

Epidemiology of Common Infections: Focus on Emerging Antimicrobial Resistance

Understanding the local epidemiology of various pathogens is essential in guiding antimicrobial therapy. This is also important for antimicrobial stewardship and the prevention of the emergence of resistant pathogens.

1- Common infections

a. *Pneumonia*

The epidemiology of community-acquired pneumonia in Lebanon is not well-defined. However, studies from other countries have found that *Streptococcus pneumoniae*, alongside respiratory viruses, are the most common etiological agents. Other common pathogens are *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus* and atypical bacteria (such as *Legionella* spp., *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*).¹

Most *S. pneumoniae* isolates are susceptible to penicillin, however in Lebanon penicillin non-susceptible *S. pneumoniae* reported up to 54%, and the reported resistance to macrolides is up to 42%.² Vigilance should be exercised in prescribing macrolides to patients who have received macrolides as empiric treatment for COVID-19 pneumonia, as increasing resistance is suspected. In addition, patients should be assessed for risk factors of methicillin-resistant *Staphylococcus aureus* (MRSA), including previous colonization/infection with MRSA, the presence for gram-positive cocci on sputum Gram stain, necrotizing pneumonia, post-influenza pneumonia, and recent IV antibiotics.¹ In Lebanon, MRSA constitute 33-36% of all *S. aureus* isolates.² On the other hand, the presence of gram-negative bacilli on sputum Gram stain, previous colonization/infection with *Pseudomonas*, and structural lung disease (bronchiectasis, chronic obstructive pulmonary disease) should prompt the use of antipseudomonal agents, such as quinolones (levofloxacin, ciprofloxacin) or antipseudomonal beta-lactams (cefepime, piperacillin-tazobactam, ceftazidime, meropenem, imipenem).

Ventilator-associated pneumonia in Lebanon was found to be mostly caused by *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. These infections are usually more serious and are more likely to be caused by multidrug resistant (MDR, organisms that are resistant to at least one antimicrobial agent in 3 or more antimicrobial classes) or extensively drug-resistant (XDR, organisms that are resistant to at least one agent in all but 2 or fewer antimicrobial categories) organisms.³ Treatment in these cases should be guided by antibiotic susceptibility testing.

b. *Urinary Tract Infections (UTIs)*

UTIs are most commonly caused by Enterobacterales (*E. coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*) and *Staphylococcus saprophyticus*.⁴ Extended-spectrum beta-lactamase (ESBL)-producing organisms are a particularly concerning etiology. These gram-negative bacteria are resistant to most beta-lactam antibiotics (penicillins and cephalosporins) and are associated with a poor outcome. In Lebanon, 32% of *Escherichia coli* and 35% of *Klebsiella pneumoniae* isolates are ESBL-producing.² They are susceptible to carbapenems (imipenem, meropenem and

ertapenem) and to some combination cephalosporin/beta-lactamase inhibitor agents (ceftolozane-tazobactam, ceftazidime-avibactam).

Another major concern is the emergence of carbapenem-resistant Enterobacterales (CRE) produce beta-lactamases that hydrolyze carbapenems (carbapenemases). The prevalence of CRE *Klebsiella pneumoniae* in Lebanon is 15%, while that of CRE *E. coli* is 6% and of CRE *Enterobacter spp.* is 8%.² Carbapenem-resistant *Pseudomonas aeruginosa* is another major concern, with a prevalence of 28%.⁵ Treatment options are limited and depend on susceptibility to antibiotics such as ceftazidime-avibactam, ceftolozane-tazobactam, aztreonam, colistin, and fosfomycin.

c. *Skin and Soft Tissue infections*

Streptococcus pyogenes is the most common culprit in skin and soft tissue infections, followed by *Staphylococcus aureus*, whereas *S. aureus* predominates in skin abscesses. Health-care exposure (recent hospitalization, recent surgery, hemodialysis, residence in a long-term care facility), HIV infection, injection drug use and prior antibiotic use are risk factors for MRSA in these cases. Additionally, MRSA outbreaks can occur in the context of prisons, military service, sharing of sports equipment or of sharp objects.⁶

2- Post-COVID-19 infections:

Bacterial and fungal co-infections and superinfections of patients with Coronavirus Disease 19 (COVID-19) are reported worldwide and at varying rates, ranging from 0.6% to up to 45%. Most worrisome is the apparent trend of rising antimicrobial resistance in this population and the higher risk of fungal infections.⁷

a. *Bacterial infections associated with COVID*

Data are still emerging on the presence of bacterial infections associated with COVID-19. Common culprits are *S. pneumoniae*, *S. aureus*, *Pseudomonas aeruginosa*, *E. coli*, *Klebsiella pneumoniae*, *Enterococcus faecium* and *Haemophilus influenzae*. Resistant organisms have been reported as well, with a rise in CRE incidence in some centers from 25.3 per 10,000 hospital days to 75.9 during the pandemic. This could be attributed to the misuse of broad-spectrum antibiotics in COVID-19 patients. In some reviews, antibiotic use was as high as 71.9% in the context of a documented bacterial infection rate of 3.5%.⁷

b. *Emergence of Candida auris*

Invasive candidiasis (including candidemia) is a serious life-threatening infection associated with elevated mortality (40-50%).⁸ In Lebanon, in concordance with the worldwide trend, non-*albicans* species have become more prevalent than *Candida albicans*, and *C. glabrata* is the predominant non-*albicans* species identified.⁸ In 2020, the first outbreak of *C. auris* was reported in Lebanon, during the COVID-19 pandemic. This is concerning as this *Candida* species is notoriously exhibits multidrug resistance, is difficult to identify and is associated with healthcare outbreaks.⁹

There are no guidelines so far for the management of *C. auris* infections, although echinocandins (casposfungin, anidulafungin and micafungin) are usually first-line therapy. Isolates from Lebanon exhibited resistance to fluconazole, varying susceptibility to amphotericin B, and were generally susceptible to echinocandins. Antifungal susceptibility testing for the isolated *Candida spp.* is essential in guiding therapy.⁹

c. COVID-associated Pulmonary Aspergillosis (CAPA)

CAPA has become a concerning infection in patients with severe COVID-19, especially due to its elevated mortality. This infection is enabled by the direct viral damage to respiratory epithelium. The diagnosis of this entity is challenging as typical risk factors and radiological features of pulmonary aspergillosis may not be present or may overlap with COVID-19 features. Voriconazole and isavuconazole are the recommended antifungal agents.¹⁰

References

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