MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

How do I interpret … *Candida* in the urine?

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ASIA FUNGAL WORKING GROUP
an ISHAM working group

How Do I interpret Candida in Urine

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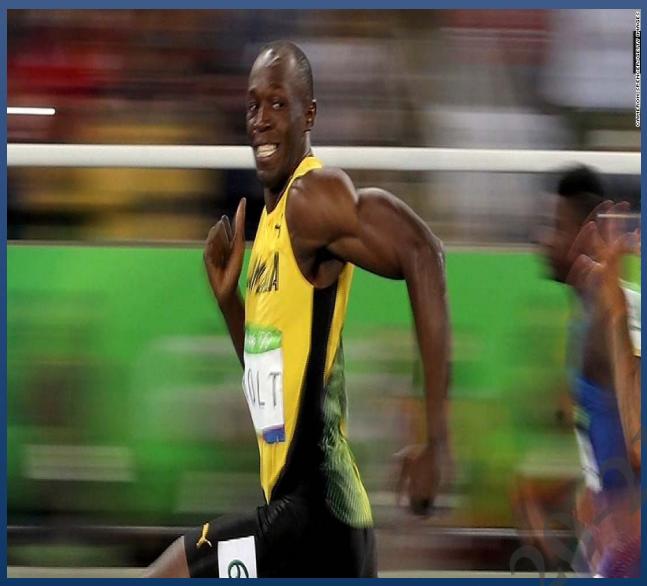


The significance of candiduria in :

1. Patient without urinary catheter
2. Patient with indwelling catheter
3. Critically ill patient

Candida in urine

Repeat a second clean-catch urine culture : MSU or Catheterization

Second urine culture : same candida spp : **Colonization vs Infection**

Symptomatic candiduria : Infection

Diagnostic dilemma in critically ill patients / paraplegic patients

Second culture is sterile : **Contamination**

Rule out Candida prostatitis/ epididymo-orchitis

Colonisation vs Infection

Bacterial UTI
Symptoms
Pyuria
Urine culture ≥ 10^5CFU/mL

In the absence of urinary catheter

- With pyuria , but need to rule out concurrent bacteriuria
- 25% of patients with candiduria also has bacteriuria

Kauffman et al, CID 2000

- Quantitative Urinary Culture (CFU/ml) : controversial
- It was thought Urine colony counts > 10^4 suggestive of infection, however biopsy- proven renal candidiasis occurred when Urinary colony 10^3 CFU/ml

Bukhary et al, Saudi J Kidney Dis Transpl 2008

Candida may multiply in urinary samples

Colonisation vs Infection

Indwelling catheter

Pyuria : not helpful

- Presence of WBC in urine due to inflammation
- Pyuria is strongly associated with Gram negative CAUTI (P=0.03) ; but not the case when pathogens are Coagulase negative staphy or enterococci (P=0.25), or Yeasts (P=0.15)

Tambyah et al, Arch Intern Med 2000

Colony counts is not useful :

as few as 10^4 CFU/mL may mean infection, > 10^5 CFU/mL may mean only colonization

Candida in urine ; with indwelling catheter

- Risk to develop candiduria was increased by 12-fold after urinary catheterization .
- Candida colonization will ensue if urinary drainage device is left in situ for long enough .
- The mean interval between ICU admission and candiduria has been reported to be 17.2 ± 1.1 days and 11.1 ±6 days (studies from Europe and India) .
- Evidence shows that the discontinuation of catheter use alone results in eradication of candiduria in almost 35-40% of asymptomatic patients.
- After a new catheter was inserted, untreated candiduria resolved in 20% of patients

Alfouzan et al, Journal de Mycologie Médicale 2017
Bougnoux et al, Intensive Care Med 2008
Jain et al, Indian J Pathol Microbiol 2011

In Summary

- absence of pyuria and low colony counts in urine tend to rule out *Candida* infection, but the reverse is not true

No urinary catheter	With urinary catheter
Symptoms + Pyuria + 2 x urinary culture (TRO contamination) grew the same Candida spp , in the absence of Bacteriuria	Fever , when no other source is found Persistent candiduria despite removal of or replacing of urinary catheter

- Any febrile patients for whom therapy for candiduria is considered , should investigate for the anatomic source of candiduria.
- The presence of granular casts containing *Candida* hyphal elements urine indicate infection to renal parenchyma

Does urinary colonization with candida predict invasive Candidiasis

- The occurrence of concomitant candidemia is low and only seen in 1—10 % of candiduric patients, with ICU patients , especially immunocompromised running the highest risk
- Candiduria generally does not predispose to the development of fungemia, but when it does occur, it usually is due to the presence of an upper-urinary-tract obstruction
- Renal candidiasis usually develops as a result of hematogenous dissemination of a fungal infection

Alfouzan et al, Journal de Mycologie Médicale 2017
Drogari-Apiranthitou et al, Mycopathologia 2017
Okulicz et al, Mycoses 2008
Dyess et al, Arch Surg 1985
Ang BS et al, CID 1993

EMPIRICAL MICAFUNGIN TREATMENT AND SURVIVAL WITHOUT INVASIVE FUNGAL INFECTION IN ADULTS WITH ICU-ACQUIRED SEPSIS, *CANDIDA* COLONIZATION, AND MULTIPLE ORGAN FAILURE **THE EMPIRICUS RANDOMIZED CLINICAL TRIAL**

Timsit et al, JAMA 2016

- Day-28 IFI–free survival in patients with a high SOFA score (>8) was not significantly different when compared between the micafungin (68%) vs placebo groups (60.2%) (HR 1.69 [95%CI 0.96-

Is candida colonization a useful tool to predict Invasive candidiasis ?

High Candida Index is only predictive of IC When combined with other risk factors

Candida colonisation

- Colonization usually precedes candidemia
- Candidemia is uncommon in those not colonised
- Candida colonization develops in up to 80% of critically ill patients with prolonged ICU stay .
- Invasive candidiasis only documented in 1-10% of those colonised
- Colonisation alone does not predict Invasive candidiasis

Eggimenn et al, J Hosp Infect 2015
Lumberg et al, 2001

In summary

- Isolated urinary candida colonization does not predict invasive candidiasis
- May be significant in critically patients with unexplained fever , Colonization ≥ 2 body sites , with multiple risk factors of IC

Empirical antifungal therapy should be considered in critically ill patients with:

no other known cause of fever, in the presence of risk factors for invasive candidiasis : recurrent gastrointestinal perforation or anastomotic leakage + Candida colonization (> 1 site)

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

IDSA

Candiduria in hematologic malignancy patients without a urinary catheter: nothing more than a frailty marker?

Georgiadouet al, Mycoses 2013

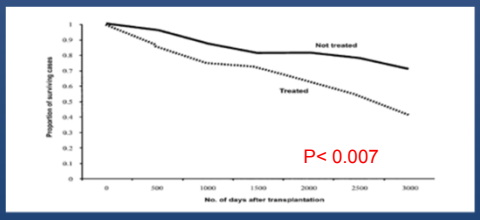
- Retrospective study , 24 patients (2001-2011)
- 54% with Acute leukemia ,62% of these cases were not in remission.
- 25% were neutropenic
- 38 % with fever , only 8% of them had urinary tract infection symptoms.
- 88 % received antifungals
- Only 1 patient (4%) had *C. glabrata* candidemia (25 days after *C. glabrata* funguria diagnosis , on caspofungin and voriconazole)
- 4 died despite treatment (1 case autopsy done , no evidence of IC)
- Isolated candiduria in patients with hematologic malignancies is not a strong predictor of subsequent invasive candidiasis.

Predictors and Outcomes of Candiduria in Renal Transplant Recipients

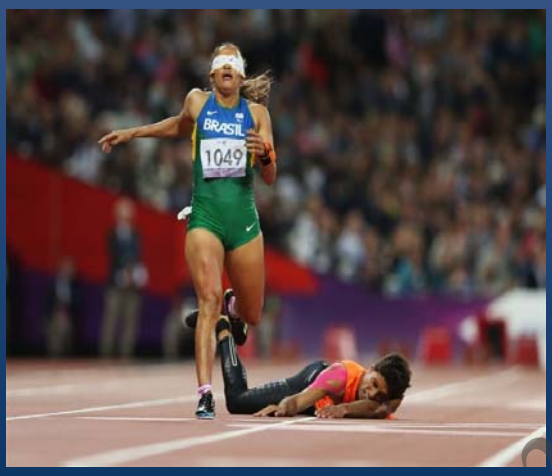
N. Safdar,[1] W. R. Slattery,[1] V. Knasinski,[1] R. E. Gangnon,[2] Zhanhai Li,[2] J. D. Pirsch,[3] and D. Andes[1,4]

CID 2005

- Case group (CANDIURIA) N=142
- Fever 25 % , Urinary symptoms < 20%
- 54 % asymptomatic candiduria
- 97 were and 95 were not treated.



- 16 cases (17%) died in the group that did not receive treatment, and 32 (33%) died in the group that received treatment.
- Treatment of asymptomatic candiduria in renal transplant recipients does not appear to result in improved outcome.



THANK YOU
FOR
YOUR ATTENTION