

1 Prevalence of Antimicrobial Resistance among Gram-Positive
2 Isolates in an Adult Intensive Care Unit at a Tertiary Care
3 Center in Saudi Arabia

4 Roaa Amer¹, Bayan T. Alzomaili² and Rana S. AlZahrani³

5 ¹ College of Medicine; King Saud Bin Abdulaziz University for Health Sciences

6 *Received: 14 December 2016 Accepted: 3 January 2017 Published: 15 January 2017*

7 **Abstract**

8 To estimate the prevalence of Grampositive infections in intensive care units (ICU), and to
9 observe the patterns of resistance against different antibiotics.Methods: A retrospective
10 cross-sectional study was conducted of all reports of Gram-positive isolates from adult ICU of
11 King AbdulAziz Medical City, Riyadh between 2010 and 2014. Organisms were identified and
12 tested by an automated system and the antibiotic susceptibility was confirmed by manual
13 method.Results: Among 2155 Gram-positive isolates, methicillininsusceptible *Staphylococcus*
14 *aureus* (MSSA) were the most commonly isolated organism followed by *Enterococcus*,
15 *Methicillin-resistant Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae*
16 and *Coagulase-negative Staphylococci*. MRSA resistance decreased to clindamycin,
17 erythromycin, and trimethoprim/sulfamethoxazole. *Coagulase-negative Staphylococcus* showed a
18 significant increase
19

20 *Index terms*— resistance; multidrug resistance; grampositive bacteria.

21 **1 Introduction**

22 uring the course of management of bacterial infections, bacteria might develop the ability to resist the bactericidal
23 or bacteriostatic effects of one or more antibiotic class (multidrug resistance (MDR)) [1]. This is usually a result
24 of the frequent and widespread use of potent antibiotics, which is the main reason why antimicrobial resistance
25 is more noted in the intensive care units (ICUs) in comparison to the other inpatient departments in hospitals
26 worldwide [2]. According to the national healthcare safety network report in the United States, host risk factors
27 for developing a nosocomial infection are age, comorbid diseases, duration of hospitalization, length of ICU stay,
28 immune status, and disease severity. It was reported that the incidence of ICU nosocomial infections worldwide
29 is between 5%-30% [3]. A study conducted in 8 European countries concluded that overuse was one of the factors
30 associated with increased antibiotic resistance [4].

31 The patterns of antimicrobial resistance vary between ICUs in different countries due to the various factors
32 leading to such a resistance including different patterns of infections and antibiotic use, the variations in local
33 infection control policies, and the effective usage of the local resistance reports directing the suitable antibiotic
34 therapies in practice, all of which will lead to different resistance patterns, and outcomes on patients and
35 healthcare systems accordingly [5]. Over the past few years, the efficacy of antibiotics against various ICU
36 pathogens has been decreasing, with MDRs on the rise [6]. Globally, Antibiotic resistance is still a continuous
37 issue however due to the differences in international and national data, a local continuous surveillance studies
38 should be conducted to identify the emergence of different bacterial resistance patterns in order to establish local
39 guidelines. This study was done to estimate the prevalence of Gram-positive infections in intensive care units
40 (ICU), and to observe the patterns of resistance against different antibiotics.
41

42 **2 II.**

43 **3 Methods**

44 **4 a) Study Design and Setting**

45 A cross-sectional retrospective study was conducted on Gram-positive isolates from the adult ICU of King
46 Abdulaziz Medical City (KAMC) between the period of 2010 and 2014. The ethics committee and institute
47 review board in King Abdullah International Medical Research Centre approved this project.

48 **5 b) Study Sample and Technique**

49 The annual antibiogram data was used to calculate the percentage of resistance in Gram-positive bacteria with
50 a total of 2155 isolates from blood, urine, sputum and respiratory aspiration. All isolates were analyzed per the
51 guidelines of the Clinical and Laboratory Standards Institute (CLSI). The species level and AST performed using
52 an automated system (The VITEK®2 system, BioMariex, France) to characterize all Gram-positive bacteria.
53 All antimicrobial susceptibility testing was confirmed by manual method. Only one isolate per patient per
54 year was used for analysis. Ampicillin, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, and
55 trimethoprim-sulfamethoxazole were tested either by the breakpoint method (with the vitek 2 system) or by
56 the ETEST method using the previously mentioned antibiotics on a Muller Hinton Agar Plate. The proportion
57 of susceptible isolates was calculated as the sum of susceptible organisms (neither intermediately susceptible nor
58 resistant) relative to the total number of organisms tested. Multidrug resistance was defined as resistance to three
59 or more antimicrobials (imipenem, ceftazidime, ciprofloxacin, pipracillin-tazobactam, and/or an aminoglycoside).

60 **6 c) Statistical Analysis**

61 The trend in the resistance rate over a 5-year period (between 2010-2014) was analyzed to identify a statistically
62 significant increasing or decreasing trend using chi-square for linear trend analysis and chi-square test was used
63 for testing the association between categorical variables. The percent of change of antibiotic susceptibility was
64 calculated as the difference between the later (e.g. 2014) and earlier (e.g. 2010) susceptibilities percentages
65 divided by the earlier one. P value <.05 was considered as statically significant. All P values were two-tailed.
66 SPSS software package for Windows (version 22.0, IBMCorp, Armonk, NY, USA) was used for all statistical
67 analyses III.

68 **7 Results**

69 **8 a) Descriptive Statistics of the Included Samples**

70 From 2010 to 2014, there were 6611 isolated organisms in total, out of which 2155 (33%) were Grampositive.
71 There were 285 Gram-positive organisms isolated in 2010, 294 in 2011, 334 in 2012, 632 in 2013, and 610 in
72 2014. Among all isolated Gram-positive organisms, methicillin-susceptible *Staphylococcus aureus* (MSSA) were
73 the most commonly isolated 849 (39%) followed by *Enterococcus* 590 (27%), methicillinresistant *Staphylococcus*
74 *aureus* (MRSA) 462 (21%), *Streptococcus pneumoniae* 135 (6%), Coagulase negative *Staphylococcus* 113 (5%),
75 and *Streptococcus viridans* 6 (0.27%). All screening samples were not included to avoid false representation of
76 colonization rather than true infection.

77 **9 b) Prevalence of Antimicrobial Resistance**

78 Over the study period, MSSA resistance increased to clindamycin until 2013 (5% to 12%, p=0.15), erythromycin
79 (5% to 13%, p=0.001), and trimethoprim/sulfamethoxazole(TMP/SMX) (1% to 4%, p=0.19). There was no
80 resistance to vancomycin, and penicillin throughout the study period (0%), however, from 2010 to 2013, MSSA
81 was 100% resistant to moxifloxacin.

82 Of 590 *Enterococcus* isolates, there was an increase in ampicillin (59% to 71%, p=0.003), and in vancomycin
83 resistance (37% to 46%, p=0.170); a decrease in the resistance to ciprofloxacin, and nitrofurantoin (96% to 76%
84 and 66% to 54%), respectively.

85 MRSA resistance decreased to clindamycin (72% to 52%, p<0.0001), erythromycin (72% to 53%, p<0.0001),
86 and TMP/SMX (60% to 46%, p<0.0001). However, no change was seen in MRSA resistance to cefazolin (1%)
87 from 2012 to 2014, and to vancomycin (0%) throughout the study period.

88 *Streptococcus pneumoniae* showed a significant decrease in resistance to cefotaxime (50% to 0%, p=0.003); an
89 increase in resistance to erythromycin (25% to 50%, p=0.428), and to penicillin (0% to 7%). On the other hand,
90 there was no change in the resistance to moxifloxacin, and vancomycin (0%) throughout the study period.

91 Coagulase negative *Staphylococcus* showed significant increase in the resistance to cefazolin (54% to 90%,
92 p<0.0001), and erythromycin (65% to 90%, p=0.02). On the other hand, Coagulase negative *Staphylococcus*
93 resistance to TMP/SMX decreased (62% to 20%, p=0.001) and showed no resistant to vancomycin from 2010 to
94 2014.

95 **10 IV.**

96 **11 Discussion**

97 Antimicrobial resistance is a global concern [1]. ICU is a potential source of multidrug resistance due to
98 the widespread use of multiple antibiotics compared to other hospital departments [2]. Methicillin sensitive
99 *Staphylococcus aureus* was found to be the most commonly isolated organism in the adult ICUs of KAMC
100 (849 isolates). Savas et al. reported that from 597 ICU isolates, 241 were *Staphylococci*, and MSSA was not
101 the most common isolates 24 (9.96%) [7]. In this study, among 1,424 *Staphylococcus* isolates, MSSA was the
102 most commonly isolated organism 849 (59.6%). Savas et al evaluated the resistance of MSSA to clindamycin,
103 erythromycin, and TMP/SMX, and it was 25%, 27%, and 21%, respectively [7]. Looking at the ranges of MSSA
104 resistance in this study, MSSA resistance increased to clindamycin (5% to 12%), erythromycin (5% to 13%), and
105 TMP/SMX (1% to 4%). In our study, vancomycin, and cefazolin remain the most effective antibiotics against
106 MSSA. Comparison of the overall resistance pattern is illustrated in table-1.

107 Although MRSA is considered an endemic in many hospitals worldwide, it is still difficult to be eradicated,
108 and remains a major concern in all ICUs [8]. MRSA is showing a significant increase in prevalence in many ICUs
109 reaching to 60% of all isolates [9]. In this study, from 2010 to 2014 and among 2155 Grampositive isolates,
110 MRSA were the third most common isolates in KAMC adult ICU 462 (21%). Vancomycin is considered the most
111 important antibiotic used for MRSA till date [10]. However, MRSA showed a resistance against vancomycin in
112 other reported studies [10]. Fortunately enough, throughout our study period, MRSA showed no resistance to
113 vancomycin in KAMC adult ICUs. Comparison of the overall resistance pattern is illustrated in table-1.

114 Enterococci are considered one of the most common causes of hospital-acquired infections. In the past 20 years,
115 Enterococci have become increasingly resistant to many antibiotics [9]. Recent studies conducted to assess the
116 incidence of multidrug resistant Gram-positive pathogens showed that *Enterococcusfaecalis* accounted for 15.7%
117 of all Grampositive isolates. In our study, we found that 27% of all Gram-positive isolates were *Enterococcus*.
118 Hällgren A et al. Evaluated the resistance of *Enterococcusfaecium* to ampicillin, vancomycin, and ciprofloxacin
119 and it was 74.3%, 1.4%, and 82.4% respectively [11]. In this study the resistance pattern of *Enterococcus* to
120 ampicillin, and ciprofloxacin was almost the same as the resistance that was reported by Hällgren A et al., 71%
121 and 76% respectively. However, *Enterococcus* was highly resistant to vancomycin 46%. V.

122 **12 Conclusion**

123 Our study revealed that antibiotic resistance among Gram-positive organisms remains a continuous issue in adult
124 ICU, KAMC-Riyadh. Among all isolated Gram-positive organisms, the most commonly isolated were MSSA
125 (39%), *Enterococcus* (27%), and MRSA (21%). Vancomycin remains the most effective drug against MSSA,
126 MRSA, *Streptococcus pneumonia*, and Coagulase-negative *Staphylococci*. The overuse of multiple antibiotics in
127 ICU is considered one of the reasons behind the significant resistance. Therefore, strict adherence to infection
128 prevention guidelines and continuous monitoring to antimicrobial resistance are essential to avoid major outbreak
129 in the future.

130 Limitation: This study was conducted in a single center in Riyadh (KAMC) and in a limited period of time
131 2010-2014 which could be considered as a limitation to our findings. In addition, the data was collected from the
132 yearly antibiogram. Therefore, Patients data such as age, sex and antibiotic use were not possible to obtain to
133 study some of the risk factors

2

Antibiotic	Resistance (%) in 2010	Resistance (%) in 2014	Trend
Enterococcus			
Ampicillin	51%	71%	?
Nitrofurantoin	66%	54%	â???"
Vancomycin	37%	64%	?
Streptococcus pneumonia			
Cefotaxime	50%	0%	â???"
Erythromycin	25%	50%	?
Moxifloxacin	0%	0%	?
Penicillin	0%	7%	?
Vancomycin	0%	0%	?
Coagulase-negative Staphylococci			
Trimethoprim/sulfamethoxazole	62%	20%	â???"
Clindamycin	62%	67%	?
Erythromycin	65%	90%	?
Vancomycin	0%	0%	?

Figure 1: Table 2 :

134 Acknowledgment: We thank Dr. NazishMasud in helping us to review this paper

135 [About Antimicrobial Resistance | Antibiotic/ Antimicrobial Resistance | CDC (2017)] *About Antimicrobial Re-*
136 *sistance / Antibiotic/ Antimicrobial Resistance / CDC*, <http://www.cdc.gov/drugresistance/about.html> May 2017. p. 29. (Internet)

138 [Van Bijnen et al. ()] 'Antibiotic Exposure and Other Risk Factors for Antimicrobial Resistance in Nasal
139 Commensal *Staphylococcus aureus*: An Ecological Study in 8 European Countries' E Van Bijnen , J Paget ,
140 E De Lange-De Klerk , C Heijer , A Versporten . *PLOS ONE* 2015. 10 (8) p. e0135094.

141 [Hallgren ()] 'Antimicrobial susceptibility patterns of enterococci in intensive care units in Sweden evaluated by
142 different MIC breakpoint systems'. A Hallgren . *Journal of Antimicrobial Chemotherapy* 2001. 48 (1) p. .

143 [Javidnia et al. ()] 'Clonal dissemination of methicillin-resistant *Staphylococcus aureus* in patients and the
144 hospital environment'. S Javidnia , M Talebi , M Saifi , M Katouli , A Rastegarlari , M Pourshafie .
145 *International Journal of Infectious Diseases* 2013. 17 (9) p. .

146 [Roberts et al. ()] 'Defining Antibiotic Levels in Intensive Care Unit Patients: Are Current ?-Lactam Antibiotic
147 Doses Sufficient for Critically Ill Patients?'. J Roberts , S Paul , M Akova , M Bassetti , J Waele , Dimopoulos
148 G Ali . *Clinical Infectious Diseases* 2014. 58 (8) p. .

149 [Doyle et al. ()] *Epidemiology of Infections Acquired in Intensive Care Units. Seminars in Respiratory and Critical*
150 *Care Medicine*, J Doyle , K Buisling , K Thursky , L Worth , M Richards . 2011. 32 p. .

151 [Chaudhry and Prajapat ()] 'Intensive care unit bugs in India: How do they differ from the Western world?'. D
152 Chaudhry , B Prajapat . *The Journal of Association of Chest Physicians* 2017. 5 (1) p. 10.

153 [Loomba et al. ()] 'Methicillin and vancomycin resistant *S. aureus* in hospitalized patients'. P Loomba , J Taneja
154 , B Mishra . *Journal of Global Infectious Diseases* 2010. 2 (3) p. 275.

155 [Savage et al. ()] 'Pathogens and antimicrobial susceptibility in critically ill patients with bloodstream infections:
156 a descriptive study'. R Savage , R Fowler , A Rishu , S Bagshaw , D Cook , P Dodek . *CMAJ Open* 2016. 4
157 (4) p. .

158 [Johani et al. ()] 'Prevalence of antimicrobial resistance among gram-negative isolates in an adult intensive care
159 unit at a tertiary care center in Saudi Arabia'. Al Johani , S Akhter , J Balkhy , H El-Saed , A Younan , M
160 Memish , Z . *Annals of Saudi Medicine* 2010. 0 (0) p. 0.

161 [Sava?l et al. ()] 'Prevalence of Methicillin-Sensitive and Methicillin Resistant *Staphylococci* in Intensive Care
162 Units in a University Hospital'. Sava?l , N Duran , Y Önlen , Sava?n , S Ocak , N ?ris . *European Journal of*
163 *General Medicine* 2005. 2 (1) p. .

164 [Brusselaers et al. ()] 'The rising problem of antimicrobial resistance in the intensive care unit'. N Brusselaers ,
165 D Vogelaers , S Blot . *Annals of Intensive Care* 2011. 1 (1) p. 47.