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The Magnificent Seven: Seven good publications in infectious diseases

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ABSTRACT

The world of infectious diseases, for various reasons, before and after the COVID-19 pandemic, capture the attention of the scientific community, either due to the epidemiological data of various microbial agents that are emerging, due to the implementation with successful results of new diagnostic strategies or due to the appearance of new therapeutic options, which encourage healthcare workers to continue on the front line.

Topics such as antimicrobial resistance, *S. aureus* bacteremia, clostridioides difficile, short treatments for tuberculosis, prosthetic joint infection or invasive fungal infections are included.

In this article, we want to highlight, among many others, seven recently published articles that deserve our attention, full of useful information to keep us updated.

Keywords: antimicrobial resistance, catheter-related bacteremia, anti-tuberculosis drugs

The broad scientific production between 2020 and 2022 has left us with a huge number of interesting scientific articles. Excluding HIV and COVID-19 we want to highlight, in an attempt to cover different topics, seven of the most impressive scientific publications.

The first article selected [1], studies the impact of antimicrobial resistance (AMR) in 204 countries. It is also reviewed the deaths and disability attributable to and associated with 23 multidrug-resistant bacteria and 88 pathogen-drug combinations. The greatest number of deaths was attributed to methicillin-resistant *Staphylococcus aureus* (MRSA), while other bacteria with multidrug-resistant spectrum such as *Escherichia*

coli, *Acinetobacter baumannii* or *Klebsiella pneumoniae* were relegated to the background. In 2019, there were 4.95 million deaths associated with antimicrobial resistance, including 1.27 million deaths that were directly attributable to bacterial AMR. The region with the highest attributable mortality in the world was Sub-Saharan Africa.

This study reveals the different epidemiology of AMR bacteria depending on the country's income. *E. coli* and *S. aureus* were more frequent in countries with high incomes, whereas *K. pneumoniae* and *S. pneumoniae* acquire more importance in those with lower incomes. The respiratory tract infections were the main source of infection in those countries with lower incomes.

Talking about *Clostridioides difficile*, we have selected the Katzman M. et al [2] article which highlights the introduction of two different interventions to reduce the incidence of *C. difficile* infections (CDI) in an university hospital, wherein despite of the cleaning and contact protocols, the incidence of CDI increases up to approximately 160 cases per year, in the last three years.

The first intervention was carried out during admission, consulting if the patient had one or more liquid stools in the last 24 hours. If the answer was affirmative, contact measures were established and CD PCR was requested. The next step consisted in the toxigenic antigen detection by enzyme immunoassay (EIA) in samples with positive result by polymerase chain reaction (PCR). If the EIA was negative, the patient did not require treatment but contact isolation, and if the toxigenic gene was detected, an internal hospital protocol was launched. Treatment with fidaxomicin was included on it.

Other minor measures were also carried out which included proton-pump inhibitors drugs reduction, usage of probiotics for some patients on antibiotics, and prophylaxis with oral vancomycin for patients receiving antibiotics who had CDI in the previous year. The results obtained one year after the implementation of these interventions confirmed a significant and

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maintained reduction in the cases of CDI over time (from 161 to 63 cases). Only 45% of patients were PCR (+)/EIA (+), and they had similar outcomes to the PCR (+)/EIA (-) patients.

Central Line-Associated Bloodstream Infections (CLABSIs) continues to be an important source of nosocomial infection. For this reason, we chose an update of the 2014 guidelines from *Strategies to Prevent Central Line-Associated Bloodstream Infections in Acute-Care Hospital* [3]. Some of the recommendations to prevent CLABSI at insertion were the usage of the subclavian site to reduce infectious complications when the catheter is placed in the Intensive Care Units (ICU) setting, guidance by ultrasound for catheter insertion and usage of an alcoholic chlorhexidine antiseptic for skin preparation. After insertion, it is recommended the routine replacement at intervals up to 7 days of administration sets not used for blood, blood products or lipid formulations. Approaches that should not be considered as a routine part of CLABSI preventions are the use of antimicrobial prophylaxis for short-term or tunneled catheter insertion or while catheters are *in situ* and not to do routinely replace of the Central Venous Catheters (CVC) or arterial catheters.

Injection drugs use is an important risk factor for the development of infective endocarditis (IE), however, advances in diagnosis and treatment have been slow. The American Heart Association along with a panel of experts have developed a scientific support document for clinicians managing IE in people who inject drugs (PWID) [4]. This document has three major sections of clinical expertise that include the integration of addiction consultation, antimicrobial therapy and cardiac valve surgery management.

The antimicrobial therapy management is focused on the treatment of *S. aureus*, as it is the most frequent attributable to injection drug use (85%). The standard of care of IE attributable to *S. aureus* has included 6 weeks of intravenous (IV) antibiotics, however the group of Baddour LM et al recognizes that 6 weeks of intravenous antibiotics is often not feasible for all PWID. Partial intravenous therapy followed by oral antibiotic treatment to complete a total of 6 weeks is growing evidence and it can be an option for patients who cannot complete 6 weeks of its treatment. For this regimen, best practice would offer oral antibiotics or long-acting lipoglycopeptides dalbavancin or oritavancin. Surgery should be postponed until the end of antibiotic treatment, except in serious cases such as heart block, persistent bacteremia, or the presence of intracardiac abscesses.

The treatment of joint prosthesis-associated infections deserves a special article in the New England Journal of Medicine [5]. This is an open-label, randomized, and controlled, non-inferiority trial to compare 6 weeks with 12 weeks antibiotic therapy in patients with confirmed prosthetic joint infection. The study enrolled 410 patients from 14 French hospitals. This trial revealed results in favor of the 12-week treatment (9.4% of persistent infections) compared to the 6-week treatment (18.1%). Results after debridement or replacement in two stages, for hip or knee prostheses, in the first episode or re-

current episode, the prognosis was more favorable in patients who completed 12 weeks of treatment, independently of these variables.

Adherence to tuberculosis treatment is a worrying issue worldwide, especially in underdeveloped countries. Our sixth article [6] is an open-label, phase 2-3, multicenter, randomized, controlled, non-inferiority trial conducted by the Tuberculosis Alliance together with Médecins Sans Frontières. The aim of the study was to evaluate the efficacy and safety of 24-week oral treatment regimen for rifampicin-resistant TB. In stage 2 of the trial, a 24-week regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPALM) was compared with a 9-to-20-month standard-care regimen. The study enrolled 301 patients who were 15 years of age or older and had rifampicin-resistant pulmonary tuberculosis. The primary outcome was an unfavourable status at 72 weeks after the randomization and the secondary outcome was to study the safety profile of treatment with BPALM regimen. The study demonstrated that 24-week BPALM regimen was non-inferior to conventional treatment with better safety profile.

Finally, we highlight the magnificent review on invasive fungal infections in COVID patients published in Nature in August 2022 [7]. This review addresses the epidemiology, risk factors, predisposing characteristics of the host, and immunological mechanisms involved in the pathogenesis of fungal co-infections by COVID-19.

The main groups of fungal pathogens cause co-infections in COVID-19 are *Aspergillus*, *Mucorales* and *Candida*, including *Candida auris*. It is to be noted the wide heterogeneity of the clinical manifestations or incidence between different geographical regions, as it occurs with COVID-19 associated mucormycosis (CAM). Rhino-orbital-cerebral disease is more frequent in Asian countries while in our media the pulmonary disease is prevalent. The diagnosis of these entities continues to be a challenge. The current tools available for diagnosis such as galactomannan, β -1,3-glucan or PCR in bronchoalveolar lavage samples offer us complex results to interpret in the clinical context of each patient. The culture of non-invasive respiratory samples has a low sensitivity and other associated pathogens are isolated in 50% of cases. The difficulties due to the low diagnostic yield of probability or possibility of invasive fungal infections of conventional cultures together with the low positive predictive value of the new techniques make it necessary to reach an equilibrium between classical techniques and biomarkers based on the patient's risk factors and their clinical and radiological data.

CONFLICT OF INTEREST

Author declares no conflict of interest.

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