HEALTH AND MEDICAL RESEARCH FUND

Surveillance of environmental contamination by antibiotics and antibiotic-resistant pathogens: abridged secondary publication

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KEY MESSAGES

1. A great diversity of antibiotic resistance genes (ARGs) including mobile colistin resistance genes are identified from sewage of Queen Mary Hospital and influent and effluent of Sandy Bay Preliminary Treatment Works.
2. A large amount of multi-drug-resistant *Escherichia coli* and *Klebsiella pneumoniae* isolates are obtained from samples.
3. Abundance of several ARGs is associated with water temperature. The use of fluoroquinolone in hospitals is positively associated with the abundance of fluoroquinolone resistance genes.
4. The resistome profile of the sewage from a hospital site has higher similarity to that of the influent at Sandy Bay Preliminary Treatment Works.

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The emergence and rapid spread of antibiotic-resistant bacteria is a major threat to global health. Antibiotic resistance is often attributed to the overuse and misuse of antibiotics in humans and animals so that bacteria acquire resistance against antibiotics through natural mutations or lateral transfer of resistance genes. This highlights the problem of mobility of antibiotic resistance genes (ARGs) from bacteria to bacteria, between bacteria and the environment, and between humans, animals, and the environment. Determining the source and dissemination pathways of ARGs is challenging and requires extensive and multi-sector collaborative efforts. Such knowledge is important for developing effective control and prevention strategies.

There have been studies investigating the emergence of antimicrobial resistance (AMR) among patients in hospitals.[1,2] Sewage surveillance to monitor AMR and other pathogens such as SARS-CoV-2 is useful to assess environmental contamination by pathogens.[3,4] In Hong Kong, such sewage surveillance for hospital AMR has not been fully assessed. Such work may provide insight into emergence of AMR in the human sector and dissemination to environments.

We conducted a 1-year longitudinal surveillance of AMR in wastewater discharged from the Queen Mary Hospital (QMH) and in the influent and effluent from the nearby wastewater treatment plant (Sandy Bay Preliminary Treatment Works, SBPTW) between February 2019 and January 2020. The study used multiple approaches to characterise the antibiotic-resistant bacteria, resistance genes, and residues in the wastewater samples. Both culture and metagenomic methods were used to delineate the bacterial-resistant profiles in phenotypic and genotypic levels. The study aimed to determine the dynamics and diversity of bacteria population, antibiotic resistance, residue, and usage in these locations over time, so as to determine the associations and factors of AMR emergence and potential dissemination.

Metagenomic sequencing identified a wide spectrum (all known classes) of antibiotic-resistant genes. The top three commonest ARGs were multidrug resistance genes, beta lactam resistance genes, and aminoglycoside resistance genes among samples from QMH, and multidrug resistance genes, aminoglycoside resistance genes, and beta-lactam resistance genes among samples from SBPTW. Notably, a wide range of mobile colistin resistant genes 1 to 10 were found.

Culture experiments revealed that the most dominant two Enterobacteriaceae species were *Escherichia coli* and *Klebsiella pneumoniae.* Antibiotic susceptibility tests showed that more than half of Enterobacteriaceae isolates were resistant to at least one antimicrobial, among which *K pneumoniae* isolates were more resistant to antimicrobials than *E coli* isolates. Notably, a significant higher number of multidrug-resistant isolates of *E coli* and *K pneumoniae* were found in wastewater samples from QMH than from SBPTW. There were temporal variations on the drug resistance profiles for *E coli* and *K pneumoniae* isolates in terms of sites and dates.

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Liquid chromatography–tandem mass spectrometry analysis showed that samples from the clinical blocks of QMH contained higher levels of antimicrobial residues (amoxicillin, ampicillin, cefuroxime, metronidazole, sulfamethoxazole, trimethoprim, and vancomycin) than those from the SBPTW. The overall antibiotic usage in QMH was associated with sewage resistance profiles in some sampling sites. For instance, the abundance of fluoroquinolone resistance genes was associated with the fluoroquinolone weekly usage; the residue of sulphonamide antibiotics was strongly associated with the sulphonamide ARGs. Abundance of a number of ARGs was positively associated with the temperature of water samples.

In conclusion, there was a great diversity of multidrug-resistant Enterobacteriaceae and different types of ARGs (such as mobile colistin resistant genes 1 to 10) in the sewage of QMH and SBPTW. There appeared to be a contamination pathway from QMH sewage to the environment, as relatively higher resistome similarity was noted between a discharge site in QMH and the influent in SBPTW. Long-term surveillance of antibiotic use through hospital sewage and treatment plant samples can be used to track the resistance emergence and spread.

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