Drug-Pathogen Concordance and its Association to Mortality in Hospitalized Patients with Enterobacteriaceae Bloodstream Infections

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Abstract

Background: Antibiotics are the mainstay of treatment in patients with bacteraemia. Drug-pathogen concordance and its impact on mortality in Africa has not been extensively studied.

Objective: We sought to describe the concept of drug-pathogen concordance and determine if there was an association with mortality in patients with *Enterobacteriaceae bacteraemia* in the African context.

Methods: We analyzed data from MBIRA - a prospective cohort study conducted between 2020 and 2022 in hospitalized patients with *Enterobacteriaceae bacteraemia* in eight African countries. Antibiotic concordance was defined as administration of a drug with *in vitro* susceptibility, at the correct dose and route. Exposure of interest was empiric antibiotic concordance, 30-day mortality was the outcome. We used logistic regression for crude and adjusted effects and tested the final model for interaction by country income status. We used McNemar's test to determine the difference in concordance between the empiric and definitive window.

Results: There was a total of 878 patients of all ages with *Enterobacteriaceae bactraemia*, of these, 787 (90%) received antibiotics in the empiric window. Antibiotic concordance in the empiric window was 44.3% (349/787), with less concordance in the empiric than the definitive window (difference -0.12 (95%CI: -1.15, -0.088: p<0.0001)). Before adjustment, there was suggestion of benefit among those that received concordant antibiotics (OR:0.80 (95%CI:0.59,1.08, p=0.14)). After adjustment, there was still no evidence of a difference in mortality between the two groups (aOR:1.05(95%CI:0.71,1.56; p=0.907). Strikingly, there was effect modification by country income (aOR:0.18 95% (0.05,0.66: p=0.009)) at the hospital in the upper-middle income setting, 1.20 (95%CI: 0.74,1.95: p=0.461 and (aOR:1.44;95% CI(0.67,3.07:p=0.348)) in the lower-middle/low income settings respectively.

Conclusion: Further studies considering confounders unique to the African context are needed to further unpack the relationship between empiric antibiotic concordance and mortality. Health leaders must consider factors beyond antibiotic use, in approaches to minimizing mortality associated with bacteraemia in African hospitals.

Public implication: As Anti-Microbial Stewardship programs (AMS) scale-up in resource-limited settings in sub Saharan Africa (SSA), they should consider the broader context of the role of antibiotics in reducing mortality for patients with bacteraemia. It may be worthwhile for researchers and policymakers to emphasize a holistic patient care approach in addition to AMR and antibiotics for patients with bacteraemia in these settings.

Key words: Drug-pathogen concordance, Association to mortality, Enterobacteriaceae bloodstream infections