



FEATURE

How covid-19 is accelerating the threat of antimicrobial resistance

Healthcare responses to the novel coronavirus may be hastening another long looming public health threat, writes **Jeremy Hsu**

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The global threat of antimicrobial resistant bacteria and other superbugs is worsening as many patients admitted to hospital with covid-19 receive antibiotics to keep secondary bacterial infections in check.

“Since the emergence of covid-19, collected data have shown an increase in antibiotic use, even though most of the initial illnesses being treated have been from covid-19 viral infection,” says Dawn Sievert, senior science advisor for antibiotic resistance at the US Centers for Disease Control and Prevention (CDC). “The resulting increased exposure to healthcare settings and invasive procedures, along with expanded antibiotic use, amplifies the opportunity for resistant pathogens to emerge and spread.”

Much remains unknown about how the pandemic is directly impacting overall levels of antimicrobial resistance (AMR), but a review of data from covid-19 cases, mostly in Asia, found that more than 70% of patients received antimicrobial treatment despite less than 10%, on average, having bacterial or fungal coinfections.¹ The same study also found frequent use of broad spectrum antibiotics—designed to kill a wide range of bacteria—that can spur AMR through overuse. Such findings give weight to researchers’ concerns that increased antibiotic use during the pandemic could increase the long term threat of AMR.

Recommended use

The World Health Organization discourages the use of antibiotics for mild cases of covid-19 while recommending antibiotic use for severe covid-19 cases at increased risk of secondary bacterial infections and death. Hanan Balkhy, assistant director general for AMR at WHO, told *The BMJ* that early data on patients with covid-19 suggest only a minority have bacterial coinfections. “WHO continues to be concerned by the inappropriate use of antibiotics, particularly among patients with mild covid-19,” Balkhy says.

One factor likely encouraging increased antibiotic use is clinical uncertainty about covid-19 infections. Such uncertainty can be amplified by urgency when physicians treat critically ill patients

whose lives hang in the balance. Some experts worry that the pandemic’s strain on healthcare systems may disrupt antibiotic stewardship programmes designed to help hospitals minimise the risk of AMR.

“There’s a lot of uncertainty about the disease process and the pathology of the infection,” says David Hyun, senior officer of the antibiotic resistance project at the Pew Charitable Trusts in Washington, DC. “When the clinician doesn’t have all the necessary information to understand truly what’s happening in the patient, it tends to drive more antibiotic use.”

Confusion and uncertainty

During the first wave of covid-19 infections in New York City, physicians working at the Montefiore Health System hospitals in the Bronx found themselves treating patients with “extreme symptoms and physiological parameters that resembled severe sepsis and shock,” says Priya Nori, medical director of the antimicrobial stewardship programme and outpatient parenteral antibiotic therapy programme at Montefiore Health System. “We were not in a position to say definitively that patients did not have concurrent bacterial infections.”

Fortunately, the hospitals had ensured they would have enough antibiotics to handle the surge in cases. But the strain on resources and staff did impact the antibiotic stewardship programme that, like many others, is designed to help minimise the risk of antibiotic misuse leading to AMR. “We didn’t face shortages but weren’t able to monitor antibiotic use as well as we would have in pre-pandemic times,” Nori says.

Since the first wave’s peak in New York City, Nori and her colleagues have reviewed their clinical data and noticed that a small percentage of patients did have both covid-19 and bacterial infections at the same time. That is not unexpected; critically ill patients are often intubated and hospitalised for weeks, which can allow “the usual cast of characters in any hospital acquired infection” to make an appearance. More ominously, the hospitals’ data also show a “slow and steady increase in

multidrug resistance” among gram negative bacteria that “can be potentially deadly coinfections with covid-19,” Nori says.²

Inadequate covid-19 testing in the US and elsewhere can also increase clinical uncertainty. Before the pandemic, 60-70% of US adults diagnosed with acute bronchitis received antibiotic prescriptions despite the fact that bronchitis is overwhelmingly caused by viral infections.³ The overlap in symptoms between bronchitis and covid-19 infections could worsen that overprescribing trend, especially when covid-19 testing remains inaccessible, says Rita Mangione-Smith, vice president for research and healthcare innovation at Kaiser Permanente Washington, a provider of healthcare and health insurance in Washington state.

Dangerous hype

Another risk of antibiotic misuse comes from premature hype surrounding possible therapies for covid-19. Notably, some media reports and political leaders amplified the possible use of the antibiotic azithromycin in combination with the drug hydroxychloroquine, which likely contributed to shortages of both drugs⁴ despite the lack of clinical evidence for their effectiveness.⁵ “If we keep having more inflammatory claims about antibiotics that may help, like azithromycin, then we’re going to have patients who come in demanding it as soon as they hear they have covid-19,” Mangione-Smith says.

The huge shift towards telehealth consultations⁶ during the pandemic could also exacerbate antibiotic overprescribing. “There was a recent paediatric study⁷ that demonstrated overprescribing is much more common in telehealth visits than in face-to-face visits,” Mangione-Smith says.

Many experts now fear the global effort to keep AMR in check could face a setback during the pandemic. Similarly, many emphasise the need to collect data on how healthcare responses to the pandemic may be affecting AMR. One example is a US Department of Defence study examining rates of secondary infections and antibiotic usage in patients with covid-19.⁸

Michael Craig, senior advisor for antibiotic resistance at the CDC, says they continue to receive data on both antibiotic usage and secondary infections from hospitals without any noticeable decline in reporting. WHO hopes its Global Antimicrobial Resistance and Use Surveillance System—with 91 countries and territories providing data—will yield results. “It will be interesting to see whether any change in profile occurred during the pandemic period, noting that this information can only be assessed and available when the pandemic has subsided,” says Balkhy.

Researchers see a need for improved data collection that goes beyond “passive surveillance” triggered by microbiology laboratory samples coming back positive for drug resistant strains. “We need clinically focused surveillance systems linking risk factors, microbiology, treatment, cost, and outcomes,” says Gemma Buckland-Merrett, science and research lead on drug resistant infections at the Wellcome Trust.

Resource gone

Wellcome is currently backing the ACORN project—organised by Oxford University in the UK and Mahidol University in Thailand—to establish an active surveillance network for AMR across low and middle income countries.⁹ The idea is to collect

data in a way that better integrates clinical information about each patient’s health condition with the microbiology laboratory results. “We spent a lot of time thinking about what we need to know about the patient to make AMR data usable,” says Paul Turner, director of the Cambodia-Oxford Medical Research Unit at the Angkor Hospital for Children in Siem Reap, Cambodia.

The ACORN project is already underway at three hospitals in Cambodia, Laos, and Vietnam, which have escaped the worst of the coronavirus outbreaks so far. But the pandemic has slowed down plans to eventually deploy at more sites across Asia and Africa, with clinical and scientific resources being diverted to either mitigating the impact of the pandemic or planning for it.

The pandemic has also stalled deployment of a new genomic surveillance initiative for the national antimicrobial surveillance programme of Nigeria, Africa’s most populous country. Backed by the Nigeria Centre for Disease Control and the UK’s National Institute for Health Research, the effort was scheduled to start prospective genome sequencing this year but border closures have made it difficult to import all the necessary laboratory materials and finish setting up equipment, says Iruka Okeke, professor of pharmaceutical microbiology at the University of Ibadan in Nigeria. Similar problems have affected the rollout of a separate genomic surveillance effort aimed at quickly detecting the spread of AMR in rural areas.¹⁰

On top of everything, Nigerian public officials currently have their hands full with both the local covid-19 outbreak and an ongoing Lassa fever outbreak. “The Nigeria Centre for Disease Control is committed to ensuring that other programmes, including AMR, are not compromised,” Okeke says. “But the reality is that emergencies will draw resources and the pinches will be felt pretty quickly when overall resources are few.”

Commissioned, not peer reviewed

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