

Comprehensive summary

Background: Antimicrobial resistance (AMR) is a global public health challenge since infection with resistant organisms may cause death, can spread across the community, and increase health care costs at individual, community and government level as more expensive antimicrobials will have to be made available for the treatment of infections caused by resistant bacteria. This calls for urgent and consolidated efforts in order to effectively curb this growing crisis, to prevent the world from slipping back to the pre-antibiotic era. The World Health Organization made a call in 2011 advocating for strengthening of surveillance and laboratory capacity as one-way of detecting and monitoring trends and patterns of emerging AMR. Knowledge of AMR guides clinical decisions regarding choice of antimicrobial therapy, during an episode of bacteraemia and forms the basis of key strategies in containing the spread of resistant bacteria. The current study focused on *Staphylococcus aureus* (SA), *Klebsiella pneumoniae* (KP), and *Pseudomonas aeruginosa* (PA), as they are common hospital acquired infections which are prone to developing resistance to multiple antibiotics.

Aim: The aim of this project was to assess and utilize the laboratory information system (LIS) at the National Health Laboratory Services (NHLS), as a tool for reporting AMR and monitoring resistance patterns and trends over time of clinical isolates of SA, KP and PA, cultured from the blood of patients admitted to seven tertiary public hospitals in three provinces in South Africa.

Methods: A retrospective and prospective analysis was done on isolates of SA, KP, PA from blood specimens collected from patients with bacteraemia and submitted to diagnostic microbiology laboratories of the NHLS at seven tertiary public hospitals in three provinces in

South Africa. These hospitals comprised the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Chris Hani Baragwanath Hospital (CBH), Helen Joseph Hospital (HJH), Steve Biko Pretoria Academic Hospital (SBPAH), Grootte Schuur Hospital (GSH), Tygerberg Hospital (TH) and the Universitas Hospital of the Free State (UH). For retrospective analysis, data submitted during the period July 2005 to December 2009 were used and for prospective analysis, data relating to AMR in SA, KP, PA, collected by the Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa, (GERMS-SA) from July 2010 to June 2011 were used. AMR in these three pathogens to commonly used antimicrobial drugs was systematically investigated. Multivariate logistic regressions models were used to assess factors associated with AMR. In addition, a systematic review of research done to date on AMR in bacterial pathogens commonly associated with hospital-acquired infections was conducted in order to understand the existing antimicrobial surveillance systems and baseline resistance patterns in South Africa.

Results: A total of 9969 isolates were reported from the retrospective dataset. These were 3942 (39.5%) SA, 4466 (44.8%) KP and 1561 (15.7%) PA. From the prospective dataset, a total of 3026 isolates were reported, 1494 (49.4%) SA and 1532 (50.6%) KP isolates respectively. The proportion of invasive bacteraemia was higher in the <5 year old children. Nearly all strains of SA in South Africa were resistant to penicillin, and >30% up to as high as 80% were resistant to methicillin-related drugs among ~560 invasive SA isolates over the two year period. Methicillin resistant *Staphylococcus aureus* (MRSA) rates significantly differed between hospitals ($p < 0.001$). The proportion of MRSA isolates in relation to methicillin-susceptible strains showed a declining trend from 22.2% in 2005 to 10.5% in 2009 ($p = 0.042$). Emerging resistance was observed for vancomycin: 1 isolate was identified in 2006 and 9 isolates between July 2010-June 2011, and all except 1 were from Gauteng hospitals. The study found increasing rates of

carbapenem-resistant KP of 0.4% in 2005 to 4.0% in 2011 for imipenem. The mean rate of extended spectrum beta lactamase (ESBL-KP) producing KP was 74.2%, with the lowest rate of 62.4% in SBPAH and the highest rate of 81.3% in UH, showing a significant geographical variation in rates of resistance ($p=0.021$). PA showed a tendency for multi-drug resistance with resistance rates of >20% to extended spectrum cephalosporins, fluoroquinolones and aminoglycosides respectively. Emerging resistance in PA isolates was observed to colistin, showing a resistance rate of 1.9% over the 5 years period. In the multivariate model, age <5 years, male gender, and hospital location were factors significantly associated with MRSA, while ESBL-KP was significantly associated with age <5 years and hospital location.

Concluding remarks: The study has clearly demonstrated that AMR is relatively common in South Africa among children <5 years. Enhancement of continued surveillance of nosocomial infections through use of routine laboratory data should be reinforced as this will facilitate effective interpretation and mapping of trends and patterns of AMR. Therefore, the LIS as a tool for gathering such data should be strengthened to provide reliable AMR data for improved understanding of the extent of the AMR, and present evidence on which future policies and practices aimed at containing AMR could be based.

Key words: Laboratory information system, Trends, Patterns, Antimicrobial resistance, Bacterial pathogens, Nosocomial infections, Surveillance, Bacteraemia, Blood culture.