International Journal of Infectious Diseases 30 (2015) 41–48

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Staphylococcus aureus bacteraemia in Gauteng academic hospitals, South Africa

Melony C. Fortuin-de Smidt [a], Ashika Singh-Moodley [a,b], Rubeina Badat [a], Vanessa Quan [a], Ranmini Kularatne [b,c], Trusha Nana [b,c], Ruth Lekalakala [d], Nelesh P. Govender [a,b], Olga Perovic [a,b,*] for GERMS-SA

[a] *National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service (NHLS), Centre for Opportunistic, Tropical and Hospital Infections, Private Bag X4, Sandringham, 2132, Gauteng, South Africa*
[b] *Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*
[c] *National Health Laboratory Service, Johannesburg, South Africa*
[d] *Department of Medical Microbiology, Faculty of Health Sciences, University of Pretoria and Tshwane Academic Division, National Health Laboratory Service, Gauteng, South Africa*

ARTICLE INFO

Article history:
Received 15 July 2014
Received in revised form 24 October 2014
Accepted 25 October 2014

Keywords:
Staphylococcus aureus
Bacteraemia
Methicillin-resistant
HIV infection
Mortality

SUMMARY

Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are responsible for longer hospital stays, increased hospital costs, and poorer outcomes compared to methicillin-sensitive *S. aureus* (MSSA) infections. We aimed to describe the epidemiology of *S. aureus* bacteraemia (SAB) and to determine factors associated with MRSA infection in South Africa.

Methods: Cases of SAB were reported from September 2012 to September 2013 from three sentinel sites. A case was defined as the isolation of *S. aureus* from a blood culture during a 21-day period. Detailed clinical information was collected. Multivariable logistic regression was done to determine factors associated with MRSA infection and mortality.

Results: There were 442 cases of SAB reported; antimicrobial susceptibility testing was performed on 240 isolates (54%). Thirty-six percent (86/240) of cases had an MRSA infection. A longer hospital stay before positive specimen collection (odds ratio (OR) 1.08, 95% confidence interval (CI) 1.02–1.13, $p = 0.004$), hospitalization in the last year (OR 15.7, 95% CI 2.5–99.5, $p = 0.003$), HIV infection (OR 4.9, 95% CI 1.05–22.90, $p = 0.044$), and antibiotic use in the previous 2 months (OR 0.1, 95% CI 0.01–0.68, $p = 0.022$) were independent predictors of MRSA. Older age, and in particular age 25–44 years (OR 22.2, 95% CI 2.7–185.5, $p = 0.004$, compared to those aged < 5 years), was the only independent predictor of mortality amongst cases with SAB. MRSA isolates were non-susceptible to more antimicrobial agents compared to MSSA isolates.

Conclusions: HIV infection was an independent risk factor for MRSA infection. The selection of appropriate empirical antimicrobial treatment is essential in patients with MRSA infections because of non-susceptibility to many other antimicrobial classes.

1. Introduction

Staphylococcus aureus, a Gram-positive bacterium, can cause bacteraemia, amongst a variety of other clinical syndromes. Due to metastatic complications, *S. aureus* bacteraemia (SAB) is strongly associated with a higher mortality compared to other bacterial bloodstream infections.[1] In a Canadian study, the mortality rate of SAB was 4–6 deaths per 100 000 persons.[2] The incidence of SAB and methicillin-resistant *S. aureus* (MRSA) bacteraemia has increased in the USA[3] due to increases in the number of invasive surgeries, use of intravascular devices, and patients with immunodeficiencies.[4] However, in the UK, a decline has been seen in MRSA incidence.[5]

* Corresponding author. Tel.: +27 11 386 6278; fax: +27 11 555 0430.
E-mail address: olgap@nicd.ac.za (O. Perovic).

http://dx.doi.org/10.1016/j.ijid.2014.10.011

Few African studies focusing only on SAB have been documented. The prevalence of MRSA bacteraemia varies greatly between African countries, with prevalence as high as 52% in Egypt, 45% in Algeria, 44% in Botswana,[6] and 19% in Morocco.[7] Even in South Africa, the prevalence of MRSA bacteraemia varies depending on the geographical location and population studied.[8–11]

Numerous reports from various countries have shown that MRSA bacteraemia results in a higher mortality compared to methicillin-sensitive *S. aureus* (MSSA) bacteraemia.[12–16] Crude mortality rates for MRSA infection vary from 29%[15] to 63%.[13] Mortality rates vary depending on how mortality is defined, the study population, location, and medical practices. MRSA is also more likely to be resistant to multiple antimicrobial agents compared to MSSA[17] and increases the length of hospital stay and costs.[12] Therefore it is important to determine risk factors that are associated with MRSA infection to assist clinicians in reducing MRSA infections and choosing appropriate empirical therapy.

The aim of this study was to describe the epidemiology of SAB and to determine factors associated with MRSA infection at three sentinel sites in Gauteng Province, South Africa.

2. Methods

2.1. Setting

Enhanced surveillance of SAB was initiated in September 2012. Three public sector sentinel sites in South Africa were involved in the surveillance: Charlotte Maxeke Johannesburg Academic hospital (CMJAH), a 1088-bed tertiary institution, Steve Biko Academic (tertiary) and Tshwane (district) hospitals (SBAH/TSH) with 832 and 197 beds, respectively, and Helen Joseph Hospital (HJH), a tertiary hospital with 700 beds. All of these hospitals are associated with universities and serve an urban population. These hospitals provide care to patients in the city of Johannesburg (approximate population 4.5 million) and the city of Tshwane (approximate population 3 million).

2.2. Study design

A cross-sectional study was conducted from September 2012 to September 2013. Surveillance officers collected demographic and clinical information through an interview and/or medical record review on a standardized case report form (CRF). Data on the following predisposing conditions were collected: chronic lung disease, chronic renal disease, diabetes mellitus, cardiac disease, cerebrovascular disease, malignancies, immunotherapy, previous surgery, aplastic anaemia, organ transplant, prematurity, decubitus ulcer, dementia, and smoking. Informed consent was obtained. CRFs were sent to the National Institute for Communicable Diseases (NICD), Johannesburg where quality checking and data capture occurred. Audits were performed quarterly to ensure complete case ascertainment.

2.3. Case definitions

A case of bacteraemia was defined when *S. aureus* was isolated from a blood culture. A positive blood culture for *S. aureus* obtained ≥21 days after the first positive blood culture was considered a new case of *S. aureus*. For cases with viable isolates, a case was defined as MRSA or MSSA depending on whether the *S. aureus* isolate was non-susceptible (MRSA) or susceptible (MSSA) to oxacillin and/or cefoxitin. A case was defined as hospital-acquired bacteraemia if the first blood culture positive for *S. aureus* was collected ≥3 days after hospital admission. Infection was defined as community-associated if the first blood culture positive for *S. aureus* was collected <3 days after hospital admission and did not fall into the hospital-associated community-onset category. Hospital-associated community-onset infection was defined if the first blood culture for *S. aureus* was obtained <3 days after hospital admission and the patient was hospitalized in the 90 days before SAB and/or had received haemodialysis and/or was a resident in a long-term care facility or nursing home. Acute severe illness was defined as a Pitt bacteraemia score of >4.[18] Empirical treatment was defined as an antimicrobial agent started prior to or less than 3 days following specimen collection. Directed treatment was defined as any antimicrobial agent that was prescribed 3 days or more after a positive specimen was collected. Appropriate antimicrobial therapy was defined as the receipt of any antimicrobial agents to which the organism was susceptible. Inappropriate antimicrobial therapy was defined if the patient received no antimicrobial agents to which the organism was susceptible or if no antimicrobial therapy was received.

2.4. Laboratory methods

Sentinel site laboratories performed initial identification and antimicrobial susceptibility testing. *S. aureus* isolates were submitted on Dorset transport medium (Diagnostic Media Products, Sandringham, South Africa) together with a laboratory report form to the NICD. Vitek 2 (bioMérieux, Durham, NC, USA) was used to confirm the identity of the isolate. Susceptibility testing was done using the MicroScan Walkaway system (Siemens Healthcare Diagnostics Inc., West Sacramento, CA, USA) and Gram-positive minimum inhibitory concentration (MIC) panel type 33. Two different systems were used for identification and antimicrobial susceptibility testing to rationalize time and costs. MICs were interpreted using Clinical and Laboratory Standards Institute guidelines.[19] Isolates not identified as *S. aureus* were excluded.

DNA was extracted from purity plates using a crude boiling method. The isolates were re-suspended in Tris–ethylenediaminetetraacetic acid buffer and boiled at 95 °C for 25 min.

Amplification and detection of *mec*A and *nuc* genes was done by multiplex real-time PCR using the LightCycler 480 II instrument (Roche Diagnostics Ltd, Rotkreuz, Switzerland) and the LightCycler 480 Probes Master kit (Roche Diagnostics, IN, USA).[20] For SCC*mec* typing, MRSA isolates were typed by conventional multiplex PCR using the Qiagen Multiplex PCR kit (Qiagen, Hilden, Germany). The multiplex PCR included 10 loci. Therefore 10 primer sets were used. These were obtained from a previously published study.[20]

2.5. Ethics

Approval was obtained from the Human Research Ethics Committee (Medical) (HREC), University of Witwatersrand, Johannesburg (protocol number M120632) and from the individual facilities.

2.6. Statistical analysis

Data were extracted from Microsoft Access and analysed in Stata 12.0 (College Station, TX, USA). The average incidence of SAB for the study period was calculated for each hospital. The number of *S. aureus* cases for the study period was the numerator and the number of admissions for the same period was the denominator. Incidence was expressed as *S. aureus* cases per 1000 admissions. The incidence of SAB was calculated using all cases (audit cases included). The MRSA incidence was calculated using only the cases where isolates were submitted to NICD, since susceptibility information was not available for audit cases. A descriptive analysis was performed comparing factors between MRSA and MSSA cases. The Chi-square test and Mann–Whitney *U*-tests were performed on categorical and non-parametric continuous data, respectively. A *p*-value of <0.05 was deemed statistically significant.