Original Article

Methicillin-resistant *Staphylococcus aureus* in Zimbabwe

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Ghana Med J 2016; 50(2): 68-71 DOI: http://dx.doi.org/10.4314/gmj.v50i2.3

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Conflict of interest: None declared

SUMMARY

Introduction: The prevalence of Methicillin Resistant *Staphylococcus* aureus (MRSA) in Africa is sparsely documented. In Zimbabwe there is no routine patient or specimen screening for MRSA. The aim of this study was to document the presence and epidemiology of MRSA in Zimbabwe.

Method: The study was done in one private sector laboratory with a national network that serves both public and private hospitals. The sample population included in-patients and outpatients, all ages, both genders, all races and only one positive specimen per patient was counted. Specimens testing positive for *Staphylococcus* aureus in this laboratory were further tested for MRSA using cefoxitin, by standard laboratory procedures. Data was collected from 1st June 2013 to 31st May 2014.

Results: MRSA was positive in 30 of 407 [7.0%] cases of *Stapylococcus aureus* reported from the laboratory. All age groups were affected from neonates to geriatrics. All specimens had similar antibiotic susceptibility pattern. Resistance was high for most widely used drugs in Zimbabwe with high sensitivity to vancomycin, linezolid and teicoplanin.

Conclusion: Although there are no recent reports in the literature of the presence of MRSA in Zimbabwe, this study documented a 7.0% prevalence. Resistance to common antibiotics is high and antibiotic oversight is required to control the emergence of resistance to these few expensive drugs.

Funding: Study was supported by Department of Anaesthesia and Critical Care funds.

Keywords: Methicillin Resistant Staphylococcus aureus, Zimbabwe, antibiotic resistance, vancomycin, teicoplanin

INTRODUCTION

The prevalence of Methicillin Resistant *Staphylococcus* aureus (MRSA) in Africa is sparsely documented. In Southern Africa only South Africa has reliable data on MRSA documented over a long period of time.[1,2] Further to the north occasional studies have been done in West Africa.[3,4] The prevalence, antibiotic susceptibility and genotypes of MRSA in Europe and North America are well characterised due to surveillance.[5] In Zimbabwe there is no routine patient or specimen screening for MRSA. There are no local guidelines or protocols for the management of MRSA colonised or infected patients. Literature in Zimbabwe on MRSA in humans is not recent although there is literature on veterinary products (pork and chicken meats).[6] The aim of this study was to document the presence and epidemiology of MRSA in Zimbabwe.

Staphylococcus aureus is a Gram-positive coccus and is part of the normal flora in the nose of 10-30% of individuals. MRSA, is a type of *Staphylococcus* aureus that is resistant to the antibiotic methicillin and other drugs in this class like penicillin, oxacillin, amoxicillin. It was first described in the UK in 1961 following the introduction of the semi-synthetic methicillin in 1959 to treat penicillin-resistant *Staphylococcus* aureus . MRSA was commonly isolated in hospital adult patients with open wounds, and with medical devices such as indwellings catheters and renal dialysis patients. The prevalence of MRSA in the UK was 2.4% in 1975, and had risen to peaks of 29% in 1990 before declining to 19% in 2009.[7,8]

MRSA develops resistance in a number of ways, but key is the possession of an extra *mecA* gene. The *Staphylococcus aureus* coat is made of peptidoglycan held together in cross-link by peptide chains. Penicillin Binding Protein (PBP) is the peptidase that forms the cross-link chains.

In sensitive organisms this is inhibited by β-lactams, cross-links fail to form and bacterial wall breaks down

resulting in bacteriolysis. In resistant *Staphylococcus aureus* organisms, a different PBP is produced [PBP2A] whose affinity for β-lactams is altered while its peptidase activity is not.

This altered PBP is the result of a *mecA* gene which confers resistance by producing an alternative PBP when a β-lactam drug is present. The *mecA* gene is inserted into the MRSA chromosome. In addition, within the cytoplasm, a 'free floating generic element' is found which contains the same *mecA* gene and a variety of other genes for drug resistance and the ability to be integrated and excised from the chromosome (ccr). This is the SCC*mec* [Staphylococcal cassette *mec*]. There are MRSA Types I to VIII depending on the combination of *mec* and ccr genes.[7,9,10]

Table 1 Virulence factors for *Staphylococcus aureus*

Virulence factor	Function	Clinical picture
leukocidin, kinases, hyaluronidase	Promotes bacterial spread	Abscess, Cellulitis impetigo
capsule, Protein A	Inhibit phagocytic engulfment	Enables *S aureus* to form vegetation
Protein A, coagulase	Immunological disguises	Protects against host immune system and evades phagocytosis
carotenoids, catalase production	Enhance their survival in phagocytes	
***hemolysins, leukotoxins, leucocidins* [incl. Panton Valentine Leucocidin]**	Membrane-damaging toxins that lyse eukaryotic cell membranes of polymorphoneucleocytes [PMN]	haemolysis cell lysis
SEA-G (superantigen enterotoxin subtypes A-G),	exotoxins that damage host tissues or otherwise provoke symptoms of disease	Staphycoccal food poison
TSST (toxic shock syndrome toxin),		Toxic shock syndrome
ET (exfoliatin toxin)		Scalded-skin syndrome

It is believed that *Staphylococcus* aureus acquired the SCC*mec* from other microbes at several different times and into several different genetic types since antibiotics came into use. The current SCC*mec* Types are the evolutionary survivors under antibiotic pressure. Whereas the earliest MRSA developed in the hospital setting (HA-MRSA), methicillin sensitive *Staphylococcus* aureus (MSSA) in the community also acquired resistance. This became known as community acquired MRSA (CA-MRSA). Although the CA-MRSA remained sensitive to a wide range of antimicrobials, this has diminished over time, so that currently that difference is disappearing.[11,12]

At the same time *Staphylococcus* aureus, which causes mostly superficial abscesses and cellulitis, can cause serious illness when it becomes systemic.[Table 1] This can be facilitated by break in the skin, contact with mucous membranes and access to the blood stream. It has a variety of virulence factors responsible for the clinical picture:

METHODS

The study was done in one private sector laboratory with a national network that serves both public and private hospitals. Specimens testing positive for *Staphylococcus* aureus were tested for MRSA using cefoxitin.[13] The sample population included in-patients and outpatients, all ages, both genders, all races. Only one positive specimen per patient was counted where one patient has more than one sampling site [eg. Blood, urine, pus swab etc].

Staphylococcal aureus was recovered from clinical specimens (swabs, blood and urine) on McConkey and Blood agars incubated at 37^0C for 24 hours. The catalase test was used for positive cultures, then a Gram stain. For in vitro identification of *Staphylococcal* aureus and a latex agglutination test [Bio Rad Pastorex ™ Staph-Plus test] was performed. Standard laboratory procedures were used for the Kirby-Bauer disk susceptibility test. Cefoxitin (30µg) was used for MRSA testing. Antibiotic susceptibility was performed in Mueller-Hinton media and incubated for 18 to 24 hours at 37/35 degrees in the presence of antibiotic discs. For the glycopeptides (vancomycin 30µg and teicoplanin 30µg) susceptibility testing of *Staphylococcus* aureus by disc diffusion method was followed by a confirmatory test of Minimum Inhibitory Concentration using Etest® (bioMerieux, SA, France). The Etest® consists of a predefined gradient of antibiotic concentration on a plastic strip to determine the MIC of the applied antibiotic.[14, 15]

The following discs were used for susceptibility testing: Ampicillin (10µg), Erythromycin (15µg), Rifampicin (5µg), Cotrimoxazole (25µg), Clindamycin (2µg), Gentamycin (10µg), Mupirocin (5µg), Fusidic Acid (10µg), Telithromycin (15µg), Tetracycline (30µg), Linezolid (30µg). The control strain was Staph aureus ATCC 29213.

The Parirenyatwa and University of Zimbabwe College of Health Sciences Joint Research and Ethics Committee approved the study (JREC/136/13).

RESULTS

From June 1st 2013 to May 31st 2014, 407 cases of *Stapylococcus aureus* were reported from the laboratory, of these thirty cases [7.0%] were MRSA positive.

One patient was reported twice, but one month apart from different body sites. A second patient was also reported twice from separate hospital admissions. There were four paediatric patients. Two neonates were positive for MRSA, one from blood specimen and another from sputum in an endotracheal tube tip at extubation. The third was pus from a wound in a six year old child and the forth was pus but site and source not indicated. All specimens had similar antibiotic susceptibility tests. The MICs as reported for vancomycin and teicoplanin were between <1.0 µg and 2 µg. The oldest patient was 83 years old and youngest 13 days. The specimenswere pus (19), blood (4), sputum (4), intravenous catheter tip (1), surface swab (1) and semen (1).

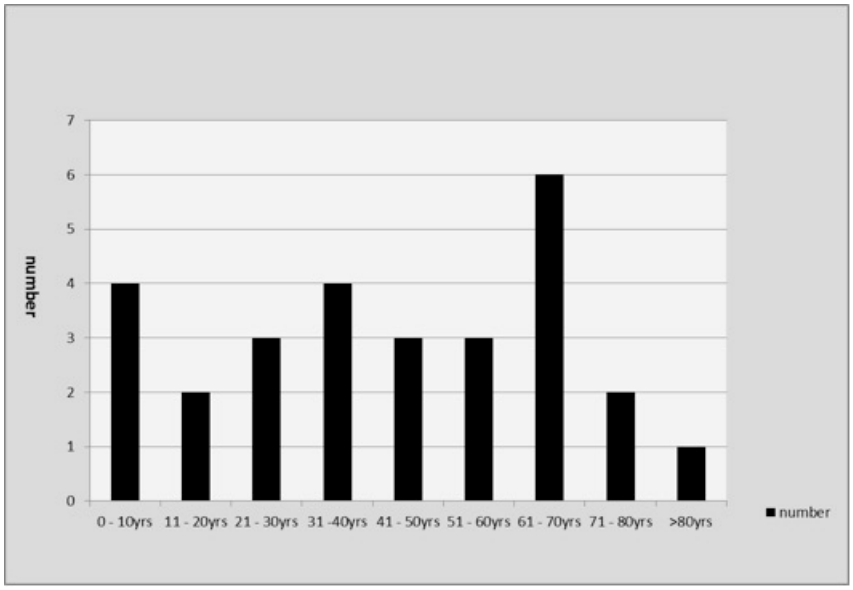

Figure 1 Age distribution of patients submitting specimens

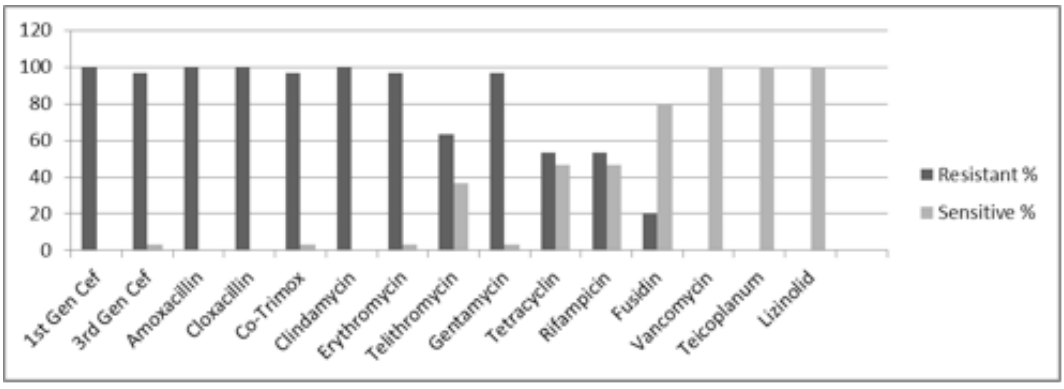

Figure 2 MRSA antibiogram: Percentage of specimens resistant or sensitive to antibiotic [n=30]

The antibiogram showed very mixed susceptibility pattern. The drugs for which there was susceptibility were the following, Tetracyline (T), Fusidine (F), Rifampicin (R), Vancomycin (V), Teicoplanin (Te), Telithromycin (Tt) and Linezolid. The commonest pattern was (TFRVTeL) at 13% followed by TFTtVTeL, FVTeL, VTeL at 10%. There is some susceptibility to telithromycin (35%), tetracyclines (46%), rifampicin (45%) and fusidin (80%) with 100% susceptibility to vancomycin, teicoplanin and linezolid.

DISCUSSION

MRSA appears to have a prevalence of 7% of *Staphylococcus aureus* cultures in this study. We could not find any recent report of MRSA prevalence or of clinical cases in Zimbabwe, the last report being in 1991, reflecting a possible lack of recognition of its presence.[16] MRSA infection occurred across all age groups. In addition the MRSA shows resistance to all commonly used antimicrobials in Zimbabwe, penicillins, cephalosporins and macrolides. This is particularly relevant for clinical areas such as Intensive Care Units and theatres. The

antibiogram patterns were diverse with the most common pattern representing only 13% of cases. A study in South Africa showed only slightly better at 18.5% but with better response to erythromycin, clindamycin and ciprofloxacin.[17]

This was a small study and a prevalence of 7% may not reflect institutional or geographic (national) prevalence. There is an urgent need for bigger study and establishment of surveillance system. The MRSA clones in this study or in the country are at present unknown and unpublished.

Rifampicin would not be a suitable drug to use because it is one of the major anti-tuberculosis drugs. Cost of drugs such as vancomycin, teicoplanum and linezolid is prohibitive in a very low income country such as Zimbabwe, and relying on treatment with ever costly drugs is not a solution. Prevention and infection control must be the first line measures. Antibiotic oversight is required in Zimbabwe to protect clinicians and patients from spread of drug resistance.

ACKNOWLEDGEMENT

Dr Charles Muronda, Ms Ilona Howard and staff at Lancet Laboratories in Harare, Zimbabwe for permission to use their laboratory. Dr Mnqabutho Dube for assisting with collection of results.

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