Zagazig J. Pharm. Sci., Dec, 2016 ISSN 1110-5089
Vol 25, Issue 2 pp 93- 97

Antimicrobial susceptibility of *Staphylococcus aureus* clinical isolates and prevalence of MRSA in ICUs of Mansoura University Hospitals

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ABSTRACT

The aim of the present study was to determine susceptibility pattern among *Staphylococcus aureus* clinical isolates from ICUs of Mansoura University Hospitals and to investigate the prevalence of MRSA in order to make continuous monitoring to the action of anti-staphylococcal drugs in Egypt and to initiate the treatment with the appropriate antibiotic to avoid failure of treatment due to resistance. A total of 100 clinical isolates were collected and identified as *Staphylococcus aureus* from blood samples of patients in ICUs of Mansoura University Hospitals. The isolates were tested for antimicrobial susceptibility against 18 different antibiotics by using disk diffusion method. Resistance rate for linezolide and vancomycin were 0%. The most effective antibiotic were clindamycin and sulphamethoxazole-trimethoprim their resistant rate were 25% and 19% respectively. Forty-five (45%) of isolates were methicillin resistant (MRSA). It is recommended by the health authority to limit the further increase of antimicrobial resistance among *Staphylococcus aureus* by declining the rational treatment regimen.

Key words : *Staphylococcus aureus*, susceptibility, disk diffusion method, antimicrobial

INTRODUCTION

Staphylococcus aureus is a major cause of bacteremia, and *S. aureus* bacteremia is associated with higher morbidity and mortality, compared with bacteremia caused by other pathogens. The burden of *S. aureus* bacteremia, particularly methicillin-resistant *S. aureus* (MRSA) bacteremia, in terms of cost and resource use is high **(Shorr and Lodise, 2006)**. The risk of infective endocarditis and of seeding to other metastatic foci increases the risk of mortality. The incidence of *S. aureus* bacteremia and its complications has increased sharply in recent years because of the increased frequency of invasive procedures, increased numbers of immunocompromised patients, and increased resistance of *S. aureus* strains to available antibiotics. This changing epidemiology of *S. aureus* bacteremia, in combination with the inherent virulence of the pathogen, is driving an urgent need for improved strategies and better antibiotics to prevent and treat *S. aureus* bacteremia and its complications **(Shorr and Lodise, 2006)**. Resistance of *S. aureus* strains to antibiotics has been increasing; thus, the ability of these pathogens to spread in both hospital and community settings has increased **(Haley *et al*., 1982)**.

Penicillin was produced in large quantities in the 1940s and many lives were saved. However, the success was short-lived. It was found that some strains of *S. aureus* quickly developed resistance to penicillin by producing ß-lactamase which could break down the penicillin molecule. A number of synthetic derivatives of penicillin, resistant to the ß-lactamases, were developed. Of these, methicillin became the standard treatment for *staphylococcus aureus*. In 1961, the first methicillin-resistant strain of *Staphylococcus aureus* was isolated in Europe. They were first reported in Australia in 1966 in the eastern states and in the United States in 1968. As well, other strains were identified that had a broad pattern of resistance, not only to methicillin, but also to the aminoglycosides and cephalosporins. In the 1970s only a small number of the Methicillin-resistant strains of *Staphylococcus aureus* were isolated (< 2%). However, in 1979, a survey in Victoria reported an increase in MRSA infections to 20-40% of all Staphylococcal isolates in six of the large teaching hospitals **(Lee and Bishop ,1997).** MRSA continues to be a major cause of serious infection to man, both in hospitals and in the community **(Shanson, 1981).** Until the early 1980s MRSA reports consisted of isolated cases, later in 1982 epidemic MRSA strains (EMRSA) were described as multi-resistant strains with special capacity to colonize patients and staff and cause widespread outbreaks. These epidemic

MRSA strains have subsequently spread to various parts of the world **(Pavillard *et al.*., 1982).**

The aim of the present study was to determine susceptibility pattern among *Staphylococcus aureus* clinical isolates from ICUs of Mansoura University Hospitals and to investigate the prevalence of MRSA isolates**.**

MATERIALS and METHODS:

One hundred isolates were collected from Mansoura University Hospitals, from blood samples of ICUs patients. Identified and verified by using the standered biochemical reactions according to **Collee *et al* (1996)**. All isolates were collected under approved ethical procedures. The susceptibility was determined by disk diffusion method according to **CLSI (2006)** on Muller-Hinton agar (Oxoid UK). The susceptibility against the clinical isolates testing was performed against 18 antimicrobial agents belonging to different groups: penicillin (10µg), ampicillin (10µg), cephazolin (30 µg), cefuroxime (30 µg), ceftriaxone (30 µg), imipenem (10 µg), vancomycin (30 µg), linezolid (30 µg), chloramphenicol (30 µg), sulphamethoxazole/trimethoprim (1.25/23.75µg), cefoxitin (30 µg), oxacillin (1 µg), clindamycin (2 µg), ciprofloxacin (5 µg), azithromycin (15 µg), tetracycline (30 µg), gentamicin (10 µg), amoxiclave (20/10 µg). The antibiotic disks were purchased from Oxoid, Hampshire, England.

RESULTS:

Forty-five (45%) of the *Staphylococcus* isolates are methicillin resistant (MRSA), while 55 isolates are methicillin sensitive (MSSA). The frequency of antibiotic resistant isolates among MRSA and MSSA isolates is represented in **Table (1).** The antibiogram typing of MRSA distinguished the isolates into 9 types and presented in **Table (2).**

DISCUSSION

The resistance of MRSA to a wide range of antimicrobials is well documented. The antibiotic sensitivity results showed that all MRSA isolates were significantly more resistant to antibiotics than MSSA isolates. The resistance of MRSA to β lactams like penicillin and ampicillin was 100% in present study. Similar findings were reported in previous studies by **Gupto *et al*. (1999); Anupurba *et al*. (2003); Choudhary (1999) and Shehab El din *et al*. (2003)**.

Resistance of MRSA isolates to gentamycin was 95.6%, comparable with 98.9% reported by **Anvikar *et al*. (2003)**. Low level of resistance (58.3%) was observed by **Shehab El din *et al* (2003).** A high level of ciprofloxacin resistance has emerged very rapidly after its introduction into general use. The resistance rate of MRSA isolates in the present study was 82.2 % consistent with that reported by **Hanumanthappa *et al*. (2003).** A high resistance rate of 95.8% was observed by **Pulimood *et al* (1996)** and **Udaya Shankar *et al* (1997),** while **Shehab El din *et al*. (2003)** reported lower level of resistance (33.3%).

For many years, Macrolides have been used as alternative to penicillin and cephalosporin in the treatment of infection caused by Gram positive bacteria, but the development of macrolide resistance has now limited the use of these antibiotics. In the present study, 91.1% of MRSA isolates were resistant to azithromycin . Similar resistance rate was observed in studies of **Anvikar *et al* (1999)** and **Gupta *et al* (1999).** About 53 % of MRSA isolates in the present study were resistant to clindamycin. A low percentage of resistance (30%) was reported by **Thouverez *et al.* (2003).**

Linezolid has shown 100% efficacy against MRSA in the present study. Similar consistent activity of linezolid against MRSA has also been reported by **Stevens *et al.* (2000).** However Linezolid resistance in MRSA has been reported by **Tsiodras *et al.* (2001)**. As linezolid's antibacterial activity is comparable with that of vancomycin in the present study, Linezolid can be used as alternative to vancomycin in treating MRSA infection.

Table (1): The frequency of antibiotic resistant isolates among MRSA and MSSA isolates.

Antibiotics	Total *S. aureus* (n = 100)		MRSA (n= 45)		MSSA (n= 55)	
	No	%	No	%	No	%
Penicillin	86	86 %	45	100	41	74.5
Ampicillin	86	86 %	45	100	41	74.5
Amoxiclave	42	42 %	42	93.3	0	0
Oxacillin	45	45 %	45	100	0	0
Cefoxitin	45	45 %	45	100	0	0
Cephazoline	45	45 %	44	97.8	1	1.8
Cefuroxime	45	45 %	45	100	0	0
Ceftriaxone	45	45 %	45	100	0	0
imipenem	37	37%	37	81.8	0	0
Azithromycin	44	44 %	41	91.1	3	5.5
Clindamycin	25	25 %	24	53.3	1	1.8
Gentamycin	47	47 %	43	95.6	4	7.3
Ciprofloxacin	39	39 %	37	82.2	2	2.9
Linzolide	0	0 %	0	0	0	0
Vancomycin	0	0 %	0	0	0	0
Tetracyclin	48	48 %	42	93.3	6	11
Chloramphenicol	19	19 %	13	28.9	6	11
sulphamethoxazole/ trimethoprim	22	22%	11	24.3	6	11

Table (2) The antibiogram typing of MRSA distinguished the isolates into 9 types

pattern	No. of antibiotic	Antibiotic resistant profile	Isolate No.
I	10	CIP,AZ,DA,AMC, T,C,SXT,IMP,CN,KZ	1, 2, 9, 10, 12, 16, 17,18, 27, 28,
IIa	9	CIP,AZ,DA,AMC,, T,C,IMP,CN,KZ	13,14
IIb		CIP,AZ,DA,AMC, T,C,SXT,IMP,KZ	30, 32
III	8	CIP,AZ,DA,AMC, T,C,CN,KZ	33,34,35,36,44,48,54,55, 62,63,64
IV	7	CIP,AZ ,AMC, T ,IMP,CN,KZ	69,70,78,79,80,81,82,83, 84,85
V	6	CIP,AZ, T,IMP,CN,KZ	66,67,68
VI	5	AZ,AMC, CN,KZ,T	90
VIIa	4	AMC, CN,KZ,T	86,87,88,89
VIIb		AZ,AMC, CN,KZ	91,92

Chloramphenicol resistance was found only in 28.9% of the isolates in this study. Low chloramphenicol resistance rate was also reported in previous studies. **Idrees *et al*. (2009)** found that the resistance rate of clinical MRSA isolates was 10%. In present study, tetracycline resistance was detected in 93.3% in MRSA. However **Randianirina *et al*. (2007)** found that 51.4% of clinical MRSA isolate were resistant to tetracycline. The infection rate of MRSA in the present study is 45% and this comparable with **El sherbini *et al*. (2013).**

In conclusion, results of the present study revealed the distributions of the resistance to various antistaphylococcal drugs among the staphylococcal isolates. Vancomycin and linezolide are still the best as antistaphylococcal drugs. Cephalosporins and azithromycin have good activity against the isolates . periodic monitoring of the antimicrobials has great importance in order to help the medical team to prescribe the optimal antistaphylococcal agents and rule out the ineffective ones from the regimen therapy as well as avoidance of emerging of multi-drug resistant strains of *S. aureus.*

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تعيين حساسية العزلات السريريه لميكروب المكورات العنقوديه ضد المضادات الحيويه بالعنايه المركزه بمستشفيات المنصوره

تهدف الدراسه الحاليه الى تقييم فاعلية المضادات الحيويه ومدى تطور المقاومه بين عزلات المكورات العنقوديه تجاه هذه الادويه. تم تجميع والتعرف على مائة عزله من المكورات العنقوديه من العنايه المركزه بمستشفيات جامعة المنصوره . تم عمل اختبار الحساسيه بطريقة الانتشار الاجاري للقرص ضد ثمانية غشره مضادات حيويه مختلفه.

اوضحت النتائج وجود مقاومه عاليه من عزلات المكورات العنقوديه تجاه كل من البنسيلين والامبيسيلين والسيفالوسبورين.بينما اظهرت النتائج فعاليه لكل من الفانكوميسين والليزوليد والكلورامفنيكول والسلفا ضد عزلات المكورات العنقوديه.كما اوصت الدراسه الحاليه بضرورة متابعة تطور المقاومه بين عزلات المكورات العنقوديه وذلك لتجنب خطورة عدم فاعلية الادويه ضد الامراض المسببه ببكتيريا المكورات العنقوديه