

# Original Research Article

## Empirical antibiotic prescription pattern among patients in a Nigerian tertiary hospital, Is there evidence of irrationality?

### ABSTRACT

**Background:** Resistance to antibiotics is spreading rapidly around the world with its associated morbidity and mortality. Infections are becoming increasingly difficult to treat resulting in increasing cost of medical care. In low income countries with high infectious disease burden, antibiotic resistance is reported to be accelerated by irrational prescriptions in health facilities. In the absence of adequate resources, many clinicians engage in empirical antibiotic prescriptions some of which their appropriateness is questionable. There is need to for laboratory evidence to justify empirical antibiotic use in the light of increasing resistance to commonly prescribed antibiotics

**Aims:** This study aims to determine empirical antibiotic prescription pattern and to determine rationality using resistance profile of common bacterial isolates in the hospital.

**Methods:** Antibiotic prescriptions in the NHIS department and antibiogram records were obtained from pharmacy and laboratory records respectively. Analysis was carried out using descriptive statistics and comparism between antibiotics prescribed and their respective resistance pattern were compared to determine rationality.

**Results/Discussion:** The Penicillins and Quinolones were the most prescribed class of antibiotics and resistance range between 30 – 90% and 3 – 23% respectively. Resistance to other antibiotics was high thus making empirical prescriptions irrational in most of the cases. These findings have been consistently reported in several studies so widespread empirical antibiotic prescriptions are not in tandem with principles of rational drug use.

**Conclusion:** Antibiotic resistance is common among hospital isolates, so there is need to emphasize that prescriptions be based on laboratory evidence of microbial sensitivity.

**Keywords:** *Antibiotics, Empirical prescription, rational drug use, Microbial resistance*

### INTRODUCTION

Antibiotics have been the cornerstone of modern medical care particularly in bacterial infections.

Since the introduction of antibiotics over eight decades ago, infections that would have otherwise

14 caused life threatening are now treatable. Infections from surgery, immunosuppression, traumatic  
15 injuries and prophylaxis have dramatically improved survival. In recent years however, reports of  
16 increasing microbial resistance have become consistent across a broad range of microorganisms  
17 [1,2,3,4,5]. Infections that were once treatable are now becoming difficult to treat resulting in increased  
18 morbidity and mortality, high cost of medical care and threatening global public health [6,7,8,9,10]. There  
19 is global evidence of the decline of effectiveness of antibiotics across all classes, there is however  
20 country and regional variations in antimicrobial resistance pattern [11].

21 Microbial resistance is reported to be a significant factor in mortality related to infectious diseases  
22 annually [12]. In less developed countries with high infectious disease burden and absence of reliable  
23 data, estimates of mortality also run into hundreds of thousands annually [13,14,15]. The rise in  
24 antimicrobial resistance in low income countries is related to a number of factors including easy  
25 availability of antibiotics, self-medication, extensive use in agriculture, and failure in infectious disease  
26 control system in healthcare facilities etc. [16,17] and irrational prescription practices [18,19,20,21,22].

27 Antibiotic prescription practices vary widely between countries and healthcare facilities; factors which  
28 have been reported to influence antibiotic use includes infectious disease burden, prescription habit of  
29 clinicians, microbial resistance pattern, regulatory control, standard treatment guidelines, availability  
30 and economic factors [23,24,25,26,27,28,29,30,31]. In resource scarce setting where routine empirical antibiotic  
31 use is widespread, prescription pattern vary widely [22]. For instance, some studies reported that  
32 Fluoroquinolones, Penicillins and Cephalosporins are the most prescribed class of antibiotics [22,32]  
33 while other studies reported high level use of Beta lactams [17,33].

34 The relationship between irrational antibiotic use and microbial resistance is well established and the  
35 current trend of antibiotic use is suggestive of an ongoing problem irrespective of healthcare setting.  
36 Among the most commonest microorganisms whose resistance to antibiotics is of global concern are  
37 *Escherichia coli*, *Streptococcus pneumoniae*, *Shigella species* *Neisseria gonorrhoea* and non typhoidal  
38 *Salmonella Typhi* [34,35,36,37,38,39,40]. Empirical antibiotic use is widely reported in literature either in the  
39 form of self-medication or irrational use in healthcare facilities, studies have reported that up to 50% of  
40 antibiotic prescriptions may be in the form of empirical prescriptions [41]. Microbial sensitivity results  
41 are rarely used in many health facilities because of poor healthcare infrastructure and paucity of  
42 qualified manpower [42,43]. In many healthcare facilities where laboratory services are available,  
43 antibiotic prescriptions are not routinely based on microbial sensitivity result which is a common cause

44 of irrational antibiotic use<sup>[26,41,44]</sup>, antibiotic prescription studies have reported high levels of irrational  
45 use and an increasing level of resistance to commonly used antibiotics<sup>[23,45]</sup>.

46 While it may be impractical to wait for antibiotic sensitivity tests before in all clinical situations, it is  
47 important that empirical prescription of antibiotics is regulated so as preserve their effectiveness and  
48 limit risk of treatment failure due to microbial resistance. It's not clear if microbial resistance  
49 containment measures such as antibiotic stewardship programs, continuing education for prescribers,  
50 patient education and regulatory control are contributing to improved antibiotic use in developing  
51 countries due to absence of reliable data<sup>[46,47,48]</sup>. In Nigeria there are few published studies that used  
52 microbial sensitivity pattern as a basis for determining level of irrational antibiotic prescriptions in  
53 healthcare facilities, so this study is an attempt in that direction.

54 In addition using World Health Organization quality prescribing indicators, it is important that antibiotic  
55 use should reflect the dynamics of prevailing microbial sensitivity pattern. Physicians have for a long  
56 time viewed antibiotics as "magic bullets" for all infectious disease, that perception should now give  
57 way to the new reality that "bugs" no long respond to therapy as before. It is expected that treatment  
58 of bacterial infections should have been based on laboratory evidence to qualify as rational antibiotic  
59 use. This appears not to be the case at the moment even in many tertiary healthcare facilities in the  
60 country; this must change as high level of microbial resistance is a potential threat to public health.

61 **Objectives:** To determine empirical antibiotic use pattern and compare with resistance of common  
62 bacterial isolates so as to assess rationality of prescriptions

## 63 **METHODS**

64 **Setting:** The study was carried out among patients insured by national health insurance scheme  
65 receiving at the University of Maiduguri teaching hospital, North east Nigeria.

66 **Study design:** This is a cross sectional retrospective study of prescriptions given to outpatients that  
67 filled their prescriptions in the NHIS pharmacy of the hospital.

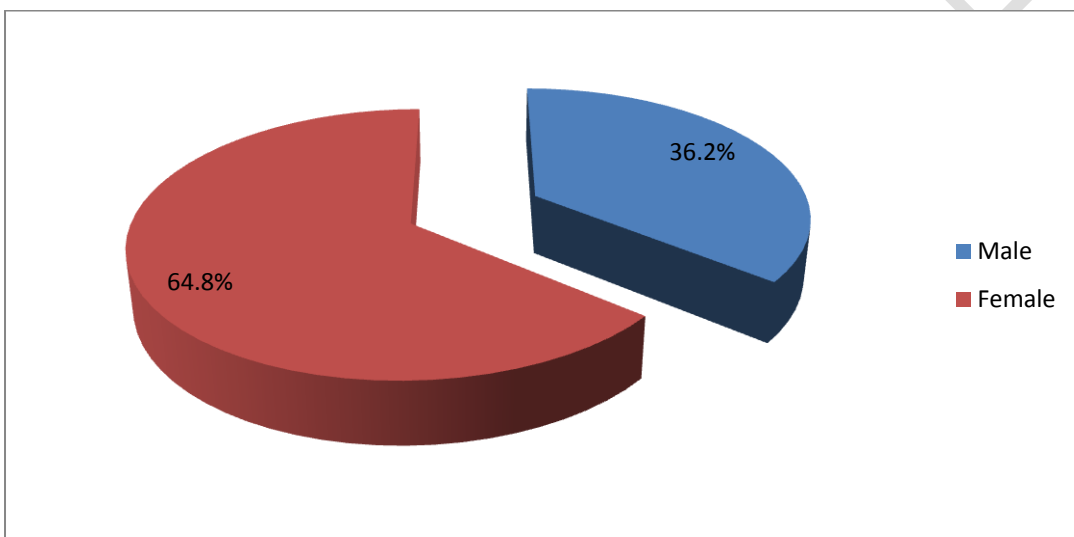
68 **Data collection:** Prescription records were obtained from National health insurance scheme [NHIS]  
69 pharmacy covering the period between January 2017 and May 2018. A total of 5079 antibiotic  
70 containing prescriptions were used for this study. All eligible prescriptions selected had patient NHIS  
71 numbers clearly indicated. Prescription records that are incomplete, illegible and those not written on  
72 NHIS prescription forms were excluded. Information relating to antibiotics, duration of therapy, number  
73 of drugs per prescription, antibiotic prescription errors and demographic data were extracted

74 **Data analysis:** The data was entered into SPSS 21 and analyzed using descriptive statistics.  
75 Irrational prescriptions were determined by comparing antibiotics prescribed and resistance level from  
76 laboratory results. Prescriptions were also reviewed for prescription errors, dosage errors, formulation  
77 errors and frequency of administration errors.

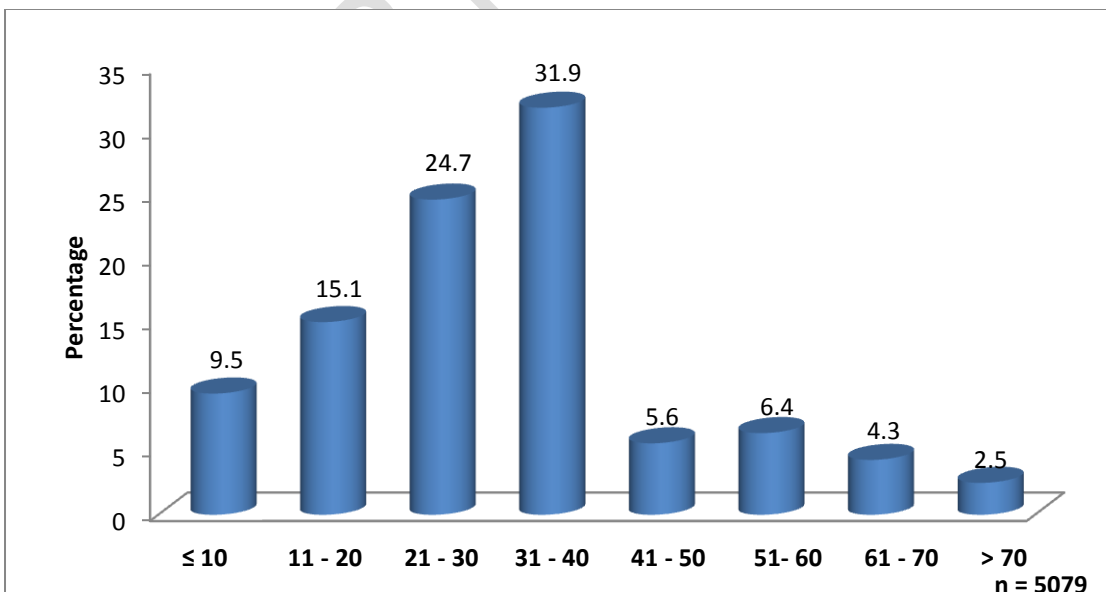
78 **Ethical approval:** This was obtained from the health research ethics committee of University of  
79 Maiduguri teaching hospital

80 **RESULTS**

81 Demographic data showed that females were about two thirds of patients and majority of them are  
82 below 40 years old [Figure 2 and 2].



83  
84 Figure 1: Gender distribution  
85



86  
87 Figure 2: Age distribution  
88

89 Prescription analysis showed that Penicillins [39%] accounted for the largest group of antibiotics given  
90 to patients. This is followed by Quinolones and Metronidazole with prescription rate of 25% and 17.8%

91 respectively. Among individual antibiotics Amoxicillin + Clavulanic acid, Metronidazole and  
92 Ciprofloxacin were the most prescribed representing 28.2%, 17.8% and 13.1% respectively.

93

94 **Table 1:** Antibiotics prescription pattern [n = 5079]

Name of drug	Number [%]
Amoxicillin + Clavulanic acid	1433 [28.2]
Amoxicillin	448 [8.8]
Ampicillin + Cloxacillin	108 [2.1]
Ciprofloxacin	663 [13.1]
Azithromycin	75 [1.5]
Cefuroxime	217 [4.3]
Ceftriaxone	13 [0.3]
Cephalexin	11 [0.2]
Erythromycin	294 [5.8]
Clarithromycin	56 [1.1]
Clindamycin	17 [0.3]
Levofloxacin	378 [7.4]
Metronidazole	906 [17.8]
Ofloxacin	146 [2.9]
Sparfloxacin	58 [1.1]
Doxycycline	187 [3.7]
Cotrimoxazole	38 [0.7]
Nitrofurantoin	23 [0.5]
Lincomycin	8 [0.2]

95

96 Antibiotic combination therapies were present in 12.8% of prescriptions; the most common is  
97 Penicillins + Metronidazole accounting for more than half of combination therapies. Metronidazole  
98 was found in 93.8% prescriptions in combination with different classes of antibiotics. The Quinolones  
99 were also found in 24.4% of prescriptions with other classes of antibiotics.

100

101 **Table 2:** Antibiotic combination therapy [n = 652]

Antibiotic combinations	Number [%]
Quinolones + Metronidazole	138 [21.2]
Penicillins + Metronidazole	357 [54.8]
Penicillins + Macrolides	13 [1.9]
Cephalosporins + Metronidazole	7 [1.1]

Macrolides + Metronidazole	49 [7.5]
Lincomycin + Metronidazole	6 [0.9]
Cotrimoxazole + Metronidazole	6[0.9]
Quinolones + Tetracycline	21 [3.2]
Penicillins + Tétracycline	7 [1.1]
Tetracycline + Metronidazole	48 [7.4]

102

103 Prescription errors involving wrong dosage and frequency of dosing were found in 15.6% of  
 104 prescriptions. A breakdown of errors showed that dosage errors accounted for 51.3% and wrong  
 105 dosing frequency occurred in 48.7% of prescriptions with errors. The highest number of errors  
 106 occurred with Cephalosporins and macrolides representing about 45% for each of them.

107 **Table 3:** Prescription errors [n - 797]

Drugs	Dosage errors [%]	Dosing frequency errors [%]
Penicillins	17 [2.1]	18 [2.2]
Cephalosporins 178 [22.3]		189 [23.7]
Macrolides	187 [23.5]	173 [21.7]
Quinolones	19 [2.4]	4 [0.5]
Lincomycins	8 [1.1]	4 [0.5]
<b>Total</b>	<b>409 [51.3]</b>	<b>388 [48.7]</b>

108

109 A comparison of empirical antibiotic prescription pattern and bacterial resistance pattern [Table 4]  
 110 reveal that most antibiotics given to patients without laboratory confirmation of sensitivity may be  
 111 considered to be irrational. For instance, resistance to most commonly prescribed Amoxicillin +  
 112 Clavulanic acid, Cotrimoxazole and Clindamycin may be inappropriate because resistance is as high  
 113 as 20 – 90%. Resistance to Quinolones is generally below 20% while that of the Macrolides is  
 114 between 6 – 40%. Empirical prescription of antibiotics against these isolates is likely to result in  
 115 treatment failure as many strains are becoming resistant to commonly used antibiotics. The result also  
 116 highlights the problem of resistance to third generation Cephalosporins and older generation  
 117 Quinolones.

118

119 **Table 4:** Comparism of microbial resistance level and antibiotic prescription pattern [%]

Drug	SA [n= 259]	EC [n = 138]	KP [n = 109]	CF [n = 99]	PS [n = 25]	PA [n = 23]	HS [n = 38]	Average resistance [%]	PIA [%] Range
Amoxicillin+ Clavulanic acid	73.4	88.0	90.3	73.3	90.9	64.4	39.7	74.3	39 - 90
Cloxacillin	66.4	32.1	23.0	31.7	---	29.8	51.2	39.0	NA
Clarithromycin	25.8	6.9	22.2	19.4	---	32.5	14.6	20.2	6 - 32

Clindamycin	49.4	20.7	21.5	22.8	---	32.5	42.7	31.6	20 – 49
Cotrimoxazole	71.3	74.2	73.5	55.5	84.1	53.5	29.7	63.1	29 – 84
Erythromycin	33.7	12.3	21.7	16.9	13.6	29.8	40.6	24.1	12 – 40
Gentamycin	12.2	30.8	40.9	26.9	27.8	10.5	9.1	22.6	NA
Ceftriaxone	10.9	41.4	50.6	30.6	42.4	36.8	6.1	31.3	6 – 50
Ampiclox	13.2	---	1.9	5.7	4.5	---	22.1	9.5	1 – 22
Amoxicillin	13.7	1.6	5.4	14.1	18.2	5.3	29.7	12.6	1 – 29
Norbactin	9.6	3.1	10.9	11.4	9.1	5.3	23.6	10.4	NA
Ciprofloxacin	11.8	14.1	8.7	6.2	4.5	5.3	22.1	10.4	4 – 23
Perfloxacin	3.9	1.6	8.9	5.7	4.5	5.3	----	4.9	NA
Nalidixic acid	6.1	10.7	15.2	14.9	13.6	5.1	6.1	10.2	NA
Streptomycin	6.4	1.6	5.4	8.6	4.5	----	6.1	5.4	NA
Ofloxacin	3.8	14.5	17.2	14.6	21.2	----	----	14.3	3 – 21
Levofloxacin	6.9	14.2	12.3	9.3	----	5.3	----	9.6	5 – 14
Chloramphenico	5.9	5.9	1.9	5.7	----	----	17.6	7.4	NA
Tetracycline	15.1	40.3	41.1	34.7	77.3	47.4	17.1	39.0	15 – 77

Key: SA = *Staph aureus*, EC = *Escherichia coli*, *Klebsiella pneumonia*, CF = *Coliform species*, PS = *Proteus species*, PA = *Pseudomonas aeruginosa*, HS = *Haemolytic streptococci*, PIA = *potentially inappropriate antibiotic*, NA = *not applicable*

## DISCUSSION

Antibiotic prescription pattern in a healthcare facility represents the overall influence of multiple factors. The result of this study showed that Penicillins, Quinolones and Macrolides were the most frequently prescribed antibiotics. Individual antibiotics prescription prevalence showed that Amoxicillin + Clavulanic acid, Metronidazole and Ciprofloxacin were the most prescribed. This result is in contrast to other studies [24,28,49,50,51,52]. Several studies have reported high rate of irrational antibiotic prescription and a significant percentage were empirically prescribed for patients [26,41,53,54].

High rate of empirical prescription of antibiotics is generally related to poor health infrastructure, inadequate human capacity, poor regulatory control and lack of antibiotic stewardship program in many developing countries like Nigeria [42,55,56]. There have been suggestions that empirical antibiotic use is not only related to inadequate or absent laboratory services, but also due to failure to utilize them even where they are available [57].

There is ample evidence in literature that variations in antibiotic prescribing practices have both clinical and non-clinical factors. Irrational empirical antibiotic prescription practice is said to be one of the major contributors to microbial resistance which is reported to be rising globally. The results of this study showed that 39 – 90% of seven common bacterial isolates were resistant to Amoxicillin + Clavulanic acid, similar high level of microbial resistance was also observed for Cotrimoxazole [29 –

139 84%], Tetracycline [17 – 77%], Ceftriaxone [6 – 50%] and Gentamycin [9 – 40%]. The high level of  
140 antibiotic resistance level in this study is comparable to many other studies, though differences exist  
141 in the magnitude<sup>[58,59,60,61,62]</sup>.

142 This high level of multidrug resistance to commonly encountered pathogens is suggestive of the fact  
143 that empirical antibiotic prescription is no longer justified. Many patients will not achieve clinical and/or  
144 bacteriological clearance of infections. Literature evidence showed that high level of resistance have  
145 been reported for *E. coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*  
146 etc.<sup>[10,63,64,65]</sup>. Antimicrobial resistance is a global phenomenon and no region or country is spared, so  
147 there is need accelerate containment effort at the facility level. To preserve low cost broad spectrum  
148 antibiotics there should be renewed focus on laboratory confirmation of microbial susceptibility results  
149 before antibiotics are prescribed<sup>[66,67,68,69]</sup>.

150 This is particularly urgent with increasing evidence of multidrug resistant strains of microorganisms  
151 being found in healthcare facilities<sup>[45,70]</sup>. Apart from the Quinolones, Methicillin and Chloramphenicol  
152 other antibiotics recorded more than 20% resistance to seven bacterial isolates; this should be a  
153 cause of concern to facility level providers and policy makers.

154 Prescription errors frequently occur and it's a common cause of irrational antibiotics use particularly  
155 as it relates to dosage, frequency of administration, formulation, timing, duration of treatment,  
156 appropriateness<sup>[71,72,73]</sup>. The prevalence of errors observed in this study associated with correct  
157 dosage and frequency of administration is totally preventable if basic standard of prescription writing  
158 are implemented. These errors can negatively affect clinical outcomes, prolong morbidity and may  
159 ultimately result in death; there is also increased risk of adverse drug reactions particularly among the  
160 most vulnerable<sup>[74,75]</sup>.

161 There is urgent need to change current antibiotic prescribing practice in the light of increasing  
162 multidrug microbial resistance to the most commonly prescribed antibiotics. Results of this study  
163 suggest that apart from the Quinolones with relatively lower resistance profile, other antibiotics may  
164 be associated with higher frequency of treatment failure. In order to achieve improvement in antibiotic  
165 prescription practices multidisciplinary teams should be set up to manage antibiotic stewardship  
166 program in the hospital. This program is being implemented worldwide as an attempt to slow down  
167 resistance in many healthcare facilities. There is evidence that successful implementation of  
168 stewardship programs in hospitals has improved antibiotic prescribing practices and use elsewhere



169 [76,77,78]. A number of studies that looked at the impact of antibiotic stewardship programs showed that  
170 most studies have differing assessment tools and there are challenges with quality of evidence  
171 [79,80,81,82]. Majority of outcomes studies showed positive improvement in both clinical and economic  
172 outcomes for patients [76,83]. While it is acknowledged that empirical antibiotic use is permissible in  
173 acute clinical conditions, it should be reserved for emergencies where laboratory confirmation of  
174 microbial sensitivity may be delayed. The healthcare system in this country and patients cannot afford  
175 further explosion of microbial resistance to cheap commonly available antibiotics.

176 **Conclusion:** Resistance to commonly prescribed antibiotics is high and that makes most empirically  
177 prescribed antibiotics to be irrational. It is imperative that emphasis be placed on laboratory  
178 confirmation of microbial sensitivity as the basis antibiotic prescription.

179 **Competing interests:** The declare no competing interests

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