

RESEARCH ARTICLE

Analysis of antimicrobial resistance pattern in a secondary care hospital

Naser Ashraf Tadvi¹, Ali Faraz², Hussain Sajid³, Khaja Mohinuddin Salar B M², Kashif Shaikh²

¹Department of Pharmacology, Ayaan Institute of Medical Sciences, Ranga Reddy, Telangana, India, ²Department of Pathology, College of Medicine, Majmaah University, Al Majmaah, Saudi Arabia, ³Department of Basic Medical Sciences, College of Medicine, Majmaah University, Al Majmaah, Saudi Arabia

Correspondence to: Naser Ashraf Tadvi, E-mail: nasertadvi@yahoo.co.uk

Received: August 19, 2019; **Accepted:** September 13, 2019

ABSTRACT

Background: Antimicrobial resistance is a grave global public health concern and has escalated in recent past. **Aims and Objectives:** This study was conducted to analyze the antimicrobial resistance pattern of commonly isolated microorganisms in a secondary care hospital in Saudi Arabia. **Materials and Methods:** This cross-sectional observational study was conducted at King Khalid Hospital, Al Majmaah. Antimicrobial resistance pattern of commonly isolated Gram-negative and Gram-positive microorganisms was checked against routinely used antimicrobials. **Results:** The prevalence rate calculated for methicillin-resistant *Staphylococcus aureus* was 44.2%. Extended-spectrum beta-lactamase *Enterobacteriaceae* was 14.70% and vancomycin-resistant enterococci were 8%. **Conclusion:** There is an increase in proportion of isolates resistant to commonly prescribed antibiotics highlighting the importance of ongoing surveillance and antibiotic stewardship program.

KEY WORDS: Antimicrobial Resistance; Extended-spectrum Beta-lactamase Producers; Methicillin-resistant *Staphylococcus aureus*; Vancomycin-resistant Enterococci


INTRODUCTION

Antimicrobial resistance is a grave global public health concern and has escalated in recent past.^[1] As a result of resistance among bacteria, the drugs that are used for treating the infections become ineffective, leading to serious concerns such as treatment failure, prolonged illness, disability, and even death.^[2] Several factors such as point mutation, transfer of resistant gene between bacteria through plasmids, transposons, and integrins have been postulated for the development of resistance.^[3] Inappropriate antibiotic usage, unhygienic practices, demographic changes, and

overcrowding are some of the reasons, which have been implicated in the emergence of antimicrobial resistance.^[4]

Antibiotics are the mainstay for many lifesaving interventions in the hospital, which depend on appropriate antimicrobial therapy for success.^[5] Unfortunately, the dependence on antimicrobials has exponentially increased the emergence of resistance as well. Misuse and injudicious antibiotic usage create a selective pressure, forcing the microbes to mutate or become resistant.^[6]

Worldwide, tons of antibiotics are used every minute, in an inappropriate and unjustified manner.^[7] Common infections such as sore throat, urinary infection, and sexually transmitted diseases are becoming increasingly difficult to treat. This is due to bacteria that have developed resistance, even to end resort lifesaving antibiotics.^[8] The multidrug-resistant (MDR) bacteria are spreading rapidly, resulting in severe financial and medical consequences globally.^[6] Every 10 min, a person succumbs to death in the United States or Europe due to untreatable resistant bacteria.^[9]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2019.9.0930813092019	

National Journal of Physiology, Pharmacy and Pharmacology Online 2019. © 2019 Naser Ashraf Tadvi, et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

Increasing prevalence of extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* has been reported in Kingdom of Saudi Arabia with many outbreaks, and mortality that ranges between 11% and 40%.^[10] There has also been a rise in resistant forms of Gram-negative bacteria such as pan-resistant *Pseudomonas* and *Acinetobacter* species.^[11] The World Health Organization (WHO) has started the global action plan on antimicrobial resistance, which was signed by many countries, including Saudi Arabia during the WHO conference held in 2015, to limit antimicrobial resistant.^[12]

The strategic objectives of this action plan include strengthening of knowledge through surveillance and research.^[13] Information on current antimicrobial resistance pattern among common pathogens helps in making an appropriate choice of empiric therapy.^[14] Hence, the present study was conducted to identify the local pattern of sensitivity and resistance of organisms in various clinical isolates of the inpatients of hospital.

MATERIALS AND METHODS

The study was conducted to analyze the antimicrobial resistance pattern of samples received in microbiology laboratory from inpatients of King Khalid Hospital, Majmaah.

This was a periodic cross-sectional observational study to analyze the antimicrobial resistance pattern of clinical isolates during the 1-year period from January 1, 2017, to December 31, 2017. Permission for the study was obtained from the college authorities before commencement.

This study included inpatients of surgical, medical, and intensive care units for whom culture and sensitivity sample had been sent. As the statistical validity of estimates of percent susceptibility for organisms for which there are fewer than 30 isolates reported is limited, only those bacterial isolates with more than 30 reports were included in the study. Beta-hemolytic streptococci susceptibility testing was not performed since resistant strains have not been recognized.

The data related to demographics of the patient, the type of sample/clinical isolate, organisms isolated from the sample, and the resistance or sensitivity to antimicrobial agents were collected from the microbiology department records.

The Microbiology Department of King Khalid Hospital has an automated system, MicroScan WalkAway by Beckman Coulter, which analyzes the samples for antimicrobial resistance and sensitivity and computerized records are maintained.

Data were entered into the Microsoft Excel and percentage of drugs having resistance against the species of isolated

organism, percentage of organisms showing source-wise resistance, and percentage of organisms having sensitivity against the isolated organisms from clinical isolates were calculated. The study was approved by the Institutional Review Board, King Fahd Medical City.

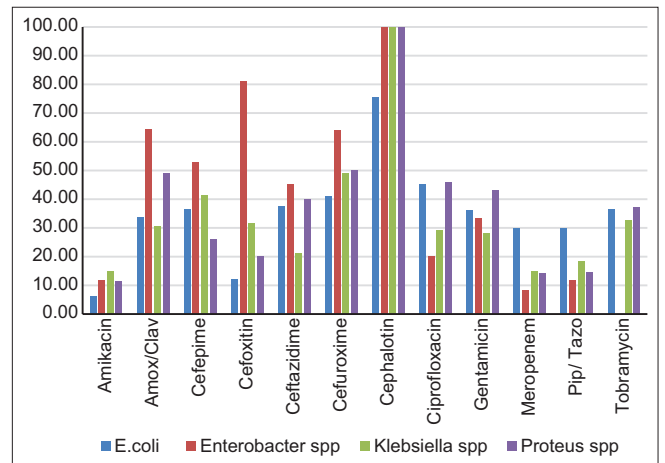


Figure 1: Resistance pattern of Gram-negative *Enterobacteriaceae* (%)

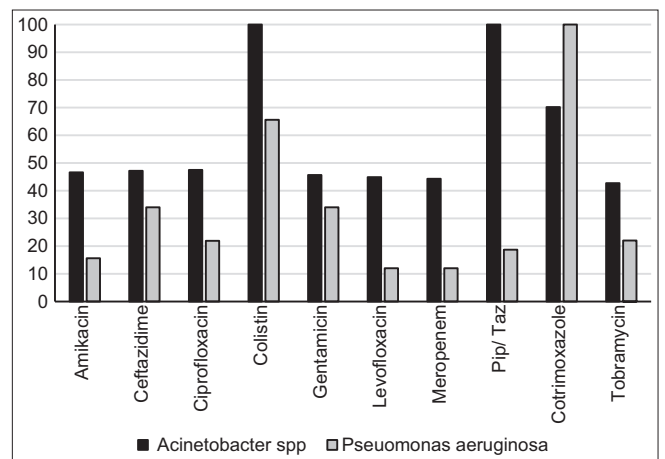


Figure 2: Resistance in non-fermenting Gram-negative rods (%)

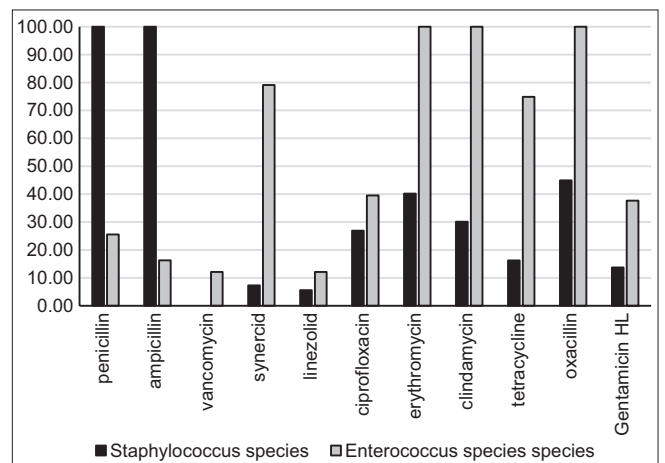


Figure 3: Antimicrobial resistance in commonly isolated Gram-positive cocci, n (%)

RESULTS

During the study period (January 2017–December 2017), a total of 1188 bacterial isolates were analyzed, but only 1134 were included in the study. Fifty-four bacterial isolates were excluded as their number was <30. The bacteria were isolated from various specimens such as blood, pus swabs/pus, urine, sputum, respiratory secretions, and other body fluids.

Pathogens and Their Susceptibility Pattern

Of these bacterial isolates, most frequently isolated pathogens were Gram-negative *Enterobacteriaceae* including *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp., *Proteus* and *Serratia* species. *Staphylococcus* species were the second most frequently isolated [Tables 1 and 2].

Of total $n = 1134$ isolates, there were 592 *Enterobacteriaceae*, 152 non-fermenting Gram-negative rods, and 390 Gram-positive cocci. MRSA trend was 44.2%, ESBL trend was 14.7%, and vancomycin-resistant enterococci (VRE) trend was 8% as detected by automated microbiology analyzer MicroScan WalkAway [Table 3 and Figures 1-3].

DISCUSSION

The widespread antimicrobial usage in health-care facilities has led to the emergence of organisms resistant to multiple antimicrobials, resulting in serious infections and increased mortality and morbidity.^[15] Over the past few decades, numerous outbreaks of infection with MDR organisms have been reported worldwide.^[16] The advent of vancomycin-resistance among Gram-positive cocci; ESBL production and, carbapenemase production in *Enterobacteriaceae* is a major threat to the use of many end resort antibiotics.^[17]

The first case of ESBL producers was reported in 1983 in Germany. Thereafter, a rapid increase in their prevalence

has been seen worldwide.^[16] In our study, the percentage of ESBL producers among *Enterobacteriaceae* was 14.7%. Similar resistance pattern among *Enterobacteriaceae* has been reported worldwide.^[18,19] Various studies conducted in the US, China, Europe, and Africa displayed an ESBL prevalence from as low as 4% to as high as 46%.^[8]

In Saudi Arabia, the prevalence of ESBL-producing isolates ranges from 4.8% to 65% as per a number of studies.^[20]

In our study, Gram-negative bacteria demonstrated significant resistance to antimicrobial groups such as quinolones, cotrimoxazole, aminoglycosides, and beta-lactam-beta-lactamase combination as shown in Table 1 and Figure 1. A sizeable percentage was multidrug resistant. The current surveillance also highlights emergence of resistance to carbapenems, used as the treatment of choice for ESBL producers.

The resistant trend among the non-fermenting Gram-negative bacteria such as *Acinetobacter* and *Pseudomonas* is a common cause of morbidity and mortality, in intensive care units as well as other hospital units. Findings of our study show significant resistance to antimicrobial groups such as aminoglycosides, carbapenems, and cephalosporins among others. Although meropenem had been an effective option to treat infections caused by these bacteria, the resistance rate 12% for *Pseudomonas* and 44.29% for *Acinetobacter* in our study is a cause of concern, and signals more caution in using meropenem for empirical therapy.

A wide-scale survey conducted in Saudi Arabia determined resistance pattern among non-fermenters, in a large sample $n = 8908$. The resistance rates among *P. aeruginosa*; 15.9% for carbapenem, 22% for amikacin, and 31.2% for gentamicin were comparable to our study.^[21]

The resistance rates among *Acinetobacter* spp. were 5.4% for carbapenems, 64% for quinolones, 76% for amikacin,

Table 1: Antimicrobial resistance pattern of Gram-negative *Enterobacteriaceae*, n (%)

Antibiotics	<i>Escherichia coli</i> ($n=328$)	<i>Entero bacter</i> species ($n=36$)	<i>Klebsiella pneumoniae</i> ($n=184$)	<i>Proteus species</i> ($n=35$)
Amikacin	20 (6.13)	4 (11.67)	28 (15)	4 (11.43)
Amoxicillin/Clavulanic acid	111 (33.79)	23 (64.17)	56 (30.5)	17 (48.86)
Cefepime	120 (36.54)	19 (52.78)	76 (41.15)	9 (25.86)
Cefoxitin	39 (11.96)	29 (80.83)	58 (31.45)	7 (20.14)
Ceftazidime	122 (37.32)	16 (44.44)	39 (21.19)	14 (40)
Cefuroxime	135 (41.12)	23 (63.88)	90 (48.91)	18 (51.42)
Cefalotin	247 (75.3)	36 (100)	184 (100)	35 (100)
Ciprofloxacin	148 (45.26)	7 (19.44)	54 (29.15)	16 (45.71)
Gentamicin	119 (36.16)	12 (33.33)	52 (28.15)	15 (43.14)
Meropenem	98 (29.84)	3 (8.33)	27 (14.80)	5 (14.29)
Piperacillin/tazobactam	97 (29.7)	4 (11.67)	34 (18.30)	5 (14.43)
Tobramycin	120 (36.62)	0 (0)	60 (32.55)	13 (37.29)

Table 2: Antimicrobial resistance in non-fermenting Gram-negative rods, n (%)

Antibiotics	<i>Acinetobacter</i> species (n=120)	<i>Pseudomonas</i> species (n=32)
Amikacin	56 (46.63)	5 (15.6)
Ceftazidime	57 (47.17)	11 (34.37)
Ciprofloxacin	57 (47.51)	7 (21.9)
Colistin	120 (100)	21 (65.6)
Gentamicin	55 (45.68)	11 (34.37)
Levofloxacin	54 (44.9)	4 (12)
Meropenem	53 (44.29)	4 (12)
Piperacillin/tazobactam	120 (100)	6 (18.7)
Cotrimoxazole	84 (70.19)	32 (100)
Tobramycin	51 (42.73)	7 (21.88)

Table 3: Antimicrobial resistance in commonly isolated Gram-positive cocci, n (%)

Antibiotics	<i>Staphylococcus</i> species (n=347)	<i>Enterococcus</i> species (n=40)
Penicillin	347 (100)	11 (25.56)
Ampicillin	347 (100)	7 (16.26)
Vancomycin	0 (0)	5 (12.12)
Quinupristin/dalfopristin	25 (7.28)	34 (79.09)
Linezolid	19 (5.56)	5 (12.12)
Ciprofloxacin	93 (26.88)	17 (39.53)
Erythromycin	139 (40.20)	43 (100)
Clindamycin	105 (30.12)	43 (100)
Cotrimoxazole	174 (50.10)	NT*
Tetracycline	56 (16.24)	32 (74.86)
Oxacillin	156 (44.92)	NT*
Gentamicin	48 (13.72)	16 (37.67)

*NT: NT means Not Tested

and 77% for gentamicin.^[18] Interestingly, our study had less resistance rates for all of these, except carbapenems; this may be due to a recent trend of overuse of meropenem for treating these infections.

The resistance in Gram-positive microorganisms has emerged as a global problem, as fewer antibiotics remain effective against them. Even more concerning is the limited discovery of newer antibiotics against these organisms.^[22] Staphylococci and enterococci have evolved mechanisms to overcome the effect of almost all newly developed antibiotics against them, inevitably leaving us with few or no choice in treating life-threatening infections by these organisms.

MRSA percentage calculated in our study was 44.2% which is close to the average international scale. MRSA prevalence rates have been found to vary from 13% to 74% worldwide.^[23]

A study conducted across five regions of Saudi Arabia analyzed MRSA data. This study showed MRSA to have a national prevalence rate of 35.6%. MRSA prevalence was highest in Riyadh region (60%) followed by Asir region (40%) while Makkah region was (25%), with Jouf being the lowest at <15%.^[24] Majmaah is a small city located in the Riyadh region, so our study agrees with the local MRSA trend.

The VRE prevalence calculated in our study is 8%. Many countries around the world have reported higher isolation rates for VRE.^[25] However, fewer studies have been conducted in Saudi Arabia in this regard and available data on epidemiology, and the prevalence of VRE in Saudi Arabia is scarce. In a study conducted in a hospital in Saudi Arabia, the prevalence of VRE was 17.3%, showing a higher prevalence rate.

CONCLUSION

The high antibiotic resistance in commonly isolated microorganisms is alarming. The antimicrobial therapy in both indoor and outdoor settings of the hospital needs to be rationalized. Ongoing surveillance and antibiotic stewardship program are key to detect and monitor antibiotic resistance trend and identify threats posed by multidrug-resistant organisms.

REFERENCES

1. Sugden R, Kelly R, Davies S. Combatting antimicrobial resistance globally. *Nat Microbiol* 2016;1:16187.
2. Antimicrobial Fact Sheet; 2017. Available from: <http://www.who.int/mediacentre/factsheets/fs194/en>.
3. Seidman JC, Anitha K P, Kanungo R, Bourgeois AL, Coles CL. Risk factors for antibiotic-resistant *E. coli* in children in a rural area. *Epidemiol Infect* 2009;137:879-88.
4. Saravanan R, Raveendaran V. Antimicrobial resistance pattern in a tertiary care hospital: An observational study. *J Basic Clin Pharm* 2013;4:56-63.
5. Teillant A, Gandra S, Barter D, Morgan DJ, Laxminarayan R. Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: A literature review and modelling study. *Lancet Infect Dis* 2015;15:1429-37.
6. Zowawi HM, Forde BM, Alfaresi M, Alzarouni A, Farahat Y, Chong TM, et al. Stepwise evolution of pandrug-resistance in *Klebsiella pneumoniae*. *Sci Rep* 2015;5:15082.
7. Zowawi HM, Harris PN, Roberts MJ, Tambyah PA, Schembri MA, Pezzani MD, et al. The emerging threat of multidrug-resistant gram-negative bacteria in urology. *Nat Rev Urol* 2015;12:570-84.
8. Zowawi HM. Antimicrobial resistance in Saudi Arabia. An urgent call for an immediate action. *Saudi Med J* 2016;37:935-40.
9. Harbarth S, Balkhy HH, Goossens H, Jarlier V, Kluytmans J, Laxminarayan R, et al. Antimicrobial resistance: One world, one fight! *Antimicrob Resist Infect Control* 2015;4:49.
10. Zowawi HM, Balkhy HH, Walsh TR, Paterson DL. n DL. DL.

- n DL. ght! urgent call fnegative pathogen isolates from the Arabian Peninsula. *Clin Microbiol Rev* 2013;26:361-80.
11. Shibl AM, Memish ZA, Kambal AM, Ohaly YA, Ishaq A, Senok AC, *et al.* National surveillance of antimicrobial resistance among gram-positive bacteria in Saudi Arabia. *J Chemother* 2014;26:13-8.
 12. World Health Organization. Global Action Plan on Antimicrobial Resistance. Geneva: World Health Organization; 2015. Available from: http://www.who.int/drugresistance/global_action_plan/en. [Last accessed on 2019 Mar 23].
 13. Ko KS, Suh JY, Peck KR, Lee MY, Oh WS, Kwon KT, *et al.* *In vitro* activity of fosfomycin against ciprofloxacin-resistant or extended-spectrum beta-lactamase-producing *Escherichia coli* isolated from urine and blood. *Diagn Microbiol Infect Dis* 2007;58:111-5.
 14. Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21st century. *Perspect Medicin Chem* 2014;6:25-64.
 15. Ventola CL. The antibiotic resistance crisis: Part 1: Causes and threats. *P T* 2015;40:277-83.
 16. Thakur S, Pokhrel N, Sharma M. Prevalence of multidrug resistant *Enterobacteriaceae* and extended spectrum e of multidrug resista*Escherichia coli* in urinary tract infection. *Res J Pharm Biol Chem Sci* 2013;4:1615-24.
 17. Rice LB, Willey SH, Papanicolaou GA, Medeiros AA, Eliopoulos GM, Moellering RC Jr., *et al.* Outbreak of ceftazidime resistance caused by extended-spectrum beta-lactamases at a Massachusetts chronic-care facility. *Antimicrob Agents Chemother* 1990;34:2193-9.
 18. Mshana SE, Kamugisha E, Mirambo M, Chakraborty T, Lyamuya EF. Prevalence of multiresistant gram-negative organisms in a tertiary hospital in Mwanza, Tanzania. *BMC Res Notes* 2009;2:49.
 19. Zhang J, Zheng B, Zhao L, Wei Z, Ji J, Li L, *et al.* Nationwide high prevalence of CTX-M and an increase of CTX-M-55 in *Escherichia coli* isolated from patients with community-onset infections in Chinese county hospitals. *BMC Infect Dis* 2014;14:659.
 20. Memish ZA, Shibl AM, Kambal AM, Ohaly YA, Ishaq A, Livermore DM, *et al.* Antimicrobial resistance among non-fermenting gram-negative bacteria in Saudi Arabia. *J Antimicrob Chemother* 2012;67:1701-5.
 21. Hassoun A, Linden PK, Friedman B. Incidence, prevalence, and management of MRSA bacteremia across patient populations-a review of recent developments in MRSA management and treatment. *Crit Care* 2017;21:211.
 22. K21: R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, *et al.* Methicillin-resistant *Staphylococcus aureus* (MRSA): Burden of disease and control challenges in Europe. *Euro Surveill* 2010;15:19688.
 23. Iyer AP, Baghallab I, Albaik M, Kumosani T. Nosocomial infections in Saudi Arabia caused by methicillin resistance *Staphylococcus aureus* (MRSA). *Clin Microbiol* 2014;3:146.
 24. O3:146. C T, Crank CW. Vancomycin-resistant enterococcal infections: Epidemiology, clinical manifestations, and optimal management. *Infect Drug Resist* 2015;8:217-30.
 25. Alotaibi FE, Bukhari EE. Emergence of vancomycin-resistant enterococci at a teaching hospital, Saudi Arabia. *Chin Med J (Engl)* 2017;130:340-6.

How to cite this article: Tadvi NA, Faraz A, Sajid H, Salar BMKM, Shaikh K. Analysis of antimicrobial resistance pattern in a secondary care hospital. *Natl J Physiol Pharm Pharmacol* 2019;9(12):1167-1171.

Source of Support: Nil, **Conflict of Interest:** None declared.