

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 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 comparison 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
18 increased morbidity and mortality, high cost of medical care and threatening global public health
19 [6,7,8,9,10]. There is global evidence of the decline of effectiveness of antibiotics across all classes,
20 there is however 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
31 empirical antibiotic use is widespread, prescription pattern vary widely [22]. For instance, some
32 studies reported that Fluoroquinolones, Penicillins and Cephalosporins are the most prescribed class
33 of antibiotics [22,32] 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
39 in the form of self-medication or irrational use in healthcare facilities, studies have reported that up to
40 50% of antibiotic prescriptions may be in the form of empirical prescriptions [41]. Microbial sensitivity
41 results are rarely used in many health facilities because of poor healthcare infrastructure and paucity
42 of 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 [26,41,44], antibiotic prescription studies have reported high levels of
45 irrational use and an increasing level of resistance to commonly used antibiotics [23,45].

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 [46,47,48]. In Nigeria there are few published studies that
52 used 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 as the basis of assessing the 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.

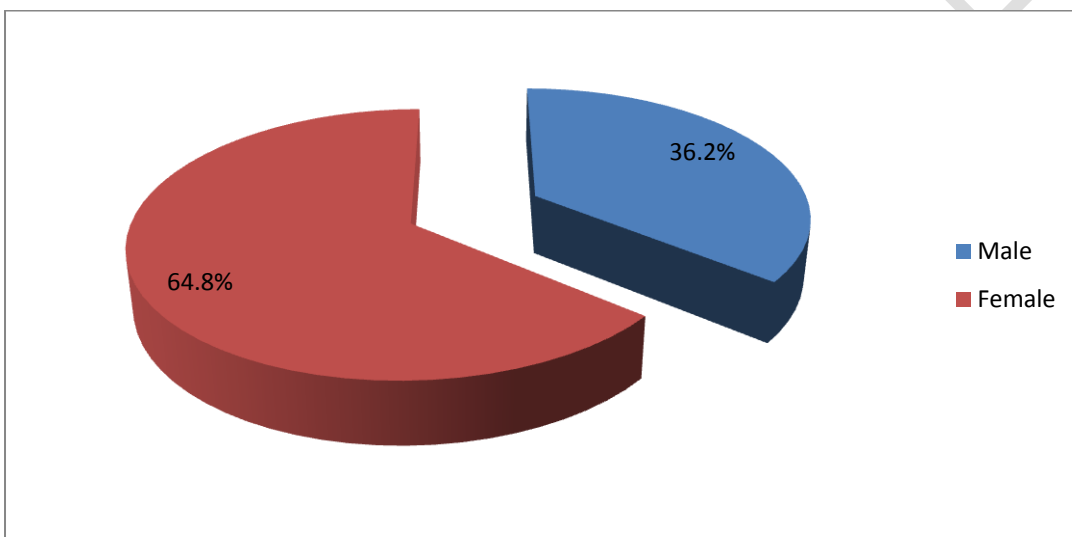
68 **Data collection:** Prescription records were obtained from National health insurance scheme [NHIS]
69 pharmacy covering the period between January 2017 and May 2018. A total of 5079 antibiotic
70 containing prescriptions were used for this study. All eligible prescriptions selected had patient NHIS
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 of outpatients. Prescriptions were also reviewed for prescription errors, dosage
77 errors, formulation errors and frequency of administration errors.

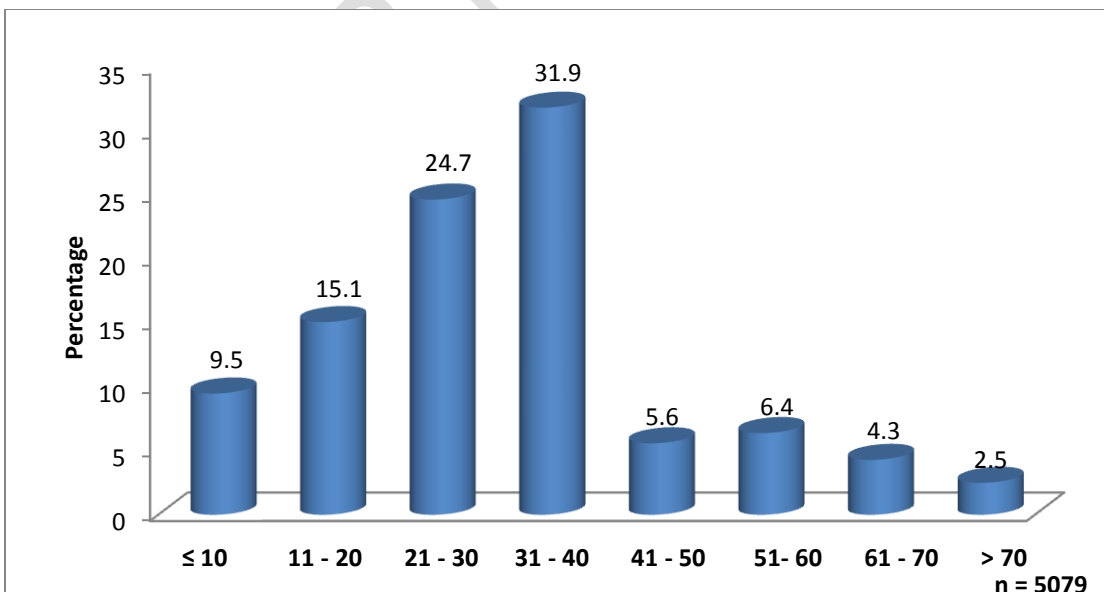
78 **Ethical approval:** This was obtained from the health research ethics committee of University of
79 Maiduguri teaching hospital

80 **RESULTS**

81 Demographic data showed that females were about two thirds of patients and majority of them were
82 below 40 years old [Figure 1 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 was followed by Quinolones and Metronidazole with prescription rate of 25% and

91 17.8% respectively. Among individual antibiotics Amoxicillin + Clavulanic acid, Metronidazole and
 92 Ciprofloxacin were the most prescribed representing 28.2%, 17.8% and 13.1% respectively [Table 1].
 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 was
 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 [Table 2].

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 [Table 3].

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]
Total	409 [51.3]	388 [48.7]

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:** Comparison 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 [58,59,60,61,62].

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. [10,63,64,65]. Antimicrobial resistance is a global phenomenon and no region or country is
147 spared, so there is need accelerate containment effort at the facility level. To preserve low cost broad
148 spectrum antibiotics there should be renewed focus on laboratory confirmation of microbial
149 susceptibility results before antibiotics are prescribed [66,67,68,69].

150 This is particularly urgent with increasing evidence of multidrug resistant strains of microorganisms
151 being found in healthcare facilities [45,70]. Apart from the Quinolones, Methicillin and
152 Chloramphenicol other antibiotics recorded more than 20% resistance to seven bacterial isolates; this
153 should be a 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 [71,72,73]. 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 [74,75].

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
170 that 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
172 economic outcomes for patients [76, 83]. While it is acknowledged that empirical antibiotic use is
173 permissible in acute clinical conditions, it should be reserved for emergencies where laboratory
174 confirmation of microbial sensitivity may be delayed. The healthcare system in this country and
175 patients cannot afford further explosion of microbial resistance to cheap commonly available
176 antibiotics.

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

180 **Competing interests:** None

181

182 REFEREES

- 183 1. Centre for disease dynamics, economics and policy. State of the world's antibiotics 2015.
184 CCDEP. Washington DC. USA
- 185 2. ECDC 2013. Antimicrobial resistance surveillance in Europe 2012. European centre for disease
186 prevention and control [ECDC] Stockholm, Sweden. Nov 15. 2013
- 187 3. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary
188 care on antimicrobial resistance in individual patients: Systematic review and Meta-analysis. *BMJ*
189 2010. 340: c2096
- 190 4. Egbule O. Antibiotic susceptibility pattern of *Escherichia coli* and *Shigella* species isolated from
191 diarrhoea stool of children. *Bayero J Pure Appl Sci* 2013. 6(1): 62 – 66
- 192 5. Abdu A, Aboderin AO, Elusiyan JB, Kolawole D, Lamikanra A. Sero-group distribution of *Shigella*
193 in Ile-Ife, Southwest Nigeria. *Trop Gastroenterol* 2013. 34(3): 164 – 169
- 194 6. Duru E, Aghahowa O, Umoren F. Bacterial agents associated with infantile diarrhoea and their
195 antimicrobial susceptibility pattern in PorthHarcourt, South-South Nigeria. *J Med Sci Public Health*
196 2014. 3(1): 1 – 12
- 197 7. Yah S, Eghafona N, Enabulele I, Aliyu H. Ampicillin usage and Ampicillin resistance [AMPR]
198 plasmids mediated *Escherichia coli* isolated from diarrhoeagenic patients attending some
199 teaching hospitals in Nigeria. *Shiraz –E Med J* 2006. 7(4): 1 – 12
- 200 8. Akinjogunla O, Eghafona N, Ekoi O. Diarrhoeagenic *Escherichia coli* [DEC]. Prevalence among in
201 and ambulatory patients and susceptibility to antimicrobial chemotherapeutic agents. *Afr J*
202 *Bacteriol Res.* 2009. 1(3): 034 – 038

- 203 9. Abdullahi M, Olonitoda S, Inabo I. Isolation of bacteria associated with diarrhoea among children
204 attending some hospitals in Kano metropolis, Kano State Nigeria. *Bayero J Pure Appl Sci* 2010.
205 3(1)
- 206 10. Nsofor CA, Iroegbu CU. Antimicrobial resistance profile of *Escherichia coli* isolated from five
207 major geopolitical zones of Nigeria. *Afr J Bacteriol Res* 2013. 5(3): 29 – 34
- 208 11. World Health Organization. Antimicrobial resistance: Global report on surveillance 2014. Geneva,
209 Switzerland. WHO 2014
- 210 12. Centre for disease control and prevention CDC 2013. Antibiotic resistance threats in the United
211 States. Atlanta.
- 212 13. Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N et al. Antibiotic
213 resistance – the need for global solutions. *The Lancet Infect Dis* 2013. 13(12): 1057 – 1098
- 214 14. Kayange N, Kamugisha E, Mwizamholya DL, Jeremiah S, Mshana SE. Predictor of positive blood
215 culture and death among neonate with suspected neonatal sepsis in a tertiary hospital, Mwanza
216 – Tanzania. *BMC Pediatr* 2010. 10(1): 39
- 217 15. Roca A, Quinto L, Abacassamo F, Morais L, Valles X, Espasa M, Sigauque B et al. Invasive
218 *Haemophilus influenzae* disease in children less than five years of age in Manhica, a rural area of
219 Southern Mozambique. *Trop Med Int Health* 2008. 13(6): 8181 – 8186
- 220 16. Marshall BM, Levy SB. Food animals and antimicrobials: impacts on human health. *Clin Microbiol*
221 *Rev* 2011. 24(4): 718 – 733
- 222 17. Chen ED, Anong DN, Akoachere J-FKT. Prescribing pattern and associated factors of antibiotic
223 prescription in primary healthcare facilities of Kumbo east and Kumbo West health district, North
224 West Cameroon. *PlosOne* 2018, 13(3): e0193353
- 225 18. Mbam LA, Monekosso GL, Asongalem EA. Indicators and pattern of prescription of antibiotics at
226 the Buea regional hospital of Cameroon. *J Health Sci Dis* 2015. 6(1): 1 - 7
- 227 19. Erah PO, Olumide GO, Okhamafe AO. Prescribing pattern in two healthcare facilities in Warri,
228 Southern Nigeria; A comparative study. *Trop J Pharm Res* 2003. 2(1): 175 – 182
- 229 20. Alam MM, Parveen F, Arah F, Igbal MJ, Saha RR. Prescribing trends in the outpatient department
230 in a territory hospital in Bangladesh. *Bangladesh Med J* 2011. 4: 2
- 231 21. Igbiks T, Joseph OE. Drug prescription pattern in a Nigerian tertiary hospital. *Trop J Pharm Res*
232 2012. 11(1): 146 – 152
- 233 22. Eshiet UI, Effiong GS, Akwaowoh AE. The use of antibiotics in a Nigerian tertiary healthcare
234 facility. *Am J Biomed Sci Engineering*. 2015. 1(3): 25 – 31
- 235 23. Anyanwu N, Arigbe-Osula M. Pattern of antibiotic use in a tertiary hospital in Nigeria. *Eur J Hosp*
236 *Pharm Sci Pract* 2012. 19: 195
- 237 24. Kaur A, Bhagat R, Kaur N, Shafiq N, Gautam V, Malhotra S, Suri V, Bhalla A. A study of antibiotic
238 prescription pattern in patients referred to tertiary care centre in Northern India. *Therap Adv Infect*
239 *Dis* 2018. 5(4): 63 – 68
- 240 25. Cui D, Liu X, Hawkey P, Li H, Wang Q, Mao Z, Sun J. Use of and microbial resistance to
241 antibiotics in China: a path to reducing antimicrobial resistance. *J Int Med Res* 2017. 45(6): 1768
242 – 1778

- 243 26. Abdu-Aguye SN, Haruna A, Shehu A, Labaran KS. An assessment of antimicrobial prescribing at
244 a tertiary hospital in North western Nigeria. *Afr J Pharmacol Therap* 2016. 5(4): 229 – 234
- 245 27. Nasir IA, Babyo A, Emeribe AU, Sani NO. Surveillance for antibiotic resistance in Nigeria:
246 challenges and possible solution. *Trends in Med Res* 2015. 10(4): 106 – 113
- 247 28. Umar LW, Isah A, Musa S, Umar B. Prescribing pattern and antibiotic use for hospitalized children
248 in a Northern Nigerian teaching hospital. *Ann Afr Med* 2018. 17(1): 26 – 32
- 249 29. Prah J, Kizzie-Kayford J, Walker E, Ampofo-Asiama A. Antibiotic prescription pattern in a Ghanaian
250 healthcare facility. *Pan Afr Med J* 2017. 28: 214
- 251 30. Akinyandenu O, Akinyandenu A. Irrational use and non-prescription sale of antibiotics in Nigeria:
252 A need for change. *J Sci Innovative Res* 2014. 3(2): 251 – 257
- 253 31. Gebeyehu E, Bantie L, Azage M. *Inappropriate use of antibiotics and its associated factors*
254 *among urban and rural communities of Bahir city administration, Northwest Ethiopia. PlosOne*
255 *2015. 10(9)*
- 256 32. Shankar RP, Partha P, Shenoy NK, Easow JM, Brahmadathan KN. Prescribing patterns of
257 antibiotics and sensitivity patterns of common micro-organisms in the internal medicine ward of a
258 teaching hospital in Western Nepal: a prospective study. *Ann Clin Microbiol and antimicrob* 2003.
259 2: 7
- 260 33. Mollahaliloglu S, Alkan A, Donortas B, Ozgulcu S, Akici A. Assessment of antibiotic prescribing at
261 different hospitals and primary healthcare facilities. *Saudi Pharm J* 2012. 21: 281 – 291
- 262 34. Kariuki S, Gordon MA, Feasey N, Parry CM. Antimicrobial resistance and management of
263 invasive Salmonella disease. *Vaccine* 2015. 33[Suppl 3]: C21 – C29
- 264 35. Reuland EA, al Naiemi N, Raadsen SA, Savelkoul PHM, Kluytmans J, Vandenbroucke-Grauls E.
265 Prevalence of ESBL – producing Enterobacteriaceae in raw vegetables. *Europ J Clin Microbiol*
266 *Infect Dis* 2014. 33(10): 1843 – 1846
- 267 36. Lu PL, Liu YC, Toh HS, Lee YL, Lui YM, Ho CM, Hsueh PR et al. *Epidemiology and antimicrobial*
268 *susceptibility profiles of gram negative bacteria causing UTI in the Asia – Pacific region 2009 –*
269 *2010 results from the study for monitoring antimicrobial resistance trends [SMART]. Int J*
270 *Antimicrob Agents* 2012. 40 [Suppl 1]: S37 – S43
- 271 37. Leopold SJ, van Leth F, Tarekegu H, Schultz C. Antimicrobial drug resistance among clinically
272 relevant isolates in sub Saharan Africa: A systematic review. *The J Antimicrob Chemother* 2014.
273 69(9): 2337 – 2357
- 274 38. Storberg V. *ESBL – producing Enterobacteriaceae in Africa: A non systematic literature review of*
275 *research published 2008 – 2012. Infect Ecology Epidemiol* 4. *Doi:10.3402/iee.v4.20342*
- 276 39. Le Doare K, Brelick J, Heath PT, Sharland M. Systematic review of antibiotic resistance rates
277 among gram negative bacteria in children with sepsis in resource limited countries. *J Pediatr*
278 *Infect Dis Soc* 2014. 4(1): 11 – 20
- 279 40. Salles MSC, Zurita J, Mejia C, Villegas MV. Persistent gram negative infections in the outpatient
280 setting in Latin America. *Epidemiol Infect* 2013. 141(12): 2459 – 2472

- 281 41. Oduyebo OO, Olayinka AT, Iregbu KC, Verspoten A, Goosens H, Nwajiobi-Princewill PI, Jimoh O,
282 Ige TO, Aigbe AI, Ola-Bello OI, Aboderin AO, Ogunsola FT. A point prevalence survey of
283 antimicrobial prescribing in four tertiary hospitals. *Ann Trop Pathol* 2017. 8: 42 – 46
- 284 42. Petti CA, Polage CR, Quinn TC, Ronald AR, Sande MA. Laboratory medicine in Africa: A barrier
285 to effective healthcare. *Clin Infect Dis* 2006. 42: 377 – 382
- 286 43. Diakema DJ, Pfalter MA. Rapid detection of antibiotic resistant organism carriage for infection
287 prevention. *Clin Infect Dis* 2013. 56: 1614 – 1620
- 288 44. Egbuchulam N, Anyika EN, Soremekun RO. Antibiotic prescribing practices for hospitalized
289 children with suspected bacterial infection in a paediatric hospital in Nigeria. *J Hosp Admin* 2018.
290 7(4): 36 – 43
- 291 45. Sani RA, Garba SA, Oyewole OA. Antibiotics resistance profile of gram negative bacteria isolated
292 from surgical wounds in Minna, Bida, Kontagora and Suleja areas of Niger State. *Am J Med Med*
293 *Sci* 2012; 2(1): 20 – 24
- 294 46. Brooks L, Shaw A, Sharp D, Hay AD. Towards a better understanding of patients perspectives of
295 antibiotic resistance and MRSA: a qualitative study. *Fam Pract* 2008. 25: 341 – 348
- 296 47. Buttler CC, Rollinick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing:
297 Qualitative study of general practitioners and patients perceptions of antibiotics for sore throat.
298 *BMJ* 1998. 317: 637 – 642
- 299 48. Kumar S, Little P, Britten N. Why do general practitioners prescribe antibiotics for sore throat?
300 Grounded theory interview study. *BMJ* 2003. 321: 138
- 301 49. Carneiro M, Ferraz T, Bueno M, Koch BE, Foresti C, Lena VF et al. Antibiotic prescription in a
302 teaching hospital: a brief assessment. *Rev Assoc Med Bras* 2011. 57(4): 414 – 417
- 303 50. Al-Johani K, Reddy SG, Mushayt AS, El-Housseiny A. Pattern of prescription of antibiotics among
304 dental practitioners in Jeddah, KSA: A cross sectional survey. *Niger J Clin Pract* 2017. 20: 804 –
305 810
- 306 51. Kourlaba G, Gkrania-Klotsas E, Kourkourni E, Mavrogeorgos G, Zaoutis TE. Antibiotic prescribing
307 and expenditures in outpatients' adults in Greece 2010 – 2015: Evidence from real world practice.
308 *Euro Surveill* 2016. 21(26): PII = 30266
- 309 52. Akram A, Megha R, Irfanul H, Pravina A, Rahul I, Ram D, Sheetal K, Isha. Study of prescription
310 pattern of antibiotics in the medicine department in a teaching hospital: A descriptive study. *Int J*
311 *Toxicol Pharmacol Res* 2014. 6(2): 43 – 46
- 312 53. Abhijit K, Jain P, Upadhyaya P, Jain S. A study monitoring pattern of antibiotics in a tertiary care
313 hospital in North India. *Int J Basic Clin Pharmacol* 2014. 3: 1006 – 1011
- 314 54. Fahmzad A, Eydian Z, Karimi A, Shiva F, Armin S, Ghanae RM, Fallah F, Tabatabaei SR,
315 Shirvani F et al. Antibiotic prescribing in neonates of seventeen Iranian hospitals. *Arch Pediatr*
316 *Infect Dis* 2017. 5(4): e61530
- 317 55. Hunter B, Harbarth S, Nathwani D; ESCMID study group for antibiotic policies [ESGAP].
318 Successful stories of implementation of antimicrobial stewardship: A narrative review. *Clin*
319 *Microbiol Infect* 2014. 20: 954 – 962

- 320 56. Tiong JJ, Loo JS, Mai CW. Global antimicrobial stewardship: A closer look at the formidable
321 implementation challenges. *Front Microbiol* 2016. 7: 1860
- 322 57. Kimang'a AN. A situational analysis of antimicrobial drug resistance in Africa. Are we losing the
323 battle? *Ethiop J Health Sci* 2012. 22: 135 – 143
- 324 58. Shahriar M, Hossain M, Kabir S. A survey of antimicrobial sensitivity pattern of different antibiotics
325 on clinical isolates of *Escherichia coli* collected for Dhaka City. Bangladesh. *J Appl Sci Environ*
326 *Manage* 2010. 14(3): 19 – 20
- 327 59. Masyeni S, Sukmawati H, Siskayani AS, Dharmayanti S, Sari K. Antimicrobial susceptibility
328 pattern of pathogens isolated from various specimens in Denpasar – Bali: A two years
329 retrospective survey. *Biomed Pharmacol J* 2018. 11(1): 493 – 502
- 330 60. Saba CKS, Amenyona JK, Kpordze SW. Prevalence and pattern of antibiotic resistance of
331 *Staphylococcus aureus* from door handles and other points of contact in public hospitals in
332 Ghana. *Antimicrob Resistance Infect Control* 2017. 6: 44
- 333 61. Fadeyi A, Zumuk CP, Raheem RA, Nwabuisi C, Desalu OO. Prevalence and antibiotic
334 susceptibility pattern of EBSL producing *Klebsiella* from clinical specimens in a Nigerian tertiary
335 hospital. *Afr J Infect Dis* 2006. 10(1): 32 – 37
- 336 62. Ray J, Paul R, Halder A, Mondol S. A study on antibiotic resistance pattern of *Escherichia coli*
337 isolated from urine specimens in east India. *Int J Med Sci Public Health* 2015. 4(12): 1670 - 1674
- 338 63. Ojo-Bola O, Oluyeye AO. Antibiotic resistance of bacteria associated with pneumonia in HIV/AIDS
339 patients in Nigeria. *Am J Infect Dis Microbiol* 2014. 2(6): 138 – 144
- 340 64. Abubakar EM. Antimicrobial susceptibility pattern of pathogenic bacteria causing urinary tract
341 infections at the specialist hospital Yola, Adamawa State, Nigeria. *J Clin Med Res* 2009. 1(1): 001
342 – 008
- 343 65. Pattanayak C, Patanaik SK, Datta PP, Panda P. A study of antibiotic sensitivity pattern of
344 bacterial isolates in the intensive care unit of a tertiary care hospital in Eastern India. *Int J Basic*
345 *Clin Pharmacol* 2013. 2(2): 153 – 159
- 346 66. Timothy OO, Olusesan FJ, Adesola BO, Temitayo AA, David FO, Ige OO. Antibiotic resistance
347 pattern of bacterial isolates from cases of urinary tract infections among hospitalized and
348 outpatients at a tertiary health facility in South Western Nigeria. *Ann Trop Med Public Health*
349 2014. 7: 130 – 135
- 350 67. Radfar M, Fallahi M, Kazemian M, Borhani S. A comparative evaluation of microbial pattern and
351 microbial sensitivity in a level III NICU between two decades. *Arch Pediatr Infect Dis* 2017. 5(2):
352 e39299
- 353 68. Ahmed NH, Hussain T. Antimicrobial susceptibility pattern of leading pathogens isolated from
354 laboratory confirmed blood stream infections in a multispecialty sanatorium. *J Global Infect Dis*
355 2014. 6(4): 141 – 146
- 356 69. Bernabe KJ, Langendorf C, Ford N, Ronat JB, Murphy RA. Antimicrobial resistance in West
357 Africa: a systematic review and Meta-analysis. *Int J Antimicrob Agents* 2017. 50: 629 – 639

- 358 70. Chakraborty S, Moshina K, Sarker PK, Alam MDZ, Sayem SMA. Prevalence, antibiotics
359 susceptibility profiles and ESBL production in *Klebsiella pneumoniae* and *Klebsiella oxytoca*
360 among hospitalized patients. *Periodicum Biologocum* 2016. 118(1): 53 – 58
- 361 71. Aronson JK. Medication errors; Definitions and classification. *Br J Clin Pharmacol* 2009. 67: 599 –
362 604
- 363 72. Patel I, Balkrishnan R. Medication error management around the globe: An overview. *Indian J*
364 *Pharm Sci* 2010. 72: 539 – 545
- 365 73. Sutradhar KB, Saha A, Huda NH et al. Irrational use of antibiotics and antibiotic resistance in
366 Southern rural Bangladesh: perspectives from both the physicians and patients. *Annual Res Rev*
367 *Biol* 2014. 4(9): 1421 – 1430
- 368 74. Stuckey ER. Prevention of medication errors in the pediatric in patient setting. *Pediatr* 2003. 112:
369 431 – 436
- 370 75. Miller MR, Robinson KA, Lubomski LH, Rinke ML, Pronovost PJ. Medication errors in pediatric
371 care : A systematic review of epidemiology and an evaluation of evidence supporting reduction
372 strategy recommendations. *Qual Saf Health Care* 2007. 16: 116 – 126
- 373 76. Davey P, Brown E, Charani E et al. Interventions to improve antibiotic prescribing practices for
374 hospital in-patients. *Cochrane Database Syst Rev* 2013. 4: CD003543
- 375 77. Schuts EC, Hulscher MEJL, Mouton JW et al. A systematic review and meta-analysis of current
376 evidence on hospital antimicrobial stewardship objectives. *Lancet Infect Dis* 2016. Pii: S1473 –
377 3099 (16) 0065 – 7
- 378 78. Jan-Willem H, Ron Hendrix D, Poleman R, Maarten J, Niesters HG, Potsma MJ, Sinha B,
379 Friedrich AW. Measuring the impact of antimicrobial stewardship programmes. *Expert Rev of*
380 *Antimicrob Infect Ther* 2016. 14(6): 569 – 575
- 381 79. Howard P, Pulcini C, Levy Hara G et al. An international cross sectional survey of antimicrobial
382 stewardship programmes in hospitals. *J Antimicrob Chemother* 2015. 70: 1245 – 1255
- 383 80. Lesprit P, Landelle C, Brun-Buisson C. Clinical impact of unsolicited post prescription antibiotic
384 review in surgical and medical wards: a randomized controlled trial. *Clin Microbiol Infect* 2013. 19:
385 91 – 97
- 386 81. Fleet E, Gopal Rao G, Patel B et al. Impact of implementation of a novel antimicrobial
387 stewardship tool on antibiotic use in nursing home: a prospective cluster randomized controlled
388 pilot study. *J Antimicrob Chemother* 2014. 69: 2265 – 2273
- 389 82. Taconelli E, Cataldo M, Paul M et al. STROBE-AMS: recommendations to optimize reporting of
390 epidemiological studies on antimicrobial resistance and inform improvement in antimicrobial
391 stewardship. *BMJ Open* 2016. 6: e010134
- 392 83. McGowan J. Antimicrobial stewardship programs – the state of the art in 2011: focus on outcome
393 and methods. *Infect Control Hosp Epidemiol* 2012. 33: 331 – 337.