

Prescribing Practices of Broad Spectrum Antibiotics in Tertiary Care Hospital: An Observational Study

* Sakina Fatima ¹, Muhammad Iyad N ¹, Subia Jamil ², Tuba Siddiqui ³

¹Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan.

²Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan.

³Department of Pharmaceutics, Faculty of Pharmacy, Federal Urdu University of Arts, Science and Technology.

Keywords: Antibiotics, Prophylactic treatment, Broad spectrum Cephalosporins, Culture sensitivity.

Author's Contribution

All the authors contributed significantly to the research that resulted in the submitted manuscripts

Article info.

Received: Feb 02, 2018

Accepted: Mar 23, 2018

Funding Source: Nil

Conflict of Interest: Nil

Cite this article: Sakina F, Iyaad N, Subia J, Siddiqui T. Prescribing practices of broad spectrum antibiotics in tertiary care hospital: an observational study. *RADS J. pharm. pharm. sci.* 2018;6(1):07-16.

Address of Correspondence

Author: sak.zaidi@gmail.com

ABSTRACT

Objective: The present study was designed to investigate the utilization of broad spectrum antibiotics in a tertiary care hospital setup.

Methods: The observational study was evaluated 685 in-patients admitted in various wards during three-months period from July-September 2015. After the data collection, it was analyzed for prevalent gender, various age groups, collected specimen, availability of culture sensitivity, Gram-Negative pathogens and prescribing trends of antibiotics alone or in combinations.

Results: The results showed that high preponderance of prescribed antibiotics was found in females with age ranges of 16-30 and 31-45 years, whereas in male patients 1-15 and >75 years. The study also revealed that 25% of patients were tested for culture sensitivity and 75% were treated with antibiotics either empirically or prophylactically. The prescribing pattern of antibiotics showed higher rate of utilization of broad spectrum cephalosporins, either alone or in combination with other antibiotics.

Conclusion: The study concluded that the utilization of broad spectrum antibiotics such as broad spectrum cephalosporins must be rationale with culture sensitivity test for antibiotic selection in clinical situations and hygienic practices in hospitals must be employed which can reduced the risk of infections. Antibiotic stewardship programs can also have reduced the inappropriate use of antibiotics.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Globally, antibiotics are the most prescribing drugs among hospitals as well as community setups [1-5]. Inappropriate use of antibiotics leads to serious consequences, more specifically antimicrobial resistance and overall cost of hospitalization for treatment of infections [4-6].

In developing countries, the irrational use of antibiotics is a leading cause of resistance in community and health care setups. The incidence is more related with the use of broad

spectrum antibiotics, more specifically with self-medication and use of antibiotics without any prescriptions [7] additionally, lesser education and unhygienic routine practices are additional major contributors. On other hand malnutrition causes severity of infections that leads to illness and death [8], whereas poverty is underlying reason associated with malnutrition [9, 10].

In some of developing countries, antibiotics used up to 90% are without prescriptions [7].

Whereas in hospital setups most of the utilization is empiric and most of prescribed antibiotics are inappropriate although prescribed by physician [11]. In infectious diseases, appropriate prescribing can be in practice along-with diagnostic tools and reliable testing methods which are unavailable to some extent in developing countries [12]. The common practice in many third world countries is before expensive testing most of the patients are preferred to use antibiotics prior [11].

Previously from Pakistan some reports were published indicated the irrational and excessive use of third generation cephalosporins among hospitalized patients in tertiary care hospitals setting [13-15].

The study was investigated as pilot study for prescribing practices of antibiotics in hospitalized patients in various wards and focused on utilization of broad spectrum antibiotics among various wards in hospital setup of Karachi, Pakistan along with the availability of culture sensitivity profile. The study has also focused the prophylactic or empiric use of antibiotics in different clinical situations.

MATERIALS AND METHODS

Study Layout

The study was single centered, conducted in a tertiary care hospital setup. It was observational and cross-sectional over of a time period of three months conducted for prescribing trends of antibiotics in patients admitted in hospital. Sampling was done by convenience random sampling method.

Studied Wards

Total studied cases were 685 patients admitted in various wards including pediatrics (Peds),

emergency room (ER), gynecology/obstetrics, urology, orthopedics, cardiac Unit and out-patient dispensing (OPD).

Data Collection and Analysis

The utilization trends of different antibiotics were evaluated in several studied wards along-with availability of culture sensitivity and prophylactic usage of antibiotics. The observational collected data were further sensitivity tests, Gram-Negative pathogens and utilization of antibiotics either alone or in combinations. analyzed for sex of patient, their age groups, collected specimen, availability of culture

RESULTS

An observational, cross-sectional study was investigated in a tertiary care hospital setting to evaluate the utilization trends of antibiotics in patients admitted in hospital.

In-patients Demographics

Mean age was found to be 28.30 ± 23.29 years, with age ranges were (1 month and 90 years). The frequency of male and female gender was 319 (46.5) and 366 (53.5) respectively. The various studied age groups were <1, 1-15, 16-30, 31-45, 46-60, 61-75 and >75. The frequency of patients in respective wards were 105, 145, 166, 114, 69, 80 and 6, among them male patients were 53, 101, 53, 26, 36, 45, 5 and females were 52, 44, 113, 88, 33, 35 and 1 respectively (Table 1). The frequencies of patients in various age groups in studied ward were depicted in Figure 1.

Table 1: Gender distribution of patients in different age groups

Age groups in years	No. of Patient n (%)	Male n (%)	Female n (%)
< 1	105 (15.3)	53 (50.5)	52 (49.5)
1-15	145 (21)	101 (70)	44 (39)
16-30	166 (24)	53 (32)	113 (68)
31-45	114 (16.6)	26 (23)	88 (77)
46-60	69 (10)	36 (52)	33 (48)
61-75	80 (11.6)	45 (56)	35 (44)
>75	6 (0.87)	5 (83)	1 (17)
Total	685 (100)	319 (46.5)	366 (53.5)

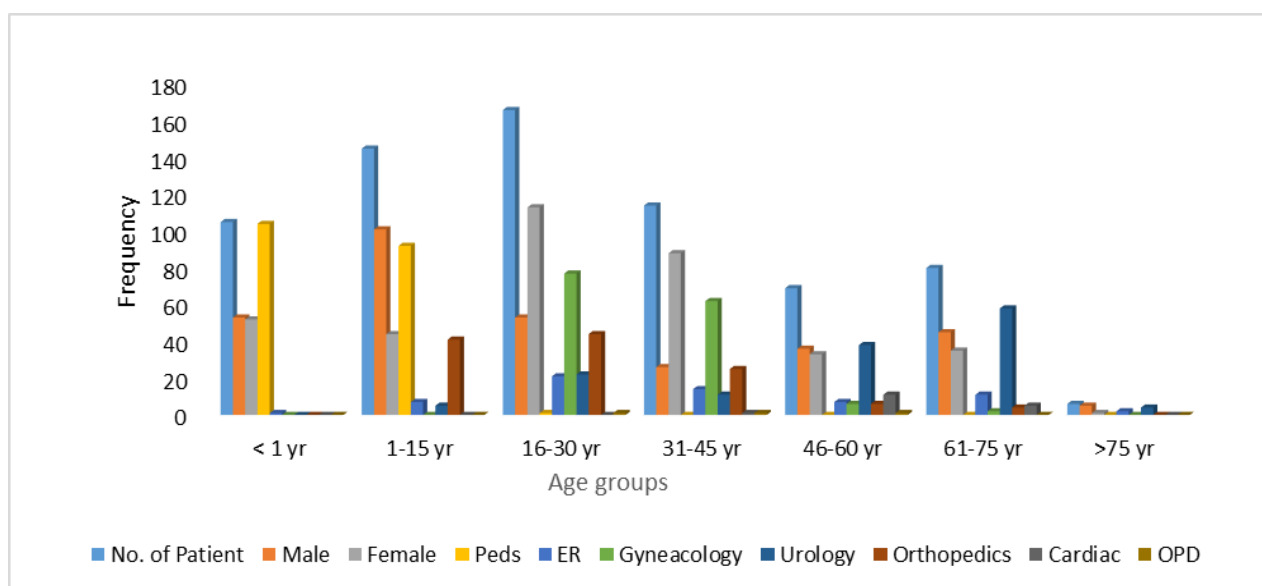


Figure 1: Gender, ward and number of patients in various age groups

Table 2: Number of Patients in various wards

Patients	Pediatrics	Emergency	Gynecology / Obstetric	Urology	Orthopedics	Cardiac	OPD
Total	197 (28.8)	63 (9.2)	147 (21.5)	138 (20.1)	120 (17.5)	17 (2.1)	3 (0.4)
Male (n=319)	117 (36.7)	23 (8.2)	0 (0)	94 (49.5)	75 (23.5)	6 (1.9)	1 (0.3)
Female (n=366)	80 (21.9)	37 (10.1)	147 (40.2)	44 (12)	45 (12.3)	11 (3)	2 (0.5)

Patient Distribution in Various Wards

In each ward frequencies of patients were 197, 63, 147, 138, 120, 17 and 3 respectively. The frequency of male patients was 117, 23, 0, 94, 75, 6 and 1 whereas number of female patients were 80, 37, 147, 44, 45, 11 and 2 respectively (Table 2).

Culture Sensitivity Test

The practice of culture sensitivity test was found in only 173 (25.3%) out of 685 cases of patients (Figure 2), in each wards culture sensitivity was done in 69, 2, 12, 61, 26, 3 and 0 respectively. Whereas, 128 (65%), 61 (96.8 %), 135 (91.8%), 77 (55.8%), 94 (78.3%), 14 (82.4%) and 3 (100%) were prescribed with antibiotics without culture sensitivity in respective wards (Table 3). Among isolated pathogens, *E. coli* was dominant and found highest in urology i.e., 41 (29.7%), 39

(19.8%) in Pediatrics, 13 (10.8%) in orthopedics and 3 (17.6%) in cardiac ward. Less frequent in gynecology/Obstetric i.e., 5 (3.4%). Whereas *P. aeruginosa* were found highest i.e., 6 (5%) in orthopedics and 4 (2.9%) in urology, whereas 1 (0.5%) in pediatrics and 4 (2.7%) in gynecology/Obstetric. *Klebsiella spp* were found 10 (5.1%), 1 (0.7%), 2 (1.4%), 3 (2.5%) in respective wards listed in Table 4.

Prescribed Antibiotics

The prescribing trends in all studied wards indicated that cephalosporins were highly prescribed antibiotics followed by quinolones either alone or in combinations (Table 5, Figure 3 and 4) in all respective wards.

Table 3: Specimen collected for culture sensitivity test

Specimen n (%)	Pediatrics	Emergency	Gynecology/ Obstetric	Urology	Orthopedics	Cardiac	OPD
Blood	49 (24.9)	0 (0)	3 (2)	11 (8)	14 (11.7)	2 (11.8)	0 (0)
Urine	6 (3)	2 (3.2)	3 (2.1)	36 (26.1)	2 (1.7)	1 (5.9)	0 (0)
Pus	2 (1)	0(0)	3 (2.1)	11 (8)	9 (7.5)	0 (0)	0 (0)
HVS*	0 (0)	0(0)	2 (1.4)	3 (2.2)	0 (0)	0 (0)	0 (0)
CSF*	2 (1)	0(0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Sputum	5 (2.5)	0(0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Swab	5 (2.5)	0(0)	1 (0.7)	0 (0)	1 (0.8)	0 (0)	0 (0)
Not tested	128 (65)	61 (96.8)	135 (91.8)	77 (55.8)	94 (78.3)	14 (82.4)	3 (100)

*HVS: High vaginal swab, OPD: Out-patient department, *CSF: Cerebral-spinal fluid

Table 4: Gram-Negative pathogens isolated in various wards

Pathogen isolated (%)	Pediatrics	Emergency	Gynecology/ Obstetric	Urology	Orthopedics	Cardiac	OPD
<i>E. coli</i>	39 (19.8)	0 (0)	5 (3.4)	41 (29.7)	13 (10.8)	3 (17.6)	0 (0)
<i>P. aeruginosa</i>	1 (0.5)	0 (0)	4 (2.7)	4 (2.9)	6 (5)	0 (0)	0 (0)
<i>K. pneumoniae</i>	10 (5.1)	0 (0)	1 (0.7)	2 (1.4)	3 (2.5)	0 (0)	0 (0)
No growth	8 (4)	2 (3.1)	0 (0)	4 (2.9)	0 (0)	0 (0)	0 (0)
Others	11 (5.5)	0 (0)	2 (1.4)	14 (10)	4 (3.3)	0 (0)	0 (0)

Table 5: Prescribed antibiotics in various studied wards

Antibiotics used	Pediatrics	Emergency	Gynecology/ Obstetric	Urology	Orthopedics	Cardiac	OPD
Penicillin	10 (5.1)	5 (7.9)	32 (21.8)	17 (12.3)	25 (20.8)	1 (5.9)	0 (0)
Cephalosporin	109 (55.3)	31 (49.2)	45 (30.6)	40 (29)	24 (20)	4 (23.5)	2 (66.7)
Quinolones	0 (0)	15 (23.8)	4 (2.7)	37 (26.8)	17 (14.2)	0 (0)	0 (0)
Aminoglycoside	0 (0)	0 (0)	1 (0.7)	2 (1.4)	2 (1.7)	0 (0)	0 (0)
Penicillin+ Cephalosporin	16 (8.1)	1 (1.6)	4 (2.7)	4 (2.9)	7 (5.8)	0 (0)	0 (0)
Penicillin+ Quinolones	0 (0)	0 (0)	2 (1.4)	1 (0.7)	27 (22.5)	0 (0)	0 (0)
Penicillin+ Aminoglycosides	6 (3)	0 (0)	0 (0)	2 (1.4)	1 (0.8)	0 (0)	0 (0)
Cephalosporin + Quinolones	0 (0)	0 (0)	1 (0.7)	11 (8)	4 (3.3)	0 (0)	0 (0)
Cephalosporin +Aminoglycoside	18 (9.1)	1 (1.6)	3 (2)	3 (2.2)	1 (0.8)	0 (0)	0 (0)
Cephalosporin+ Glycopeptide	23 (11.7)	1 (1.6)	6 (4.12)	2 (1.4)	5 (4.2)	0 (0)	0 (0)
Carbapenem	0 (0)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)
Other antibiotic	10 (5.07)	8 (12.7)	38 (25.8)	15 (10.9)	4 (3.3)	3 (17.6)	1 (33.3)
No antibiotics	3 (1.5)	1 (1.6)	2 (1.4)	3 (2.2)	0 (0)	9 (53)	0 (0)

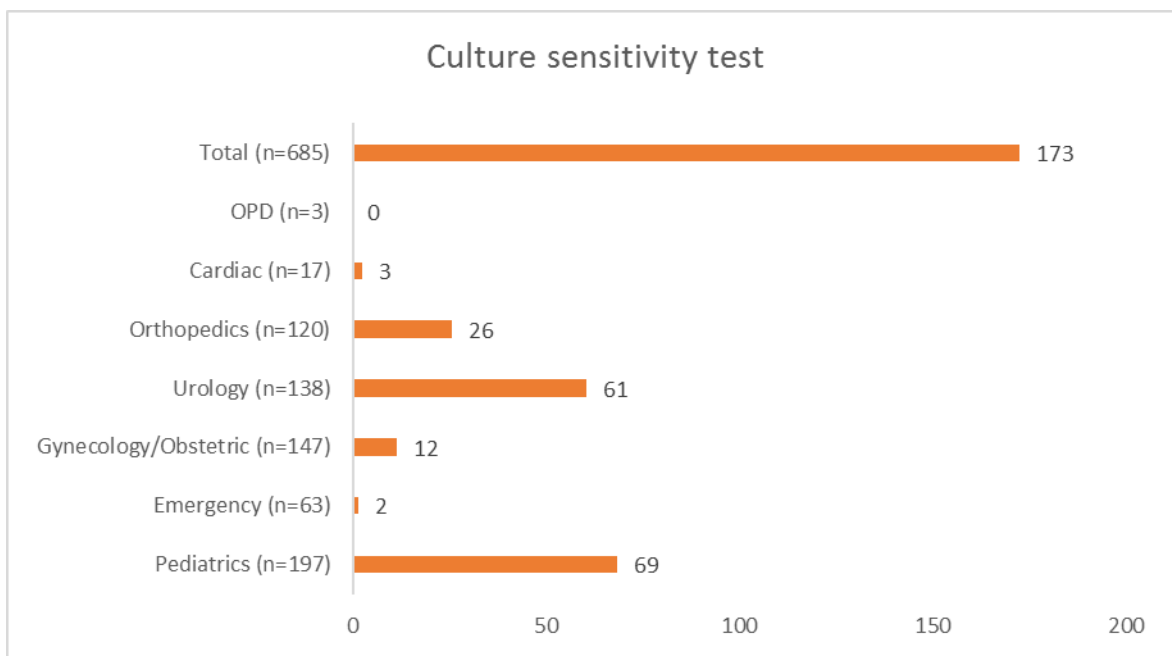


Figure 2: Number of culture sensitivity test in various wards

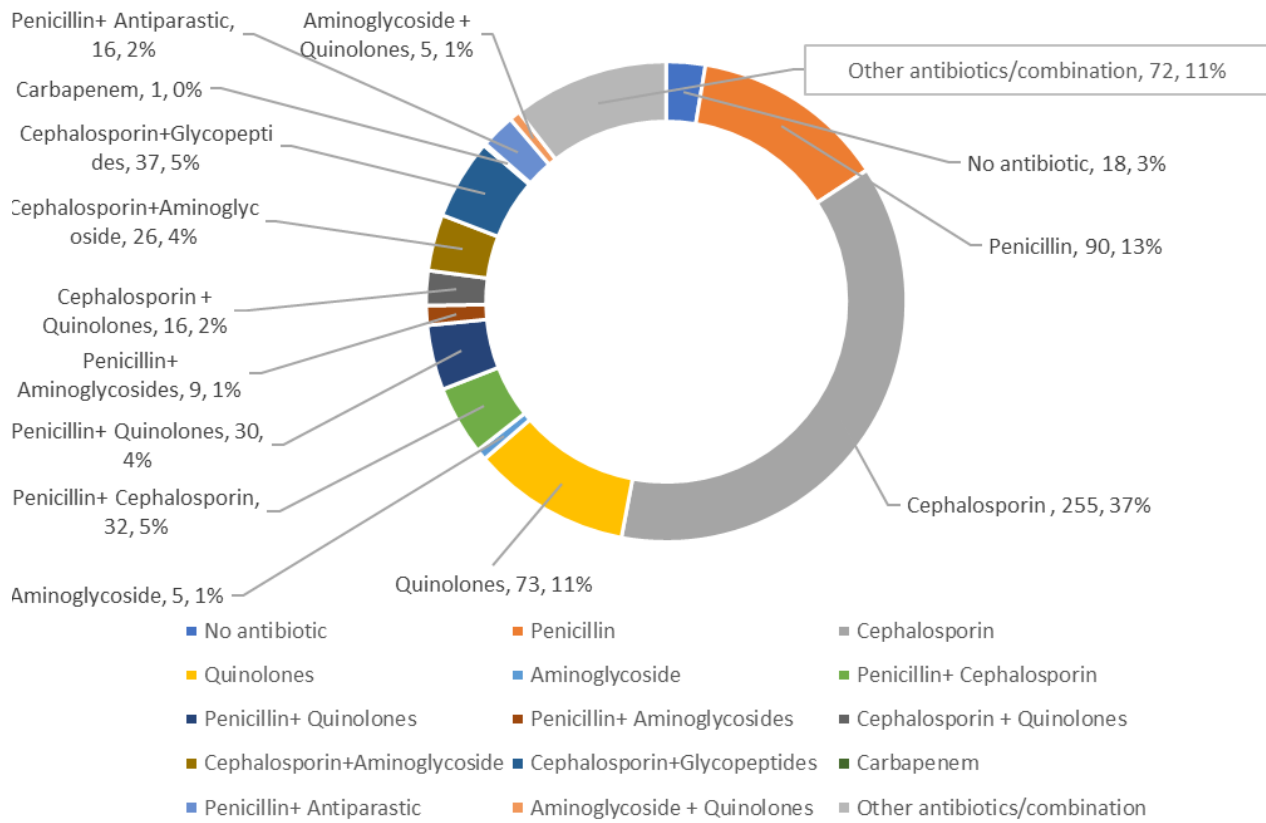


Figure 3: Prescribed antibiotics in patients

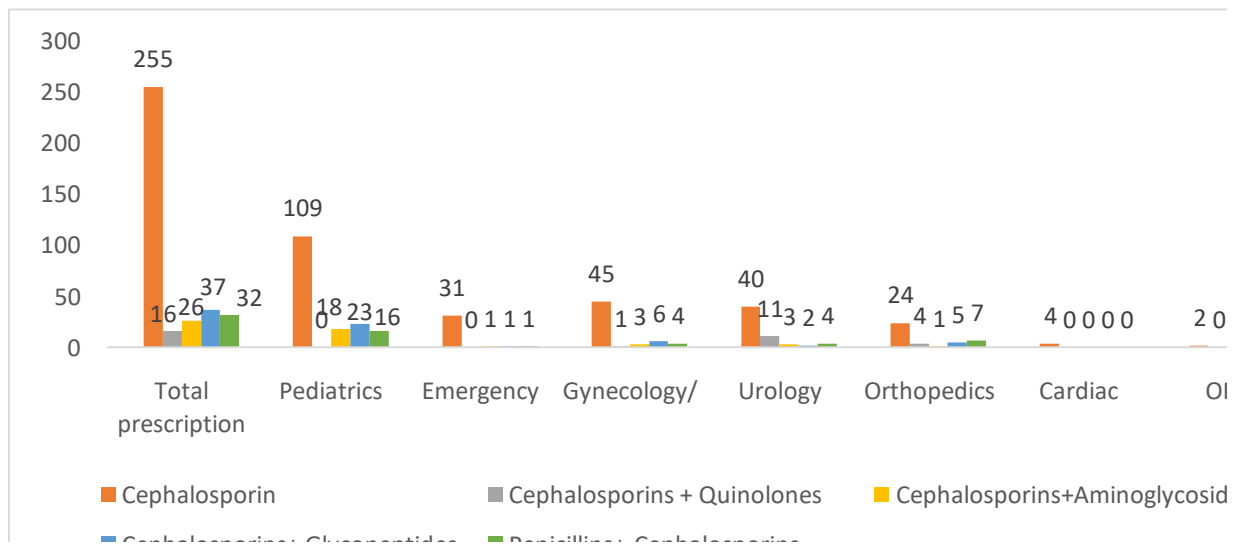


Figure 4: Prescribing pattern of cephalosporins alone or in combination in patients

DISCUSSION

Irrational use of antibiotics leads to serious consequences of various resistance mechanisms [5]. The present study was an observational and cross-sectional evaluated for the suggesting trends of broad spectrum antibiotics in a tertiary care hospital setting. The utilization was analyzed in patients of various wards with respect to different age groups and availability of culture sensitivity test.

In the present study, the pattern of utilization of antibiotics in relation to their age, gender, site of infection, availability of culture sensitivity results and wards were investigated in total of 685 patients for duration of three months. The study reported that 366 (53.5%) female patients and 319 (46.5%) male patients were prescribed with antibiotics (Table 1). The patients were stratified in different age groups (Table 2, Figure 1) that showed high female preponderance of prescribed antibiotics in age ranges of 16-45 years. Whereas the number of antibiotic prescriptions in male gender was highest in patients belongs to young and elderly age groups.

The present study also observed that different wards have varying pattern of antibiotics use that was highest in Pediatrics, followed by Gynecology/obstetrics, Urology, Orthopedics, Emergency, Cardiac and OPD patients (Figure 1). In Pediatrics ward, the prevalent type of infections was found to be respiratory tract infections, gastric or diarrheal illness and meningitis. Whereas the age of 52% (104/197) of patients in pediatric ward was less than a year. Previous studies have reported that major illness rate of children under five years were diarrheal diseases and acute respiratory tract infections [16, 17]. In respiratory tract infections, several associated risk factors were poverty, limited family income, low education level of parents, under-weight birth rate, malnutrition, and breastfeed lacking [17]. The life threatening diarrheal disease can be reduced with

acceptable nutrition, sanitation practices and safe water for drinking instead of antibiotics utilization [18]. The adequate and healthy nutritive diet can reduce the incidence of mortality related with diarrheal illness and respiratory tract infection [19].

The patients in Emergency (ER) were 9.19% in the present study, patients came with diarrhea/enteric fever, accidents and infections. The number of patients prescribed with antibiotics in gynecology and obstetrics were highest in maternal cases with fertile ages i.e., 16-30 and 31-45 years. In Pakistan, females are at more risk of infections and hospitalization due to multiple pregnancies and surgical procedures during child birth, early age of menarche and young age marriages [20]. Furthermore lower rate of contraceptive utilization was found to be one of the cause [21].

In current findings, male patients were dominant in urology department associated with prevalent illness of urinary tract infections, chronic kidney disease and abscess. Previously published studies revealed male gender, elderly ages [22] and Diabetes mellitus [23] were commons risks associated with UTIs in males. However, it is thus suggested that unhygienic and inadequate sanitation practices can increased the risk of incidence UTIs.

The use of diagnostic tests for infectious diseases is lower in developing countries due to inadequate diagnostic facilities [12] additionally these tests are expensive to afford by the patients [11]. The present study revealed that only 25% of patients were tested for culture sensitivity whereas, 75% were treated with antibiotics either empirically or prophylactically (Figure 2). A previously published report is in alliance with the present study that 44% of antibiotics were prophylactic and 78.4% antibiotics were used as an empiric treatment in Turkey [24], another study reported that almost 95% empiric antibiotics were prescribed in lower respiratory tract infections in Egypt [25]. The

frequency of culture sensitivity test in present study was found to be higher in Pediatrics, Urology and Orthopedics respectively (Table 3). The reason behind higher prevalence of culture sensitivity tests in the above stated wards was higher number of cases associated with Gram-negative pathogens such as *E. coli*, *K. pneumoniae* and *P. aeruginosa* (Table 4). Previous studies reported that the higher resistance rate were developed in *E. coli*, *K. pneumoniae* [26] and *P. aeruginosa* [27].

Hospitals setups are major infection source due to inappropriate hygienic practices [28], Furthermore in developing countries other associated reasons are crowding and lack of hospital infection control practices [29]. An increased prophylactic use of antibiotics is thus found to be practiced for reduction of hospital acquired infections. The prescribing pattern of antibiotics in present study showed higher rate of utilization of cephalosporins, either alone or in combination with other antibiotics (Figure 3). A study reported 68% and 29.7% of empiric and prophylactic use of third generation cephalosporins respectively in Spain [30]. From Pakistan a report indicated high utilization of third generation cephalosporins in secondary care hospital setups [31], another study revealed that intensive care unit (ICU) were prescribing higher rates of third generation cephalosporins [32].

The one major reason of ESBLs global dissemination is intensely associated with the extended spectrum cephalosporins use as well as third generation cephalosporins, according to the study there is a strong correlation among resistance and third generation cephalosporins [33]. The prophylactic and empiric use of cefotaxime is related with increased risk of incidence of ESBLs in neonatal intensive care unit according to another study [34] and this risk of ESBLs emergence can be declined with targeted use of cephalosporins [35, 36]. High prevalence of ESBL producing isolates were reported in Pakistan according to various studies

[37-40]. The utilization of extended spectrum cephalosporins was found to be highest among studied patients (Table 5), Figure 4 showed that the prescribed cephalosporins alone or in combination in various wards were 53.4% (366/685). The inappropriate exposure of broad spectrum cephalosporins in hospitals must be limited with rationality and microbiological screening.

CONCLUSION

The use of extended spectrum cephalosporins in hospital cannot be restricted, the main challenges of prescribing practices are rationality and diagnostic tools for microbiological screening of infection. Antibiotic stewardship programs must be utilized to educate practitioners, to reduce the risk associated with inappropriate prescribing of antibiotics in hospitals.

REFERENCES

1. Polk, R., *Optimal use of modern antibiotics: emerging trends. Clinical infectious diseases*, 1999. **29**(2): p. 264-274.
2. Guillemot, D., et al., *Trends in antimicrobial drug use in the community—France, 1981–1992. Journal of Infectious Diseases*, 1998. **177**(2): p. 492-497.
3. Gonzales, R., J.F. Steiner, and M.A. Sande, *Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. Jama*, 1997. **278**(11): p. 901-904.
4. Fridkin, S.K., et al., *Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. Clinical infectious diseases*, 1999. **29**(2): p. 245-252.
5. Bantar, C., et al., *A hospitalwide intervention program to optimize the quality of antibiotic use: impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. Clinical infectious diseases*, 2003. **37**(2): p. 180-186.
6. John Jr, J.F. and N.O. Fishman, *Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital. Clinical infectious diseases*, 1997. **24**(3): p. 471-485.
7. Morgan, D.J., et al., *Non-prescription antimicrobial use worldwide: a systematic review. The Lancet infectious diseases*, 2011. **11**(9): p. 692-701.
8. Müller, O. and M. Krawinkel, *Malnutrition and health in developing countries. Canadian Medical Association Journal*, 2005. **173**(3): p. 279-286.

9. Thomas, D. and E. Frankenberg, Health, nutrition and prosperity: a microeconomic perspective. *Bulletin of the World Health Organization*, 2002. **80**(2): p. 106-113.
10. Sachs, J.D. and J.W. McArthur, *The millennium project: a plan for meeting the millennium development goals. The Lancet*, 2005. **365**(9456): p. 347-353.
11. Laxminarayan, R. and D.L. Heymann, Challenges of drug resistance in the developing world. *BMJ (Clinical research ed)*, 2012. **344**.
12. Berkley, J.A., et al., Diagnosis of acute bacterial meningitis in children at a district hospital in sub-Saharan Africa. *The Lancet*, 2001. **357**(9270): p. 1753-1757.
13. Khan, M.S., et al., Common trend of antibiotics usage in a tertiary care hospital of Peshawar, Pakistan. *Journal of Ayub Medical College Abbottabad*, 2010. **22**(1): p. 118-120.
14. Nausheen, S., R. Hammad, and A. Khan, Rational use of antibiotics--a quality improvement initiative in hospital setting. *Journal Pakistan Medical Association*, 2013. **63**(1): p. 60.
15. Naveed, S., et al., Use of 3rd generation cephalosporins in different age groups in tertiary health care centers of Karachi. *Journal of Scientific and Innovative Research*, 2014. **3**(2): p. 1-4.
16. Kotloff, K.L., et al., Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *The Lancet*, 2013. **382**(9888): p. 209-222.
17. Cashat-Cruz, M., J.J. Morales-Aguirre, and M. Mendoza-Azpiri. Respiratory tract infections in children in developing countries. in *Seminars in pediatric infectious diseases*. 2005: Elsevier.
18. Thapar, N. and I.R. Sanderson, Diarrhoea in children: an interface between developing and developed countries. *The Lancet*, 2004. **363**(9409): p. 641-653.
19. Rice, A.L., et al., Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization*, 2000. **78**(10): p. 1207-1221.
20. Udry, J.R. and R.L. Cluquet, A cross-cultural examination of the relationship between ages at menarche, marriage, and first birth. *Demography*, 1982. **19**(1): p. 53-63.
21. Hakim, A. and M. Sultan, *Pakistan Reproductive Health and Family Planning Survey (2000-01). Preliminary report*. 2001.
22. Azap, Ö., et al., Risk factors for extended-spectrum β -lactamase positivity in uropathogenic *Escherichia coli* isolated from community-acquired urinary tract infections. *Clinical microbiology and infection*, 2010. **16**(2): p. 147-151.
23. Saleem, M. and B. Daniel, Prevalence of Urinary Tract Infection among Patients with Diabetes in Bangalore City. *Int. J. Emerg. Sci*, 2011. **1**(2): p. 133-142.
24. Usluer, G., I. Ozgunes, and H. Leblebicioglu, A multicenter point-prevalence study: antimicrobial prescription frequencies in hospitalized patients in Turkey. *Annals of clinical microbiology and antimicrobials*, 2005. **4**(1): p. 16.
25. Ahmed, M., A. ELMaraghy, and E. Andrawas, Study of prescription patterns of antibiotics in treating lower respiratory tract infections at Sohag Chest Hospital. *Egyptian Journal of Chest Diseases and Tuberculosis*, 2016. **65**(1): p. 143-155.
26. Hanson, N.D., et al., Surveillance of community-based reservoirs reveals the presence of CTX-M, imported AmpC, and OXA-30 β -lactamases in urine isolates of *Klebsiella pneumoniae* and *Escherichia coli* in a US community. *Antimicrob agents and chemother*, 2008. **52**(10): p. 3814-3816.
27. Hugbo, P. and P. Olurinola, Resistance of *Pseudomonas aeruginosa* to antimicrobial agents: implications in medicine and pharmacy. *Nig J Pharm Sci*, 1992. **4**: p. 1-10.
28. Weinstein, R.A., Controlling antimicrobial resistance in hospitals: infection control and use of antibiotics. *Emerging infectious diseases*, 2001. **7**(2): p. 188.
29. Istúriz, R.E. and C. Carbon, Antibiotic use in developing countries. *Infection Control & Hospital Epidemiology*, 2000. **21**(06): p. 394-397.
30. Pereira, L.M.P., et al., Third generation cephalosporin use in a tertiary hospital in Port of Spain, Trinidad: need for an antibiotic policy. *BMC infectious diseases*, 2004. **4**(1): p. 59.
31. Ali, S.R., S. Ahmed, and H. Lohana, Trends of empiric antibiotic usage in a secondary care hospital, Karachi, Pakistan. *International journal of pediatrics*, 2013. **2013**.
32. Akhtar, N., Hospital acquired infections in a medical intensive care unit. *J Coll Physicians Surg Pak*, 2010. **20**(6): p. 386-390.
33. Daoud, Z., et al. Prevalence and Molecular Epidemiology of ESBL producing *E. coli* and *K. pneumoniae* in Lebanese Medical Centers; Strong Correlation between Antibiotic Consumption and Resistance to Cephalosporins and Ciprofloxacin. in *Open Forum Infectious Diseases*. 2014: Oxford University Press.
34. Le, J., et al., Impact of empiric antibiotic use on development of infections caused by extended-spectrum β -lactamase bacteria in a neonatal intensive care unit. *The Pediatric infectious disease journal*, 2008. **27**(4): p. 314-318.
35. Kim, J.Y., et al., Control of extended-spectrum β -lactamase-producing *Klebsiella pneumoniae* using a computer-assisted management program to restrict third-generation cephalosporin use. *Journal of Antimicrobial Chemotherapy*, 2008. **62**(2): p. 416-421.
36. Apisarnthanarak, A., et al., Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clinical Infectious Diseases*, 2006. **42**(6): p. 768-775.
37. Ullah, F., S. Malik, and J. Ahmed, Antibiotic susceptibility pattern and ESBL prevalence in nosocomial *Escherichia coli* from urinary tract infections in Pakistan. *African Journal of Biotechnology*, 2009. **8**(16): p. 3921-6.
38. Jabeen, K., A. Znfar, and R. Hasan, Frequency and sensitivity pattern of Extended Spectrum beta Lactamase producing isolates

in a tertiary care hospital laboratory of Pakistan. JOURNAL-PAKISTAN MEDICAL ASSOCIATION, 2005. 55(10): p. 436.

39. Shah, A., et al., *Extended-spectrum beta-lactamases in Enterobacteriaceae: related to age and gender. The new microbiologica, 2002. 25(3): p. 363-366.*

40. Ahmed, N., et al., *Frequency of Extended Spectrum Beta Lactamases in Enterobacteriaceae in Urinary Isolates Related to Age and Gender. Medical Channel, 2016. 22(2): p. 16-20.*