

Invasive Salmonellosis in HIV-uninfected Patients in South Africa 2003-2013

Karen H. Keddy^{1,2}, Prasha Mahabeer^{3,4}, Vindana Chibabhai^{2,5}, Arvinda Sooka¹

¹Centre for Enteric Diseases (CED), National Institute for Communicable Diseases; ²Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; ³National Health Laboratory Service, King Edward VIII Hospital, Durban South Africa; ⁴Faculty of Health Sciences, University of the Kwazulu-Natal, Durban, South Africa; ⁵National Health Laboratory Service, Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa

Background: HIV-associated invasive nontyphoidal *Salmonella* (iNTS) infection has responded to antiretroviral programmes in South Africa. HIV-uninfected patients can acquire infection in association with predisposing immunosuppressive conditions. This study aimed to define risk factors for mortality in HIV-uninfected patients, to improve patient management.

Methods: *Salmonella* isolates received from diagnostic laboratories around South Africa were serotyped in CED and antimicrobial susceptibility testing done. Data including basic demographic information, HIV status, outcome and other risk factors was collected at selected sites.

Results: Between 2003 and 2013, we identified 8617 iNTS cases; HIV status was known for 3285 (38.1%): 615 (18.7%) were HIV-uninfected. Incidence rates per 100,000 population increased from 2003 (22 cases [0.06/100,000]) to 2013 (98 cases [0.21/100,000]) (incidence rate ratio [IRR] 1.11, 95% confidence interval (CI)=1.09-1.14, P<0.001). Males numbered 318/615 (51.7%). Ages were available for 613/615 (99.7%): <5 years: 375 (61.2%); 5-14 years: 29 (4.7%); 15-24 years: 27 (4.4%); 25-54 years: 135 (22.0%); ≥55 years: 47 (7.7%). Risk factors were identified in 308 (50.1%) patients: including malignancy (32/308; 10.4%) and protein energy malnutrition (children) (64/376; 17.0%). Two (0.6%) patients had malaria. Outcome was known for 602 (97.9%) patients: 96 (15.6%) died. On univariate analysis, mortality was associated with age ≥55 years (Odds Ratio [OR]=6.6; 95 % CI=3.4-12.8; P<0.001), severity of illness (OR=4.8; 95% CI=1.8-12.3; P=0.001), nosocomial infection (OR=1.7; 95% CI=1.0-3.2.8; p=0.05) and comorbidity (OR=2.6; 95% CI=1.6-4.2; P<0.001). *Salmonella* serotype and multidrug resistance were not contributory. On multivariate analysis, mortality was associated with age ≥55 years (adjusted OR [AOR]=5.5; 95% CI=2.5-12.4-12.9; p<0.001) severity of illness (AOR=4.7; 95% CI=1.7-12.8; p=0.003) and comorbidity (AOR=2.3; 95% CI=1.3-4.1; p=0.006).

Conclusions: Mortality due to iNTS in HIV-uninfected patients in South Africa is primarily associated with older age and disease severity. Reasons for increasing incidence rates remain undefined but may be associated with increasing poverty and food security issues.