Role of Procalcitonin in Antimicrobial Stewardship

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CDC prioritized bacteria in our set up:

Urgent Threats

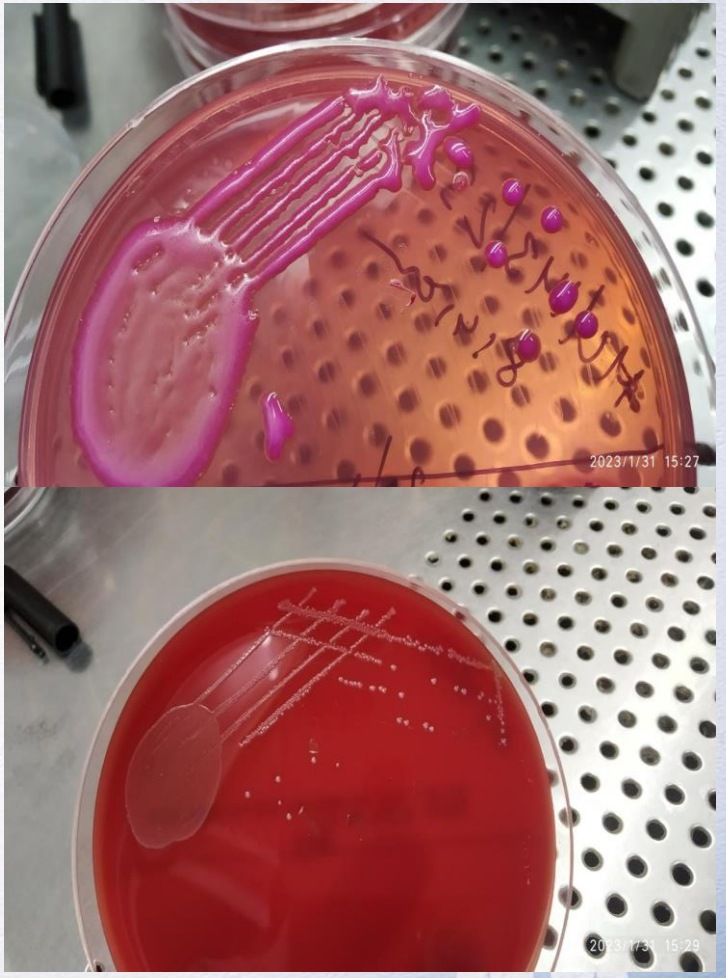
- Clostridium difficile
- Carbapenem-resistant Enterobacteriaceae (CRE)

Serious Threats

- Multidrug-resistant Acinetobacter
- Fluconazole-resistant Candida
- Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant Enterococcus (VRE)
- Multidrug-resistant Pseudomonas aeruginosa
- Methicillin-resistant Staphylococcus aureus (MRSA)
- Drug-resistant TB

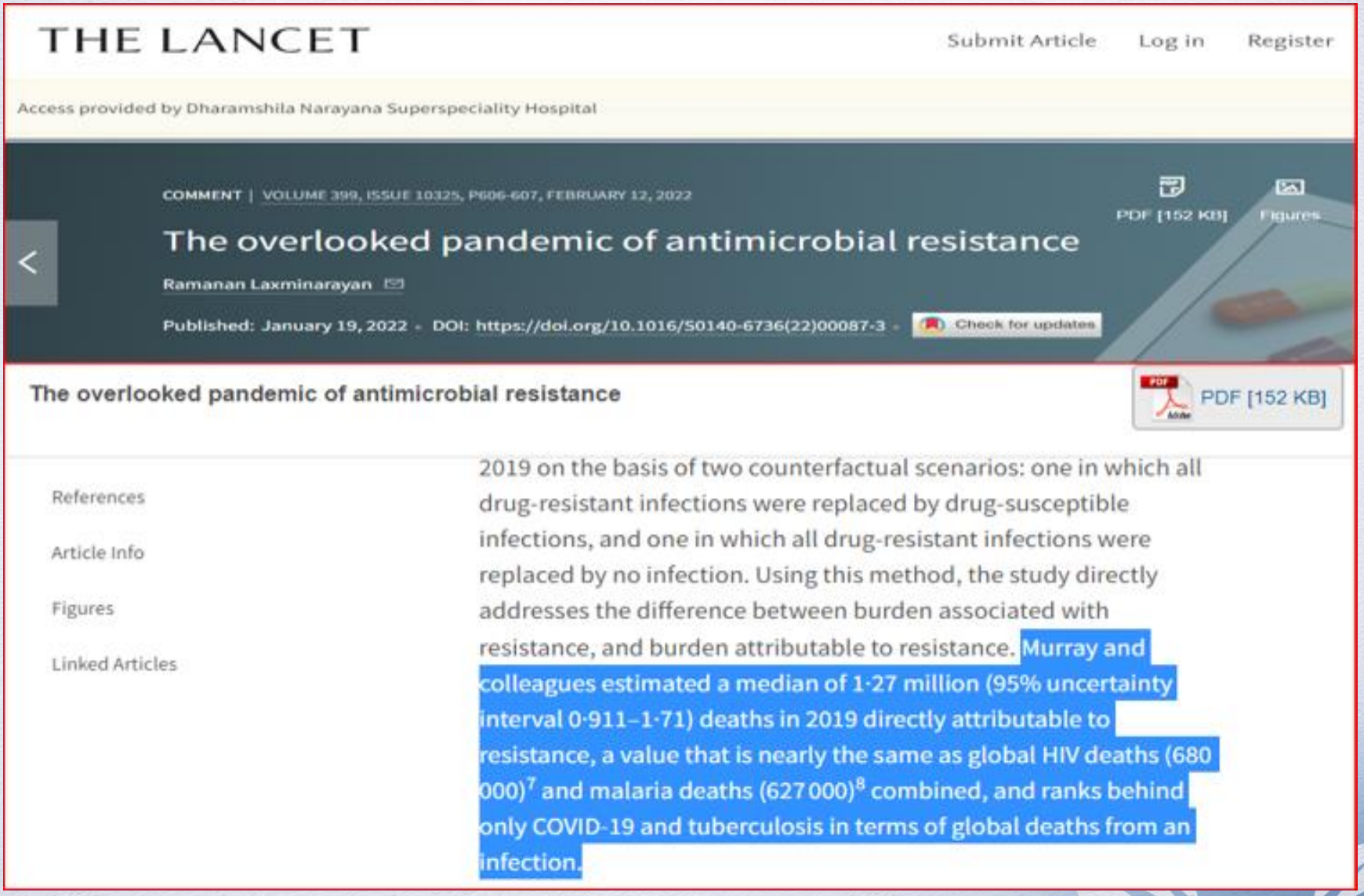
Concerning Threats

- Vancomycin-resistant Staphylococcus aureus (VRSA)



Human says Covid-19 causes pandemic but they don’t know that we are also doing the same!

OVERLOOKED PANDEMIC



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COMMENT | VOLUME 399, ISSUE 10325, P606-607, FEBRUARY 12, 2022

PDF [152 KB] Figures

The overlooked pandemic of antimicrobial resistance

Ramanan Laxminarayan

Published: January 19, 2022 - DOI: https://doi.org/10.1016/S0140-6736(22)00087-3 - Check for updates

The overlooked pandemic of antimicrobial resistance

PDF [152 KB]

References

Article Info

Figures

Linked Articles

2019 on the basis of two counterfactual scenarios: one in which all drug-resistant infections were replaced by drug-susceptible infections, and one in which all drug-resistant infections were replaced by no infection. Using this method, the study directly addresses the difference between burden associated with resistance, and burden attributable to resistance. Murray and colleagues estimated a median of 1·27 million (95% uncertainty interval 0·911–1·71) deaths in 2019 directly attributable to resistance, a value that is nearly the same as global HIV deaths (680 000)[7] and malaria deaths (627 000)[8] combined, and ranks behind only COVID-19 and tuberculosis in terms of global deaths from an infection.

Indian Journal of Medical Microbiology 41 (2023) 19–24

Contents lists available at ScienceDirect

Indian Journal of Medical Microbiology

journal homepage: www.journals.elsevier.com/indian-journal-of-medical-microbiology

Original Research Article

Delhi's network for surveillance of antimicrobial resistance: The journey, challenges and output from first year

Saxena Sonal [a,*], Sharma Anuj [b], Andrews A. Amala [c], WINSAR-D Network members [1]

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WINSAR-D Network Members: Anita Pandey, Abhilasha Kochhar, Anupama Mittal, Deepali Saini, Devjani De, Navin Dang, Gitali Bhagawati, Iqbal Kaur, Karnika Saigal, N P Singh, Namita Jaggi, Naveen

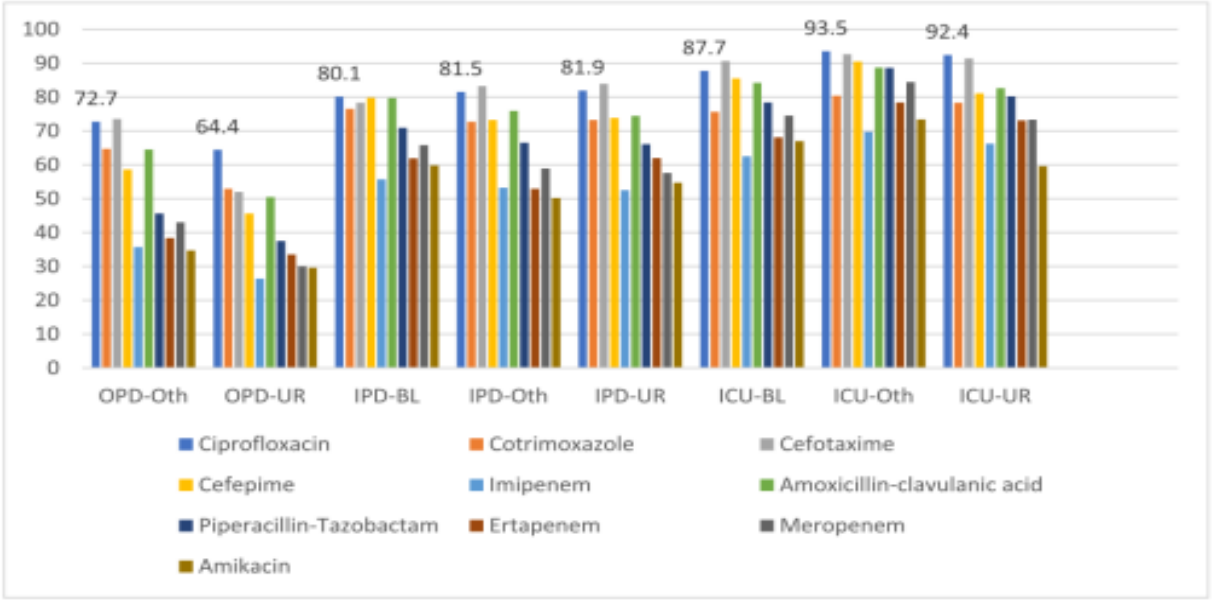


Fig 5. Location wise % resistance profile of Klebsiella spp. isolated from blood, urine, pus and sterile body fluids. Key: Tri-sulpha: Trimethoprim sulphamethoxazole, Amoxi-clav: Amoxicillin clavulanic acid, Pip-Taz: Piperacillin tazobactamOPD: Outpatient department, IPD: inpatient department, ICU: intensive care unit, Oth: Pus and sterile body fluids.

AMR: Man Made Phenomenon

- Over prescription of antibiotics (>30%)
- Incomplete course of treatment
- Over the counter sale of antibiotics
- Poor infection control practices (Improper Hand hygiene)
- Poor sanitation
- Use of antibiotics in live stock

Role of Antibiotic stewardship program (AMSP) in AMR

Antibiotic stewardship (AS) encompasses all activities intended to **improve patient outcomes** from infection while **minimizing negative consequences** such as **AMR.**

5 ‘D’s of Antibiotic stewardship

- Optimal **D**iagnosis
- **D**rug selection
- **D**osage
- **D**e-escalation and
- **D**uration

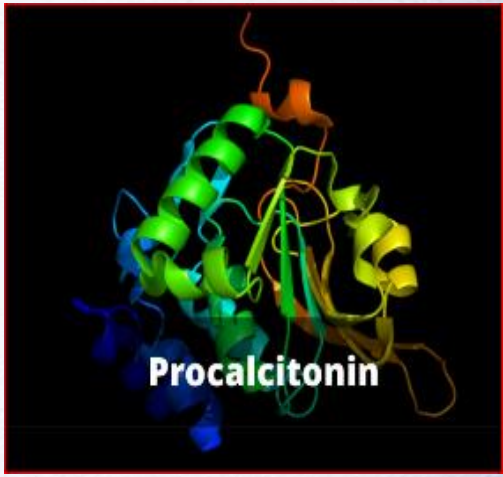
Biomarkers in AMSP

BMs are helpful for 3 D's are

- Optimal **D**iagnosis
- **D**e-escalation and
- **D**uration

PCT in Bacterial infection

- Bacterial cell wall releases Cytokines and endotoxins → Blunting of final step in conversion of PCT to calcitonin
  PCT ↑↑ (cytokines IL-6, TNF-α, IL-1β)



PCT as Biomarker

Procalcitonin – Included into national and international clinical guidelines

"... measurement of procalcitonin levels can be used to support **shortening the duration of antimicrobial therapy** in sepsis patients. "
"... procalcitonin levels can be used to support the **discontinuation of empiric antibiotics** in patient Surviving Sepsis Campaign Guideline 2016 s who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection."

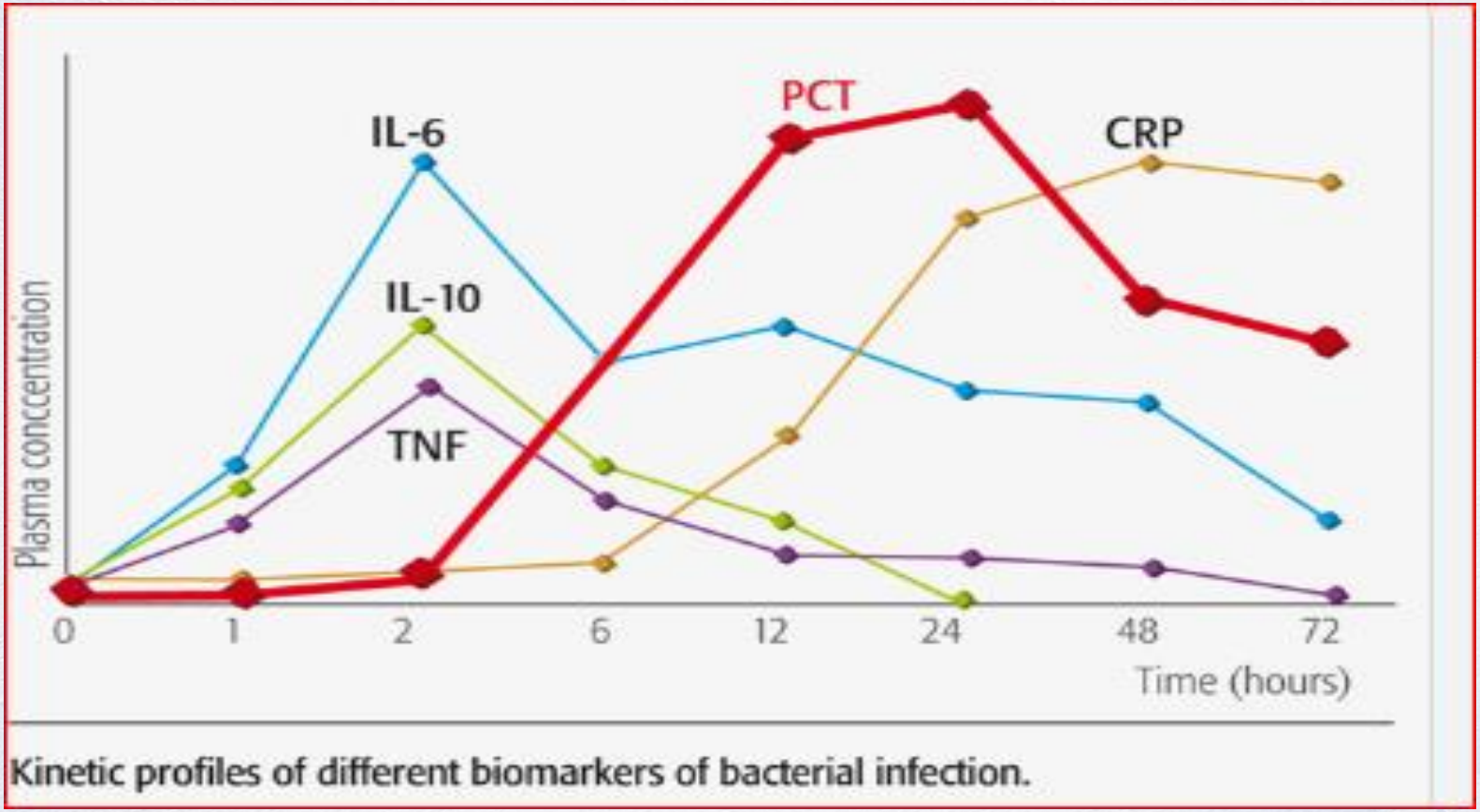
Surviving Sepsis Campaign
Guideline 2016 [1]

Procalcitonin is the **ONLY recommended biomarker** for antibiotic stewardship in sepsis and LRTI.

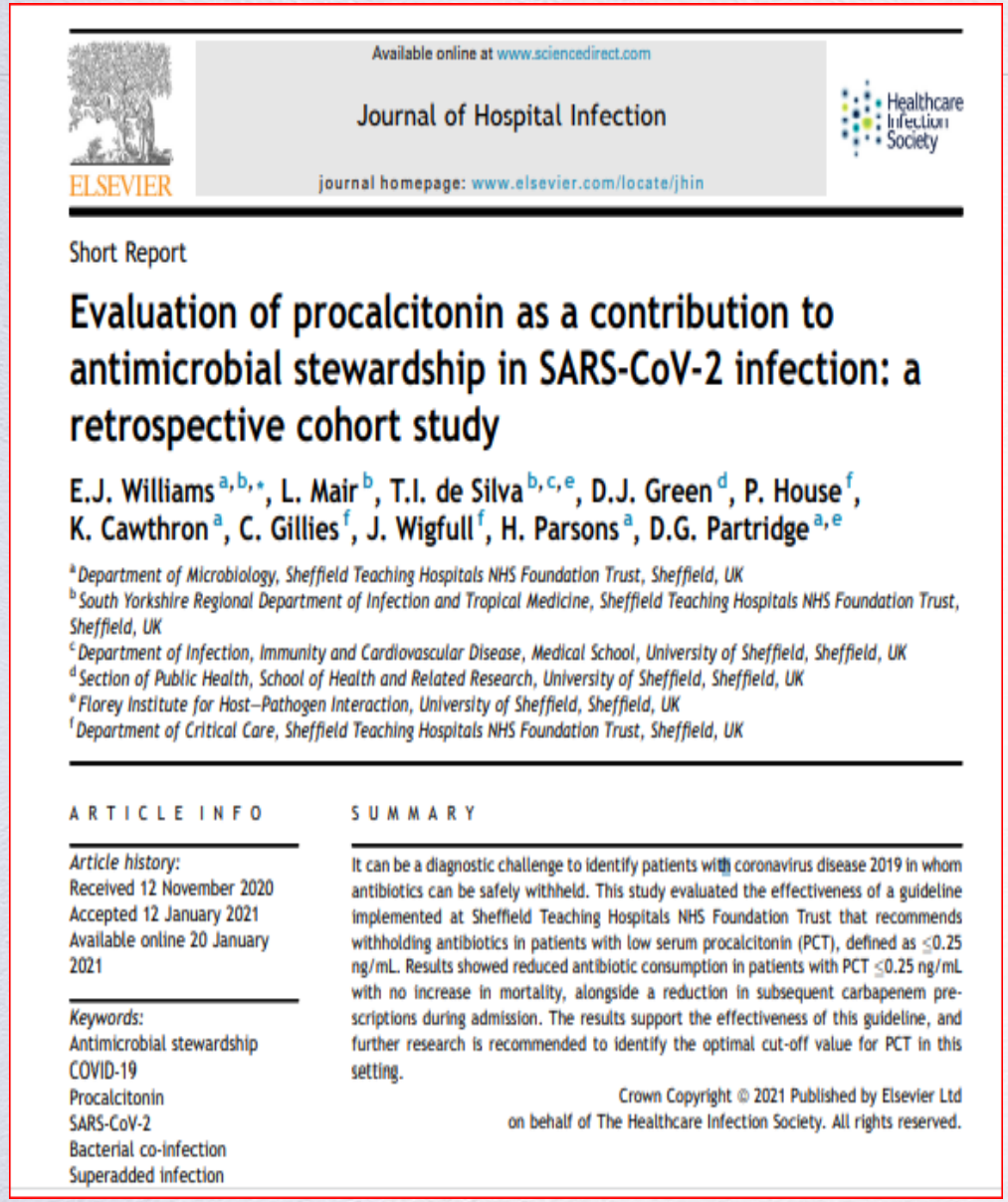
World Health Organization
Essential In Vitro Diagnostics List 2019 [2]

1 Rhodes A. et al., Intensive Care Med 2017;43 (3),Mar: 304-377
2 https://www.who.int/medical_devices/publications/Second_WHO_Model_List_of_Essential_In_Vitro_Diagnostics/en/

Kinetic of PCT in Bacterial infection



Kinetic profiles of different biomarkers of bacterial infection.



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Short Report

Evaluation of procalcitonin as a contribution to antimicrobial stewardship in SARS-CoV-2 infection: a retrospective cohort study

E.J. Williams[a,b,*], L. Mair[b], T.I. de Silva[b,c,e], D.J. Green[d], P. House[f], K. Cawthron[a], C. Gillies[f], J. Wigfull[f], H. Parsons[a], D.G. Partridge[a,e]

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ARTICLE INFO

Article history:
Received 12 November 2020
Accepted 12 January 2021
Available online 20 January 2021

Keywords:
Antimicrobial stewardship
COVID-19
Procalcitonin
SARS-CoV-2
Bacterial co-infection
Superadded infection

SUMMARY

It can be a diagnostic challenge to identify patients with coronavirus disease 2019 in whom antibiotics can be safely withheld. This study evaluated the effectiveness of a guideline implemented at Sheffield Teaching Hospitals NHS Foundation Trust that recommends withholding antibiotics in patients with low serum procalcitonin (PCT), defined as ≤0.25 ng/mL. Results showed reduced antibiotic consumption in patients with PCT ≤0.25 ng/mL with no increase in mortality, alongside a reduction in subsequent carbapenem prescriptions during admission. The results support the effectiveness of this guideline, and further research is recommended to identify the optimal cut-off value for PCT in this setting.

- This study carried out in Sheffield Teaching Hospitals NHS Foundation Trust
- They recommend- withholding antibiotics in patients with low serum procalcitonin (PCT), [0.25 ng/mL].
- Results showed reduced antibiotic consumption in patients with PCT 0.25 ng/mL with **no increase in mortality**, alongside a **reduction in subsequent carbapenem prescriptions** during admission.

PCT concentration

Table 1. Interpretation of PCT concentration. Adapted from Meisner M.[13]

PCT (μg/L)	Interpretation
< 0.05	Healthy adult
0.05 – <0.5	Systemic infection is unlikely although localised infection is possible
0.5 – <2	Systemic infection is possible but other conditions (e.g. major trauma, recent surgery, severe cardiogenic shock) may also induce significant PCT rises.
2 – <10	Systemic infection is likely
≥ 10	High likelihood of severe bacterial sepsis or septic shock

PCT α *Severity of infection*

PCT in Antibiotic Stewardship

- Initiation of antibiotic therapy

- Discontinuation of antibiotic therapy

Guideline for use of PCT

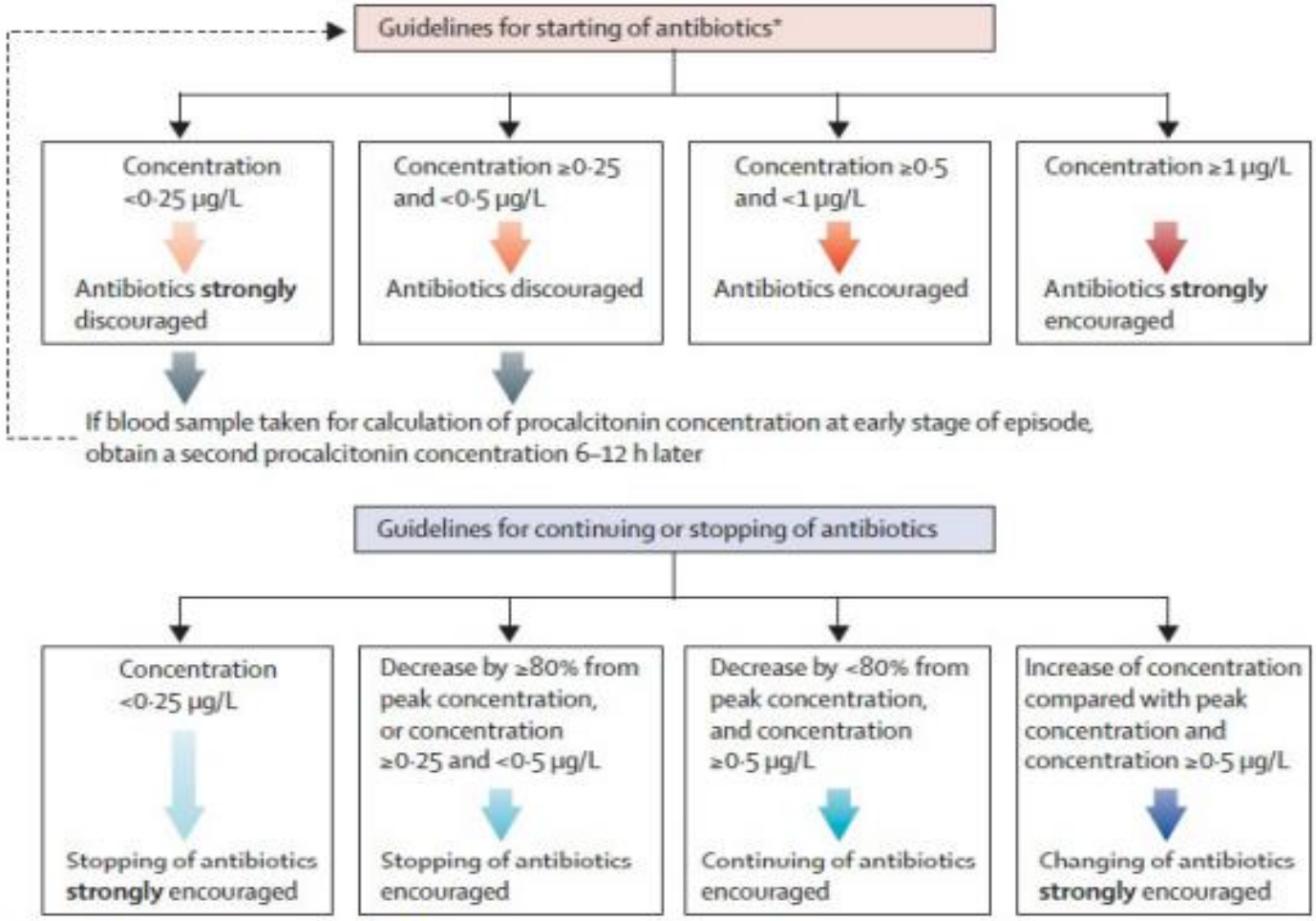


Figure 3. Algorithms for initiating and discontinuing antibiotic therapy in ICU.

Reprinted from The Lancet, 375, Bouadma L et al, Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a randomised, controlled, open-label trial, pages 463-74, 2010, with permission from Elsevier.

Other causes of increase in PPT

- Major surgery
- Severe trauma
- Severe burns
- Prolonged cardiogenic shock
- Medication which stimulate cytokine release e.g., OKT3 (Muromonab-CD3), antilymphocyte globulins, Alemtuzumab, IL-2, granulocyte transfusion etc.
- Newborn babies (baseline PCT is higher than adults)
- Chronic kidney disease

Dysregulated PCT production

- Paraneoplastic syndromes due to medullary thyroid, small cell CA Lung etc.

Low or Normal PCT

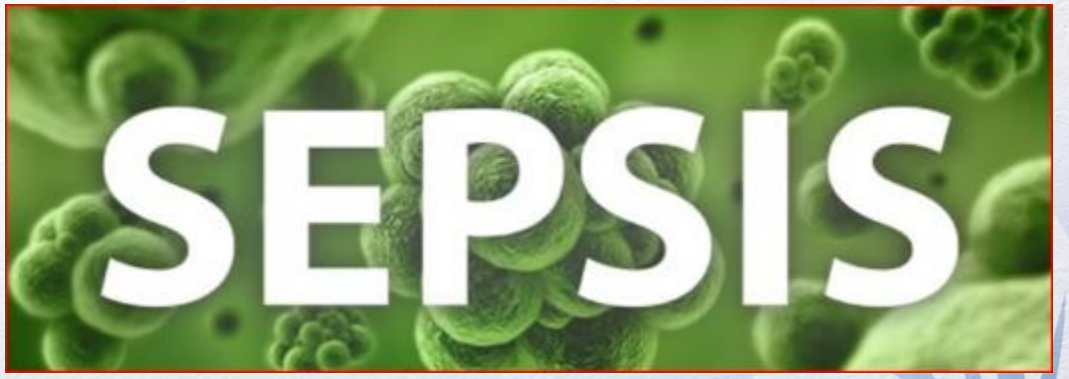
- Early course of bacterial infection
- Localised infection like Osteomyelitis, empyema etc.
- Subacute infective endocarditis

Advantages of PCT over other Biomarkers:

- Rapidly increases after the onset of infection
- Rapid decline within 48 hours in non-infected patients
- PCT has higher specificity in mixed bacterial infections
- PCT is not affected by the use of Non-steroidal anti-inflammatory agents
- PCT is not affected by the use of Steroids
- PCT levels have not shown to be affected by comorbidities like SLE, Gout etc.

Sepsis panel

- Procalcitonin
- Paired Blood culture



Take Home Message

- PCT can be considered as a standard and convincing BM for Initiation and Discontinuation of Antibiotics
- If it is <0.5 µg/L- antibiotics discouraged

THANK YOU

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