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Original Research Article

A comparative study of antibiotic profile of community acquired and hospital acquired isolates of staphylococcus aureus in a tertiary care hospital, Kashmir

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Abstract

Introduction: *Staphylococcus aureus* is a virulent pathogen in humans capable of surviving in the hospital environment as a saprophyte and in the human body as a normal commensal. It is a gram positive cocci which is capable of causing serious and life threatening infections like bacteremia and pneumonia with high morbidity and mortality. Presence in the blood increases its chances of metastasis and the risk of fatality. The choice of antibiotic therapy has conventionally relied to a large extent on the susceptibility of the pathogen to methicillin. In our study we intend to analyze the cases of different infections caused by *Staphylococcus aureus* both from the community and hospital environment with main focus on methicillin resistant strains.

Keywords: Methicillin resistant Staphylococcus aureus (MRSA), Methicillin susceptible Staphylococcus aureus (MSSA), Hospital acquired Methicillin resistant Staphylococcus aureus (HAMRSA), Community acquired Methicillin resistant Staphylococcus aureus (CAMRSA), Out-patient department (OPD), In-patient department (IPD).

Introduction

Staphylococcus aureus is the most important human pathogen among the Staphylococci. It has developed resistance against most of the therapeutic agents. Being a versatile human pathogen it causes infections ranging from a mild involvement of the skin and the soft tissue, to life-threating sepsis and pneumonia. The capability of this pathogenic gram positive cocci to produce numerous cell surface and secreted virulence factors as well as the propensity to develop resistance to multiple antibiotics leads to an increase in its propensity to cause systemic and invasive diseases. The ubiquity of these bacteria in nature makes the interpretation of their recovery from patient specimens occasionally difficult, unless the clinical manifestations of disease are apparent. *Staphylococcus aureus* may reside in approximately 20-40% of healthy adults in the anterior nares followed by the axillae, the vagina, the perineum and lower gut as other sites of colonization.[1]

Originally, penicillin was the drug of choice for the *Staphylococcus aureus* infections. Most of the penicillin-resistant strains of *Staphylococcus aureus* produce β lactamase, which hydrolyzes the β-lactam ring of the antibiotic. Soon after methicillin was introduced into the clinical use in 1961, resistance to methicillin and other β lactamase resistant penicillins was first observed in *Staphylococcus aureus*.[2] The first case of an MRSA infection recorded in Australia, was in Sydney in 1965.[3,4] The first case of a community associated MRSA (CAMRSA) infection in the United States was reported in 1980.

The HA-MRSA isolates do circulate in the community, especially among adults. Additionally, many reports have demonstrated that the MRSA clones bear Staphyloccocal Cassette Chromosome (mec type IV gene).

The CA-MRSA strains are genetically and phenotypically distinct from the HA-MRSA strains. They typically resemble some strains of methicillin-susceptible *S. aureus* (MSSA) in being susceptible to a wider range of anti-staphylococcal antibiotics (some are resistant only to β lactams), and they often produce panton valentine leucocidine (PVL), a toxin that destroys the white blood cells and is a staphylococcal virulence factor.[5,6]

Many of the MRSA isolates are becoming multidrug resistant and they are susceptible only to the glycopeptide antibiotics such as vancomycin. A low level resistance, even to vancomycin, is emerging. A prolonged hospital stay and the indiscriminate use of antibiotics before hospitalization are the common factors responsible for emergence of MRSA infections globally. These affected patients act as the root cause for the spread of the infections to the hospital staff who may act as carriers adding more complications to the treatment.

Aims and Objectives

1. To determine the incidence of occurrence of community acquired and hospital acquired *Staphylococcus aureus* infection.
2. To study the antibiotic sensitivity pattern of these infections.

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http://doi.org/10.18231/j.ijmmtd.2019.032

Materials and Methods

The present study was carried out in the department of Microbiology, in a tertiary care hospital in Srinagar for a period of two years (Jan 2017- Dec 2018).

The study material consisted of 573 non-repetitive isolates of *Staphylococcus aureus* which were obtained from various clinical samples of the out-patients and the in-patients treated in various clinical departments.

Methodology

1. All clinical samples were properly collected under strict aseptic precautions and appropriately delivered to the microbiology laboratory.
2. After an initial direct gram staining technique, all samples were inoculated on the routine laboratory media like nutrient agar, blood agar, MacConkey agar and chocolate agar following the standard microbiological techniques.[7]
3. Any growth obtained after overnight incubation at 37^{o}C was put to confirmation by various spot tests like catalase, coagulase and modified oxidase or biochemical tests and hemolytic pattern.[8]
4. Antibiotic sensitivity testing of the identified growth of *Staphylococcus aureus* was performed on Mueller Hinton agar media using the Kirby-Bauer disc diffusion technique according to clinical laboratory standards institute (CLSI) guidelines 2017.[9]
   The following antibiotics were tested for the isolates of gram positive cocci: Ampicillin (10µg), clindamycin (2µg), erythromycin (15µg), azithromycin (15µg), linezolid (30µg), vancomycin (30µg), teicoplanin (30µg), penicillin (10units), amoxicillin/clavulanic acid (20/10µg), amikacin (30µg), gentamycin (30µg), ciprofloxacin (5µg), ofloxacin (5µg), chloramphenicol (30µg), co-trimoxazole (25µg), cefoxitin (30µg), cefotaxime(30µg), and levofloxacin (5µg).
5. Culture plates with no growth obtained after 48 hours incubation were labeled as sterile. In case of blood samples, plates were re incubated till 72 hours and observed for any growth to be processed under steps 2-4. No growth obtained even after 72 hours was labeled as sterile.

Detection of methicillin resistant *Staphylococcus aureus*

The detection of MRSA was done phenotypically by using cefoxitin (30µg) disc. A zone of inhibition equal to or more than 21mm was considered as susceptible.

Categorization of *Staphylococcus aureus* isolates into hospital acquired and community acquired.

Based on the history of the patient, the MRSA isolates were categorized into Community acquired or Hospital acquired. An infection occurring among the in-patients with a *Staphylococcus aureus* isolate earlier than 48 hours of hospitalization or among out-patients is considered as community acquired, and that occurring after 48 hours of hospitalization or from a patient with a history of hospitalization for surgery or dialysis, intervention, or of an admission in day-care is considered as hospital acquired.

Results

A year-wise prevalence of *Staphylococcus aureus* infection was studied among various samples. Highest prevalence was observed among exudates during these two years whereas very low prevalence was observed among blood and urine samples. All blood samples with positive growth of *Staphylococcus aureus* were collected from IPD (Table 1).

Table 1: Prevalence of *Staphylococcus aureus* among hospital and community patients

Clinical sample	Year	Total number of samples	Culture positive samples	Total no. of *S.aureus* isolated	*S.aureus* isolated (IPD)	*S.aureus* isolated (OPD)	%age of *S.aureus* isolated
Exudates	2017	2180	502	201	78	123	40.03%
	2018	2300	519	313	101	212	60.30%
Blood	2017	1270	204	29	29	_	14.21%
	2018	1548	114	28	28	_	24.56%
Urine	2017	2172	443	4	2	2	0.90%
	2018	2340	509	5	2	3	0.98%
Total		11810	2291	580	240	340	

A higher percentage of MRSA was observed among OPD exudates during both the years. There was however no significant difference among MRSA and MSSA isolated from IPD exudates during the year 2018. However during the same year, percentage of MRSA isolated from blood samples was much higher compared to MSSA. Rate of isolation of *Staphylococcus aureus* was much lower among urine samples (Table 2).

Table 2: Year wise prevalence of Community and Hospital acquired MRSA and MSSA

Clinical sample	Year	MRSA OPD	MSSA OPD	MRSA IPD	MSSA IPD
Exudates	2017	71 (57.71%)	52 (42.27%)	48 (61.53%)	30 (38.46%)
	2018	148 (69.81%)	64 (30.I0%)	49 (48.51%)	52 (51.48%)
Blood	2017	-	-	16 (55.17%)	13 (44.82%)

	2018	-	-	17 (60.7%)	11(39.28%)
Urine	2017	1 (50%)	1 (50%)	2 (100%)	0
	2018	2 (66.6%)	1 (33.33%)	1 (50%)	1 (50%)
Total		222	118	133	107

A comparison of antibiotic sensitivity pattern among *Staphylococcus aureus* isolates from hospital and community revealed a higher resistance to most of the drugs among isolates from hospital samples. However, more isolates from community samples were resistant to drugs like penicillin, erythromycin and ciprofloxacin. The difference in sensitivity was however observed to be of less significance to most drugs except co-trimoxazole where 60% of the isolates from community samples were observed sensitive compared to 41.76% of sensitive isolates from hospitalized patients. Highest sensitivities were observed for teicoplanin, vancomycin and linezolid among isolates from both OPD and IPD (Table3).

Table 3: Antibiotic sensitivity pattern of Hospital acquired and community acquired *Staphylococcus aureus.*

Antibiotics	**Hospital acuired *Staphylococcus aureus* (Percentage sensitive)**	**Community acuired *Staphylococcus aureus* (Percentage sensitive)**
Penicillin	40 (16.6%)	42 (12.35%)
Cefoxitin	107 (44.59%)	118(34.71%)
Amoxyclav	129 (53.75%)	204 (60%)
Nitrofurantoin*	2 (50.00%)	3 (60%)
Erythromycin	190 (55.8%)	117 (48.75%)
Ciprofloxacin	163 (47.9%)	150 (44.11%)
Ofloxacin	163 (47.94%)	203 (59.70%)
Amikacin	271 (79.70%)	289 (85%)
Gentamicin	211 (62.05%)	240(70.5%)
Clindamycin	243(71.4%)	258 (75.88%)
Cotrimoxazole	142 (41.76%)	204 (60%)
Teicoplanin	239 (99.58%)	340 (100%)
Vancomycin	239 (99.58%)	340 (100%)
Linezolid	239 (99.58%)	340 (100%)

An overall higher percentage of *Staphylococcus aureus* isolates were cultured from exudates and blood samples collected from male patients. However among the urine samples, *Staphylococcus aureus* was isolated from 7 urine samples belonging to female patients in comparison to just 2 urine samples from male patients (Table 4).

Table 4: Gender wise prevalence of *Staphylococcus aureus* infection

Clinical sample	**Male**	**Female**	**Total**
Exudate	341(66.34%)	173(33.65%)	514
Blood	34(59.64%)	23(40.35%)	57
Urine	2(22.22%)	7(77.77%)	9
Total	377(65%)	203(35%)	580

Discussion

Among the gram-positive pathogens, *Staphylococcus aureus* is a common cause of skin and soft tissue infection in hospitalized as well as community-acquired infections.

Of the 580 total non-repetitive isolates of *S aureus* detected from January 2017 to December 2018, 234(40.34%) were isolated in 2017 and 346(59.65%) were isolated in 2018. Majority of the patients were referred from Dermatology department followed by departments of General surgery, Orthopedics, Gynaecology and Obstretics and Medicine. The prevalence of CAMRSA was found to be 346(62.53%) and that of HAMRSA was 234(37.46%). This is in concordance with a study made by D'Souza *et al* [10] in 2010 where prevalence of MRSA amongst the outpatient was 54% and study by Avneet Kaur *et al*[11] in 2017 where 49% prevalence rate was reported. This may partly be attributed to the fact that a large percentage (60%) of samples from skin and soft tissue infections were reported to be *Staphylococcus aureus* as in case of study by Sangeeta Joshi *et al*[12] and study by D'Souza *et al.*[10] CAMRSA is increasing, even in USA, where 50% or more of *Staphylococcus aureus* infections presenting to the emergency department may be methicillin resistant. These occur in otherwise healthy individuals with no recent healthcare contacts.[13] CAMRSA strains cause the same range of infections as HAMRSA strains and these may include blood stream infections (BSI), skin and soft tissue infections and severe pneumonia.[13] This could be partly attributed to the fact that the CAMRSA strains produced skin disease whereas HAMRSA are associated with risk factors including recent hospitalization or surgery.

In our study we observed that the percentage of males (65%) was significantly more than females (35%) and this number was 377 and 203 respectively. This was in contrast to study by Abbas *et al*[14] where no significant difference was found. A total of 355(61.20%) MRSA strains were detected from various clinical samples using cefoxitin disc diffusion technique. This is significantly higher than other studies in India by Mittal *et al* [15] (40.38%) and Mohanasoundaram *et al*[17] (39.16%) and Iran by Seifi *et al*[16] (41.7%). Different studies from India have reported the prevalence of MRSA ranging from 40-50% including studies by Patel *et al*[18] in 2010; Gopalakrishnan *et al*[19] and Arora S. *et al*[20] in 2010 and Sangeeta Joshi *et al*[12] in 2013.

Highest isolation of MRSA among different clinical samples was observed from pus samples (88.62%), followed by Blood (9.8%) and Urine (1.55%). This is in concordance with a study done by Tiwari *et al* which showed 71.20% MRSA from pus samples.[21]

The present study revealed that 99.58% of HAMRSA were sensitive to linezolid, vancomycin and teicoplanin. One isolate among the HAMRSA isolated from an orthopedic implant was found to be pan-drug resistant which is in contrast to study by Abbas *et al*[14] where 100% MRSA isolates were found to be sensitive to vancomycin, linezolid and teicoplanin. About 79.70% isolates of hospital acquired *Staphylococcus aureus* were sensitive to amikacin followed by clindamycin (71.4%), gentamycin (62.05%), erythromycin (55.8%), amoxiclav (53.75%), cefoxitin (44.59%) and cotrimoxazole (41.76%). Among the community acquired *Staphylococcus aureus*, 100% isolates were sensitive to vancomycin, linezolid and teicoplanin, 85% isolates were sensitive to amikacin followed by clindamycin (75.88%), gentamycin (70.5%), amoxiclav (60%), cotrimaxazole (60%) and cefoxitin (34.71%).

Conclusion

This study demonstrates that MRSA is a common cause of therapeutic problem in health care facilities. Injudicious use of over-the-counter antibiotics is the major cause behind this trend. The current challenging problem is the spread of MRSA among the community. There is a need to study epidemiology of such infections as this appears to be a changing trend. Robust antimicrobial stewardship, strengthened infection control measures most importantly hand hygiene practices are required to prevent spread and reduce emergence of resistance. Glycopeptides and linezolid continues to remain the mainstay for treatment for MRSA infections. However de-escalation of vancomycin to β lactams once the culture sensitivity results reveal a MSSA isolate should be encouraged. Cephalosporins are the drugs of choice for the treatment of MSSA infection. Amikacin, chloramphenicol, clindamycin and teicoplanin are to be kept as reserved drugs and drugs like vancomycin and linezolid which should be used for life-threatening infections.

Source of Funding

None.

Conflict of Interest

None.

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How to cite this article: Rashid A, Qayoom S, Kohli A, Masoodi T, Khursheed S. A comparative study of antibiotic profile of community acquired and hospital acquired isolates of staphylococcus aureus in a tertiary care hospital, Kashmir. *Int J Med Microbiol Trop Dis* 2019;5(3):145-9.