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Antimicrobial resistance and gender

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According to the WHO, antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi, and parasites no longer respond to the most effective antimicrobials.[1] AMR has been identified as one of the most important threats to human health and life.

In 2019, bacterial AMR caused around 5 million deaths associated with resistance, and it is estimated that this number could rise to 10 million per year by 2050.[1] In the European Union and the European economic area alone, approximately 33,000 people die each year due to infections caused by antibiotic-resistant bacteria. The cost of AMR is very high, varying from country to country: in Europe, it is around 9 billion euros per year, and in the USA, it exceeds 20 billion dollars.[2]

The drivers of AMR are numerous; the main ones include the overuse or misuse of antimicrobials, lack of adequate water, sanitation, and hygiene (WASH) facilities, as well as various factors such as living and working conditions, access to healthcare and vaccination programs, geography, race, ethnicity, level of education, religion, migration status, and gender identity.[3]

However, when focusing on AMR and gender, despite the clear interconnections between antimicrobial use (especially antibiotics) and gender, this topic remains underexplored in the current literature.[3,4] Moreover, the most important epidemiological studies on the global burden of bacterial AMR do not even report data disaggregated by sex.[1]

To our knowledge, one of the few papers presenting data on AMR disaggregated by sex was published in *The Lancet Regional Health-Western Pacific* in February 2024. This was a systematic analysis of AMR in China, reporting 1.3 million infection-related deaths, with more than 600,000 clearly associated with AMR in 2019.[5] Males were 1.5 times more affected than females.[5] These differences are consistent with previously published data, which show that not only are males more susceptible to infections than females, but they also have a higher mortality rate.[6] The higher male mortality is generally due to infections caused by bacteria, fungi, viruses, and parasites that are resistant to antimicrobials.

There is substantial evidence that the greater susceptibility, prevalence, and severity of infections in males are due to both weaker innate and adaptive immunity.[7] On the other hand, the stronger immune response in females contributes to a different behavioral pattern in infections, such as a higher prevalence of autoimmune diseases and a lower incidence of many tumors.[7]

Gender inequalities, especially in low- and middle-income countries, have significant consequences for AMR. In these regions, women, due to ancient socio-cultural norms, often have lower levels of education and face greater challenges in accessing adequate WASH facilities, particularly during pregnancy, childbirth, or abortion. They also have reduced access to financial resources, low participation in the workforce, and limited access to health information, including infection screening.[4]

Poverty also compromises women's health by limiting their decision-making power within the household, reducing their access to healthcare facilities. For example, in Tanzania, treatment for male children is often prioritized over that of girls, and in Afghanistan, women are not allowed to be examined by male doctors.[4]

Poor women have greater exposure to AMR due to their responsibilities in cooking, animal care, and caring for children and the elderly. In agricultural and husbandry settings, they are often forced to take on servile or low-paying jobs, which can increase their contact with animals carrying drug-resistant organisms (DRO).[8] However, this risk is not limited to low-income countries; it can also occur in high-income countries like the Netherlands, the UK, and the USA, where women work as farmers and are involved in poultry farming.[4]

Another high-risk occupation for exposure to DRO is work in healthcare settings. Women, in fact, make up the majority of employed staff in hospitals and other healthcare facilities, not only as nurses or physicians but also as cleaners and receptionists. It is well known that inadequate sterilization or hygiene practices (such as lack of gloves, soap, disinfectants, water facilities, and a contaminated environment) can put them at risk of infection by DRO.[4]

Continuing to review the main drivers of AMR and their relationship with gender, it is important to emphasize the role of the abuse, overuse, and misuse of antibiotics. In high-income countries, women are 27% more likely to receive antibiotic prescriptions compared to

men. In a meta-analysis conducted by Schöder and colleagues on several European countries, the amount of antibiotics prescribed to women was 36-40% greater than that prescribed to men in the age group of 16 to 54 years.[9]

Some authors have investigated the reasons for the gender gap in antibiotic prescribing. The most reliable publication on this topic is by Smith and collaborators, who examined more than 4 million prescriptions from English primary care, disaggregated by sex and type of infection. Their conclusion was that the gender gap can largely be explained by consultation behavior, which is significantly higher for women.[10]

Gender can also influence the prescribing behavior of general practitioners: female doctors prescribe fewer antibiotics, especially to female patients, compared to male doctors.[11]

Switching from primary care to hospital wards, several studies have described a positive association between male gender and infections caused by drug-resistant bacteria.[5-7,12]

One of the most interesting papers was recently published by a group of researchers in Germany. It reported on all national notifications of invasive infections and colonizations with methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant *Acinetobacter* spp. (CRA), and *Enterobacterales* (CRE) over a period of 10 years (2010-2019).[12]

They found a significant difference in the incidence rates of infections between the two sexes. Male patients experienced approximately double the rate of infections with CRA and CRE, and more than three times the rate of MRSA compared to females.[12]

The causes of these differences between the two sexes can be attributed to several factors: biological differences (such as immunity and hormones), antibiotic prescribing practices, poorer male compliance with hand hygiene, higher alcohol consumption, and greater hospitalization rates, especially among older men.[12]

In conclusion, we can summarize the data and reflections on antimicrobial resistance and gender presented in this editorial with the following statements:[13, 14]

- Research and literature on AMR and gender are very limited. Data on AMR are not generally disaggregated by sex, and even less so by other social constructs related to gender.
- The lack of research and data on this topic is more pronounced in low- and middle-income countries compared to high-income countries, exacerbating gender inequalities among impoverished populations.
- There are significant differences between the sexes in the risk of acquiring infections, including drug-resistant diseases. Men experience more severe infections and have a higher risk of death from AMR.
- A gender-focused approach to AMR is necessary to advance gender equality and promote more effective solutions to reduce the incidence, severity, and mortality of infections caused by resistant microorganisms.

References

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399:629-55.
2. Dadgostar P. Antimicrobial resistance: implications and costs. Infect Drug Resist. 2019;12:3903-10.
3. Charani E. Navigating socio-cultural disparities in relation to infection and antibiotic resistance: the need for an intersectional approach. JAC Antimicrob Resist. 2021;3(4):1-7.
4. WHO. Tackling antimicrobial resistance together. Working paper 5.0. Enhancing the focus on gender and equity.2018.
5. Zhang C. Burden of infectious diseases and bacterial antimicrobial resistance in China: a systematic analysis for the global burden of disease study 2019. Lancet Reg Health West Pac. 2023;43:100972.
6. Vom Steeg LG, Klein SL. SeXX matters in infectious disease pathogenesis. PLoS Pathogen. 2016;12(2):e1005374.
7. Klein SL, Flanagan KL. Sex differences in immune responses. Nature Rev. 2016; 16:626-38.
8. Depshikha B, Shristi G [Internet]. Antimicrobial resistance and gender. Available from: https://cddep.org/posts/antimicrobial-resistance-and-gender/.
9. Schröder W, Sommer H, Gladstone BP, Foschi F, Hellman J, Evengard B, Tacconelli E. Gender differences in antibiotic prescribing in the community: a systematic review and meta-analysis. J Antimicrob Chemother. 2016;71(7):1800-6.
10. Smith DRM, Dolk FCK, Smieszek T, Robotham JV, Pouwels KB. Understanding the gender gap in antibiotic prescribing: a cross-sectional analysis of English primary care. BMJ Open. 2018;8(2):e020203.
11. Eggermont D, Smit MAM, Kwestroo GA, Verheij RA, Hek K, Kunst AE. The influence of gender concordance between general practitioner and patient on antibiotic prescribing for sore throat symptoms: a retrospective study. BMC Fam Pract. 2018;19(1):175-83.
12. Brandl M, Hoffmann A, Willrich N, Reuss A, Reichert F, Walter J, Eckmanns T, Haller S. Bugs that can resist antibiotics but not men: gender-specific differences in notified infections and colonisations in Germany, 2010-2019. Microorganisms. 2021;9(5):894-904.
13. Gautron JMC, Tu Thanh G, Barasa V, Voltolina G. Using intersectionality to study gender and antimicrobial resistance in low- and middle-income countries. Health Policy Plan. 2023;38(9):1017-1032.
14. Lynch I, Fluks L, Manderson L, Isaacs N, Essop R, Praphasawat R, Middleton L, Naemiratch B. Gender and equity considerations in AMR research: a systematic scoping review. Monash Bioeth Rev. 2024 Apr 27.