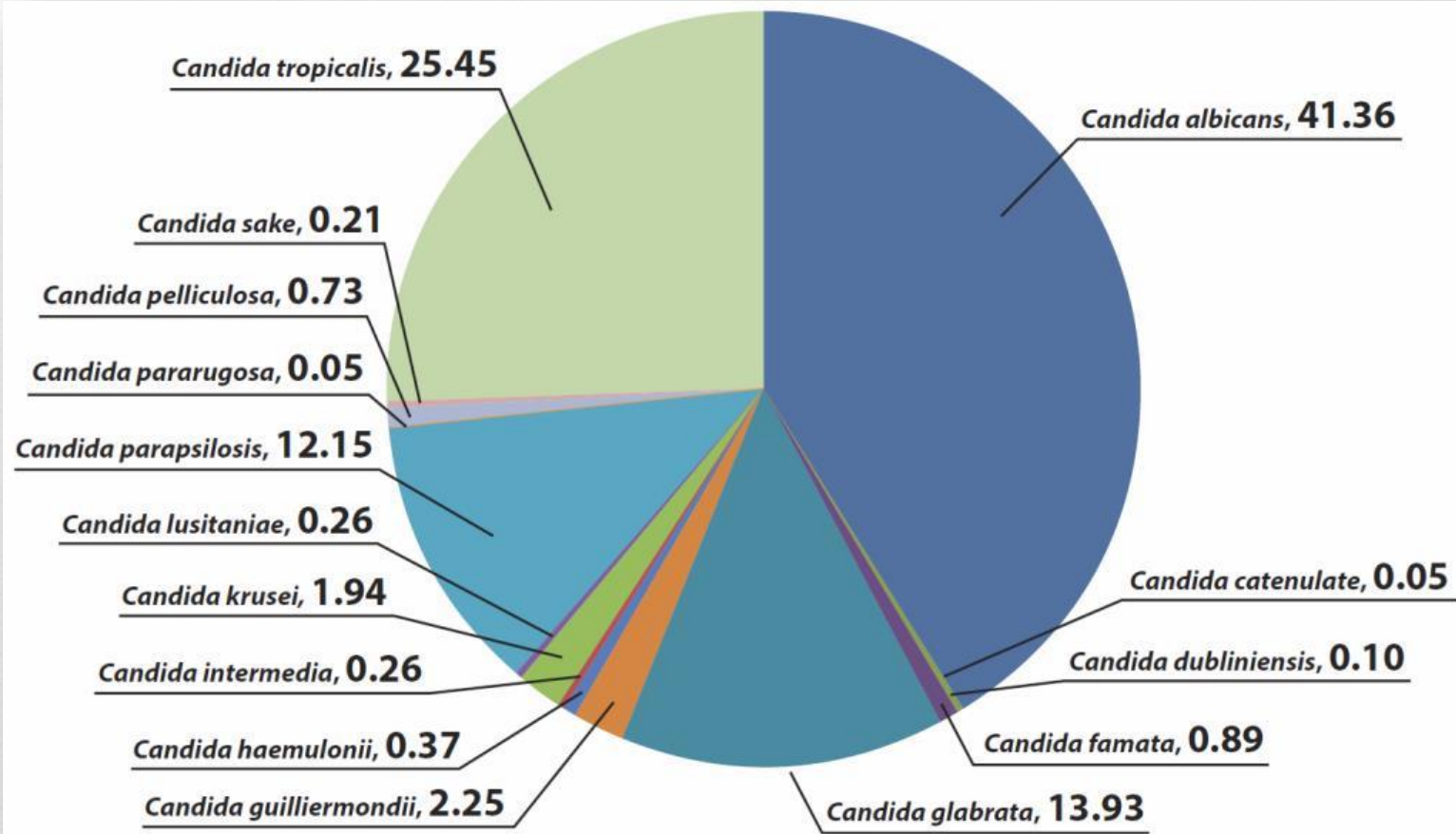
- 1,601 episodes of candidaemia among 1.2 million discharges.
- Overall incidence: 1.22 episodes per 1000 discharges
 - Varied among the hospitals (range 0.16–4.53 per 1000 discharges)
 - Varied among countries (range 0.25–2.93 per 1000 discharges).

- 1,910 blood isolates evaluated
 - *Candida albicans* was most frequently isolated (41.3%)
 - Followed by *Candida tropicalis* (25.4%)
 - *Candida glabrata* (13.9%)
 - *Candida parapsilosis* (12.1%)

Although *C. albicans* was the most common *Candida* species, it accounted for <40% of candidaemia in 12 of 25 hospitals.

Candida tropicalis was the leading non-*albicans* species

Species distribution in Asia, 1910 non-duplicate blood *Candida* isolates



C. tropicalis

- Leading NAC species overall
- The most common NAC species in 18 hospitals:
 - China (6/10),
 - Hong Kong,
 - India (3/4),
 - Singapore,
 - Taiwan (4/6) and
 - Thailand (3/3)

- Proportion of *C. tropicalis* was higher in tropical areas (India, Thailand and Singapore) than other geographical regions (46.2% versus 18.9%, p 0.04).

C. glabrata

- The most common NAC species in 3 of 25 hospitals (two in China; one in Taiwan).
- Up to 26% of candidaemia was caused by *C. glabrata* in two hospitals (one in China; one in Singapore).

C. parapsilosis/ C. krusei

- *C. parapsilosis* was the most common NAC species in 3 of 25 hospitals
 - 33% of candidaemia cases in one Indian hospital.
 - 26% in a Chinese hospital and
 - 14% in a Taiwanese hospital.
- *Candida krusei* was rare, but contributed to 12.2% of *Candida* blood isolates in one Indian hospital.

Is there a difference between East and West?

- The species distribution is different from Western countries.
- Both geographic and healthcare factors contribute to the variation of species distribution.

Country or region	Setting or population	Study period	No. of episodes	Incidence (range)	Incidence density (range)	Reference
Hospital-based survey						
China	9 hospitals	2010–2011	310	0.38 per 1000 discharges (0.16–0.74)	0.05 per 1000 patient-days (0.01–0.06)	Current study
Hong Kong	1 hospitals	2010–2011	30	0.25 per 1000 discharges	0.07 per 1000 patient-days	Current study
India	3 hospitals	2010–2011	333	1.94 per 1000 discharges (0.30–4.53)	1.24 per 1000 patient-days (0.30–1.77)	Current study
Singapore	1 hospitals	2010–2011	73	NA	0.15 per 1000 patient-days	Current study
Taiwan	6 hospitals	2010–2011	1104	2.93 per 1000 discharges (1.99–3.89)	0.37 per 1000 patient-days (0.20–0.56)	Current study
Thailand	3 hospitals	2010–2011	130	1.31 per 1000 discharges	0.17 per 1000 patient-days	Current study
Asia	25 hospitals in 6 countries/ regions	2010–2011	1601	1.22 per 1000 discharges (0.16–4.53)	0.15 per 1000 patient-days (0.01–1.77)	Current study
Latin American	21 tertiary care hospitals in 7 countries	2008–2010	672	1.18 per 1000 admissions (0.21–2.98)	0.23 per 1000 patient-days (0.06–0.39)	[4]
Italy	34 hospitals	2009	467	1.19 per 1000 admissions		[5]
UK	A tertiary referral center.	2005–2008	107		0.109 per 1000 bed-days	[6]
Intensive care units (ICUs)						
Asia	ICUs in 25 hospitals in 6 countries/regions	2010–2011	370	11.7 per 1000 discharges		Current study
India	27 ICUs	2011–2012	1,400	6.51 per 1000 ICU admission		[7]
China	67 adult ICUs	2009–2011	306	3.2 per 1000 ICU admission		[8]
Italy	18 adult ICUs	2007–2008	92	16.5 cases per 1000 admissions		[9]
Germany	682 ICUs	2006–2011	523	0.24 per 1000 patients	0.07 per 1000 patient-days	[10]
Population-based survey						
Spain	Population survey (29 hospitals in five municipal areas)	2010–2011	773	8.1 cases per 100 000 inhabitants 0.89 per 1000 admissions	1.36 per 10 000 patient-days	[11]
USA	Population survey	2008–2011	2675	13.3 per 100 000 person-years in Atlanta; 26.2 per 100 000 person-years in Baltimore		[12]
Australia	Nationwide survey	2000–2004	1095	1.81 per 100 000 population and 0.21 per 1000 separations		[13]
Iceland	Nationwide survey	2000–2011	208	5.7 per 100 000 population/year		[14]
Finland	Nationwide survey	2004–2007	603	2.86 per 100 000 population		[15]

¹Pubmed search using the following phrase: ((candidemia[Title/Abstract]) OR invasive candidiasis[Title/Abstract])) AND (“2010/1/1”[Date - Publication] : “2014/1/1”[Date - Publication]) AND incidence[Text Word], accessed on 1 January 2014, limited to European and American countries, and excluded those limited to specific patient population or specific *Candida* species. When more than one publication was found, the publication most representative of the country/region was selected.



Original Article

Antifungal susceptibility of invasive *Candida* bloodstream isolates from the Asia-Pacific region

Thean Yen Tan^{1,*}, Li Yang Hsu², Marissa M. Alejandria³,
Romanee Chaiwarith⁴, Terrence Chinniah⁵, Methee Chayakulkeeree⁶,
Saugata Choudhury⁷, Yen Hsu Chen^{8,9,10}, Jong Hee Shin¹¹,
Pattarachai Kiratisin⁶, Myrna Mendoza¹², Kavitha Prabhu⁵,
Khuanchai Supparatpinyo⁴, Ai Ling Tan¹³, Xuan Thi Phan¹⁴,
Thi Thanh Nga Tran¹⁴, Gia Binh Nguyen¹⁵, Mai Phuong Doan¹⁵,
Van An Huynh¹⁶, Su Minh Tuyet Nguyen¹⁶, Thanh Binh Tran¹⁷
and Hung Van Pham¹⁷

Table 1. Distribution of *Candida* species from participating countries.

Organism	All		Brunei		Korea		Philippines		Singapore		Taiwan		Thailand		Vietnam	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<i>Candida albicans</i>	309	35.9	13	26.0	39	39.0	17	22.1	62	34.3	51	51.0	66	33.0	61	39.9
<i>Candida tropicalis</i>	264	30.7	14	28.0	17	17.0	26	33.8	44	24.3	29	29.0	74	37.0	60	39.2
<i>Candida parapsilosis</i>	135	15.7	18	36.0	26	26.0	24	31.2	20	11.0	11	11.0	24	12.0	12	7.8
<i>Candida glabrata</i>	116	13.6	5	10.0	9	9.0	5	6.5	48	26.5	6	6.0	31	15.5	12	7.8
<i>Candida guilliermondii</i>	7	0.8			3	3.0	1	1.3			2	2.0			1	0.7
<i>Candida pelliculosa</i>	6	0.7			3	3.0	3	3.9								
<i>Candida rugosa</i>	6	0.7													6	3.9
<i>Candida krusei</i>	6	0.7							3	1.7	1	1.0	2	1.0		
<i>Candida dubliniensis</i>	3	0.3							3	1.7						
<i>Candida spp.</i> [¶]	9	1.0			3	3	1	1.3	1	0.6			3	1.5	1	0.7
Total	861		50		100		77		181		100		200		153	

[¶]Note: *Candida fabianii* (n = 2), *Candida nivariensis* (n = 1), *Candida intermedia* (n = 1), *Candida famata* (n = 1), *Candida norvegensis* (n = 1), *Candida pseudohaemulonii* (n = 1), *Candida haemulonii* (n = 1), *Candida lusitanae* (n = 1).

- Invasive isolates of *C. albicans*, *C. parapsilosis* complex and *C. tropicalis* remain highly susceptible to fluconazole (>90% susceptible).

Candida bloodstream isolates, Asia-Pacific region

Species	Antifungal name	Brunei		Korea		Philippines		Taiwan		Thailand		Singapore		Vietnam	
		%I	%S	%I	%S	%I	%S	%I	%S	%I	%S	%I	%S	%I	%S
<i>Candida albicans</i>	Anidulafungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Caspofungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Fluconazole*	0	100	0	97.4	0	100	0	100	0	100	0	100	0	100
	Micafungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Voriconazole*	0	100	0	100	0	100	0	100	0	100	0	100	0	100
<i>Candida tropicalis</i>	Anidulafungin	0	100	0	100	0	100	0	96.6	0	100	2.3	97.7	0	100
	Caspofungin	0	100	0	100	0	100	0	100	0	100	2.3	97.7	0	100
	Fluconazole*	14.3	85.7	0	100	0	100	6.9	82.8	9.5	70.3	6.8	72.7	3.3	61.7
	Micafungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Voriconazole*	7.1	92.9	0	100	3.8	96.2	13.8	82.8	16.2	64.9	25	63.6	25	46.7
<i>Candida parapsilosis</i>	Anidulafungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Caspofungin	0	100	0	100	0	100	0	100	0	100	0	100	0	100
	Fluconazole*	11.1	83.3	3.8	96.2	4.2	87.5	9.0	91.0	0	100	0	95	0	100
	Micafungin	5.6	94.4	0	100	0	100	0	100	0	100	0	100	0	100
	Voriconazole*	0	100	0	100	4.2	95.8	0	100	0	100	0	100	0	100
<i>Candida glabrata</i>	Anidulafungin	0	100	0	100	0	100	0	100	0	96.8	0	100	0	100
	Caspofungin	0	100	22.2	77.8	0	100	0	100	3.2	93.5	8.2	89.8	0	100
	Fluconazole*	80	n/a	100	n/a	100	n/a	100	n/a	93.5	n/a	93.9	n/a	100	n/a
	Micafungin	0	100	0	100	0	100	0	100	3.2	96.8	2	98	0	100

Invasive *C. glabrata* complex isolates

- The following are increasing in prevalence:
 - Fluconazole resistance (6.8-15%)
 - Isolates with non-wild-type phenotype for itraconazole (3.9-10%) and voriconazole (5-17.8%) susceptibility
 - Echinocandin resistance
(2.1-2.2% in anidulafungin and 2.2% in micafungin)

C. tropicalis

- Nonsusceptible rate to fluconazole 5.7-11.6% : China
- Voriconazole 5.7-9.6%: China

Arctic Ocean

China

Pacific Ocean

Indian Ocean

Taiwan



2009-11 Candidemia

0.8/ 1000 hospital discharges

C. tropicalis: 29%

C. albicans: 23%

C. Parapsilosis 19.5%

Susceptibility

Voriconazole: 98%

Itraconazole: 69.5

Fluconazole: 46%

26 % Mortality; *C. trop*: Highest

Risk Factors: Abdominal/ CTVS

Elderly patients; Candidemia

C. albicans: 43%

C. trop: 25%

C. parapsilosis: 14%

C. glabrata: 11%

C. krusei: 4.8%

C. famata: 1.6%

SAME as young population

Resistance to azoles was double as compared to younger population

Higher mortality

2006-11

Invasive candidiasis

C. albican > *tropicalis* >
parapsilosis > *glabrata*

Fluconazole R

C albicans: 7%

Tropicalis: 11%

Glabrata: 15%

West China Neonatal infections

2012-15

Prevalence: 1.4%

NAC: 56.5%

Glabrata: 33%

Tropicalis: 20%

Parapsilosis: 1.4

Kefyr: 1.4%

2010-12

Invasive Candidiasis in ICUs

92%: *Candida*

6%: *Cryptococcus*

2%: Other non *candida*
yeasts

Flu R: 4% in *C. albicans*;

10%: *trop*; 14% *glabrata*; 4%
parapsilosis

Arctic Ocean

Pacific Ocean

Thailand

OnTheWorldMap.com

Indian Ocean



2006-2009

- 147 patients with clinically significant candidemia
- The four most common *Candida* species
 - *C. albicans* (39%)
 - *C. tropicalis* (28%)
 - *C. glabrata* (22%)
 - *C. parapsilosis* (6%)
- Only 47% received appropriate antifungal therapy within 72 hours.
- 28-day all-cause mortality was 59%.

- The independent risk factors associated with mortality:
 - Neutropenia from chemotherapy
 - Septic shock
 - ICU admission
 - Inappropriate antifungal therapy within 72 hours
 - Renal failure

Arctic Ocean

2012

Candidemia: 6%

NAC: 91%

***Parapsilosis*: 36.4%**

***Lusitaniae*: 30%**

***Tropicalis*: 21%**

***Glabrata*: 4%**

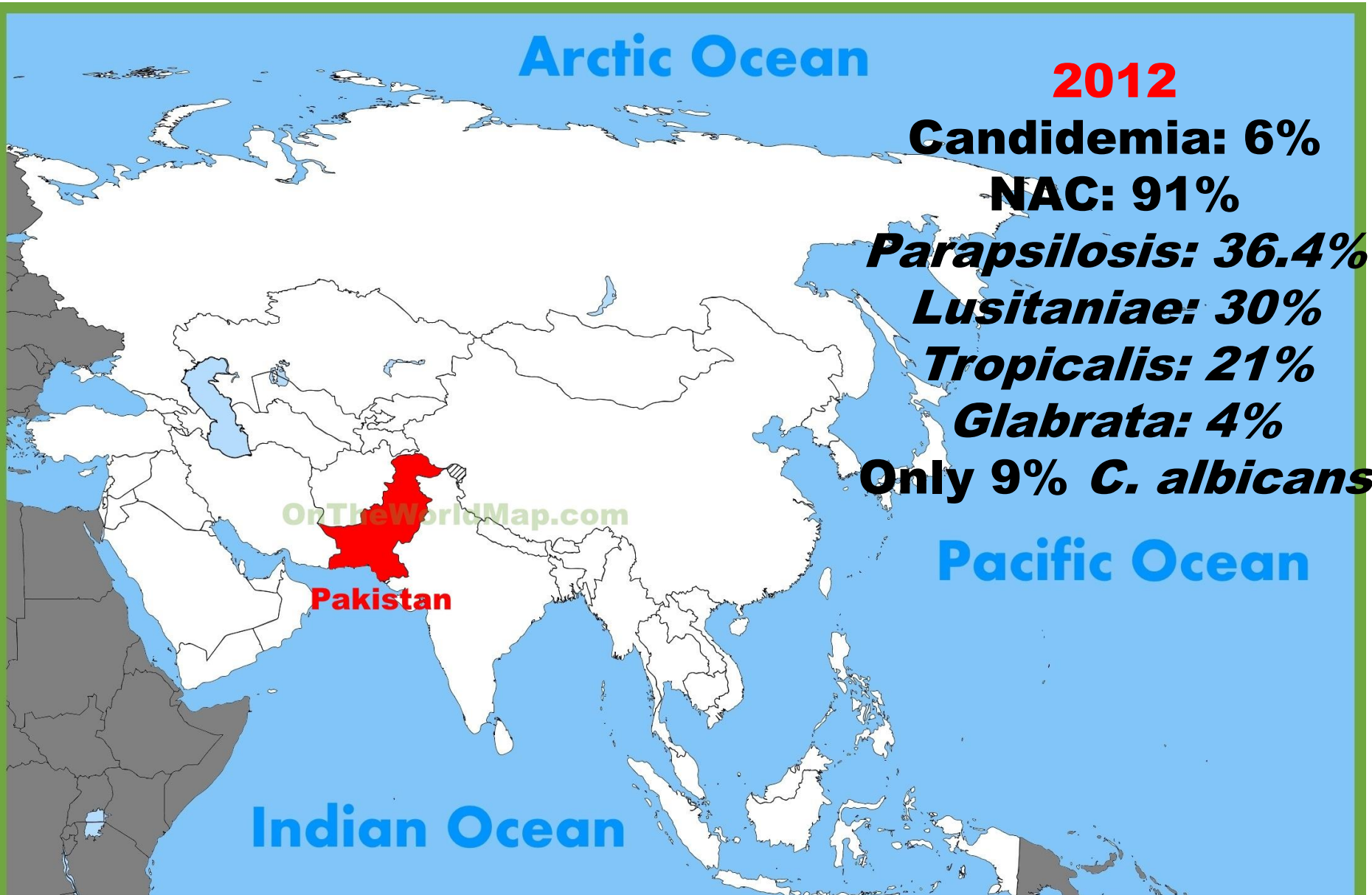
Only 9% *C. albicans*

Pacific Ocean

OnTheWorldMap.com

Pakistan

Indian Ocean



Arctic Ocean

NICU & PICU

- 15.2/ 1000 admissions
- Risk factors

CVC

Mech Ventilation

Parenteral nutrition

- *C. albicans*: 57%
- *Parapsilosis*: 24%
- *Orthopsilosis*, *glabrata*, *dublinensis*, *lusitaniae*, *kefyr*, *intermedia*:
all 11%

- NAC: almost half

- Overall mortality: 42.5%

Iran

Indian Ocean

Pacific Ocean

Arctic Ocean

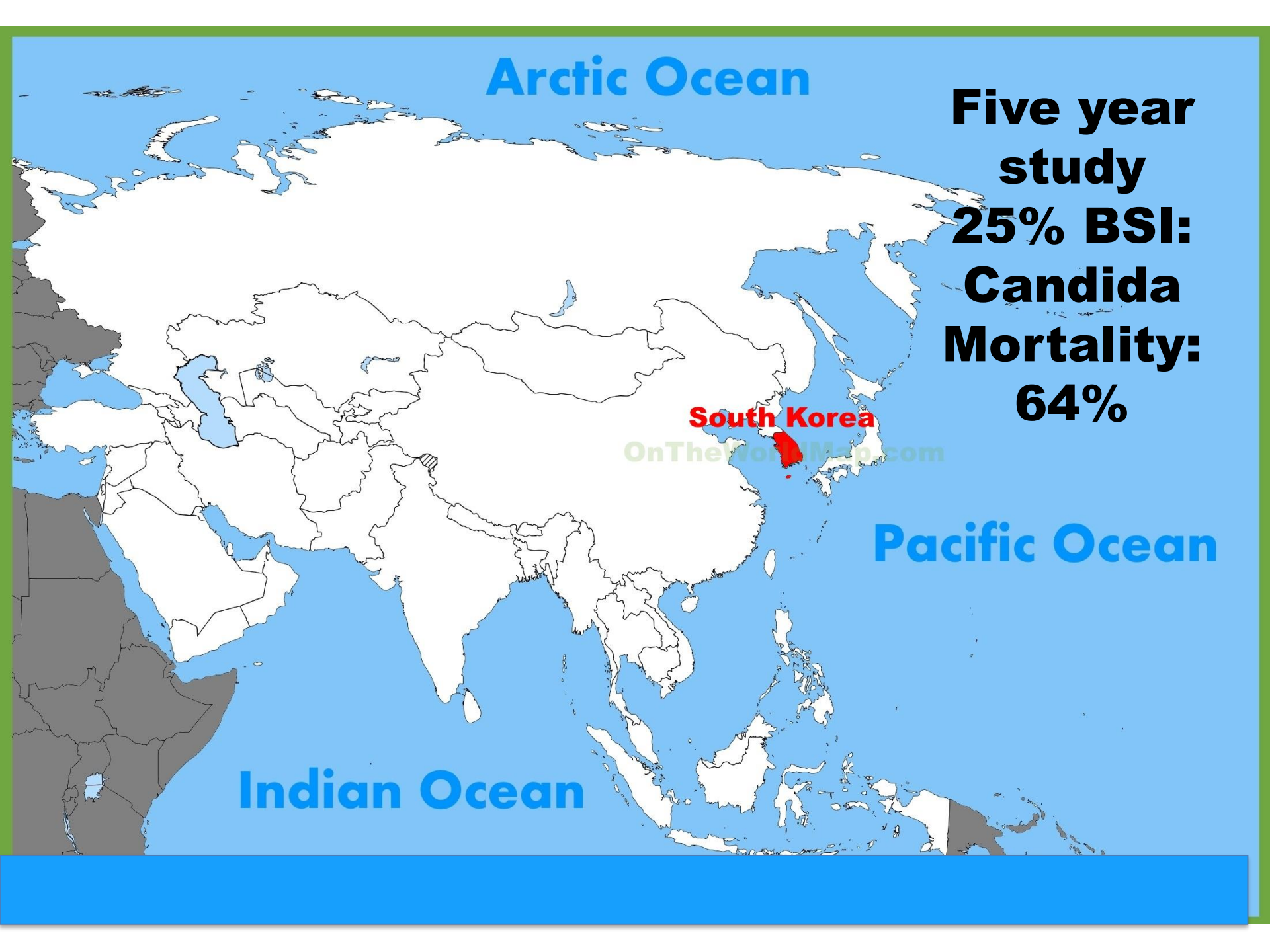
**Five year
study
25% BSI:
Candida
Mortality:
64%**

South Korea

OnTheWorldMap.com

Pacific Ocean

Indian Ocean



Arctic Ocean

Turkey

Indian Ocean

Pacific Ocean

CAUTION
Candida sp: Most common
34.7%

C. albicans: 52.4%

All *C. albicans* were
Sensitive to fluconazole

A world map with a light blue background and white landmasses. The map is centered on the Pacific Ocean. The text is overlaid on the map, with the Arctic Ocean at the top, the Pacific Ocean on the right, and the Indian Ocean at the bottom. A red dot marks Singapore in Southeast Asia.

Arctic Ocean

2012 to 2015

261 candidemia episodes.

The overall incidence was

0.14/1000

***C. glabrata* (31.4%), *C. tropicalis*
(29.9%), *C. albicans* (23.8%)**

**The incidence of *C. glabrata*
significantly increased from 2008
to 2015**

Pacific Ocean

Indian Ocean

Singapore

Fluconazole resistance was detected primarily in *C. tropicalis* (16.7%) and *C. glabrata* (7.2%).



Special Article

National Trends in the Distribution of *Candida* Species Causing Candidemia in Japan from 2003 to 2014: A Report by the Epidemiological Investigation Committee for Human Mycoses in Japan

Epidemiological Investigation Committee for Human Mycoses in Japan: Hiroshi Kakeya¹, Koichi Yamada¹, Yukihiro Kaneko², Katsunori Yanagihara³, Kazuhiro Tateda⁴, Shigefumi Maesaki⁵, Yoshio Takesue⁶, Kazunori Tomono⁷, Jun-ichi Kadota⁸, Mitsuo Kaku⁹, Yoshitsugu Miyazaki¹⁰, Katsuhiko Kamei¹¹, Kazutoshi Shibuya¹², Yoshitihō Niki¹³, Minoru Yoshida¹⁴ and Yoshihiro Sei¹⁵

Med. Mycol. J. Vol. 59 (No. 1) , 2018

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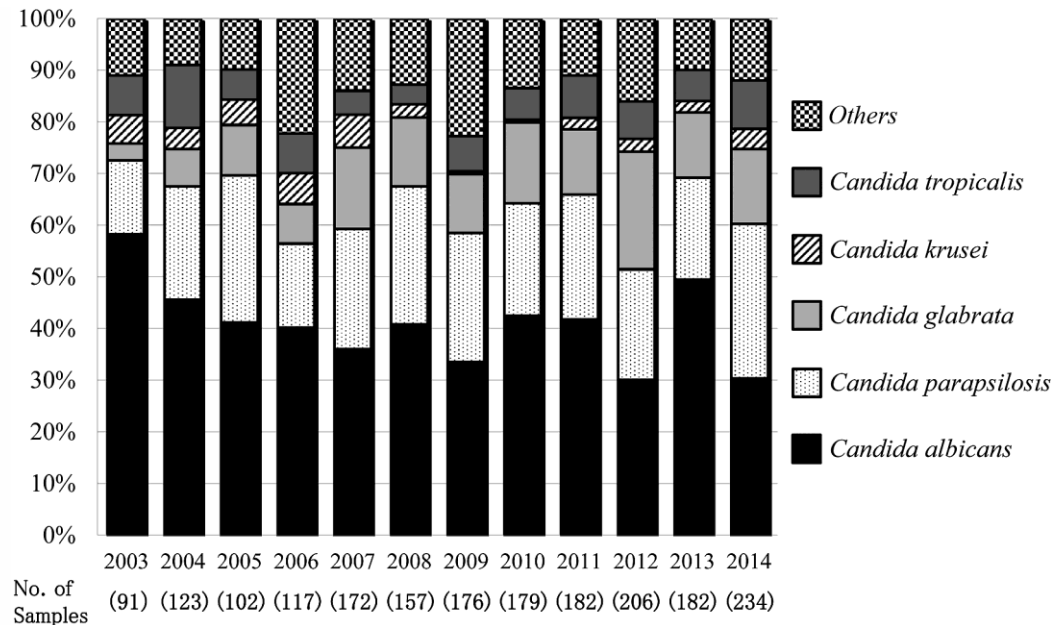


Fig. 1. *Candida* species distributions during 2003-2014.

Table 1. Major *Candida* isolates

Species	Isolates, n (%)
<i>Candida albicans</i>	758 (39.5%)
<i>Candida parapsilosis</i>	447 (23.3%)
<i>Candida glabrata</i>	254 (13.2%)
<i>Candida krusei</i>	61 (3.2%)
<i>Candida tropicalis</i>	137 (7.1%)
Others	264 (13.7%)

Arctic Ocean

Pacific Ocean

India

Indian Ocean

OnTheWorldMap.com



Incidence, characteristics and outcome of ICU-acquired candidemia in India.

Chakrabarti A¹, Sood P, Rudramurthy SM, Chen S, Kaur H, Capoor M, Chhina D, Rao R, Eshwara VK, Xess I, Kindo AJ, Umabala P, Savio J, Patel A, Ray U, Mohan S, Iyer R, Chander J, Arora A, Sardana R, Roy I, Appalaraju B, Sharma A, Shetty A, Khanna N, Marak R, Biswas S, Das S, Harish BN, Joshi S, Mendiratta D.

ICU-acquired candidemia in India



- 1,400 ICU-acquired candidemia cases
- overall incidence of 6.51 cases/1,000 ICU admission,
- 65.2 % were adults
- acquisition occurred early after admission to ICU (median 8 days), even infecting patients with lower APACHE II score at admission .

- 31 *Candida* species
- *Candida tropicalis*: 41.6 %
- Azole and multidrug resistance were seen in 11.8 and 1.9 % of isolates.
- 30-day crude and attributable mortality rates of candidemia was 44.7 and 19.6 %
- Independent predictors of mortality:
 - Admission to public sector hospital, APACHE II score at admission, underlying renal failure, central venous catheterization and steroid therapy.

ICU-acquired candidemia in India



Antifungal	AFST	All species (n = 918)	<i>C. tropicalis</i> (n = 382)
Amphotericin B	MIC ₅₀ (µg/ml)	–	0.50
	MIC ₉₀ (µg/ml)	–	1.00
	Resistant (%)	2.1 %	4 (1.0)
	MIC percentile (25–75)	–	0.25–1
Fluconazole	MIC ₅₀ (µg/ml)	–	0.50
	MIC ₉₀ (µg/ml)	–	2.00
	Resistant (%)	6.2 %	10 (2.6)
	SDD (%)	11.0 %	9 (2.4)
Itraconazole	MIC percentile (25–75)	–	0.25–1
	MIC ₅₀ (µg/ml)	–	0.06
	MIC ₉₀ (µg/ml)	–	0.12
	Resistant (%)	1.2 %	1 (0.3)
Posaconazole	SDD (%)	9.3 %	27 (7.1)
	MIC percentile (25–75)	–	0.03–0.12
	MIC ₅₀ (µg/ml)	–	0.03
	MIC ₉₀ (µg/ml)	–	0.25
Voriconazole	MIC percentile (25–75)	–	0.03–0.12
	MIC ₅₀ (µg/ml)	–	0.12
	MIC ₉₀ (µg/ml)	–	0.50
	Resistant (%)	5.6 %	31 (8.1)
Anidulafungin	SDD (%)	22.9 %	128 (33.5)
	MIC percentile (25–75)	–	0.06–0.25
	MIC ₅₀ (µg/ml)	–	0.03
	MIC ₉₀ (µg/ml)	–	0.25
Caspofungin	Resistant (%)	1.7 %	8 (2.1)
	Intermediate (%)	1.6 %	8 (2.1)
	MIC percentile (25–75)	–	0.03–0.06
	MIC ₅₀ (µg/ml)	–	0.25
Micafungin	MIC ₉₀ (µg/ml)	–	0.50
	Resistant (%)	5.6 %	16 (4.2)
	Intermediate (%)	10.1 %	50 (13.1)
	MIC percentile (25–75)	–	0.12–0.25
	MIC ₅₀ (µg/ml)	–	0.03
	MIC ₉₀ (µg/ml)	–	0.12
	Resistant (%)	1.7 %	5 (1.3)
	Intermediate (%)	2.2 %	11 (2.9)
	MIC percentile (25–75)	–	0.03

Central India
2010-2012

NAC> *C. albicans* in pediatric
and geriatric populations

Resistance

Amph B: 30%

Flu: 6%

Itra: 4.2%

Voric: 2.5%

All *C. krusei*: Resistant to
Fluconazole

Sir Gangaram Hospital, New Delhi
Out of 22,491 blood cultures, 2840 were
positive

18% positive for Candida
Drastic shift towards NAC
High R to azoles

Uttarakhand
NICU candidemia

NAC: 80%; Parapsilosis: 25%; Tropicalis: 22%; Albicans: 19.7
Glabrata: 14.3; Krusei: 10.6%

60% sensitive to fluconazole

73%: Itraconazole

96%: Amph B

NAC: (Except glabrata and krusei) were more R to azoles than
albicans

Trauma Center, AIIMS, New Delhi
2008-09

0.71 per 1000 patient days

NAC: > 80%

C. rugosa: 18.4%

6% R to Fluconazole

No resistance to Amph B, flucytosine,
voriconazole

Trauma Center, AIIMS, New Delhi
2011-2012

Candida sp: 12% of all BSI causing organisms

C. tropicalis: 55%

C. albicans: 18%

C parapsilosis: 10.5%

Rugosa, glabrata, haemulonii: 5% each

RESEARCH ARTICLE

Alarming rates of antimicrobial resistance and fungal sepsis in outborn neonates in North India

Mamta Jajoo¹, Vikas Manchanda², Suman Chaurasia³, M. Jeeva Sankar^{3*}, Hitender Gautam², Ramesh Agarwal^{3*}, Chander Prakash Yadav^{4,5}, Kailash C. Aggarwal⁶, Harish Chellani⁶, Siddharth Ramji⁷, Monorama Deb⁸, Rajni Gaind⁸, Surinder Kumar⁹, Sugandha A^{2nd short course on Public Health Informatics}⁴, Arti Kapil¹⁰, Purva Mathur¹¹, Reeta Rasaily¹², Ashok K. Deorari³, Vinod K. Paul³, Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration, New Delhi, India¹¹

- 2588 neonates enrolled
- About a quarter of infections were caused by *Candida* spp. (n = 91; 22.7%); almost three-fourths (73.7%) of these infections occurred in neonates born at or after 32 weeks' gestation and about two-thirds (62.1%) in those weighing 1500 g or more at birth.

The Unexpected and Troubling Rise of *Candida auris*

Tom Chiller, MD

DISCLOSURES | August 24, 2017

DISPATCHES

New Clonal Strain of *Candida auris*, Delhi, India

**Anuradha Chowdhary, Cheshta Sharma,
Shalini Duggal, Kshitij Agarwal,
Anupam Prakash, Pradeep Kumar Singh,
Sarika Jain, Shallu Kathuria,
Harbans S. Randhawa, Ferry Hagen,
and Jacques F. Meis**

The yeast isolates were oval without pseudohyphae and germ tube formation. They appeared pink on CHROMagar *Candida* medium (Difco, Becton Dickinson, Baltimore, MD, USA) and grew at 37°C and 42°C. VITEK2 (bioMérieux, Marcy l'Etoile, France) misidentified 10 isolates as *C. haemulonii* and 2 as *C. famata*. Similarly, API20C (bioMérieux) also misidentified them as *C. sake*. *C. auris* isolates from India assimilated *N*-acetylglucosamine (NAG) in contrast to the isolates from Japan and South Korea.

Molecular identification was done by sequencing internal transcribed spacer (ITS) and D1/D2 regions (5–7). ITS sequences (GenBank accession nos. KC692039–

[Microbiol Immunol](#). 2009 Jan;53(1):41-4. doi: 10.1111/j.1348-0421.2008.00083.x.

Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital.

[Satoh K¹](#), [Makimura K](#), [Hasumi Y](#), [Nishiyama Y](#), [Uchida K](#), [Yamaguchi H](#).

 **Author information**

Erratum in

[Corrigendum](#). [[Microbiol Immunol](#). 2018]

Abstract

A single strain of a novel ascomycetous yeast species belonging to the genus *Candida* was isolated from the external ear canal of an inpatient in a Japanese hospital. Analyses of the 26S rDNA D1/D2 domain, nuclear ribosomal DNA ITS region sequences, and chemotaxonomic studies indicated that this strain represents a new species with a close phylogenetic relationship to *Candida ruelliae* and *Candida haemulonii* in the *Metschnikowiaceae* clade. This strain grew well at 40 degrees C, but showed slow and weak growth at 42 degrees C. The taxonomic description of *Candida auris* sp. nov. is proposed (type strain JCM15448T= CBS10913T= DSM21092T).

Multidrug-resistant endemic clonal strain of *Candida auris* in India.

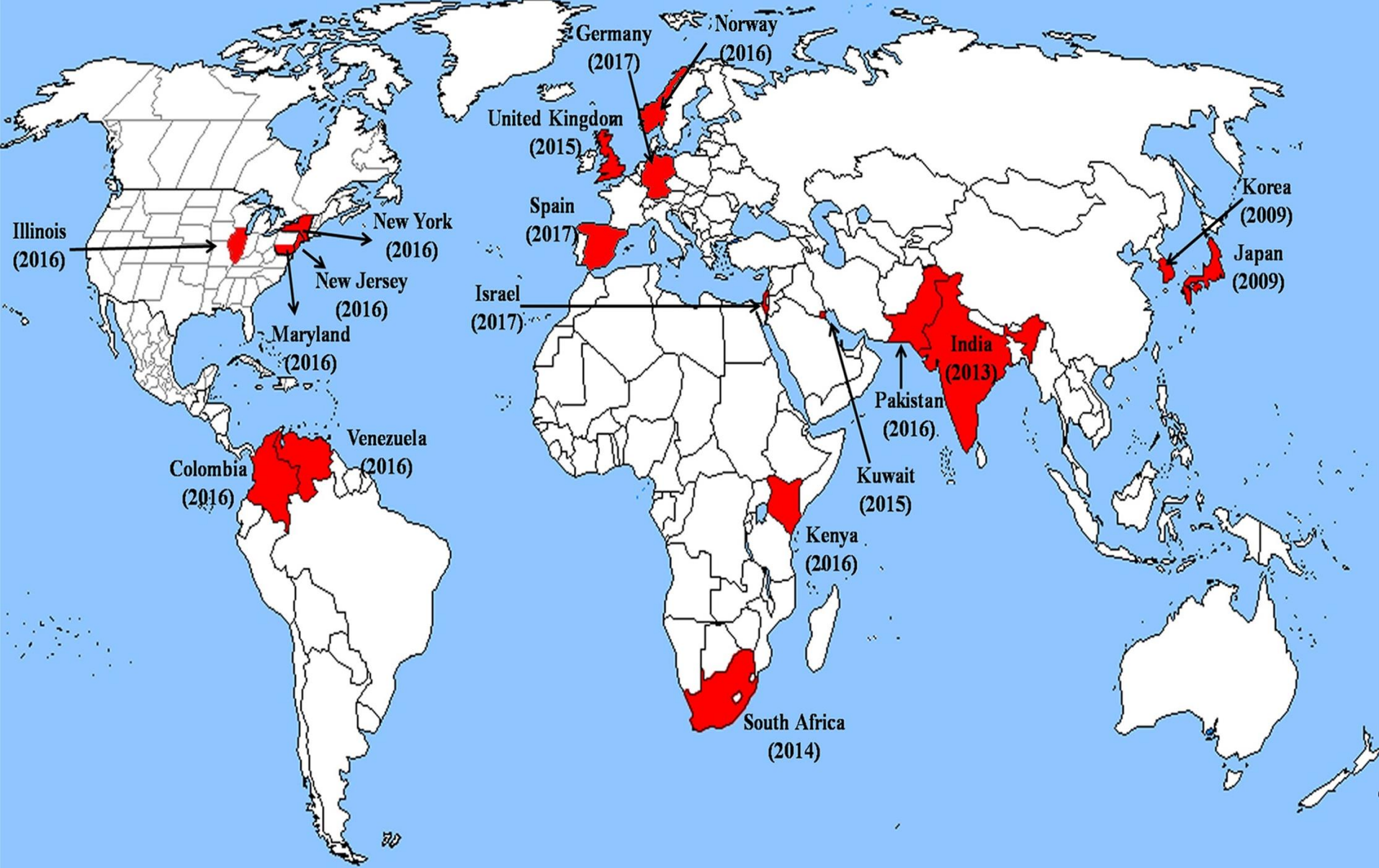
Chowdhary A¹, Anil Kumar V, Sharma C, Prakash A, Agarwal K, Babu R, Dinesh KR, Karim S, Singh SK, Hagen F, Meis JF.

 **Author information**

Abstract

Candida auris is a recently described rare agent of fungemia. It is notable for its antifungal resistance. A total of 15 *C. auris* isolates originating from seven cases of fungemia, three cases of diabetic gangrenous foot, and one case of bronchopneumonia from a tertiary care hospital in south India, were investigated. All of the 15 isolates were identified by sequencing and 14 of these along with 12 *C. auris* isolates previously reported from two hospitals in Delhi, north India, two each from Japan and Korea were genotyped by amplified fragment length polymorphism (AFLP). In vitro antifungal susceptibility testing (AFST) was done by the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method. *Candida auris* isolates were misidentified as *Candida haemulonii* by VITEK. All were resistant to fluconazole [geometric mean minimum inhibitory concentration (MIC) 64 µg/ml] and 11 isolates were resistant to voriconazole (MIC ≥1 µg/ml). Forty-seven percent of the *C. auris* isolates were resistant to flucytosine (MIC ≥64 µg/ml) and 40% had high MIC (≥1 µg/ml) of caspofungin. Breakthrough fungemia developed in 28.6% of patients and therapeutic failure occurred in 66.7% patients. Interestingly, the 26 Indian *C. auris* isolates from north and south India were clonal and phenotypically and genotypically distinct from Korean and Japanese isolates. The present study demonstrates that *C. auris* is a potential emerging pathogen that can cause a wide spectrum of human mycotic infections. The prevalence of a *C. auris* endemic clonal strain resistant to azoles and other antifungals in Indian hospitals with high rates of therapeutic failure in cases of fungemia is worrisome.

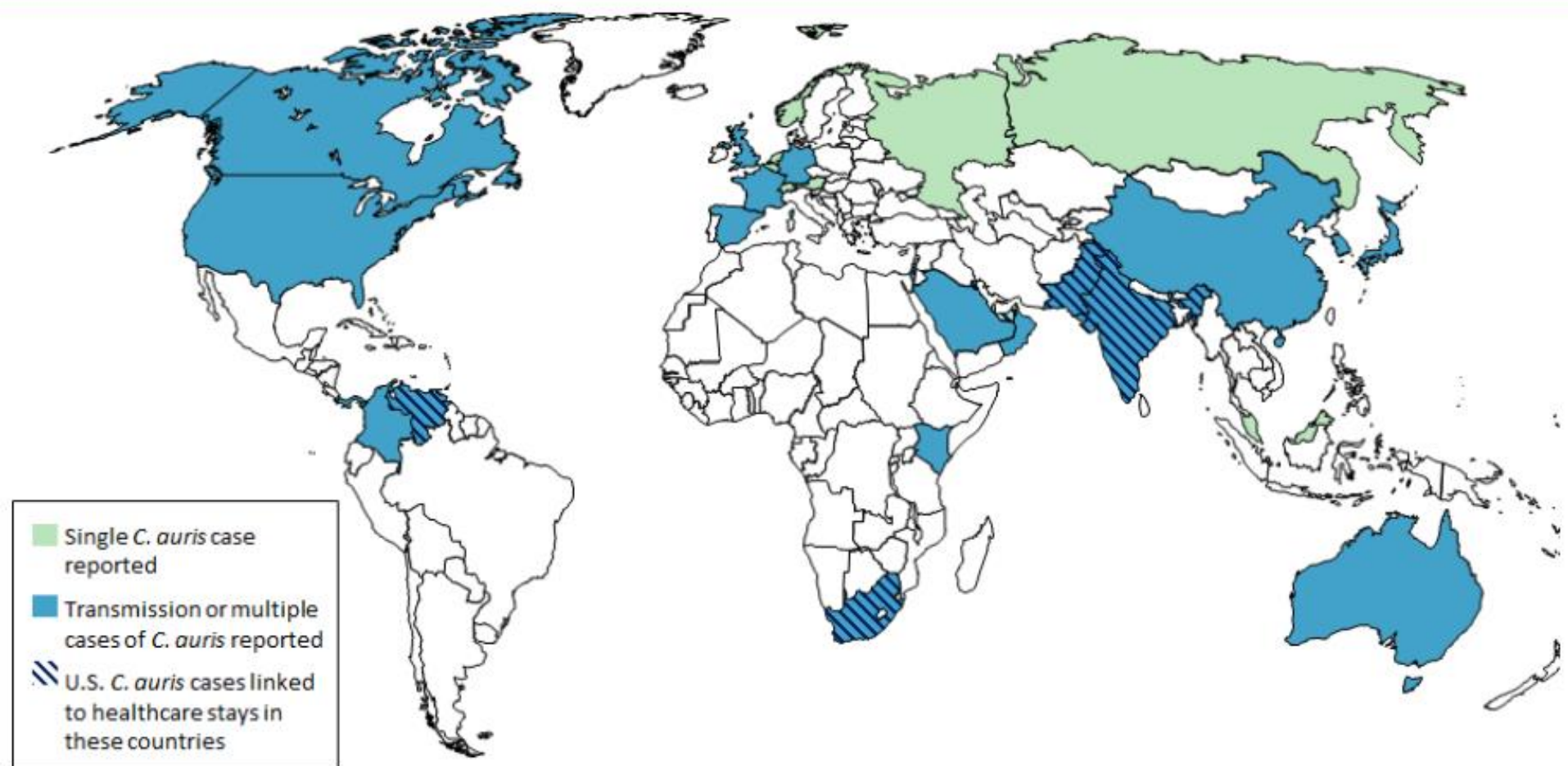
- *Candida auris* has emerged as the multi-drug resistant non-albican candida species in critically ill patients admitted ICU causing bloodstream and other infections.
- It has often been misidentified as *Candida famata*, *Candida sake*, *Rhodotorula glutinis*, or *Saccharomyces cerevisiae* and *Candida haemulonii* by automated identification systems.
- *C. auris* is notable because of its resistance to azole antifungal agents and its potential for clonal transmission.



A global map depicting rapid emergence of multidrug-resistant clinical *Candida auris* strains in 5 continents.

The value in parentheses denotes the year of report of *C. auris* from the respective country or state.

Countries from which *Candida auris* cases have been reported, as of July 31, 2018



- Single cases of *C. auris* have been reported from Austria, Belgium, Malaysia, the Netherlands, Norway, Russia, Singapore, Switzerland, and the United Arab Emirates.
- Multiple cases of *C. auris* have been reported from Australia, Canada, China, Colombia, France, Germany, India, Israel, Japan, Kenya, Kuwait, Oman, Pakistan, Panama, Saudi Arabia, South Africa, South Korea, Spain, the United Kingdom, the United States (primarily from the New York City area, New Jersey, and the Chicago area) and Venezuela; in some of these countries, extensive transmission of *C. auris* has been documented in more than one hospital.
- U.S. cases of *C. auris* have been found in patients who had recent stays in healthcare facilities in India, Kuwait, Pakistan, South Africa, the United Arab Emirates, and Venezuela, which also have documented transmission.
- Other countries not highlighted on this map may also have undetected or unreported *C. auris* cases.


A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009–17) in India: role of the *ERG11* and *FKS1* genes in azole and echinocandin resistance

Anuradha Chowdhary ✉, Anupam Prakash, Cheshta Sharma, Milena Kordalewska, Anil Kumar, Smita Sarma, Bansidhar Tarai, Ashutosh Singh, Gargi Upadhyaya, Shalini Upadhyay, ... [Show more](#)

Journal of Antimicrobial Chemotherapy, Volume 73, Issue 4, 1 April 2018, Pages 991–999 <https://doi.org/10.1093/jac/dlx490>

- 90% *C. auris* were fluconazole resistant
- 2% and 8% were resistant to echinocandins and amphotericin B, respectively.
- Overall, 25% and 13% of isolates were MDR and multi-azole resistant, respectively.

Five-year profile of candidaemia at an Indian trauma centre: High rates of *Candida auris* blood stream infections

Purva Mathur¹ | Fahmi Hasan¹ | Pradeep K. Singh² | Rajesh Malhotra^{3,4} |
Kamini Walia⁵ | Anuradha Chowdhary² 

- All patients diagnosed with candidaemia between 2012 and 2017 were studied.
- The isolates were identified using conventional methods, VITEK 2 and MALDI-TOF MS.
- The isolates not identified by MALDI-TOF were sequenced.
- Antifungal susceptibility testing was done by the CLSI broth microdilution method and VITEK 2.

- A total of 114 isolates of *Candida* species were analysed.
- *Candida tropicalis* (39.4%) > *C. auris* (17.5%) > *C. albicans* (14%) > *C. parapsilosis* (11.4%).
- *Diutina mesorugosa* isolates (n = 10) were not identified by MALDI- TOF and were confirmed by sequencing.

- *C. auris*: 55% isolates had high MICs.
- A high rate of errors in antifungal susceptibility was noted with the VITEK 2 as compared to the CLSI method.

Capacity Building and Strengthening of Hospital Infection Control to detect and prevent antimicrobial resistance in India



HEALTHCARE ASSOCIATED INFECTION SURVEILLANCE IN INDIA

The project will strengthen the national capacity for surveillance of HAIs, report the magnitude & types of AMR & HAI threats affecting India. This project will also serve the need for reliable AMR data to support successful patient care.

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ABOUT THE PROJECT

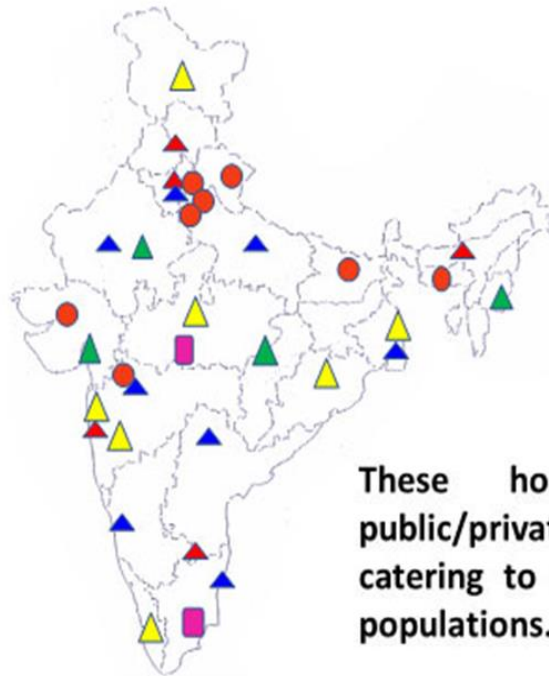
The **All India Institute of Medical Sciences (AIIMS), New Delhi** is collaborating with the **Centers for Disease Control and Prevention (CDC)** and the **Indian Council of Medical Research (ICMR)** to leverage the existing capacities for microbiology and robust academic capabilities of the ICMR-Antimicrobial resistance network to implement a step-wise, scalable process for quantifying, strengthening, and expanding the ability of the healthcare systems in India to generate, apply and report accurate data of Healthcare Associated Infections and AMR. This work, being conducted under the broader umbrella of **Global Health Security** includes more than 25 hospitals, representing almost all regions and states of India.



[LIST OF NETWORK CENTRES](#)

Participating Centers

- ICMR- AIIMS centres- 24 (23 Functional)
- NCDC centres- 4
- Centers trained under Swachhata Action Plan- 7



These hospitals are a mix of public/private/missionary/army hospitals, catering to a diverse category of patient populations.

ICUs Included

- Total ICUs included in the surveillance
93
- Number of ICUs reporting in surveillance-
86

BSI cases - ICU wise

ICU Type	BSI cases (CRFs); N (%)
Medical/Surgical ICU	433 (25)
Medical ICU	291 (16.8)
Neonatal ICU	290 (16.8)
Surgical ICU	224 (13)
Pediatric Medical ICU	149 (8.6)
Neurosurgical ICU	90 (5.2)
Trauma ICU	76 (4.4)
Gastrointestinal ICU	60 (3.4)
Cardiothoracic Surgical ICU	33 (1.9)
Respiratory ICU	25 (1.4)
Oncologic Medical ICU	19 (1)
Pediatric Medical/Surgical ICU	11 (0.6)
Burn ICU	9 (0.5)
High Dependency Unit	8 (0.4)
Oncologic Surgical ICU	5 (0.2)
Cardiac ICU	2 (0.1)
Total BSI CRFs	1,725

Blood stream Infections

Data from May, 2017 to June, 2018

BSI Rates

BSI Type	Number
CLABSI	778 (45%)
Non CLABSI	569 (33%)
Secondary BSI	378 (22%)
Total	1,725

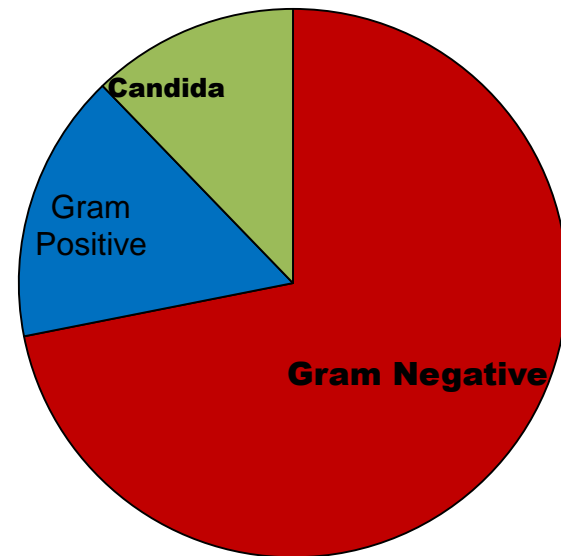
BSI Rates

Patient Days	260,033	Total BSI Rate	6.62
Central Line Days	89,301	CLABSI Rate	8.77
CLABSI	783	Sec. BSI Rate	1.42
NON- CLABSI	569	NON-CLABSI Rate	2.19
Secondary BSI	369		

Organisms causing BSIs

Organism Type	Number
Gram Negative	1,335
Gram Positive	295
Candida	227 (12%)
Total	1,857

Distribution of organisms causing BSI



BSI causing Organisms distribution

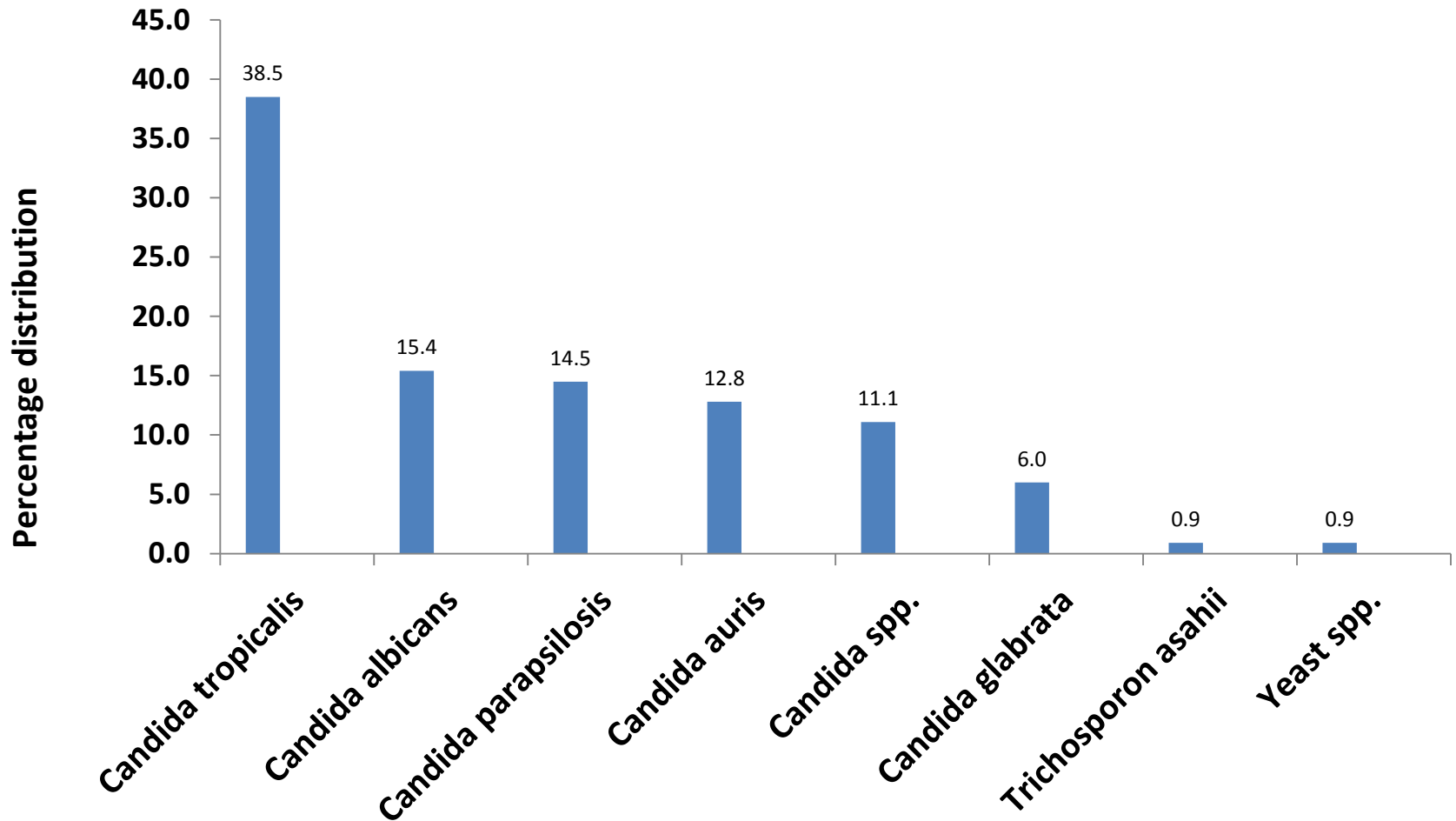
Organisms	Number
<i>Klebsiella</i> spp.	428
<i>Acinetobacter</i> spp.	387
<i>Candida</i> spp.	221
<i>Enterococcus</i> spp.	152
<i>Staphylococcus</i> spp.	141
<i>Pseudomonas</i> spp.	127
<i>Escherichia coli</i>	104
<i>Enterobacter</i> spp.	75
<i>Burkholderia</i> spp.	70
Others	42
<i>Citrobacter</i> spp.	34
<i>Stenotrophomonas</i> spp.	29
<i>Serratia</i> spp.	26
<i>Chryseobacterium</i> spp.	10
<i>Proteus</i> spp.	7
<i>Ralstonia</i> spp.	4
Total	1857

Percentage distribution of *Candida* Sp.

Organisms	Number (%)
<i>C. tropicalis</i>	68 (30)
<i>C. utilis</i>	43 (19)
<i>C. albicans</i>	27 (12)
<i>C. auris</i>	23 (10)
<i>C. parapsilosis</i>	23 (10)
<i>C. glabrata</i>	18 (8)
<i>Candida</i> spp.	7 (3)
<i>C. pelliculosa</i>	5 (2)
<i>C. haemulonii</i>	3 (1)
<i>C. lusitaniae</i>	2 (1)
<i>Non albican candida</i>	2 (1)

Organisms	Number (%)
<i>Trichosporon ashaii</i>	2 (0.9)
<i>Cryptococcus neoformans</i>	1 (0.4)
<i>Geotrichum capitatum</i>	1 (0.4)
<i>Kodamaea ohmeri</i>	1 (0.4)
<i>Yeast</i> spp.	1 (0.4)
Total	227

Percentage distribution of Fungi causing CLABSI



Antimicrobial Susceptibility Profile

Candida spp.; n= 221

Antibiotic name	Number	%R
Anidulafungin	17	5.9
Caspofungin	152	1.3
Fluconazole	184	18.5
Itraconazole	11	45.5
Voriconazole	186	3.2

UTI

UTI Rates

Patient Days	260,013
Urinary Catheter Days	162,569
CAUTI	474
NON- CAUTI	31

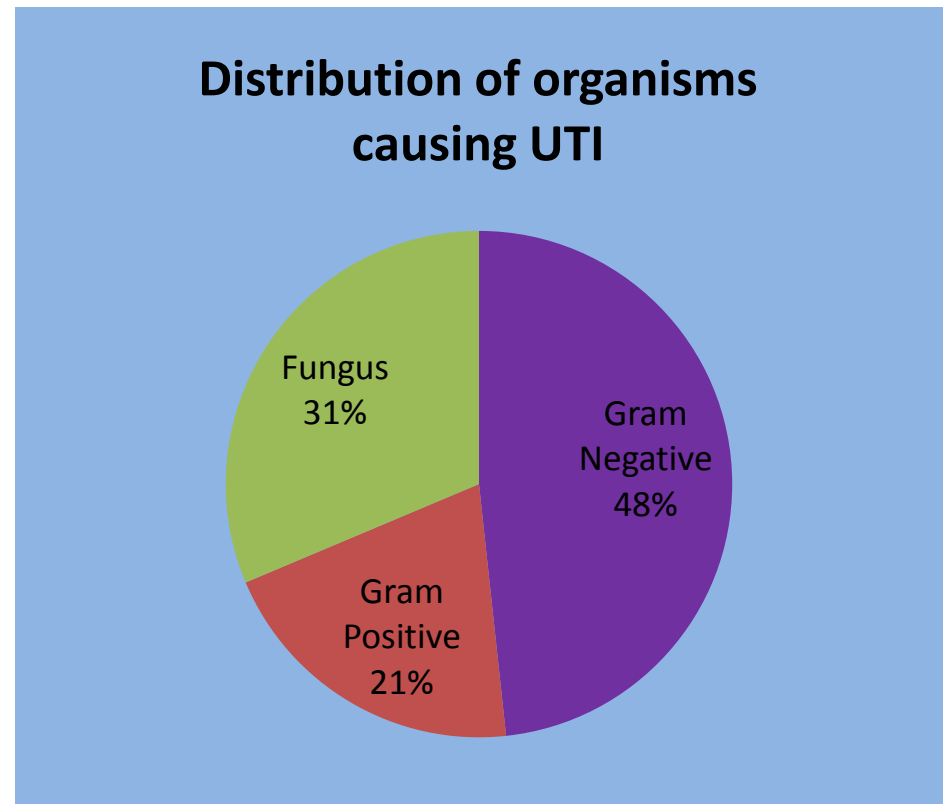
Total UTI Rate	1.94
CAUTI Rate	2.92
NON-CAUTI Rate	0.12

Data from May, 2017 to June, 2018

UTI Type	Number
CAUTI	479 (94%)
Non CAUTI	31
Total	510

Data from May, 2017 to June, 2018 (Organisms causing UTI)

Organism Type	Number
Gram Negative	268
Candida	174 (31%)
Gram Positive	113
Total	555



UTI causing Organisms

Organisms	Number
<i>Candida spp.</i>	167
<i>Enterococcus spp.</i>	111
<i>Escherichia coli</i>	90
<i>Klebsiella spp.</i>	68
<i>Pseudomonas spp.</i>	39
<i>Acinetobacter spp.</i>	23
<i>Proteus spp.</i>	11
<i>Citrobacter spp.</i>	9
<i>Providencia spp.</i>	9
<i>Enterobacter spp.</i>	7
<i>Trichosporon spp.</i>	7
<i>Myroides spp</i>	4
<i>Morganella morganii</i>	3
<i>Staphylococcus aureus</i>	2
<i>Burkholderia spp</i>	1
<i>Chryseobacterium sp</i>	1
<i>Ralstonia spp.</i>	1
<i>Serratia marcescens</i>	1
<i>S. maltophilia</i>	1
Total	555

Distribution of Candida sp causing UTI

Organism Name	Number (%)
<i>Candida spp.</i>	43 (24.7)
<i>Candida tropicalis</i>	41 (23.6)
<i>Candida albicans</i>	39 (22.4)
<i>Candida auris</i>	11 (6.3)
<i>Candida glabrata</i>	9 (5.2)
<i>Candida parapsilosis</i>	8 (4.6)
<i>Trichosporon ashaii</i>	6 (3.4)
<i>Candida utilis</i>	4 (2.3)
<i>Candida lusitaniae</i>	3 (1.7)
<i>Candida non-albicans</i>	3 (1.7)
<i>Candida cryptococcus laurentii</i>	1 (0.6)
<i>Candida famata</i>	1 (0.6)
<i>Candida kefyr</i>	1 (0.6)
<i>Candida krusei</i>	1 (0.6)
<i>Candida pelliculosa</i>	1 (0.6)
<i>Candida pseudotropicalis</i>	1 (0.6)
<i>Trichosporon spp.</i>	1 (0.6)
Total	174

Candida spp.; N= 167

Antibiotic name	Number	%R
Anidulafungin	19	26.3
Caspofungin	74	4.1
Fluconazole	117	18.8
Itraconazole	15	40
Voriconazole	109	8.3

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Thank you