İNVAZİV FUNGAL ENFEKSİYONLAR KURSU

COVID-19 ile İlişkili Kandidemiler

Dr.Nagehan Didem Sarı

10. TÜRKİYE EKMÜD BİLİMSEL KONGRESİ

EPİDEMİYOLOJİ

- ABD'de nasokomial Kan dolaşımı enfeksiyonu (KDE)4.,Kateter ilişkili KDE 3.sırada KDE %8-10
- Avrupa'da KDE 6.sırada %2-3'den sorumlu 0,2-0,38/1000 hasta başvurusu
- Ülkemizde 1-5.4/10.000 hasta günü
- Candidemi olgularının 2/3'ü YBÜ hastası
- Mortalitesi %39-63
- C.albicans %40-60 etken

10 TÜRKİYE EKMUD BİLİMSEL KONGRESİ

EPİDEMİYOLOJİ

- Duyarlı populasyon artıyor
- Yeni türler tanımlanıyor
- Proflakside flukonazol kullanımı artıyor.

- SONUÇ: non albicans türleri artıyor.

Profilakside posakonazol, itrakonazol ve flukonazol kullanımı ile

- Kolonize hasta sayıları artışı yanında

*Flukonazol kullanımı ile 2 kat *C. krusei* artışı

*Posakonazol ve itrakonazol kullanımı ile 2-4 kat *C. glabrata* artışı

**C. glabrata*'da MİK artışları

Mann PA et al. Antimicrob Agents Chemother 2009 Asano Mori Y. Int J Hematol 2010

10 TÜRKİYE EKMÜD BİLİMSEL KONGRESİ

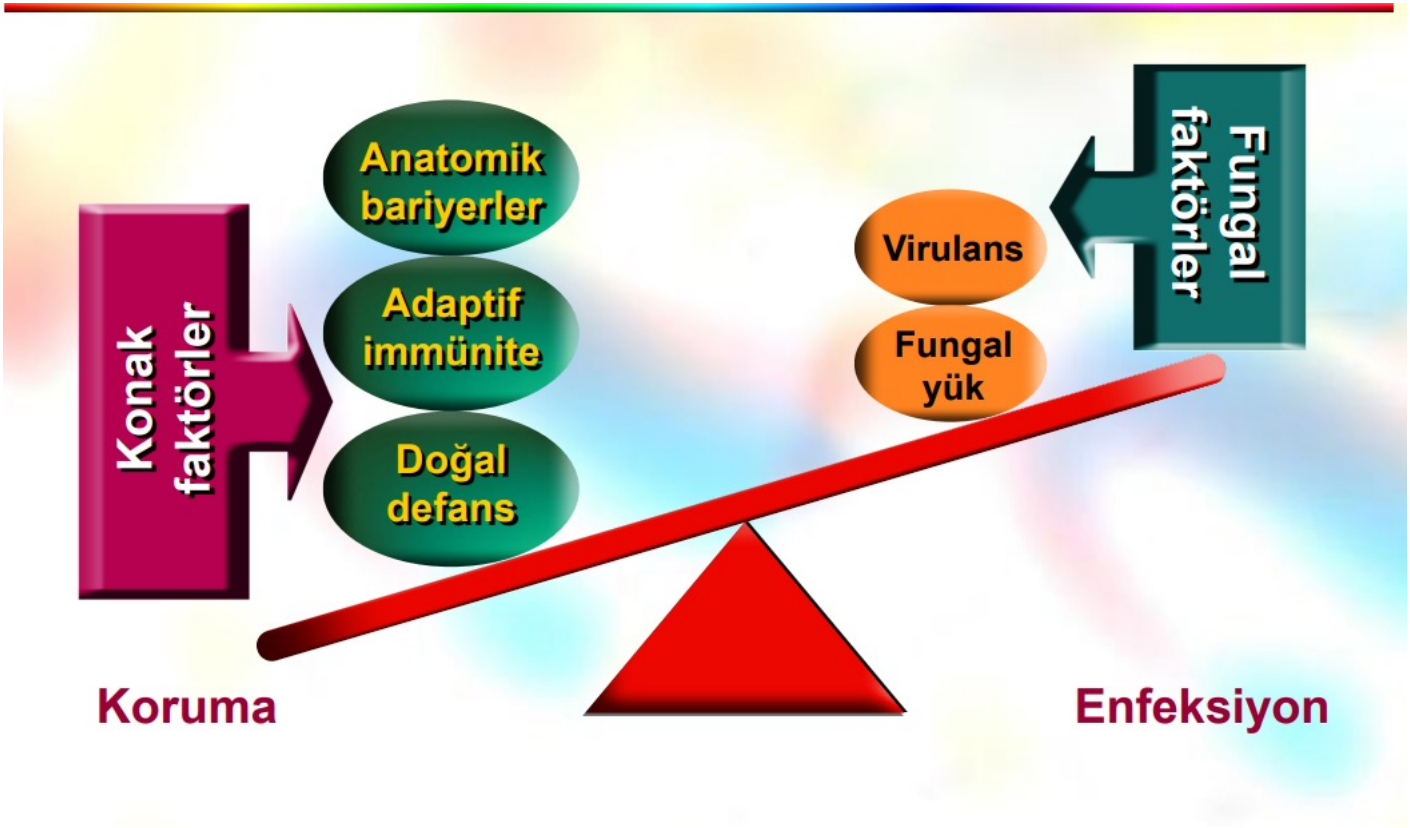
Non-albicans candidalar

- *C.parapsilosis*:YBÜ'de daha yaygın,SVK ve TPN ile ilişkili
- *C.glabrata*: yaşlı ve onkolojik tedavi görenlerde, DM hastalarda daha sık. mortalitesi YBÜ'de daha yüksek

Patogenezi

- İnvaziv fungal enfeksiyonlar immün yetmezliği ve yoğun bakımda olan hastalar için önemli bir mortalite nedenidir.
- Yaş, diyet, cinsiyet, yaşanılan bölgeye göre mikrobiyom farklılaşır.
- Virulans faktörleri ve konak direnci arasındaki dengenin bozulması enfeksiyonlara yol açar.

Patogenezi


Konak faktörler
Anatomik bariyerler
Adaptif immünite
Doğal defans
Fungal faktörler
Virulans
Fungal yük
Koruma
Enfeksiyon

KONAK DEFANS MEKANİZMALARI

DOĞAL DEFANS

- Nötrofiller
- Makrofajlar
- Dendritik hücreler
- Çözünebilir ögeler

ADAPTİF İMMÜNİTE

- T ve B lenfositler
- Aktive fagositler
- Çözünebilir ögeler

ANATOMİK BARİYERLER

- Mukozal yüzeyler
- Cilt

Konak cevapları, anatomik bölge ve fungus morfotipine göre değişir....

Fungal enfeksiyonlarda etkili olan virulans faktörler

- Yüksek sıcaklıklarda büyüme
- 37 °C ve üzeri aralıkta (38-42 °C) büyümeleri kolaydır.
- Adherens
  - Fiziksel olarak elimine edilmeye direnç
  - Kendilerinde bulunan adhezyon molekülleri yardımı ile hücrelerin yüzeylerindeki spesifik reseptörlere bağlanarak tutunur ve kolonize olabilirler, daha derinlere ulaşabilir ve vücuda yayılabilirler.

Penetrasyon ve disseminasyon faktörleri

- Enfeksiyonun ilk adımı konağa giriş
- Sonrasında lokal enfeksiyon veya hematojen yolla yayılım ile sistemik enfeksiyon
- *C. albicans* endotel hücrelerini enfekte edebilir.

Candida virülans faktörleri

- *Candida türlerinin patojenitesine; (*Konak savunmasından kaçma kabiliyeti)
  - Mukozaya yapışma, biyofilm oluşumu kapasitesi önemli bir virülans faktörüdür
  - Doku yapısını bozan hidrolitik enzimler
- Hidrolitik enzimlerin salgılanması da virulans faktörler açısından önemlidir.
  - Lokal olarak üretilen bu enzimler arasında;
    - Aspartil proteinazlar (Saps),
    - Fosfolipazlar,
    - Lipazlar,
    - Hemolizinler yer almaktadır.
- *C. albicans* diğer candida türlerinden daha fazla fosfolipaz üretmektedir.
- Candida'nın maya ve hif büyüme formları arasında geçiş yapma yeteneği de virülans ile ilgilidir.

Candida enfeksiyonuna karşı konak savunma mekanizmaları

*Sağlam mukokutanöz bariyerler

Yaralar, intravenöz kateterler, yanıklar, ülserasyonlar

*Fagositik hücreler – Granülositopeni

*Polimorfonükleer lökositler- Kronik granülomatöz hastalık

* Monositik hücreler -Miyeloperoksidaz eksikliği

*Kompleman -Hipokomplementemi

*İmmünoglobulinler -Hipogammaglobulinemi

*Hücre aracılı bağışıklık - Kronik mukokutanöz kandidiyaz, diabetes mellitus, siklosporin A, kortikosteroidler, HIV enfeksiyonu

*Mukokutanöz koruyucu bakteri florası - Geniş spektrumlu antibiyotikler

RİSK FAKTÖRLERİ

KONAĞA AİT FAKTÖRLER

- Granülositopeni
- Hematolojik maligniteler, Solid kanserler
- kemoterapi veya radyasyon ted
- kortikosteroidler
- Yanıklar, Şiddetli travma
- Uzun süreli hastanede yatış
- Son bakteriyel enfeksiyon
- GİS Cerrahisi
- Erken doğum
- hemodiyaliz
- Akut ve kronik böbrek yetmezliği

TEDAVİYE İLİŞKİN FAKTÖRLER

- Kemik iliği nakli, Solid organ nakli (karaciğer, böbrek)
- Parenteral hiperalimentasyon
- Foley kateterler
- Geniş spektrumlu antibiyotikler
- Santral kateterler
- 3 günden uzun mekanik ventilasyon

Increased prevalence of pre-existing conditions favoring IFI

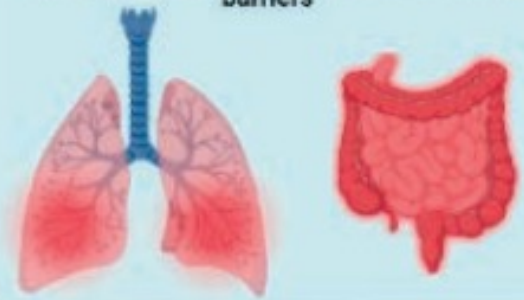
- Diabetes
- Immune-suppression
- Older age

Increased prevalence of healthcare-associated risk factors for IFI

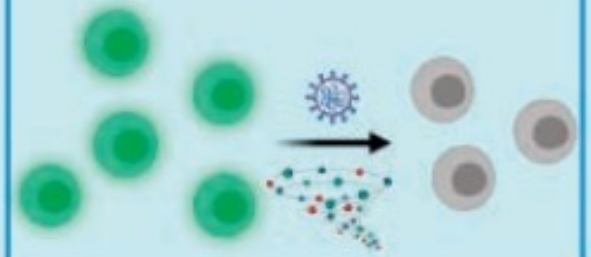
- Acute illness and ICU stay
- Indwelling medical devices
- Broad-spectrum antibiotics
- Immunomodulating therapies

SARS-CoV-2-associated pathological modifications

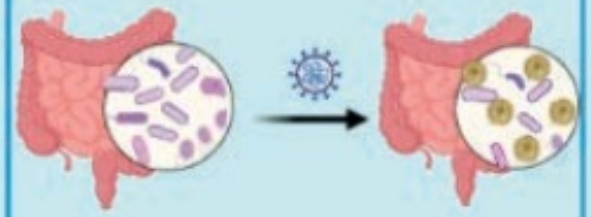
- **Infection and damage of enterocytes and pneumocytes**
- **Inflammation and dysruption of epithelial barriers**



- **Dysregulated inflammatory response**
- **Lymphopenia**
- **Functional exhaustion of immune cells**



- **Increased intestinal permeability and microbial translocation**
- **Shift of gut microbiota towards increased prevalence of fungal species**



Respiratory Medicine 188 (2021) 106619

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journal homepage: www.elsevier.com/locate/rmed

Candida spp. co-infection in COVID-19 patients with severe pneumonia: Prevalence study and associated risk factors

Gonzalo Segrelles-Calvo [a,b], Glauber R. de S Araújo [c], Estefanía Llopis-Pastor [a], Javier Carrillo [a,d], Marta Hernández-Hernández [a], Laura Rey [a], Nestor Rodríguez Melean [a], Inés Escribano [a,b], Esther Antón [a], Celia Zamarro [a], Mercedes García-Salmones [a,d], Susana Frases [c,*]

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[d] Servicio de Neumología, Hospital Universitario Infanta Elena, Madrid, Spain

1 Şubat-30 Nisan 2020

215----31 Candidemi : yaş, cinsiyet, komorbidite açısından fark yok

Candidemililerde MuLBSTA yüksek,radyolojik bulgular daha ağır,YBÜ yatış günü 21,7 (Candidemi olmayanlarda 12,1) mortalitesi %90(Candidemi olmayanlarda %40)

Journal of *Fungi*

MDPI

Communication

Is the Frequency of Candidemia Increasing in COVID-19 Patients Receiving Corticosteroids?

Cezar V. W. Riche [1,3], Renato Cassol [2] and Alessandro C. Pasqualotto [3,4,*]

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2 Hospital Nossa Senhora da Conceição, Porto Alegre 91350-200, Brazil; renato.cassol@gmail.com
3 School of Medicine, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre 90050-170, Brazil
4 Santa Casa de Misericordia de Porto Alegre, Porto Alegre 90020-090, Brazil
* Correspondence: pasqualotto@santacasa.org.br

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Brezilya'da 2 hastaneden retrospektif, aynı dönemde COVİD-19 olan ve olmayan hastalarda Candidemi insidansı karşılaştırılmış

COVİD -19 (-) lerde 1,43-1,15/1000 hasta günü

COVİD-19(+)lerde 11,83-10,23/1000 hasta günü en önemli ayrım yüksek doz steroid

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19
A Meta-analysis

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

12 ülke 26 şubat-6 temmuz 2020 prospektif
628 hasta (hidrokortizon,dexametazon,metil prednizolon) 28 gün mortalite bakılmış %2,8 azalmış

Table 1. Characteristics of Included Trials

	DEXA-COVID 19	CoDEX	RECOVERY	CAPE COVID	COVID STEROID	REMAP-CAP	Steroids-SARI[a]
ClinicalTrials.gov identifier	NCT04325061	NCT04327401	NCT04381936	NCT02517489	NCT04348305	NCT02735707	NCT04244591
Planned sample size	200	350	NA	290	1000	NA[b]	80
Eligibility criteria	• Intubation • Mechanical ventilation • Moderate to severe ARDS per Berlin criteria[9] • Confirmed COVID-19	• Intubation • Mechanical ventilation • Moderate to severe ARDS per Berlin criteria[9] • Onset of ARDS <48 h before randomization • Probable or confirmed COVID-19	Criteria[c] used for this meta-analysis: Intubation Suspected or confirmed COVID-19	• Minimal severity • Admitted to ICU or intermediate care unit • Oxygen (≥6 L/min) • Probable or confirmed COVID-19	• Oxygen (≥10 L/min) • Confirmed COVID-19	• Admitted to ICU receiving high-flow nasal oxygen with FIO_2 ≥0.4 at ≥30 L/min, noninvasive or invasive ventilatory support, or receiving vasopressors • Probable or confirmed COVID-19	• Admitted to ICU with PaO_2:FIO_2 <200 mm Hg on positive pressure ventilation (invasive or noninvasive) or high-flow nasal canulae >45 L/min • Confirmed COVID-19
Corticosteroid							
Drug name	Dexamethasone	Dexamethasone	Dexamethasone	Hydrocortisone	Hydrocortisone	Hydrocortisone	Methylprednisolone
Dosage and administration	20 mg/d intravenously × 5 d and then 10 mg/d intravenously × 5 d	20 mg/d intravenously × 5 d and then 10 mg/d intravenously × 5 d	6 mg/d orally or intravenously	Continuous intravenous infusion × 8 d or 14 d (200 mg/d × 4 d or 7 d; 100 mg/d × 2 d or 4 d; 50 mg/d × 2 d or 3 d)	200 mg/d intravenously × 7 d (continuous or bolus dosing every 6 h)	50 mg intravenously every 6 h × 7 d[d]	40 mg intravenously every 12 h × 5 d
Dose classification	High	High	Low	Low	Low	Low	High
Control intervention	Usual care	Usual care	Usual care	Placebo	Placebo	Usual care	Usual care
Primary outcome	60-d mortality	Ventilator-free days	28-d mortality	21-d treatment failure (death or persistent requirement for mechanical ventilation or high-flow oxygen therapy)	Days alive without life support at 28 d	Composite of hospital mortality and ICU organ support-free days to 21 d	Lower lung injury score at 7 d and 14 d
Mortality outcome, d	28	28	28	21	28	28	30
Serious adverse event definitions	• Secondary infections of pneumonia, sepsis, or other similar • Pulmonary embolism	• Mortality • Infections • Insulin use	• Cause-specific mortality • Ventilation • Dialysis • Cardiac arrhythmia (in a subset) • Other that were believed to be related to study treatment	• Any • Excluded some listed in protocol • Excluded expected adverse events related to the patient's disease or comorbidity	• New episodes of septic shock (Sepsis-3 criteria) • Invasive fungal infection • Clinically important gastrointestinal bleeding • Anaphylaxis	• Per ICH good clinical practice guidelines (events not already captured as a trial end point; eg, mortality) • When the event may reasonably have occurred because of study participation	• Secondary bacterial infections • Barotrauma • Severe hyperglycemia • Gastrointestinal bleeding requiring transfusion • Acquired weakness
Location	Spain	Brazil	UK	France	Denmark	Australia, Canada, European Union, New Zealand, UK, US	China

- COVID-19 tanısı alan hastaların tanı esnasında bakteriyel veya viral ko enfeksiyon nadiren görülür.

Rawson T.M., Moore L.S.P., Zhu N., Ranganathan N., Skolimowska K., Gilchrist M., et al. (2020). Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. Clinical Infectious Diseases. 71, 2459-2468.

- Ancak hastalığı şiddetinin artışıyla birlikte yatış süresinin uzaması ve YBÜ ihtiyacıyla, invasiv uygulamalarla birlikte ko enfeksiyon insidansı artmaktadır.

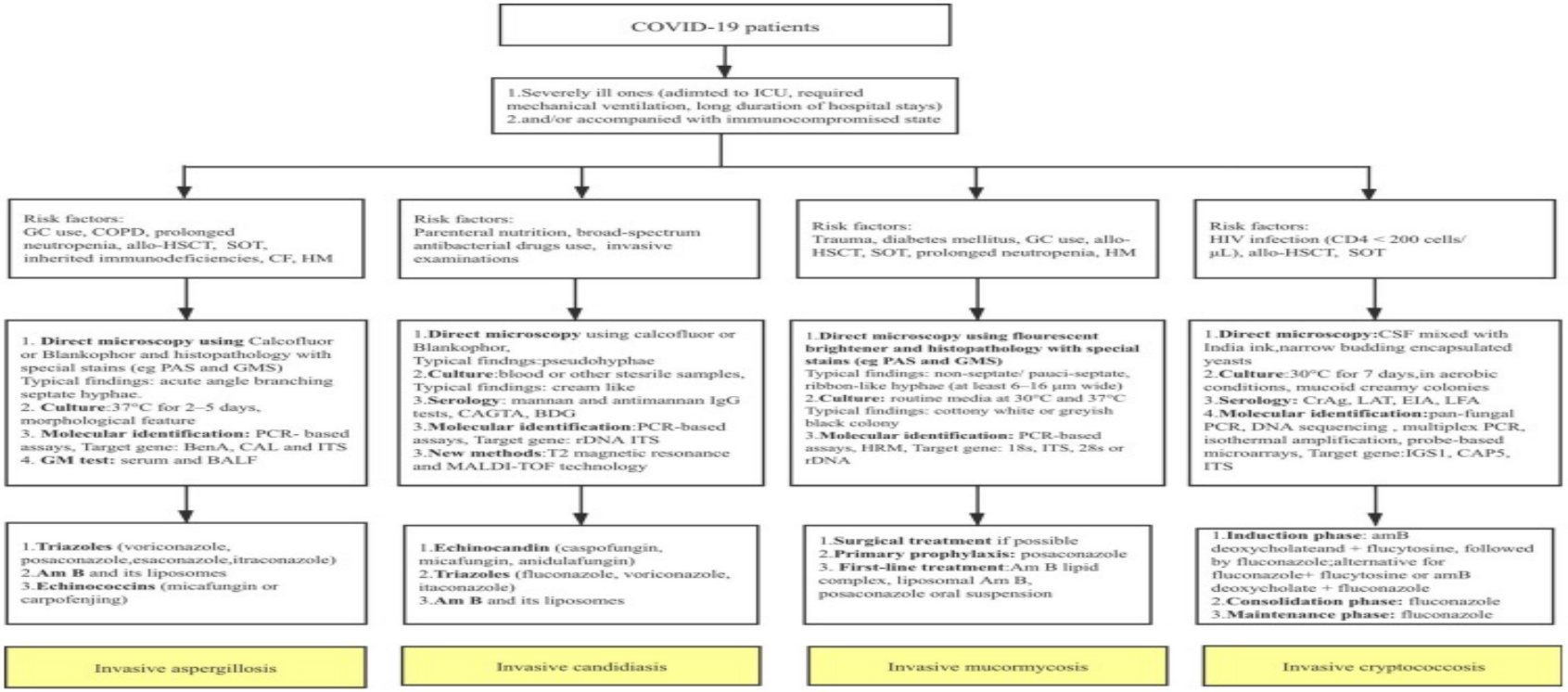
- Langford B.J., So M., Raybardhan S., Leung V., Westwood D., MacFadden D.R., et al. (2020). Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect. 26, 1622-1629

Mycopathologia
https://doi.org/10.1007/s11046-020-00462-9

EDITORIAL

Fungal Co-infections Associated with Global COVID-19 Pandemic: A Clinical and Diagnostic Perspective from China

Ge Song · Guanzhao Liang · Weida Liu



SARS-CoV

- 2003'de fungal koenfeksiyon %14,8-27
- Ağır hastalarda %21,9-%33
- Mortalite %25-73,7
- Candida koenfeksiyonu İnfluenza'da %19
  mortalite %28-51

SONUÇ: COVİD-19'da candidemi tanınamıyor

CHEST

16 hastada Candida ve aspergiloz (%2)

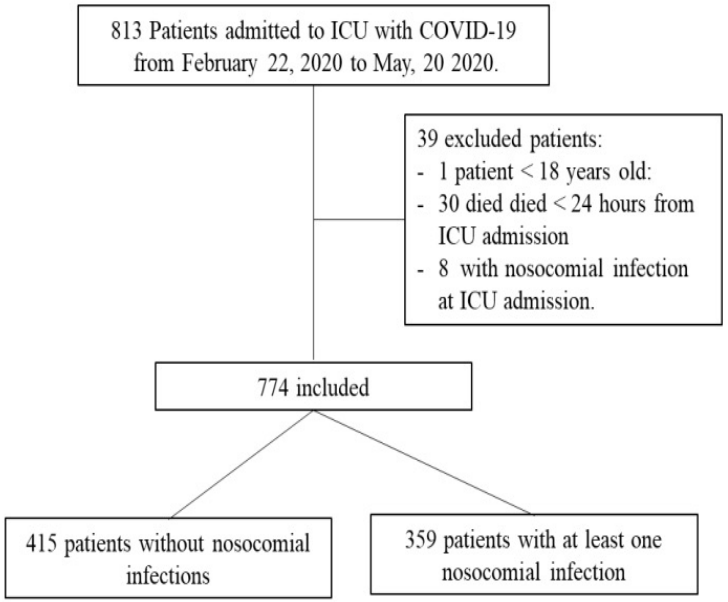
Hospital-Acquired Infections in Critically Ill Patients With COVID-19

Giacomo Grasselli, MD; Vittorio Scaravilli, MD; Davide Mangioni, MD; Luigia Scudeller, MD; Laura Alagna, MD; Michele Bartoletti, MD; Giacomo Bellani, PhD; Emanuela Biagioni, MD; Paolo Bonfanti, MD; Nicola Bottino, MD; Irene Coloretti, MD; Salvatore Lucio Cutuli, MD; Gennaro De Pascale, MD; Daniela Ferlicca, MD; Gabriele Fior, MD; Andrea Forastieri, MD; Marco Franzetti, MD; Massimiliano Grecc
Marianna Meschiari, MD; Antonio Messina, MD; Gianpaola Mon
Simone Redaelli, MD; Flavia Stefanini, MD; Tommaso Tonetti,
Giuseppe Foti, MD; Roberto Fumagalli, MD; Massimo Girardis,
Mario Raviglione, MD; Antonio Pesenti, MD; Andrea Gori, MD;

İtalya'dan 8 merkez, retrospektif,
20 mart-20 mayıs YBÜ'da takip edilen hastalar
774 hastanın 359'unda 759 HAİ tespit edilmiş. %64 Gr (-), %34 Gr(+) bakteri
Hastaların %70'inde amprik geniş spekturumlu antibiyotik
HAI :insidans 44.7/1000 hasta günü, VİP %50,BSI %34, Kateter BSI %10.

Additional Results

e-Figure 1. Patients Flowchart.



ICU, Intensive Care Unit

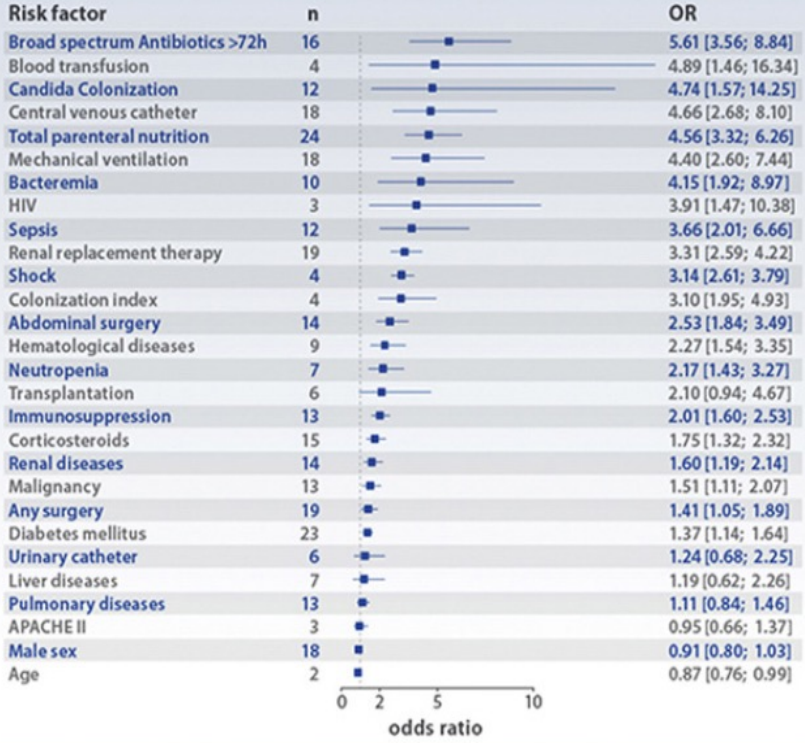
What Risk Factors for Invasive Candida Infection Can Be Identified by a Systemic Review and Meta-analysis?

STUDY DESIGN

- Systematic review and meta-analysis of **34 studies** in the assessment of **29 possible risk factors** for invasive Candida infection
- Risk factors included
  - Demographic factors
  - Comorbid conditions
  - Medical interventions

RESULTS

- **Comorbid conditions and medical interventions** while in the ICU have a significant impact
- Demographic factors **do not** play a significant role
- Dependence between various risk factors is probably high



There are multiple correlated risk factors for invasive Candida infection in the ICU. Comorbid conditions and medical interventions during ICU are associated with increased risk, but odds ratios are small.

Thomas-Rüddel D, et al. *CHEST* February 2022 | @journal_CHEST | https://doi.org/10.1016/j.chest.2021.08.081

frontiers in Medicine

BRIEF RESEARCH REPORT
published: 28 October 2020
doi: 10.3389/fmed.2020.583897

3 hastada fungal enfeksiyon

IL-6 Inhibition in Critically Ill COVID-19 Patients Is Associated With Increased Secondary Infections

Lucas M. Kimmig[1,2†], David Wu[1,2†], Matthew Gold[1], Natasha N. Pettit[1,3], David Pitrak[1,3], Jeffrey Mueller[4], Aliya N. Husain[4], Ece A. Mutlu[5] and Gökhan M. Mutlu[1,2]*

[1] Department of Medicine, University of Chicago, Chicago, IL, United States, [2] Section of Pulmonary and Critical Care Medicine, University of Chicago, Chicago, IL, United States, [3] Section of Infectious Diseases, University of Chicago, Chicago, IL, United States, [4] Department of Pathology, University of Chicago, Chicago, IL, United States, [5] Section of Gastroenterology and Hepatology, Rush University, Chicago, IL, United States

Tosilizumab kullanan ve kullanmayan hastalar sekonder enfeksiyon açısından 8 hafta takip edilmiş.

Toplam 111 hasta (54'ü tosilizumab kullanmış)

Tosilizumab kullanan hastalarda sekonder bakteriyel enfeksiyon %48, Fungal Enfeksiyon %5,6. Kullanmayan grupta sekonder enfeksiyon %28, fungal enfeksiyon yok

Received: 1 April 2021 | Revised: 28 May 2021 | Accepted: 31 May 2021

DOI: 10.1111/myc.13332

ORIGINAL ARTICLE

mycoses WILEY

Characteristics of candidemia in COVID-19 patients; increased incidence, earlier occurrence and higher mortality rates compared to non-COVID-19 patients

Bircan Kayaaslan[1] | Fatma Eser[1] | Ayşe Kaya Kalem[1] | Zeynep Bilgic[2] | Dilek Asilturk[2] | Imran Hasanoglu[1] | Muge Ayhan[2] | Yasemin Tezer Tekce[2] | Deniz Erdem[3] | Sema Turan[3] | Ipek Mumcuoglu[4] | Rahmet Guner[1]

1 mart 2019-1 mart 2020 pre pandemik dönem (non COVİD :131)

1 mart 2020-1 mart 2021 pandemik dönem (COVİD 105)

Sonuç: Candida türleri ve dirençleri arasında farklılık yok

Candidemi tespiti COVİD 13. Gün, Non COVİD'de 27. Gün(fark 14 gün)

YBÜ'de Candidemi tespit edilen COVİD'lilerde mortalite %90,

Olguların 1/3'ü tedavi alamadan kaybedilmiş.

251 hasta,
pandemik (64 %25,5) : nisan –ağustos 2019 YBÜ yatışı, MV,SVK, immunsüpresif kullanma 1,3 fazla
pre pandemik : nisan –ağustos 2020 solid organ TM,Karaciğer hastalığı,ameliyatlar 3 kat fazla

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

The Landscape of Candidemia During the Coronavirus Disease 2019 (COVID-19) Pandemic

Emma E. Seagle,[1,2] Brendan R. Jackson,[2] Shawn R. Lockhart,[2] Ourania Georgacopoulos,[2] Natalie S. Nunnally,[2] Jeremy Roland,[3] Devra M. Barter,[4] Helen L. Johnston,[4] Christopher A. Czaja,[4] Hazal Kayalioglu,[5] Paula Clogher,[5] Andrew Revis,[6,7,8] Monica M. Farley,[6,9] Lee H. Harrison,[10] Sarah Shrum Davis,[11] Erin C. Phipps,[11] Brenda L. Tesini,[12] William Schaffner,[13] Tiffanie M. Markus,[13] and Meghan M. Lyman[2]

[1]ASRT, Inc, Atlanta, Georgia, USA; [2]Mycotic Disease Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [3]California Emerging Infections Program, Oakland, California, USA; [4]Colorado Department of Public Health and Environment, Denver, Colorado, USA; [5]Connecticut Emerging Infections Program, Yale School of Public Health, New Haven, Connecticut, USA; [6]Atlanta VA Medical Center, Atlanta, Georgia, USA; [7]Foundation for Atlanta Veterans Education and Research, Atlanta, Georgia, USA; [8]Georgia Emerging Infections Program, Atlanta, Georgia, USA; [9]Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; [10]Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [11]New Mexico Emerging Infections Program, University of New Mexico, Albuquerque, New Mexico, USA; [12]University of Rochester School of Medicine, Rochester, New York, USA; and [13]Vanderbilt University School of Medicine, Nashville, Tennessee, USA

Seagle EE, Jackson BR, Lockhart SR, Georgacopoulos O, Nunnally NS, Roland J, Barter DM, Johnston HL, Czaja CA, Kayalioglu H, Clogher P, Revis A, Farley MM, Harrison LH, Davis SS, Phipps EC, Tesini BL, Schaffner W, Markus TM, Lyman MM. The Landscape of Candidemia During the Coronavirus Disease 2019 (COVID-19) Pandemic. Clin Infect Dis. 2022 Mar 9;74(5):802-811. doi: 10.1093/cid/ciab562. PMID: 34145450.

Table 1. Demographic Characteristics of Candidemia Cases by Cohort and COVID-19 Status in the 30 Days Before Candidemia

Characteristic	Pandemic Cohort Cases				Pre-Pandemic Cohort Cases	
	All, n (%) (N = 251)	With COVID-19, n (%) (n = 64)	Without COVID-19, n (%) (n = 187)	P[a]	All, n (%) (N = 472)	P[a,b]
Age at candidemia diagnosis						
<1 year old	2 (0.8)	0	2 (1.1)	.0030	5 (1.1)	.9254
1–18 years old	5 (2.0)	0	5 (2.7)		10 (2.1)	
19–44 years old	45 (17.9)	3 (4.7)	42 (22.5)		112 (23.7)	
45–64 years old	88 (35.1)	29 (45.3)	59 (31.6)		161 (34.1)	
≥65 years old	111 (44.2)	32 (50.0)	79 (42.3)		184 (39.0)	
Sex						
Female	99 (39.4)	23 (35.9)	76 (40.6)	.5063	203 (43.0)	.5793
Male	152 (60.6)	41 (64.1)	111 (59.4)		269 (57.0)	
Race						
White	120 (47.8)	18 (28.1)	102 (54.6)	.0455	265 (56.1)	.6542
Black/African-American	78 (31.1)	24 (37.5)	54 (28.9)		144 (30.5)	
Asian	11 (4.4)	3 (4.7)	8 (4.3)		12 (2.5)	
American Indian/Alaska Native	1 (0.4)	0	1 (0.5)		2 (0.4)	
Native Hawaiian/Pacific Islander	4 (1.6)	2 (3.1)	2 (1.1)		2 (0.4)	
Multiracial	2 (0.8)	0	2 (1.1)		4 (0.9)	
Unknown	35 (13.9)	17 (26.6)	18 (9.6)		43 (9.1)	
Ethnicity						
Hispanic/Latino	45 (17.9)	20 (31.3)	25 (13.4)	.0015	35 (7.4)	.0112
Not Hispanic/Latino	179 (71.3)	38 (59.4)	141 (75.4)		397 (84.1)	
Unknown	27 (10.8)	6 (9.4)	21 (11.2)		40 (8.5)	

Abbreviation: COVID-19, coronavirus disease 2019.

[a]Chi-square or Fisher's exact test; excludes unknown category for statistical comparison.

[b]Comparison between all pre-pandemic cohort cases and pandemic cohort cases without COVID-19.

Table 2. Underlying Conditions and Social History of Candidemia Cases by Cohort and COVID-19 Status in the 30 Days Before Candidemia

Characteristics	Pandemic Cohort Cases				Pre-Pandemic Cohort Cases	
	All, n (%) (N = 251)	With COVID-19, n (%) (n = 64)	Without COVID-19, n (%) (n = 187)	P[a]	All, n (%) (N = 472)	P[a,b]
Underlying health conditions						
Chronic pulmonary disease	54 (21.5)	12 (18.8)	42 (22.5)	.5330	103 (21.8)	.8586
Diabetes	104 (41.4)	34 (53.1)	70 (37.4)	.0278	187 (39.6)	.6041
Cardiovascular disease[c]	86 (34.3)	21 (32.8)	65 (34.8)	.7770	188 (39.8)	.2275
Gastrointestinal disease[d]	25 (10.0)	2 (3.1)	23 (12.3)	.0344	58 (12.3)	.9968
HIV/AIDS	3 (1.2)	0	3 (1.6)	.5726	5 (1.1)	.6940
Hematopoietic stem cell transplant	3 (1.2)	1 (1.6)	2 (1.1)	1.0000	7 (1.5)	1.0000
Solid-organ transplant	7 (2.8)	3 (4.7)	4 (2.1)	.3757	4 (0.9)	.2325
Chronic liver disease[e]	25 (10.0)	1 (1.6)	24 (12.8)	.0093	55 (11.7)	.6737
Hepatitis C	24 (9.6)	2 (3.1)	22 (11.8)	.0425	60 (12.7)	.7398
Hematologic malignancy	11 (4.4)	2 (3.1)	9 (4.8)	.7343	24 (5.1)	.8853
Solid-organ malignancy	41 (16.3)	4 (6.3)	37 (19.8)	.0115	83 (17.6)	.5092
Neurologic disease[f]	72 (28.7)	21 (32.8)	51 (27.3)	.3977	112 (23.7)	.3418
Plegias/paralysis	6 (2.4)	3 (4.7)	3 (1.6)	.1750	25 (5.3)	.0341
Chronic kidney disease	64 (25.5)	18 (28.1)	46 (24.6)	.5764	137 (29.0)	.2527
Skin condition[g]	56 (22.3)	16 (25.0)	40 (21.4)	.5494	104 (22.0)	.8570
Obesity/morbid obesity	55 (21.9)	21 (32.8)	34 (18.2)	.0146	75 (15.9)	.4753
Chronic dialysis[h]	14 (5.6)	5 (7.8)	9 (4.8)	.3620	53 (11.2)	.0127
Social history[i] (prior year[i])						
Smoking						
Yes	61 (24.3)	5 (7.8)	56 (30.0)	.0003	169 (35.8)	.1692
No	184 (73.3)	58 (90.6)	126 (67.4)		294 (62.3)	
Alcohol abuse						
Yes	23 (9.2)	1 (1.6)	22 (11.8)	.0148	55 (11.7)	.9705
No	221 (88.1)	61 (95.3)	160 (85.6)		404 (85.6)	
Injection drug use						
Yes	18 (7.2)	0	18 (9.6)	.0087	61 (12.9)	.2400
No	233 (92.8)	64 (100)	169 (90.4)		411 (87.1)	

Table 3. Medical Encounters and Receipt of Medications Among Candidemia Cases by Cohort and COVID-19 Status in the 30 Days Before Candidemia

Characteristic[a]	Pandemic Cohort Cases				Pre-Pandemic Cohort Cases	
	All, n (%) (N = 251)	With COVID-19, n (%) (n = 64)	Without COVID-19, n (%) (n = 187)	P[b]	All, n (%) (N = 472)	P[b,c]
Medical encounters						
Previous hospitalization[d] (prior 90 days[e])						
Yes	99 (39.4)	15 (23.4)	84 (44.9)	.0025	236 (50.0)	.2784
No	149 (59.4)	48 (75.0)	101 (54.0)		235 (49.8)	
Long-term care[f] (prior 90 days[e])						
Yes	48 (19.1)	15 (23.4)	33 (17.7)	.2655	102 (21.6)	.2764
No	203 (80.9)	49 (76.6)	154 (82.4)		370 (78.4)	
Surgery (prior 90 days[e])						
Yes	53 (21.1)	3 (4.7)	50 (26.7)	.0002	142 (30.1)	.3940
No	198 (78.9)	61 (95.3)	137 (73.3)		330 (69.9)	
Intensive care unit[g] (prior 14 days[e])						
Yes	135 (53.8)	52 (81.3)	83 (44.4)	<.0001	194 (41.1)	.3797
No	114 (45.4)	12 (18.8)	102 (54.6)		278 (58.9)	
Renal replacement therapy[h] (prior 30 days[e])						
Yes	38 (21.0)	24 (37.5)	14 (12.0)	<.0001	Not collected in 2019	
No	143 (79.0)	40 (62.5)	103 (88.0)			
Invasive mechanical ventilation[h] (prior 30 days[e])						
Yes	93 (51.4)	51 (81.0)	42 (35.6)	<.0001	Not collected in 2019	
No	88 (48.6)	12 (19.0)	76 (64.4)			
Central venous catheter (prior 2 days[e])						
Yes	159 (63.4)	51 (79.7)	108 (57.8)	.0017	284 (60.2)	.5691
No	92 (36.7)	13 (20.3)	79 (42.3)		188 (39.8)	
Urinary catheter (prior 2 days[e])	131 (52.2)	47 (73.4)	84 (44.9)	<.0001	174 (36.9)	.0561
Respiratory indwelling device (prior 2 days[e])	92 (36.7)	46 (71.9)	46 (24.6)	<.0001	116 (24.6)	.9951
Gastrointestinal indwelling device (prior 2 days[e])	54 (21.5)	17 (26.6)	37 (19.8)	.2548	69 (14.6)	.1036
Case classification[i]						
Community-onset	34 (13.6)	3 (4.7)	31 (16.6)	.0001	67 (14.2)	.7269
Healthcare-associated community-onset	70 (27.9)	9 (14.1)	61 (32.6)		162 (34.3)	
Healthcare-onset	147 (58.6)	52 (81.3)	95 (50.8)		243 (51.5)	
Location of specimen collection						
Inpatient, intensive care unit	121 (48.2)	50 (78.1)	71 (38.0)	<.0001	189 (40.0)	.8481
Inpatient, non–intensive care unit	72 (28.7)	7 (10.9)	65 (34.8)		154 (32.6)	
Other	58 (23.1)	7 (10.9)	51 (27.3)		128 (27.1)	
Medications						
Systemic corticosteroids (prior 30 days[e])						
Yes	79 (31.5)	34 (53.1)	45 (24.1)	<.0001	Not collected in 2019	
No	159 (63.4)	29 (45.3)	130 (69.5)			
Tocilizumab (prior 30 days[e])	13 (5.2)	12 (18.8)	1 (0.5)	<.0001	Not collected in 2019	
Systemic antibiotics (prior 14 days[e])						
Yes	207 (82.5)	57 (89.1)	150 (80.2)	.1416	357 (75.6)	.1581
No	42 (16.7)	7 (10.9)	35 (18.7)		113 (23.9)	
Total parenteral nutrition (prior 14 days[e])						
Yes	36 (14.3)	4 (6.3)	32 (17.1)	.0283	90 (19.1)	.6327
No	211 (84.1)	60 (93.8)	151 (80.8)		381 (80.7)	
Antifungals (prior 13 days[e] or culture date)						
Yes	29 (11.6)	2 (3.1)	27 (14.4)	.0133	61 (12.9)	.5612
No	219 (87.3)	62 (96.9)	157 (84.0)		410 (86.9)	
Antifungals after *Candida* culture[e]						
Yes	204 (81.3)	53 (82.8)	151 (80.8)	.8310	412 (87.3)	.0453
No	45 (17.9)	11 (17.2)	34 (18.2)		58 (12.3)	

Table 4. Microbiological Factors of Candidemia Cases by Cohort and COVID-19 Status in the 30 Days Before Candidemia

Characteristic	Pandemic Cohort Cases				Pre-Pandemic Cohort Cases	
	All, n (%) (N = 251)	With COVID-19, n (%) (n = 64)	Without COVID-19, n (%) (n = 187)	P[a]	All, n (%) (N = 472)	P[a,b]
Candida species						
Candida albicans	95 (37.9)	28 (43.8)	67 (35.8)	.6874	153 (32.4)	.3746
Candida glabrata	79 (31.5)	17 (26.6)	62 (33.2)		143 (30.3)	
Candida parapsilosis	27 (10.8)	8 (12.5)	19 (10.2)		78 (16.5)	
Candida tropicalis	14 (5.6)	4 (6.3)	10 (5.4)		38 (8.1)	
Candida dubliniensis	10 (4.0)	3 (4.7)	7 (3.7)		9 (1.9)	
Candida lusitaniae	10 (4.0)	3 (4.7)	7 (3.7)		14 (3.0)	
Candida krusei	3 (1.2)	0	3 (1.6)		8 (1.7)	
Candida guilliermondii	1 (0.4)	0	1 (0.5)		1 (0.2)	
Candida, other	5 (2.0)	0	5 (2.7)		17 (3.6)	
Candida, unknown species	2 (0.8)	1 (1.6)	1 (0.5)		0	
>1 species	5 (2.0)	0	5 (2.7)		11 (2.3)	
Other *Candida* infections[c]						
Yes	121 (48.2)	34 (53.1)	87 (46.5)	.4418	219 (46.4)	.8101
No	126 (50.2)	30 (46.9)	96 (51.3)		252 (53.4)	

Abbreviation: COVID-19, coronavirus disease 2019

Grasseli'nin çalışmasında fungal co- enfeksiyonlara spesifik olmamakla birlikte immunsüpresif KS ve diğer ajanların sekonder enfeksiyon riskinin güçlü bir şekilde ilişkilendirememiştir.

Grasselli G., Scaravilli V., Mangioni D., Scudeller L., Alagna L., Bartoletti M., et al. (2021). Hospital-acquired infections in critically-ill COVID-19 patients. Chest

Richi , Antinori ve Kimmig 'in küçük vaka serilerinde Tosiluzumab ve KS kullanılan hastalarda fungal enfeksiyon riskinin arttığını

Kimmig L.M., Wu D., Gold M., Pettit N.N., Pitrak D., Mueller J., et al. (2020). IL-6 Inhibition in Critically Ill COVID-19 Patients Is Associated With Increased Secondary Infections. Front Med (Lausanne) 7, 583897

Antinori S., Bonazzetti C., Gubertini G., Capetti A., Pagani C., Morena V., et al. (2020). Tocilizumab for cytokine storm syndrome in COVID-19 pneumonia: an increased risk for candidemia? Autoimmun Rev. 19, 102564.

Riche C.V.W., Cassol R., Pasqualotto A.C. (2020). Is the Frequency of Candidemia Increasing in COVID-19 Patients Receiving Corticosteroids? Journal of Fungi. 6, 286. https://doi.org/10.3390/ jof6040286

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DOI: 10.1111/myc.13225

ORIGINAL ARTICLE

mycoses WILEY

Increased incidence of candidemia in a tertiary care hospital with the COVID-19 pandemic

Marcio Nucci | Gloria Barreiros | Luiz Felipe Guimarães | Vitor A.S. Deriquehem | Anna Carla Castiñeiras | Simone A. Nouér

Variable	Total n = 41	COVID-19 n = 9	Non-COVID-19, period 1 n = 16	Non-COVID-19, period 2 n = 16
Candida species				
C albicans	17 (41.5)	5 (55.6)	7 (43.8)	5 (31.3)
C tropicalis	10 (24.4)	2 (22.2)	3 (18.8)	5 (31.3)
C parapsilosis	7 (17.1)	0	4 (25.0)	3 (18.8)
C glabrata	4 (9.8)	1 (11.1)	2 (12.5)	1 (6.3)
Other[a]	3	1	2	

Ocak 2019-Şubat 2020 ----1. Period--- 16 hasta---1,54/1000

Mart 2020-Eylül 2020 ----2.Period---- 25 hasta -----7,44/1000

Nucci M, Barreiros G, Guimarães LF, Deriquehem VAS, Castiñeiras AC, Nouér SA. Increased incidence of candidemia in a tertiary care hospital with the COVID-19 pandemic. Mycoses. 2021 Feb;64(2):152-156. doi: 10.1111/myc.13225. Epub 2020 Dec 10. PMID: 33275821; PMCID: PMC7753494.

Candida auris

- YBÜ'de yüksek mortalite ile seyreden, 44 ülkede salgın yaptığı bildirilmiş.
- Multidrug rezistan, hasta ortamında cansız yüzeylerde uzun süre yaşabilir.Sağlık çalışanları aracılığıyla salgın yapabilir.
- Diabetes mellitus, böbrek hastalığı, akciğer hastalığı, travma, kulak hastalığı, Hipertansiyon gibi altta yatan hastalığı olanlar,
- Uzun süreli yoğun bakım ünitesinde kalış, santral venöz katerter gibi mekanik ventilasyon ve önceki antibiyotik kullanımı, iyatrojenik risk faktörleri COVID-19 pandemisinden önce C. auris enfeksiyonları ile önemli ölçüde ilişkiliydi.
- Aynı risk faktörleri ağır COVİD -19 içinde geçerli.

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DOI: 10.1111/myc.13258

ORIGINAL ARTICLE

mycoses WILEY

Epidemiology and Mycology of Candidaemia in non-oncological medical intensive care unit patients in a tertiary center in the United States: Overall analysis and comparison between non-COVID-19 and COVID-19 cases

Precious Macauley | Oleg Epelbaum

Candida Species	Non-COVID	COVID	Total
C. albicans	11	4	15
C. glabrata	12	2	14
C. parapsilosis	7	3	10
C. tropicalis	5	2	7
C. dubliniensis	3	1	4
C. krusei	1	0	1
Other non-C.albicans	0	1	1
	39[a]	13[b]	52

Non-COVİD (n:38) %1.1-insidans 11/1000 başvuru

Mayıs 2014-Ekim 2020

COVİD (n: 12) %5.1 - insidans 51/1000 başvuru

SONUÇ: COVİD SOFA skoru düşük,Uzun yatış ve CVP kateteri,mortalitesi aynı, kortikositreod belirgin risk

- Altta yatan hastalık ve sırasındaki invaziv tıbbi prosedürler COVID-19 hastalarında hastanede kalış, onları C. auris enfeksiyonlarına/ kolonizasyonuna karşı oldukça duyarlı hale getirir. Farklı ülkelerde COVID 19 pandemisi sırasında C. auris enfeksiyonlarının patlak verdiği rapor edilmiştir.
- Birden fazla çalışmaya göre, *C. auris* prevalansı kandidemi hastaları içinde (COVID-19 olmayan vakalar) %5-30 arasında değişmektedir.
- Ayrıca güney Afrika , Hindistan ve Avrupa ve ABD'de kolonize bir çok vaka bildirilmiştir.

Open Forum Infectious Diseases
MAJOR ARTICLE

HİNDİSTAN

A High Frequency of *Candida auris* Blood Stream Infections in Coronavirus Disease 2019 Patients Admitted to Intensive Care Units, Northwestern India: A Case Control Study

Ekadashi Rajni,[1] Ashutosh Singh,[2] Bansidhar Tarai,[3] Kusum Jain,[2,4] Ravi Shankar,[5] Kalpana Pawar,[2] Vedprakash Mamoria,[1] and Anuradha Chowdhary[2]

[1]Department of Microbiology, Mahatma Gandhi University of Medical Science & Technology, Jaipur, Rajasthan, India, [2]Medical Mycology Unit, Department of Microbiology, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India, [3]Department of Microbiology, Max Hospital, New Delhi, India, [4]Department of Zoology, Ramjas College, University of Delhi, Delhi, India, [5]Department of Biostatistics, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India

Toplam 33 hastada kandidemi gelişti ve ortalama YBÜ'de kalış süresi 24 gün, genel insidans ,%1.4,15/1000 hasta günü. COVID-19 olmayan hastalara kıyasla COVID-19'da kandidemi insidansında 2 kat artış gözlendi. Çok değişkenli regresyon analizi, tocilizumab kullanımını, yoğun bakımda kalış süresi (24'e 14 gün) ve yüksek ferritin düzeyi kandidemi gelişimi için bağımsız risk faktörü. Candida auris baskın türdü (%42), ardından Candida tropikalis geldi.

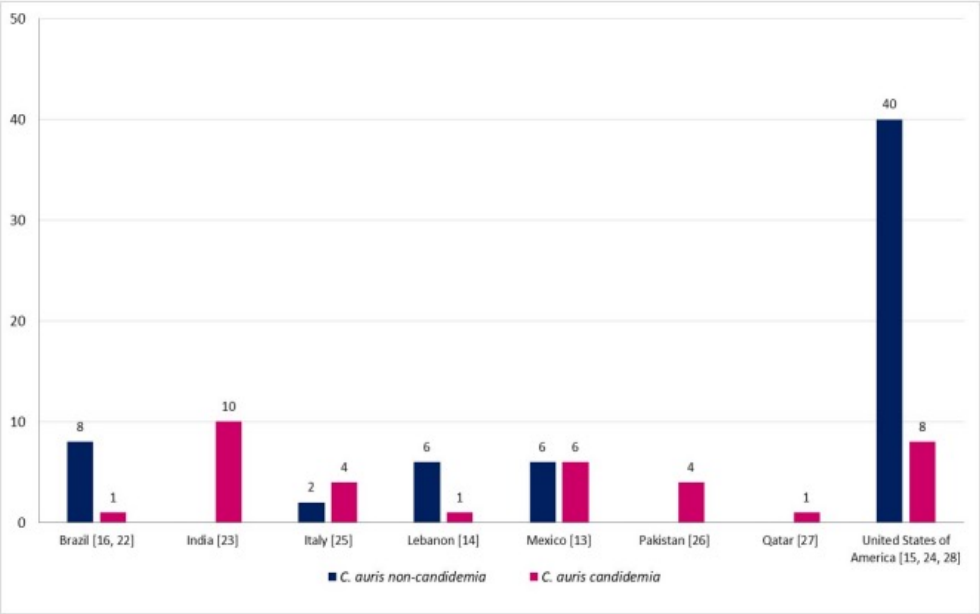
SONUÇ:dirençli suşların hastane kaynaklı bulaşmasına ilişkin endişeleri artırmaktadır

Review > Mycoses. 2022 Apr 20. doi: 10.1111/myc.13447. Online ahead of print.

Prevalence, Risk Factors, Treatment and Outcome of multidrug resistance Candida auris Infections in Coronavirus Disease (COVID-19) Patients: A Systematic Review

Kalaiselvi Vinayagamoorthy [1], Kalyana Chakravarthy Pentapati [2], Hariprasath Prakash [3]

Affiliations + expand



Preferred Reporting Items for Systematic reviews and Meta-Analyses(PRISMA) 2020

C. auris candidemia (CAC): n=35, 56.5% :22.8 GÜN

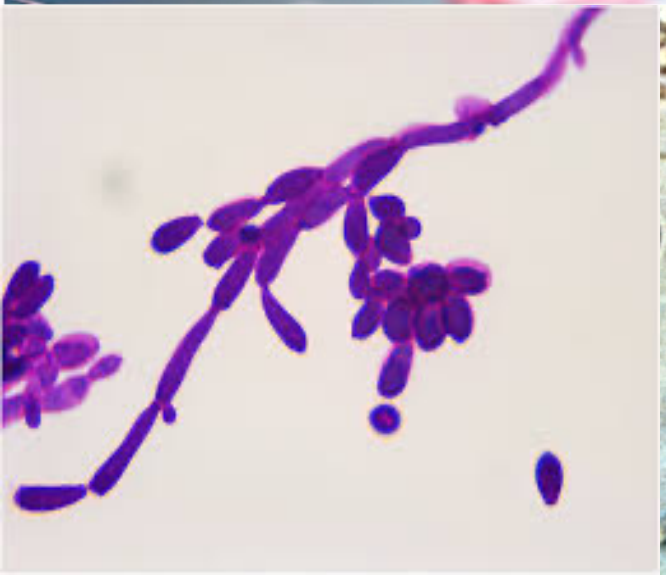
C. auris non-candidemia/ colonised (CANC): (n=27, 43.5%) 27.7 GÜN,

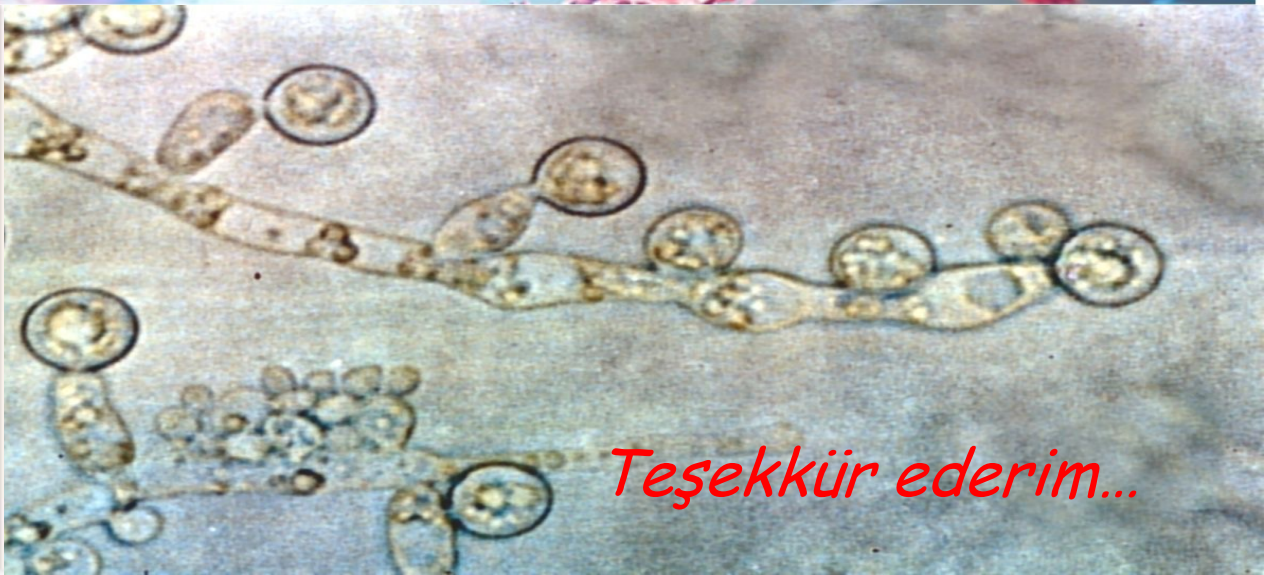
Komorbiditeler ve YBÜ endikasyonları, iatrojenik girişimler arasında fark yok.

10. TÜRKİYE EKMÜD BİLİMSEL KONGRESİ

AKLIMIZDA KALACAKLAR

- YBÜ yatışı gerektiren ağır COVİD-19 hastalarıyla Candidemi ihtimali taşıyan hastalar aynı risk faktörlerine sahip
- Yerel epidemiyoloji ampirik tedavi seçiminde önemli
- Geçikmiş tanı ve tedavi mortalitede belirgin rol oynuyor.





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