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2
3 **Endogenous methicillin resistant staphylococcus aureus as a**
4 **source of post operative surgical site infections**

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12
13 **Abstract**

14 **Objectives:** To determine frequency of Endogenous Methicillin Resistant
15 Staphylococcus aureus (MRSA) in pre operative patients and its frequency in
16 Surgical Site Infections (SSIs) Post operatively.

17 **Methods:** It was a descriptive cross sectional conducted at Department of
18 Microbiology, Fauji Foundation Hospital Rawalpindi (FFH), Pakistan. Samples
19 were collected from 1st November-31st May 2018. Total 75 samples were
20 collected during the period. Consecutive non-probability sampling technique
21 was utilized. Specimens were collected from nose, axilla and groin of
22 preoperative patients. Methicillin Resistant Staphylococcus aureus was
23 identified if only isolated from these sites. Patients were followed till his/her
24 discharge from the hospital and if they developed infection post operatively, pus
25 specimen from infected site was also collected and identified.

26 **Results:** Out of 75 specimen preoperatively, 14.7% (n=11) were identified as
27 endogenous MRSA. From these, 44% (n=33) developed Surgical site infections
28 (SSIs), among them 57% (n=19) were MRSA (09 endogenous, 10 exogenous),

29 21.2% (n=7) were *Escherichia coli*, 9.1% (n=3) were *Klebsiella pneumoniae*,
30 9.1% (n=3) were *Enterococcus faecalis* and 3% (n=1) was Methicillin Sensitive
31 *Staphylococcus aureus*.

32 **Conclusion:** The results of this study determined that Endogenous Methicillin
33 Resistant *Staphylococcus aureus* (MRSA) could be isolated from patients going
34 for surgery if microbiological screening was done at the time of admission. This
35 could prevent patients from Surgical Site Infection Post operatively by these
36 endogenous MRSA. This search and wipe out strategy is able to curtail the
37 events of outbreak, reduce hospital stay and decrease budget of the hospital by
38 providing guidance in choice of empirical therapy for infection.

39 **Keywords:** Endogenous MRSA, Surgical site infection, Surveillance,
40 Antibiotics resistance.

42 Introduction

43 *Staphylococcus aureus* is capable of establishing a broad spectrum of
44 interactions with human. It can be a part of the normal flora and cause a variety
45 of illnesses ranging from mild infections compromising skin, soft-tissues to
46 severe diseases such as necrotizing pneumonia, bacteremia, osteomyelitis, toxic
47 shock syndrome, urinary tract infections and surgical site infections (SSIs).¹

48 *Staphylococcus aureus* acquired resistance to many antimicrobial agents. The
49 first isolation of methicillin-resistant *S. aureus* (MRSA) was reported in 1960.²

50 Since then, the occurrence of MRSA in SSIs is increasing³ and accounts for
51 24.45% of SSI in general hospitals.¹ An increasing cases of SSIs produced by

52 MRSA acquired in the community have been reported. They were called as
53 community associated methicillin-resistant *S. aureus* (CA MRSA). These can be

54 prevented by antibiotic prophylaxis as bacteria implicated in SSIs include those,
55 which are conceded by patients themselves (endogenous flora), or those that

56 might be acquired in the operating room (exogenous flora), which are known as
57 hospital associated methicillin-resistant *S. aureus* (HA MRSA).⁴ Infection

58 caused by microorganisms from endogenous source is more common than an
59 external source following surgery.⁵ Recent studies have suggested that these
60 endogenous MRSA might be encroaching on hospital settings⁶ and significant
61 proportion of them are caused by the same strain that colonizes nasal mucosa.⁷
62 Epidemiologic and molecular typing methods exist for classifying CA MRSA
63 infections and HA MRSA. In addition, phenotypic methods (e.g., using
64 antibiotic susceptibility and biochemical testing) can be used to identify MRSA
65 strain type.⁸

66 Endogenous MRSA could be easily prevented by eliminating their carriage
67 through proper targeted screening and source control. This would not only
68 decrease burden of disease but also have a significant impact on hospital
69 budgets and patient's health, their diagnosis must be anticipated and therapy
70 improved. Therefore, the purpose of this study was to determine the frequency
71 of colonized MRSA in patient's different body areas like nose, axilla and
72 inguinal region pre operatively and post operative if they are isolated as a source
73 of wound infection.

74

75 **Methods**

76 The study was carried out at Department of Microbiology, FFH from 1st
77 November 2018 to 31st May 2019. After taking consent, a total of 75 swabs
78 were included in the study. Keeping the Confidence level 95%, anticipated
79 population proportion for MRSA in SSIs 0.25.¹ Sample size was calculated by
80 WHO calculator.⁹ The samples were taken from Nose, axilla and Inguinal area
81 of the patients who reported in outdoor clinics for admission for surgery in
82 different wards of FFH, Rawalpindi like Gynecology, General surgery, Urology
83 and Neurosurgery, and MRSA was identified if isolated from these sites. These
84 isolate were labeled and stored for further assessment. The patients were
85 followed till his/her discharge from the hospital and if patient developed
86 infection post operatively within his stay in the hospital, pus specimen from

87 infected site was collected and MRSA, if present, was identified. If MRSA was
88 identified preoperatively, both the isolates were assessed whether they are the
89 same strains. All duplicate samples, patients already on treatment or taken
90 antibiotics within last 48hour were excluded from study.

91 We applied phenotypic method to assess strain similarity, which included
92 extended antibiogram and extended biochemical tests. If both the strains were
93 found similar, then the source of post operative MRSA infection was labeled as
94 endogenous. Clinical samples were inoculated on Blood and MacConkey's agar
95 and incubated at 37°C for 18 to 24h. Staphylococcus aureus was identified by
96 its colony morphology, positive Gram reaction, positive catalase and coagulase
97 tests.¹⁰ Methicillin resistance of isolated Staphylococci was detected by agar
98 disk-diffusion method (Kirby-Bauer) using a 30µg cefoxitin disk, according to
99 the guidelines by Clinical and Laboratory Standards Institute guidelines
100 (CLSI).¹¹ According to CLSI, a zone diameter of ≤ 21 mm was taken as resistant
101 and a zone diameter of ≥ 22 mm, as susceptible. Susceptibility to other
102 antimicrobial agents was determined by the disk diffusion method in accordance
103 with CLSI. The other antibiotics tested included Penicillin 10µg, Ciprofloxacin
104 5µg, Doxycycline 30µg , Gentamicin 10µg, Rifampicin 5µg, Linezolid 30µg,
105 Chloramphenicol 300µg , Co-trimoxazole 25µg, Erythromycin 15µg, and
106 Clindamycin 2µg (Oxoid Ltd). E-strip was used to assess susceptibility of
107 vancomycin as recommended by CLSI. S. aureus strain ATCC 25913 was used
108 as quality control.

109 Data was analyzed using Statistical Package for Social Sciences version 22.
110 Descriptive analysis was done for qualitative and quantitative variables.
111 Frequency and percentages were calculated for qualitative variables like type of
112 wards, gender, growth positive and negative cultures of MRSA isolates, SSIs
113 and post operative MRSA. In-vitro efficacy of antibiotics was calculated as
114 frequency percentages of sensitive and resistant organisms. Mean and standard
115 deviation were calculated for quantitative variables like age of patients.

116 All ethical considerations and obligations were duly addressed and the study
117 was conducted after approval of ethical committee.

118

119 **Results**

120 Total 75 patients were included according to the inclusion criteria of the study.

121 Descriptive statistics of age (years) of patient was also calculated in terms of
122 mean and standard deviation. Mean age (years) in the study was 45.63 ± 17.81
123 with ranges from 18 to 75 years. Distribution of gender of patient was also
124 calculated in terms of frequency and percentage of male and female patients.
125 There were 40% (n=30) male and 60% (n=45) female patients who were
126 included in the study according to inclusion criteria.

127 There were 14.7% (n=11) cases of Endogenous MRSA in preoperative patients.

128 Out of 75 cases, there were 25.3% (n=19) cases of cultural growth positive of
129 MRSA postoperatively, which included 9 endogenous and 10 exogenous
130 MRSA. Whereas, frequencies of postoperative surgical site infections were
131 44% (n=33) cases out of 75, which included 57.6% (n=19) MRSA and 14 other
132 organisms like, 9.1% (n=3) Enterococcus, 21.2% (n=7) E.coli, 9.1% (n=3)
133 Klebsiella and 3% (n=1) Methicillin sensitive Staphylococcus aureus (MSSA).
134 (Table: 1)

135 Ward wise distribution of MRSA showed that Gynecology has the highest rate
136 of Surgical Sites Infections 18.1% (n=6) followed by orthopedics 15.1% (n=5)
137 & general surgery 12.1% (n=4) respectively. (Table: 2).

138 Susceptibility of Endogenous & Exogenous MRSA to various antibiotics is
139 shown in (Table: 3)

140

141 **Discussion**

142 MRSA has ability to cause widespread diseases which range from soft tissue
143 infection to more life threatening sepsis. Its remarkable resistance towards many
144 drugs and the deadly outcome of its infections has become a big problem.^{12, 13}

145 Surgical patients are at soaring threat of infection if they are colonized with
146 MRSA or if MRSA is inoculated into their surgical wound by unhygienic hands
147 or instruments.¹⁴

148 Mean age (years) in this study was 45.63 ± 17.81 with ranges from 18 to 75
149 years. A high proportion of patients in our study were observed from old age.
150 Garcia supported our results regarding higher susceptibility in old age and
151 recommended age as considerable factor in antibiotic selection.¹⁵ Comparable
152 findings were of Naz R et al,¹⁶ who reported that peak incidence of SSI was
153 observed in age group greater than 45 years. However, Ajao et al concluded that
154 age does not bear a major impact in MRSA infections.¹⁷

155 The collected samples in our study had a slightly higher proportion (60%) of
156 female patients. This is incongruity with previous study conducted on the
157 subject within the country, which observed proportion of samples collected
158 from male patients as 58%.¹⁸ A higher infection rate in male population was
159 also observed in other countries as well for example in Poland.¹⁹ The main
160 reason behind this discrepancy is basically FFH is a welfare organization for
161 families of retired army personal.

162 MRSA (57.6%) was the predominant isolate from surgical site infections from
163 our hospital, which is comparable to other local studies.^{5, 12} as well as study
164 from India.^{1, 20} The predominance of MRSA seen in our study is related with
165 endogenous source as the organism is a member of normal skin and nasal flora
166 of the patients. Extended antibiogram showed that there were 27.2% (n=9)
167 MRSA out of 57.6% (n=19) causing postoperative SSIs having the same
168 antibiogram as the endogenous MRSA isolated preoperatively from same
169 patients. These could be easily prevented by stringent surveillance and
170 preoperative antibiotics. Extended antibiogram was also used by Yang from
171 University of California, USA which suggested that difference in sensitivity
172 could be used to label CA- MRSA and HA- MRSA.²¹ While a study from

173 Uruguay proved this by using genotyping and Pulse Field Gel Electrophoresis
174 along with antibiogram, which is the limitation of this study.²²

175 In our study, out of 75 cases majority of MRSA were from obstetrics &
176 gynecology (18.1%) followed by and orthopedics (15.1%) surgery department
177 (12.1%). These results are comparable to studies from neighboring country⁵ as
178 well as local study from Karachi.²³

179 Surgical Site Infections are the main contributor of health care associated
180 infections. Rate of SSIs in our study was 33 out of 75, 44% which was in
181 tandem with a local study carried out in Abbottabad, which showed an infection
182 rate of 34% with 32 patients developing SSIs out of 95 patients.²⁴ But frequency
183 of SSI varied from 2.5-41.9%.²⁵ Rate of SSIs is an important gauge of quality of
184 surgical procedures in a hospital and it is different in different set-ups.

185

186 **Conclusion**

187 The results of this study determined that Endogenous Methicillin Resistant
188 Staphylococcus aureus (MRSA) could be isolated from patients going for
189 surgery if microbiological screening was done at the time of admission. This
190 could prevent patients from Surgical Site Infection Post operatively by these
191 endogenous MRSA. This search and wipe out strategy is able to curtail the
192 events of outbreak, reduce hospital stay and decrease budget of the hospital by
193 providing guidance in the choice of empirical therapy for infection.

194

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Table 1: Frequency of Endogenous MRSA in Preoperative /Post Operative patients

Sr.No	Total sample N=75	% (n)	
1.	Endogenous MRSA in Preoperative patients	14.7% (n=11)	
2.	Frequency of cultural growth positive MRSA Post operatively out of total samples N=75	25.3% (n=19)	
	Endogenous MRSA		n=9
	Exogenous MRSA		n=10
3.	Frequency of Post operatively SSIs	44%(n=33)	

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Table 2: Wards wise distribution of MRSA in SSIs

Wards	Frequency of sample N=75 100%	MRSA 57.6% (n=19) in SSIs	Non MRSA 42.4% (n= 14) in SSIs	Total SSIs 44% (n= 33)
Gynecology	24.0% (n=18)	18.1%(n=6)	12.1%(n=4)	30.3%(n=10)
Neuro surgery	13.3% (n=10)	3.0%(n=1)	Nil	3.0%(n=1)
Urology	21.3% (n=16)	9.0%(n=3)	9.0% (n=3)	18.1%(n=6)
General surgery	22.6% (n=17)	12.1%(n=4)	12.1% (n=4)	24.2%(n=8)
Orthopedics	18.6% (n=14)	15.1%(n=5)	9.0% (n=3)	24.2%(n=8)

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307**Table. 3: Antibiotic resistance pattern of Endogenous & Exogenous MRSA**

Antibiotics	Endogenous MRSA (Pre OP) % (n= 11)		Endogenous MRSA (Post OP) % (n=9)		Exogenous MRSA (Post OP) % (n=10)	
	Resistance	Sensitive	Resistance	Sensitive	Resistance	Sensitive
Penicillin	90% (10)	10% (1)	90% (8)	10% (1)	100%(10)	Nil
Ciprofloxacin	63% (7)	37% (4)	66% (6)	34% (3)	90% (9)	10% (1)
Doxycycline	9% (1)	91% (10)	11% (1)	89% (8)	30% (3)	70% (7)
Gentamicin	36% (4)	64% (7)	33% (3)	67% (6)	60% (6)	40% (4)
Rifampicin	9% (1)	91% (10)	11% (1)	89% (8)	20% (2)	80% (8)
Linezolid	Nil	100%(11)	Nil	100%(09)	Nil	100%(10)
Chloramphenicol	27% (3)	73% (8)	22% (2)	77% (7)	40% (4)	60% (6)
Co-trimoxazole	63% (7)	37% (4)	66% (6)	34% (3)	90% (9)	10% (1)
Erythromycin	63% (7)	37% (4)	66% (6)	34% (3)	90% (9)	10% (1)
Clindamycin	27% (3)	73% (8)	22% (2)	77% (7)	30% (3)	70% (7)
Vancomycin	Nil	100%(11)	Nil	100% (9)	Nil	100%(10)