COVID-19 Mortality from Secondary Acquired Infections

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How life has changed: COVID-19 and AMR
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Why do COVID-19 patients die?

- Diffuse alveolar damage causing acute respiratory distress syndrome (ARDS)
- Thromboembolic disease
- Multisystem organ failure
- Immune depletion and dysregulation

Do patients die of secondary infections?

37% of COVI-19 autopsies have histopathologic findings in lungs that are consistent with superimposed bronchopneumonia or pulmonary infection

- Findings due to superimposed infection or COVID-19?
- Very limited microbiology and AMR data
- More often focal process rather than diffuse disease
- Often not recognized or treated with antimicrobials ante-mortem

Sizeable minority of COVID-19 decedents die with, but not necessarily from, superimposed bacterial or (less often) fungal infections

Types of COVID-19 secondary infections

Microbiology and AMR will reflect local epidemiology and host risk factors

Bloodstream infections
- Endocarditis, septic emboli, abscesses

Urinary tract infections

Skin and soft tissue infections
*Clostridiodes difficile* infections

Lung:
*P. aeruginosa, K. pneumoniae, C. koseri, S. maltophilia*

Urine:
*E. Coli, Proteus, K. pneumoniae*

● MDR, ESBL, CRE infections diagnosed

Blood:
*S. aureus*, coag negative *Staph, Strep* spp., *Candida*

Co-infections
- Community acquired pneumonia, urinary tract infection, skin/soft tissue infection, *C difficile* infection, febrile neutropenia

Secondary infections
- Hospital/ventilator pneumonia, bloodstream infection, urinary tract infection, *C. difficile* infection

VAPHS experience, through 7/31/20


- Present w co-infxn, 9%
- Develop secondary infxn, 19%
- No co- or secondary infxn, 72%

Lung: *P. aeruginosa, K. pneumoniae, C. koseri, S. maltophilia*

Urine: *E. Coli, Proteus, K. pneumoniae*

- MDR, ESBL, CRE infections diagnosed

Blood: *S. aureus*, coag negative *Staph, Strep* spp., *Candida*
COVID-19: Antimicrobial stewardship strategies

<table>
<thead>
<tr>
<th>Stewardship group</th>
<th>Stewardship objectives</th>
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<tr>
<td>1. No treatment</td>
<td>Limit unnecessary use, include rapid diagnostics (negative predictive values)</td>
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<tr>
<td>2. Empiric treatment</td>
<td>Target most likely pathogens, rapid de-escalation, limit duration, aggressive diagnostic testing (NPVs)</td>
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<td>3. Treat co-infection</td>
<td>Promote narrow spectrum, short course, oral</td>
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<tr>
<td>4. Treat secondary infection</td>
<td>Target nosocomial pathogens, promote narrow spectrum, short course</td>
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Gp 1. No antimicrobials 41%
Gp 2. Empiric treatment, no infxn diagnosed 31%
Gp 3. Treat for co-infxn 9%
Gp 4. Treat for secondary infxn, 19%
Impact of COVID-19 on hospital antibiotic use

VAPHS Days of therapy (DOT)

VAPHS bed days of care (BDOC)

VAPHS DOT/1,000 BDOC

Non-antipseudomonal PNCs

DOT/1,000 BDOC

Macrolides

DOT/1,000 BDOC

Significantly increased DOT/1000 BDOC of agents vs. CAP

- Patients with CAP/suspected CAP disproportionately presenting to hospital?
- Over-treatment of suspected CAP?

Outpatient antibiotic use

Significant reductions in prescription fills in April 2020 for the ten most commonly prescribed outpatient antibiotics

- No significant rebound, April-July 2020: Azithromycin, amoxicillin-clavulanate, levofloxacin
- Rebound April-July 2020, but still below baseline: Amoxicillin, doxycycline

Prescription fills for outpatient antibiotics recommended against CAP or commonly used against respiratory tract infections remain significantly below baseline

- Patients not seeking care? Clinicians less likely to prescribe (unnecessary) agents?
Will COVID-19 result in increased AMR?

**Pro**

- Antibiotic prescribing in excess of secondary infections, suggesting inappropriate use
- Many COVID-19 epicentres also AMR epicentres
- Burden of antibiotic use in hospitalized patients increased, even outside of epicentres
- Reports of HAI outbreaks associated with breakdowns in infection prevention
- Effects of COVID-19 on public health infrastructure, sanitation, healthcare delivery, governance may indirectly impact AMR and transmission
- Secondary infections may increase as COVID-19 treatment evolves (e.g., dexamethasone)
- Co-circulation of SARS-CoV-2 and influenza may fuel inappropriate antibiotic prescribing

**Con**

- Overall antibiotic use in humans has decreased in many places
- Major determinant of AMR rates is spread, which may be decreased with COVID-19 travel restrictions, enhanced attention to infection prevention, etc.
- Better COVID-19 outcomes may decrease pools of high risk critically ill patients, including those on ventilators, receiving hemodialysis, etc.
- Increased emphasis on diagnosing respiratory viral infections may decrease inappropriate antibiotic treatment
- Data from southern hemisphere suggest that impact of influenza may be lessened by COVID-19 precautions

COVID-19 and AMR story will be dynamic, and likely to differ from region to region, hospital to hospital, and unit to unit within hospitals

- AMR was a major problem before COVID-19, and it will remain a problem

COVID-19 and AMR: Needs moving forward

• Report our experiences and data
• More rigorous microbiology and definitions of superimposed infections in clinical and postmortem studies
• Surveillance data on antimicrobial use and AMR
• Education
  • It’s OK not to get/give an antibiotic
  • AMR has not gone away