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Bacterial Resistance to Commonly Prescribed Antibiotics in a Tertiary Care Hospital: A Retrospective Review of Evidence

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Authors' contributions

This research was carried out in collaboration between the two authors. Author OOP designed the study, performed literature review, manuscript writing and was also involved in data collection and analysis. Author SA was involved with data collection and processing, statistical analysis, manuscript writing and editing. We have read and approved the final manuscript.

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ABSTRACT

Background: Antibiotic resistance is a growing global healthcare challenge and efforts to contain it are being outpaced by rapid emergence of resistant microbes. Common environmental pathogens have been reported to be manifesting resistance to several antibiotics to which they were once sensitive. In hospital setting, close contact between patients and caregivers allow resistant strains to easily spread in hospital wards. Evidence of antibiotic resistance is needed to inform rational selection of drugs for infectious diseases.
Aim: The aims of this study were to determine common pathogenic bacterial isolates among patients and their antibiotic sensitivity profiles.
Methods: This was a cross sectional retrospective study using laboratory records of antibiotic resistance profiles of bacterial isolates obtained from patient medical samples. Antibiogram records for one year period were obtained and relevant data extracted for analysis
Results and Discussion: The most commonly isolated bacteria included *Staphylococcus aureus, Escherichia coli* and *Klebsiella pneumoniae* which together accounted for over two thirds of all isolates. Most of the isolates were resistant to at least four antibiotics; Penicillins, Sulphonamides

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and Tetracyclines exhibited the highest level of resistance. Resistance to these antibiotics is well reported in literature and their empirical prescription threatens their efficacy in the management of infectious diseases.

Conclusion: Antibiotic resistance among pathogenic bacteria was high, there is need to emphasize evidence based prescriptions to not only improve clinical outcomes but also to preserve the efficacy of current antibiotic stock.

Keywords: Bacterial resistance; antibiotic resistance; tertiary care hospital; infectious diseases.

1. INTRODUCTION

Antimicrobial resistance is a rising global problem particularly in low to middle income countries where regulatory controls and health care systems are weak. A combination of high infectious disease burden, poor access to quality medicines and diagnostic services as well as low availability of second line antibiotics all combine to increase morbidity and mortality [1,2,3]. Antimicrobial resistance is widespread and it's now threatening future public health making infectious diseases difficult to manage. In recent years emerging evidence have shown that irrational use of antibiotics in both animals and humans is accelerating the development of multiple microbial resistance to commonly prescribed antibiotics particularly in low income countries [4,5,6,7].

In many developing countries where a combination of weak healthcare systems and poor regulatory controls allow antibiotics to be freely available without medical prescription, irrational prescription and misuse of antibiotics is reported to be contributing to emergence of new resistant bacterial strains [Lim et al. 2015, Zimmer 2015]. In Nigeria, several studies have reported high level of irrational prescription of antibiotics in healthcare facilities [8,9,10,11]. While prevalence of antibiotic misuse may vary widely between countries, frivolous antibiotic prescription is a global problem [12,13,14].

Antibiotic resistance is well documented, particularly among five common bacterial pathogens [*Staphylococcus aureus*, *Escherichia coli*, *Proteus spp*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, alpha *Haemolytic streptococci* etc.]. A recent study in China reported that resistance of *Escherichia coli* to Quinolones is in the range of 53 – 56% and about 31 – 70% for third generation Cephalosporins. Resistance of *Klebsiella pneumoniae* was also reported to be between 25 – 52% [15].

In sub Saharan Africa, some studies reported resistance of *Escherichia coli* and *Klebsiella pneumonia to* Ampicillin averaged 75.4% and 97% of strains respectively, while a third of these organisms were reported to be resistant to Amoxicillin + Clavulanic acid [Adjei et al. 2012] [16,17,18,19,20,21,22]. There is emerging literature evidence to indicate that *Escherichia coli* has become a leading cause of urinary tract infections globally [23,24] often resulting morbidity and mortality [25].

Resistance of pathogenic bacteria to Quinolones is becoming a major concern among clinicians globally [26,27,28,29,30,31]. The prevalence of Methicillin resistant *Staphylococcus aureus* [MRSA] is reported to vary widely between countries and sometimes between various departments of the same hospital [32,33,34,35,36], while its occurrence is decreasing in developed countries because of sustained action, the reverse is the case in many developing countries.

The emergence of multidrug resistant strains of *Pseudomonas aeruginosa*, *Klebsiella* spp and MRSA in hospital settings is well reported in literature [Rice 2006, Misic et al. 2014, Iredell et al. 2016]. For instance resistance of gram negative bacterial isolates to Aminoglycosides and Quinolones is reported to have increased in recent years [37,38]. While prevalence is highly variable, there is consistent evidence to conclude that high levels of resistance of both gram positive and negative bacteria pose significant risks to public health [39,40,41,42,43,31].

Multidrug resistance above 50% have been reported with many bacterial strains in many sub Saharan African countries [44]. In one study, it was observed that 84% of *Klebsiella pneumonia* strains were resistant to Cephalosporins; about 47% of Enterobacteriacea isolates were resistant to third generation Cephalosporins and 31 – 94% of isolates were resistant to Chloramphenicol [45].

Overall, high rates of resistance of gram positive pathogens in hospital acquired infections are reported to be highly resistant to first line

antibiotics [46]. Evidence of high level resistance to commonly prescribed antibiotics is yet to significantly influence treatment guidelines of many common invasive bacterial infections. The impact of rising antimicrobial resistance due to empirical antibiotic prescription practices is yet to be widely evaluated in healthcare facilities in low and middle income countries like Nigeria. The cost of microbial resistance and impact on patient clinical outcomes has also received little research attention in low income countries [47]. Microbial sensitivity to antibiotics has changed and evidence from healthcare facilities can provide valuable insight into trends, spread and severity. This will help in formulating antibiotic use guidelines in hospitals and research evidence will help guide cautious use of broad spectrum and new generation antibiotics.

2. OBJECTIVES

The aims of this study are to determine the level of microbial resistance to commonly prescribed antibiotics and investigate prevalence of pathogenic bacteria in laboratory samples

3. METHODS

3.1 Setting

The study was carried out in the microbiology department of the University of Maiduguri teaching hospital, Borno State Nigeria.

3.2 Study Design

This was a cross sectional retrospective study using microbial sensitivity test records in the Microbiology laboratory of the hospital.

3.3 Data Collection

Records of bacterial isolates from all patient samples and their sensitivity/resistance results were extracted into data collection forms. Isolates were from Urine, Blood, Sputum, swab [HVS, wound and pus]. Antibiogram followed standard test procedures using antibiotic impregnated test discs in appropriate growth medium. The level of bacterial resistance to each antibiotic was demonstrated by zones of inhibition of bacterial growth.

3.4 Data Analysis

The data was entered into SPSS 20 for descriptive analysis. Results were expressed as percentages and average.

4. RESULTS

Demographic data indicated that females were the majority of patients from where over two thirds of samples were obtained [67.2%] and males represented about a third of the population [Fig. 1].

Age distribution showed that majority of patients was below 50 years [81.4%] of which those within 21 – 30 year old bracket represented the largest age group [Fig. 2].

A total of 4691 laboratory samples were tested for the presence of pathogenic bacteria of which 829 [17.6%] returned with positive results. Distribution showed that Sputum samples returned with the most positive results [57.1%] compared with blood samples which had about 6.7% positive result [Fig. 3].

The most common pathogenic bacterial isolates were *Staphylococcus aureus* [37.3%], *Escherichia coli* [22.7%] and *Klebsiella* pneumoniae [13.1%]. These bacteria were found in all laboratory samples obtained from patients compared with *Proteus* species, *Pseudomonas aeruginosa* and coliforms which were largely found in urine and swab samples [Table 1].

The overall prevalence of pathogenic bacteria in all clinical isolates showed that *Staphylococcus aureus* accounted for over a third of pathogenic bacteria while *Proteus* species were the least commonly encountered isolate [Fig. 4].

All the pathogenic isolates were resistant to between 3 – 6 commonly prescribed antibiotics in the hospital with an average resistance of 4 antibiotics [Table 2].

The prevalence of multidrug resistant strains showed that resistance was found in about 90% of *Staphylococcus aureus* and over 50% of *Escherichia coli* isolates. A similar pattern of resistance was observed for other bacterial isolates though resistance level was lower [Fig. 5].

The pattern of resistance showed that it was highest with the Penicillins and Cotrimoxazole, moderate with Ceftriaxone, Tetracycline, Erythromycin and Gentamycin and least with the Quinolones [Table 3].

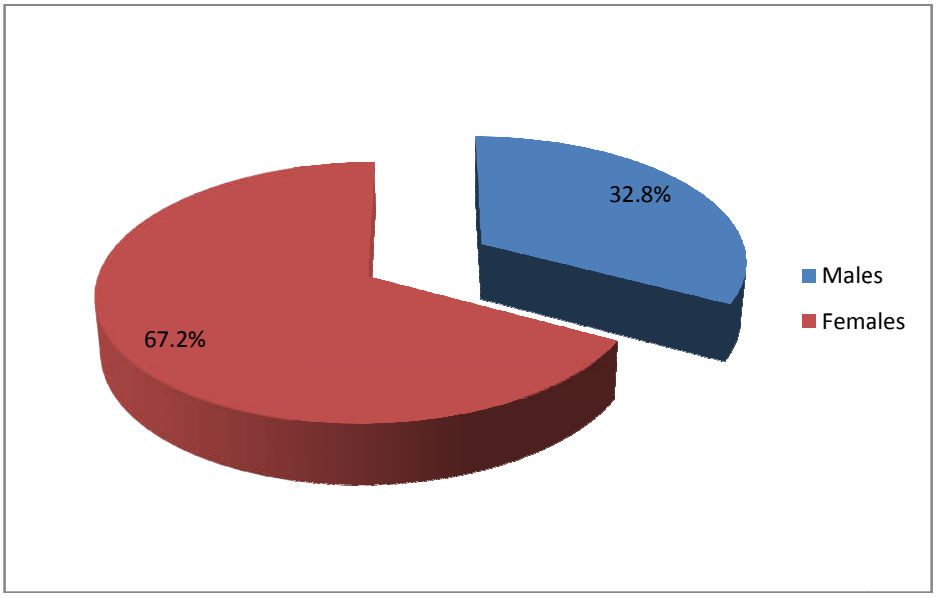

Fig. 1. Gender distribution

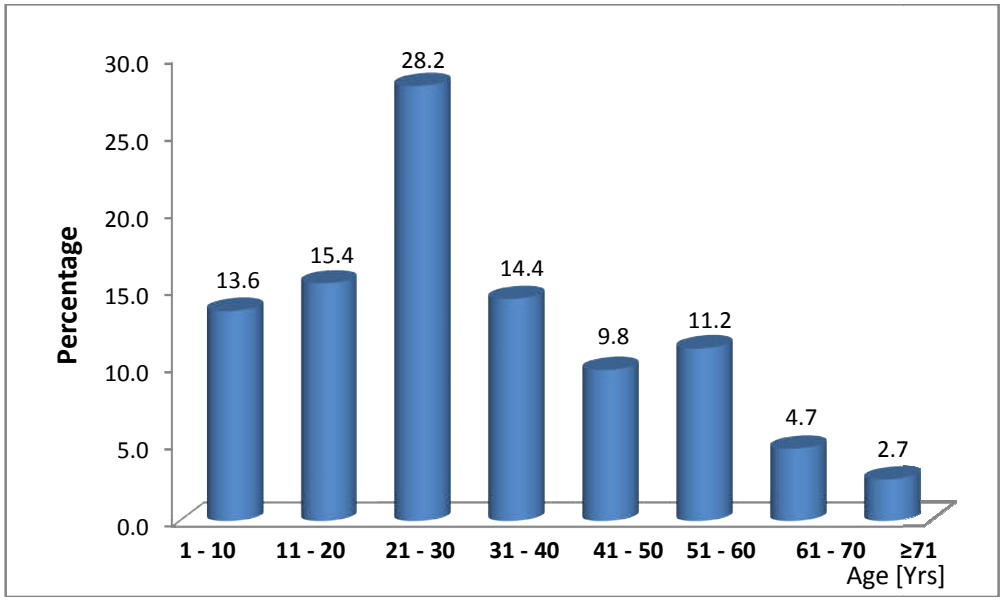

Fig. 2. Age distribution

Table 1. Bacteria found in all laboratory samples

Specimen	SA	EC	KB	PT	PS	HS	CF
Swab	244	64	58	27	29	7	36
Urine	23	114	36	8	10	--	52
Sputum 10	3	9	--	4	39	4	
Blood	32	7	6	--	--	--	7
Total	309	188	109	35	43	46	99

Key: SA = Staph aureus, EC = E. coli, KP = Klebsiella pneumoniae, PT = Proteus spp, PS =Pseudomonas aeruginosa, Haemolytic streptococci HS, CF = Coliforms

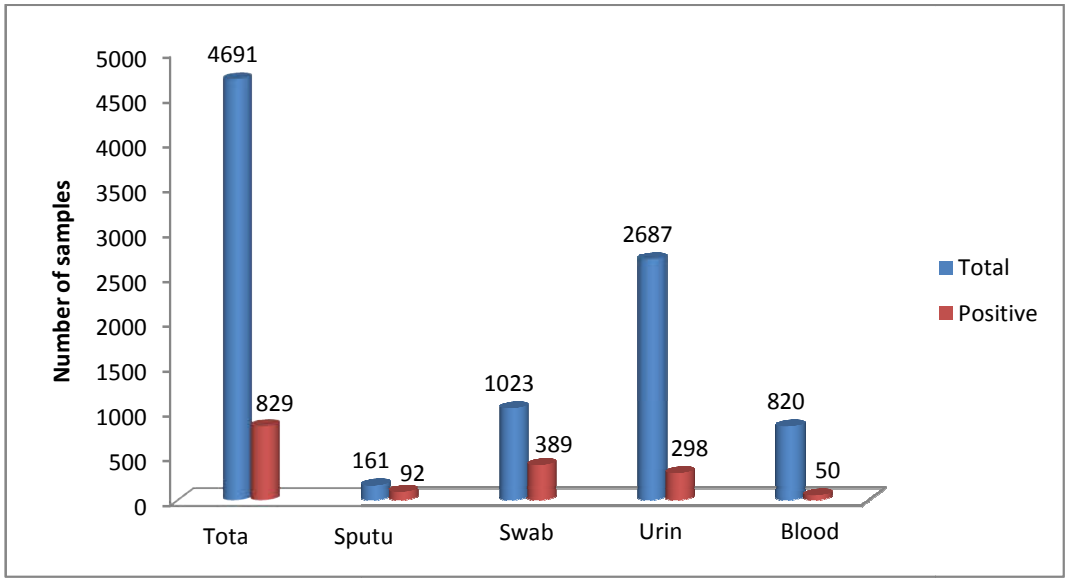

Fig. 3. Distribution of pathogenic bacterial isolates among clinical samples

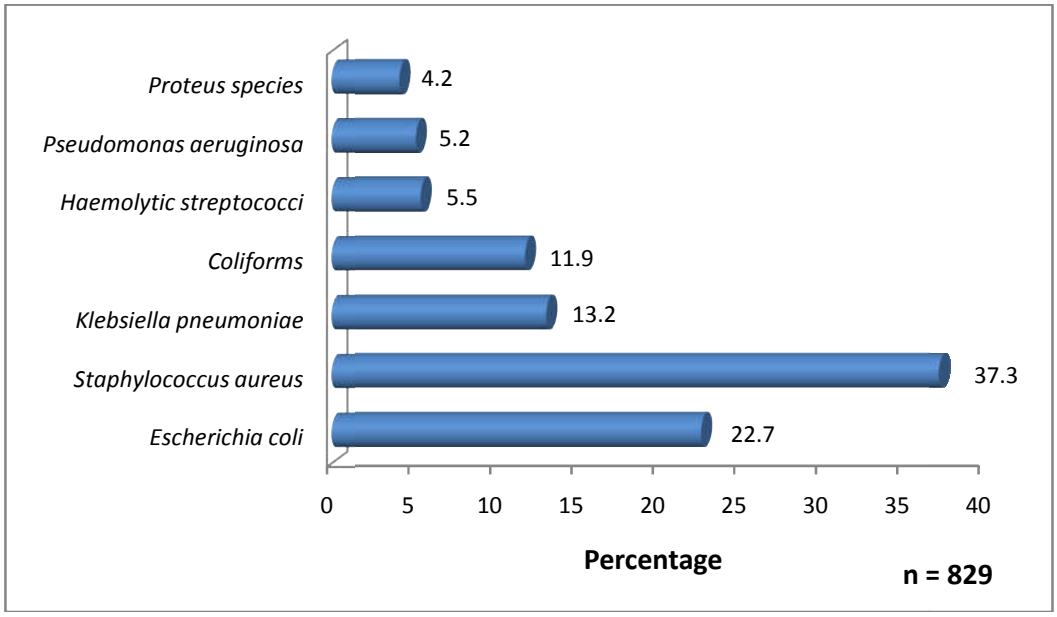

Fig. 4. Distribution of pathogenic bacterial isolates

Table 2. Mean number of resistant antibiotic strains [n = 829]

Bacteria	Number	Antibiotic resistant strains Mean ± SD
Escherichia coli	188	4.06 ± 1.78
Staphylococcus aureus	309	4.11 ± 1.92
Klebsiella pneumonia	109	4.82 ± 1.57
Coliforms	99	4.18 ± 1.72
Proteus spp	35	4.56 ± 1.18
Pseudomonas aeruginosa	43	4.58 ± 1.38
Haemolytic streptococci	46	3.78 ± 1.42

Table 3. Resistance to antibiotics

Drug	EC[%] n = 188	SA[%] n = 309	COL[%] n = 99	KP[%] n = 109	PT[%] n = 35	PS[%] n = 43	HS[%] n = 46	Resistance range [%]
Cloxacillin	30[15.9]	154[49.3]	22[22.2]	29[26.6]	4[11.4]	6[13.9]	17[36.9]	11.4 – 49.8
Clindamycin	21[11.2]	36[11.5]	17[17.2]	21[19.3]	1[2.1]	7[16.3]	17[36.9]	2.1 – 36.9
Amx + CLA	131[69.7]	208[66.7]	86[86.9]	94[86.2]	23[65.7]	20[46.5]	15[32.6]	32.6 – 86.9
Cotrimoxazole	110[58.5]	183[58.7]	67[67.7]	81[74.3]	18[47.4]	15[34.9]	18[39.1]	34.9 – 74.3
Clarithromycin	19[10.1]	74[23.7]	18[18.2]	22[20.2]	6[17.1]	7[16.3]	4[8.7]	8.7 – 23.9
Tetracycline	60[31.9]	56[17.9]	38[38.4]	51[46.8]	17[48.6]	9[20.9]	5[10.8]	10.8 – 48.6
Ceftriaxone	51[27.1]	46[14.7]	31[31.3]	50[45.9]	6[17.1]	7[16.3]	2[4.3]	4.3 – 45.9
Gentamycin	36[19.1]	33[10.6]	28[28.3]	41[37.6]	9[23.7]	2[4.7]	NA	4 7 – 37.6
Methicillin	11[5.9]	8[2.6]	10[10.1]	9[8.2]	5[14.3]	NA	NA	2.6 – 14.3
Erythromycin	12[6.4]	108[34.6]	14[4.1]	21[19.3]	3[3.6]	7[16.3]	10[21.7]	3.6 – 34.9
Ofloxacin	19[10.1]	10[3.2]	13[13.1]	14[12.8]	3[8.6]	NA	NA	3.2 – 13.1
Levofloxacin	7[3.7]	8[2.6]	5[5.1]	10[9.2]	NA	NA	NA	2.6 – 9.2
Ciprofloxacin	4[2.1]	23[7.4]	5[5.1]	9[8.2]	1[2.9]	1[2.3]	9[19.6]	2.1 – 19.6
Nalidixic acid	9[4.8]	18[5.8]	9[9.1]	12[11.0]	3[8.6]	1[2.3]	2[4.3]	2.3 – 11.0
Ampiclox	NA	15[4.8]	2[2.0]	1[0.9]	1[2.9]	NA	9[19.6]	1.0 – 19.6
Amoxicillin	1[0.5]	20[6.4]	5[5.1]	3[2.7]	4[11.4]	1[2.3]	14[30.4]	1.0 – 30.4
Norbactin	2[1.1]	20[6.4]	4[4.0]	6[5.5]	2[5.7]	1[2.3]	10[21.7]	1.1 – 21.7
Perfloxacin	1[0.5]	8[2.6]	3[3.0]	5[4.6]	1[2.9]	NA	NA	1.0 – 4.6
Streptomycin	1[0.5]	13[4.2]	3[3.0]	3[2.7]	1[2.9]	NA	NA	1.0 – 4.2

Key: EC = Escherichia coli, SA = Staphylococcus aureus, COL = Coliforms, KP = Klebsiella pneumonia, PT = Proteus spp, PS = Pseudomonas aeruginosa, HS = Haemolytic streptococci, AMX+CLA = Amoxicillin + Clavulanic acid, NA = not applicable

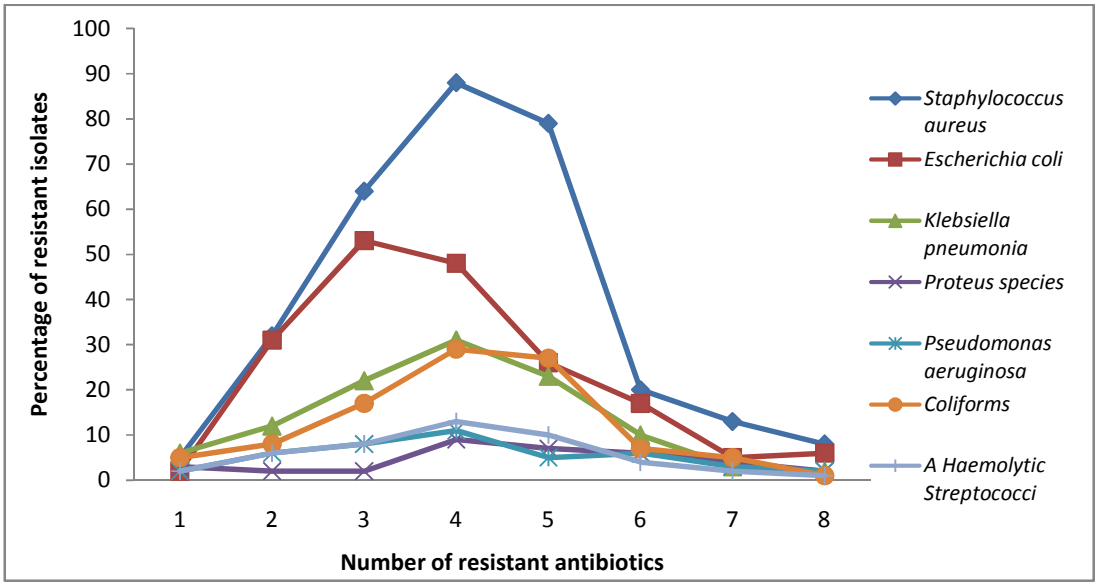

Fig. 5. Percentage of multidrug resistant isolates

5. DISCUSSION

The emergence and rapid spread of resistance in sub Saharan Africa is endangering efficacy of antibiotics and limiting treatment options in the face of high infectious disease burden. Healthcare facilities have been recognized as a place where resistance to antibiotics can easily be spread among patients. The results of this study showed that *Staphylococcus aureus* accounted for more than a third of all isolates from clinical samples followed by *Escherichia coli*. These two bacteria account for more than two thirds of all isolates comparable to an earlier study [18], but lower than that reported in previous studies [49,50]. Many clinical samples had *Staphylococcus aureus,* however *Escherichia coli* were predominantly found in urine samples [51,52]. Several studies reported that *Staphylococcus aureus* is found in many clinical specimens across African countries with prevalence that is as high as 60.9% [53, Opoku-Okrah et al. 2013]. A number of gram negative bacteria such as *Klebsiella, Proteus* and *Pseudomonas aeruginosa* have also been reported clinical specimens with varying level of prevalence [54, 55], [Fadeyi et al. 2016]. Majority of alpha *haemolytic Streptococci* were isolated from sputum specimens similar to previous studies [48].

In many developing countries, prevalence of *Klebsiella* infections is higher compared to the findings of this study [56,57,58]. Similar pattern of varying prevalence of bacterial isolates was reported for *Pseudomonas aeruginosa*, *Proteus* species, *Klebsiella* and *coliforms* which are in contrast to the results of this study [59,60,61,62,63,64, 65].

The emergence of antibiotic resistance is known to be due to a complex interplay of several factors that include overuse/irrational use and environmental factors. Evidence from this study showed that bacterial isolates were resistant to 3 – 6 antibiotics on the average. This high level of resistance presents a unique challenge in this setting where empirical antibiotic treatment is widespread. It also raises doubt as to the efficacy and appropriateness of existing guideline recommendations for syndromic treatment of infections [Bernabe et al. 2017]. Antibiotics with high level resistance included Amoxicillin + Clavulanic acid, Cotrimoxazole, Cloxacillin, Tetracycline and Ceftriaxone in that order of decreasing frequency. Quinolones have the least resistance which was below 20% for these commonly isolated bacteria.

The level of resistance to Amoxicillin + Clavulanic acid in this study is lower than that earlier reported [51, Saba et al. 2017, 66], but comparable to results of another studies [Masyeni et al. 2016]. Resistance of *Staphylococcus aureus* to Cotrimoxazole and Macrolides in this study is considerably higher compared to previous studies [67, 68]. In the case of *Escherichia coli*, resistance to Amoxicillin + Clavulanic acid, Cotrimoxazole and

Ceftriaxone is comparatively higher [Ray et al. 2015, 69]. Penicillins and Macrolides have showed consistently comparable level of resistance to several strains of bacteria as reported in previous studies [70,71,72]. The level of resistance to Quinolones found in this study is lower than previous studies, though some reports indicated that resistance is higher [73,61].

A similar pattern of resistance was also observed with *Pseudomonas aeruginosa* and *Haemolytic Streptococci*, though resistance to Quinolones have been reported to have higher [74,75], however one study reported lower level of resistance [76]. The high level of multidrug resistance observed in this study has also been reported around the world [77, 78]. One of the major driving factors is inappropriate prescribing and self-medication in the community [79, 80]. In Nigeria, poor regulatory controls, misuse and inappropriate prescribing habits is compounding the problems of resistance. Many patients only report to hospital when self-medication fail to address their health problems.

Evidence from this study and several others clearly indicate that routine empirical antibiotic prescription can no longer be justified as rational. There is therefore an urgent need to review antibiotic use policies to emphasize microbial susceptibility testing as a means of ensuring that cost effective treatment outcomes are achieved.

6. CONCLUSION

Antibiotic resistance to commonly used antibiotics is very high. There is need to de-emphasize empirical prescriptions and rely more on evidence based susceptibility testing of pathogens before initiation of a suitable course of antibiotic therapy.

7. LIMITATIONS

There are a number of limitations of this study

- The data were extracted from records and there may be errors in entry and/or test procedures
- The quality of materials and adherence to standard test procedures could not be ascertained
- The presence of antibiotic tainted samples due to previous antibiotic therapy or self-medication may influence results

ETHICAL APPROVAL

It was received from human ethics research committee of University of Maiduguri teaching hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist

REFERENCES

1. World Health Organization. The evolving threat of antimicrobial resistance: Options for action. Geneva, Switzerland. WHO; 2012.
2. World Health Organization. Antimicrobial resistance – Global report on surveillance. Geneva. Switzerland. WHO; 2014.
3. Frean J, Perovic O, Fensham V, McCarthy K, von Gottberg A, de Gouveia L et al. External quality assessment of national public health laboratories in Africa 2002 – 2009. Bull World Health Organization. 2012;90:191–191A.
4. Levy SR, Marshall B. Antibacterial resistance worldwide: Causes, challenges and responses. Nat Med. 2004;10(Suppl 12):S122–S129.
5. Lateef A. Antibiotics use and misused in developing countries. World J Microbiol. 2004;20:167– 170.
6. Nsofor CA, Iroegbu CU. Antibiotic resistance profile of *Escherichia coli* isolated from apparently healthy livestock in south eastern Nigeria. J Cell Animal Biol. 2012;6(6):2445–2450.
7. Ohi CA, Luther VP. Antimicrobial stewardship for inpatients facilities. J Hosp Med. 2011;6(Suppl 1):S4–S15.
8. Umar LH, Isah A, Musa S, Umar B. Prescribing pattern and antibiotic use for hospitalized children in a northern Nigerian teaching hospital. Ann Afr Med. 2018;17:26–32.
9. Eshiet UI, Effiong GS, Akwaowoh AE. The use of antibiotics in a Nigerian tertiary health care facility. Am J Biomed Sci Engineering. 2015;1(5):25–31.
10. Akinyandenu O, Akinyandenu A. Irrational use and non-prescription sale of antibiotics in Nigeria: A need for change. J Sci Innovative Res. 2014;3(2):251–257.
11. Oduyebo OO, Olayinka AT, Iregbu KC, Versporten A, Goossens H, Nwajiobi-

Princewill PI, Jimoh O, Ige TO, Aigbe AI, Ola-Bello OI, Aboderin AO, Ogunsola FT. A point prevalence survey of antimicrobial prescribing in four Nigerian tertiary hospitals. Ann Trop Pathol. 2017;8:42–46.

12. Kourlaba G, Gkrania-Klotsas E, Kourkouni E, Mavrogeorgos G, Zaoutis TE. Antibiotic prescribing and expenditures in outpatient adults in Greece, 2010 – 2013: Evidence from real world practice. Euro Surveill. 2016;21(26):PII–302266.
13. Akram A, Megha R, Irfanul H, Pravina A, Rahul I, Dasari R, Kuriakose S, Patel I. Study the prescription pattern of antibiotics in the medicine department in a teaching hospital: A descriptive study. Int J Toxicol Pharmacol Res. 2014;6(4):43–46.
14. Kaur A, Bhagat R, Kaur N, Shafiq N, Gautam V, Malhotra S, Suri V, Bhalla A. A study of antibiotic prescription pattern in patients referred to tertiary care center in Northern India. Ther Adv Infect Dis. 2018;5(4):63–68.
15. Cui D, Liu X, Hawkey P, Li H, Wang Q, Mao Z, Sun J. Use of and microbial resistance to antibiotics in China: a path to reducing antimicrobial resistance. J Int Med Res. 2017;45(6): 1768–1778.
16. Oli AN, Okafor CI, Ibezim EC, Akujiobi CN, Onwunzo MC. The prevalence and bacteriology of asymptomatic bacteruria among antenatal patients in Nnamdi Azikiwe University teaching hospital Nnewi, South eastern Nigeria. Niger J Clin Pract. 2010;13:409–412.
17. Oladeinde BH, Omoregie B, Olley M, Anunibe JA. Urinary tract infection in a rural community of Nigeria. N Am J Med Sci. 2011;3:75–77.
18. Muoneke V, Ibekwe M, Ibekwe R. Childhood urinary tract infections in Abakiliki: Etiological organisms and antibiotic sensitivity pattern. Ann Med Health Sci Res. 2012;2:29–32.
19. Rabasa AI, Shattima D. Urinary tract infections in severely malnourished children at the University of Maiduguri teaching hospital. J trop Pediatr. 2002;48:359–361.
20. Okwori EE, Nwadioha SI, Jombo GTA, Nwokedi EOP, Odimayo MS. A comparative study of bacterial isolates from the urine samples of AIDS and non AIDS patients in Benue, Nigeria. Asian Pacific J Trop Med. 2010;3:382–385.
21. Mava Y, Bello M, Ambe JP, Zailani SB. Antimicrobial sensitivity pattern of organisms causing urinary tract infections in children with sickle cell anaemia in Maiduguri, Nigeria. Niger J Clin Pract. 2012;15:420–423.
22. Sire JM, Nabeth P, Perrier-Claude JD, Bahsoun I, Silby T, Macondo EA, et al. Antimicrobial resistance in outpatient *Escherichia coli* urinary isolates in Dakar – Senegal. J Infect Dev Ctries. 2007;1:263–268.
23. Stamm WE, Norby SR. Urinary tract infections: Disease panorama and challenges. J Infect Dis. 2001;183(Suppl 1):S1–S4.
24. Russo TA, Johnson JR. Medical and economic impact of extra-intestinal infections due to *Escherichia coli*: Focus on an increasing important endemic problem. Microbes Infect. 2003;5(5):449-456.
25. Dehbanipour R, Rastaghi S, Sedighi M, Maleki N, Faghri J. High prevalence of multidrug resistance uropathogenic *Escherichia coli* strain. Isfahan, Iran. J Nat Sci Biol Med. 2016;7(1):22–26.
26. Pitout JD, Laupland KB. Extended spectrum beta-lactamase producing Enterobacteriacea: An emerging public health concern. Lancet Infect Dis. 2008;3(3):159–166.
27. Urban C, Mariano N, Bradford PA, Tuckman M, Segal-Maurers JR, et al. Identification of CTX-M- beta-lactamases in *Escherichia coli* from hospitalized patients and residents of long term care facilities. Diagn Microbiol Infect Dis. 2010;66(4):402–406.
28. Amabile–Cuevas CF, Arredondo–Garcia JL, Cruz A, Rosas I. Fluoroquinolone resistance in clinical and environmental isolates of *Escherichia coli* in Mexico City. J Appl Microbiol. 2010;168(1):158–162.
29. Silva-Sanchez J, Cruz-Trujillo E, Barrios H, Reyna-Flores F, Sanchez-Perez A, Garcia-Ramos U. Characterization of plasmid mediated quinolone resistance [PMQR] gene in extended spectrum beta-lactamase producing Enterobacteriacea in pediatric clinical isolates in Mexico. Plos One. 2013;8(10):e77968.
30. Paniagua-Contreras GL, Monroy-Perez E, Rodriguez-Moctezuma JR, Dominguez-Trejo P, Vaca-Paniagua F, Vaca S. Virulence factors, antibiotic resistance phenotypes and O sero-groups of *Escherichia coli* strains isolated from community acquired urinary tract infection

patients in Mexico. J Microbiol Immunol Infect. 2017;50(4):478–485.
31. Center for disease dynamics, economics and policy. State of the world's antibiotics 2015. Washington DC; 2015.
32. Robicsek A, Beaumont JL, Paule SM, et al. Universal surveillance for Methicillin resistant *Staphylococcus aureus* in 3 affiliated hospitals. Ann Intern Med. 2008;148(6):409–418.
33. Gordon JR, Lowy FD. Pathogenesis of MRSA infection. Clin Infect Dis. 2008;46(5):S350–S359.
34. Jarvis WR, Schlosser J, Chinn RY, Tweeten S, Jackson M. National prevalence of methicillin resistant *Staphylococcus aureus* in inpatients at a US healthcare facilities. Am J Infect Control. 2007;35(10):631–637.
35. Haznedaroglu T, Oncul T, Hosbul S, Cavuslu O, Ozyurt M et al. Methicillin resistance in *Staphylococcus aureus* strains isolated from hospitalized patients: three year trend. TAF Prevent Med Bull. 2010;9(6):585–590.
36. Ramirez-Castillo, Flor Y, Adriana C, Moreno-Flores, Francisco J, Avelar-Gonzalez, Francisco–Marquez-Diaz, Josee H, Alma L, Guerrero-Barrera. An evaluation of multidrug resistant *Escherichia coli* isolates in urinary tract infections from Aguascalientes, Mexico: Cross section study. Ann CLin Microbiol Antimicrob. 2018;17:34.
37. Bubonja-Sonje M, Matovina M, Skrobonja J, Bedemic B, Abram M. Mechanism of Carbanepem resistance in multidrug resistant clinical isolates of *Pseudomonas aeruginosa* from a Croatian hospital. Microbiol Drug Resist. 2015;21(3):261–269.
38. Labarca JR, Salles MJ, Seas C, Guzman-Blanco M. Carbanepem resistance in *Pseudomonas aeruginosa* and *Acinebacter baumanii* in the nosocomial setting in Latin America. Critical Rev Microbiol. 2016;42(2):276–292.
39. Nsofor CA, Anyanwu NC, Ogbulie TE. High antibiotic resistance pattern observed in bacterial isolates from a tertiary hospital in South east Nigeria. Int J Res Pharm Biosciences. 2016;3(1):1–6.
40. Jombo GT, Emanghe UE, Amefule EN, Damen JG. Urinary tract infections at a Nigerian University hospital, causes and antimicrobial susceptibility profile. J Microbiol Antimicrob. 2011;3:53–59.
41. Muluye D, Wondimeneh Y, Ferede G, et al. Bacterial isolates and their antibiotic susceptibility pattern among patients with pus and /or wound discharge at Gondar University hospital. BMC Res Notes. 2014;7(1):619.
42. Ruiz J, Villareal E, Gordon M, Frasquet J, Castellanos A, Ramirez P, et al. From MIC creep to MIC decline: *Staphylococcus aureus* antibiotic susceptibility evolution over the last 4 years. Clin Microbiol Infect. 2016;22(8):741–742.
43. Trojan R, Razdan L, Singh N. Antibiotic susceptibility pattern of bacterial isolates from pus samples in a tertiary care hospital of Punjab, India. Int J Microbiol; 2016. [Article ID 9302692] Available:http://dx.doi.org/10.1155/2016/9302692
44. Kariuki S, Gordon MA, Feasey N, Parry CM. Antimicrobial resistance and management of invasive Salmonella disease. Vaccine. 2015;33(Suppl 3):C21–C29.
45. Le Doare K, Bielicki J, Heath PT, Sharland M. Systematic review of antibiotic resistance rates among gram negative bacteria in children with sepsis in resource limited countries. J Pediatr Infect Dis Soc. 2014;4(1):11–20.
46. Leopold SJ, van Leth F, Tarekegn H, Schultsz C. Antimicrobial drug resistance among clinically relevant bacterial isolates in sub Saharan Africa: A systematic review. J Antimicrob Chemother. 2014;69(9):2337–2353.
47. Blomberg B, Jureen R, Manji RP, Tamin BS, Nwakagile DSM, Urassa WK, et al. High rate of fatal causes of pediatric septicemia caused by gram negative bacteria with extended spectrum beta-lactamases in Dar es Salam, Tanzania. J Clin Microbiol. 2005;43:745–749.
48. Masyeni S, Sukmawati H, Siskayani AS, Dharmayanti S, Sari K. Antimicrobial susceptibility pattern of pathogens isolated from various specimens in Denpasar – Bali: A two years retrospective survey. Biomed Pharmacol J. 2018;11(1):493–502.
49. Sewunat T, Demissie Y, Mihret A, Abebe T. Bacterial profile and antimicrobial susceptibility pattern of isolates among burn patients at Yekatit 12 hospital burn centre, Adis Ababa, Ethiopia. Ethiopian J Health Sci. 2013;23(3):209–216.
50. Dilnessa T, Bitwe A. Prevalence and antimicrobial susceptibility pattern of

Methicillin resistance *Staphylococcus aureus* isolated from clinical samples at Yekatit 12 hospital medical college, Adis Ababa, Ethiopia. BMC Infect Dis. 2016;398.

51. Ragbetli C, Parlak M, Bayram M, Guducuoglu H, Ceylan N. Evaluation of antimicrobial resistance in *Staphylococcus aureus* isolates by years. Interdisciplinary Perspect Infect Dis. 2016;ID9171395. Available:http://dx.doi.org/10.1155/2016/9171395
52. Ramirez–Castillo FY, Moreno–Flores A, Avelar–Gonzalez FF, Marquez–Diaz F, Harel J, Guerrero–Barrera AL. An evaluation of multidrug resistant *Escherichia coli* isolates in urinary tract infections from Aquascalientes. Mexico: Cross sectional study. Ann Clin Microbiol. 2018;17:34.
53. Acquah SE, Quaye L, Sagbe K, Ziem JB, Bromberger P, Amponsem AA. Susceptibility of bacterial etiological agents to community used antimicrobial agents in Children with sepsis at the Tamale teaching hospital. BMC Infect Dis. 2013;18(13):89.
54. Mordi RM, Momoh MI. Incidence of *Proteus* species in wound infection and their sensitivity pattern in University of Benin teaching hospital. Afr J Biotech. 2009;8(5):725–730.
55. Kehinde AO, Ademola SA, Okesola AO, Oluwatosin OM, Bakare RA. Pattern of bacterial pathogens in burn wound infection in Ibadan, Nigeria. Ann Burns Fire Disasters. 2004;17(1):12– 15.
56. Hansen DS, Auken HM, Abiola T, Podschun R. Recommended test panel for differentiation of *Klebsiella* species on the basis of trilateral inter-laboratory evaluation of 18 biochemical tests. J Clin Microbiol. 2004;42:3665–3669.
57. Chakraborty S, Moshina K, Sarker PK, Alam MDZ, Sayem SMA. Prevalence, antibiotics susceptibility profiles and ESBL production in *Klebsiella pneumoniae* and *Klebsiella oxytoca* among hospitalized patients. Periodicum Biologocum. 2016;118(1):53–58.
58. Olowe OS, Oladapo GO, Makajuola OA, Olaitan JO. Prevalence of extended spectrum beta – lactamases [ESBLs] carrying genes in *Klebsiella* species from clinical samples at Ile – Ife, South west Nigeria. Int J Pharm Med Biosci. 2012;1(2):129–138.
59. Mahmoud AM, Tarig MSA, Osama MS, Mariam MA. Prevalence and antimicrobial resistance pattern of bacterial strains isolated from patients with urinary tract infections in Messalata central hospital, Libya. Asian Pacific J Trop Med. 2016;9(8):771–778.
60. Putil HV, Patil VC. Incidence, bacteriology and clinical outcome of ventilator associated pneumonia at tertiary care hospital. J Natr Sci Biol Med. 2017;8(1):46–55.
61. Akter J, Masadil Azad Chowdhury AM, Forkan M. Study on prevalence and antibiotic resistance pattern of *Klebsiella* isolated from clinical samples in South east region of Bangladesh. Am J Drug Delivery Dev. 2014;4(1):73–79.
62. Riaz S, Faisal M, Hasnain S. Prevalence and comparism of beta-lactamase producing *Escherichia coli* and *Klebsiella* species from clinical and environmental sources in Lahore, Pakistan. Afr J Microbiol Res. 2012;6:465–470.
63. Sarathbau R, Ramani TV, Bhaskara K, Panda S. Antibiotic susceptibility pattern of *Klebsiella pneumoniae* isolated from sputum, urine and pus samples. J Pharm Biol Sci. 2012;1:4–9.
64. Prasad RR, Shree V, Sagar S, Kumar S, Kumar P. Prevalence and antimicrobial susceptibility pattern of *Proteus* species in clinical samples. Int J Curr Microbiol App Sci. 2016;5(4):962–968.
65. Bahashwan SA, El Shafey HM. Antimicrobial resistance pattern of *Proteus* isolates from clinical isolates from clinical specimens. Europ Sci J. 2013;9(27):1857–1881.
66. Bernabe KJ, Langendorf C, Ford N, Baptiste Ronat J, Murphy R. Antimicrobial resistance in West Africa: A systematic review and meta – analysis. Int J Antimicrob Agents. 2017;50:629–639.
67. Aydin N, Gultekin B, Eyigor M, Gurel M. The antibiotic resistance of *Staphylococuss aureus* isolated of clinical specimens. Adan Menderes Universitesi Tip Fakultesi Dergisi. 2001;2(3):21–26.
68. Ozkalp B, Baybek H. *In vitro* susceptibility to various antibiotics of *Staphylococcus aureus* isolated from clinical specimens. Genel Tip Derg. 2003;13(2):65–68.
69. Ali Abdel Rahim KA, Ali Mohamed AH. Prevalence of extended spectrum beta – lactamase producing *Klebsiella pneumoniae* in clinical isolates.

Jundishapur J Microbiol. 2014;7(11): e17114.
70. Dash M, Padhi S, Mohanty I, Panda P, Parida B. Antimicrobial resistance in pathogens causing urinary tract infections in a rural community of Odisha, India. Indian J Family Community Med. 2013;20:20–26.
71. Niranjan V, Malini A. Antimicrobial resistance pattern in a *Escherichia coli* causing urinary tract infections among inpatients. Indian J Med Res. 2014;139:945–948.
72. Dugal S, Purohit H. Antimicrobial susceptibility profile and detection of extended spectrum beta-lactamases production by gram negative uropathogens. Int J Pharm Pharm Sci. 2013;5:434– 438.
73. Olorunmola FO, Kolawole DO, Lamikanra A. Antibiotics resistance and virulence properties in *Escherichia coli* strains from cases of urinary tract infections. Afr J Infect Dis. 2013;7(1):1–7.
74. Sharma J, Singh S, Kaur Gill A, Kaur A. Prevalence and antimicrobial susceptibility pattern of *Pseudomonas aeruginosa* isolated from pus samples in a tertiary care hospital. Bathinda. Int J Contemporary Med Res. 2016;3(12):3481–3483.
75. Khan F, Khan A, Kazmi SU. Prevalence and susceptibility pattern of multidrug resistant clinical isolates of *Pseudomonas aeruginosa* in Karachi. Pak J Med Sci. 2014;30(5):951–954.
76. Naik TB, Nadagir SD, Biradar A. Prevalence of Beta – *Hemolytic Streptococci* groups A, C and G in patients with acute pharyngitis. J Lab Physician. 2016;8(1):45–49.
77. Rossolini GM, Arena F, Pecile P, Pollini S. Update on the antibiotic crisis/ Clin Opin Pharmacol. 2014;18:56–60.
78. Golkar Z, Bagazra O, Pace DG. Bacteriophage: A potential solution for the antibiotic resistance crisis. J Infect Dev Ctries. 2014;8(2):129–136.
79. Bartlett JG, Gilbert DN, Spellberg B. Seven ways to preserve the miracle of antibiotics. Clin Infect Dis. 2013;56(10): 1445–1450.
80. Luyt CE, Brechot N, Trouillet JL, Chastre J. Antibiotic stewardship in the intensive care unit. Crit Care. 2014;18(5):480.

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