

Higher incidence of prescribing rates and utilization of broad spectrum cephalosporin in young patients: A retrospective observational study in a tertiary care hospital

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Abstract: Frequent use of antibiotics has been developed resistance and the use of broad spectrum cephalosporin must be limited in children. The study evaluated the association of prescribing patterns of third generation cephalosporin with diagnosis, age, availability of cultural sensitivity report and gender. It is an observational study that was carried out in the duration of six months in a low socio-economic tertiary care hospital. The data of six hundred and eighty-five (685) patients were collected from the medical records of the tertiary hospital. The cephalosporin are the most prescribed antibiotics in children 118/217 (54.3%) followed by adults 119/403 (29.5%) and teenagers 18/65 (27.6%). Whereas, 75/217 (34.5%), 126/403 (31.2%) and 22/65 (33.8%) were prescribed cephalosporin with combination in patients respectively. The culture sensitivity was performed only in 25% of patients i.e., 173/685, Of 173 culture reports 70 and 91 cases from children and adults respectively. Blood is mostly examined specimen in children and urine in adults. *Escherichia coli* was highly recovered pathogen in culture sensitivity report. The study concluded broad spectrum cephalosporin antibiotics were highly prescribed in children. The culture sensitivity was performed in limited number of patients. Antibiotics stewardship programme will be implemented to reduce the prescribing of broad spectrum cephalosporin in young patients.

Keywords: Broad spectrum cephalosporin, antibiotics, children, culture sensitivity test, antibiotics stewardship.

INTRODUCTION

Antibiotics are most prescribed medication and an important part of regimen in hospitals to treat infections. Antibiotics can be prescribed as prophylactic therapy or an empiric treatment to control the infection in hospitalized patients. The unnecessary use of antibiotics leads to development of ineffectiveness due to bacterial resistance (Laxminarayan *et al.*, 2013). The prescribing of antibiotics are common in clinical settings and practiced unnecessarily in children (Watson *et al.*, 2017, Hersh *et al.*, 2011). However, the utilization of broad spectrum antibiotics are common to treat infections in young patients, raising concerns for antimicrobial resistance (Hersh *et al.*, 2011). The investigation associated with utilization of pediatric antibiotics is significant because antibiotic use in children is associated with a transferal in intestinal micro biome and increased risk of obesity and asthma (Korpela *et al.*, 2016, Azad *et al.*, 2014, Marra *et al.*, 2009)

The cephalosporin is one of highly prescribed antibiotic in hospital settings due to broad spectrum activity against

Gram-Negative bacteria. The mechanism of action is the inhibition of peptidoglycan chain in the wall ultimately breaks the cell wall of bacteria (Khan *et al.*, 2019a). The overuse and excessive prescribing leads to the resistance mechanisms (Shankar *et al.*, 2005). An important aspect of the global distribution issue has highlighted that antibiotic resistance lead to the lack of fast and inexpensive diagnostics in detecting the disease. Researchers are working all over the world for more effective antibiotics. The spectrum ranging from new drugs to patients could bring relief to combat of antibiotic resistance in hospitals (Costelloe *et al.*, 2010).

If the antibiotics are not prescribed rationally, it could lead to adverse drug effect. The resistance of antibiotics could badly affect the health of the patients as it would eventually lead to the ineffective treatment and increase the cost of the treatment. Regular audit of the hospitals is essential so that physicians can be given feedback about the prescription of the medications. (Sabir *et al.*, 2014, Shah *et al.*, 2014) Culture sensitive reports play vital and significant role in identifying the bacteria and then prescribing the antibiotic accordingly (Singha *et al.*, 2020).

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Broad spectrum cephalosporin when prescribed in children with meningitis and other infections causes high resistance and the combination is more useful to treat the infections (Klugman *et al.*, 1995). The rising relevance of antibiotics in children causing higher rate of infectious pathogens in environment which is more dangerous to treat children and thus serious notice should be taken before prescribing broad spectrum antibiotics (Logan *et al.*, 2014).

Therefore, this study was conducted with the purpose to investigate the pattern of antibiotics in tertiary care hospitals of Karachi and then recommend the effective ways to prescribe the antibiotics in an appropriate manner.

MATERIALS AND METHODS

The study is based on quantitative methodology to analyse the data. The purpose of this study is to examine the prescribing pattern of cephalosporin in tertiary care hospitals in Karachi. The research focused on secondary data, gathered through information collection of patients from the medical records of the tertiary hospitals in Karachi during January-June 2018. The demographic and medical treatment records were collected, such as, age category and sex of the patient, medical ward in which patients were admitted, diagnosis on the basis of the drug were prescribed, availability of culture-sensitive reports, organism found in culture report, number of prescribed drugs and duration of treatment. The purpose of this quantitative, co-relational research study was to assess and examine the factors on the basis of which broad spectrum cephalosporin antibiotics were prescribed to the patients in tertiary care hospitals of Karachi.

Experimental setting

This is the cross-sectional, single centre tertiary care hospital of low socio economic status. This study was carried out in low socio-economic tertiary care hospitals in Karachi. Various wards were included in the study and the data was collected through medical records which were maintained in their medical files. The sample size was 685 and collected through convenient sampling method.

Eligibility criteria

- Gender: both male and female

a. Inclusion criteria

- Records of all patients receiving antibiotics for treatment or prophylaxis were included.
- Patients from all age groups from infants to old age were included.
- Patients from all available wards were enrolled.

b. Exclusion criteria

- Patients with incomplete data
- Patients with no records of prescribed antibiotics

Data collection

Data is collected from different wards of a low socioeconomic tertiary care hospital. The collected data was based on availability of medical records of patients admitted in various wards. The available information related to age, gender, diagnosis, prescribed antibiotics, culture sensitivity report, specimen of culture reports and pathogen.

Ethical approval

The study was approved by the Board of advance studies and research of Jinnah University for Women with Reference No: BASR/Extr./62nd Proc/Dec.

STATISTICAL ANALYSIS

The descriptive statistics was analysed and all results are expressed as the frequency and percentages. Data were therefore cross tabulated to expressed results in association with various age categorization. All statistical analysis was carried out by using SPSS version 20.

RESULTS

The accession criteria were based on total number of antibiotics prescribed in children, teenage and adults patients. The results are collected in three categories with the correlations of diagnosis, culture sensitivity, specimen and recovered pathogen.

Age of patient

Total number of (N=685) data related to patients were studied. Highest number of patients were adults 403 (58.8%) followed by children 217(31.6%) and teenagers 65(9.4%) patients.

Association of age with prescribed antibiotics

Table 1 revealed that cephalosporin are the most prescribed drugs that showed highest percentage in children 118 (17.2%) followed by adults 119 (17.3%) and teenagers 18 (2.6%). The second most prescribed antibiotic is penicillin that is most frequently prescribed in adults 60 (8.7%) followed by teenagers 16 (2.2%) and the children 15 (2.1%).

Combination antibiotic therapy with cephalosporin was seen most frequently in adults 126 (18.3%) followed by teenagers 22(3.2%) and children 75 (10.9%). while other drugs showed variable pattern of occurrence as shown in data.

Association of age and diagnosis

Table 2 revealed that Respiratory tract infection is the most common diagnosis for antibiotic prescription that is more prevalent in children 83 (12.1%) followed by adults 11 (1.6%) and teenagers 2 (0.2%). The second most common diagnosis was found to be gynecological problems that has high occurrence but only in female

Table 1: Association of age with prescribed antibiotics

Age Category	Number Of Prescribed Drugs In n (%)										Total
	Penicillin	Cephalosporin with combination	Cephalosporin	Macrolides	Quinolones	Aminoglycosides	Tetracycline	Carbapenem	Glycopeptide	Antiparasytic	
Children	15 (2.1)	75 (10.9)	118 (17.2)	1 (0.1)	3 (0.4)	0 (0)	1 (0.1)	0 (0)	1 (0.1)	0 (0)	217 (31.7)
Teenager	16 (2.2)	22 (3.2)	18 (2.6)	1 (0.1)	6 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.2)	65 (9.5)
Adults	60 (8.7)	126 (18.3)	119 (17.3)	1 (0.1)	63 (9.1)	5 (0.7)	0 (0)	1 (0.1)	7 (1)	6 (0.8)	403 (58.8)
Total	91 (13.3)	223 (32.6)	255 (37.2)	3 (0.4)	72 (10.5)	5 (0.7)	1 (0.1)	1 (0.1)	8 (1.2)	8 (1.2)	685 (100)

Table 2: Association of age and diagnosis

Age Category	Diagnosis (%)										Total		
	Respiratory Tract Infection	Urinary Tract Infection	Meningitis	Other Infections	Topical Infections	Orthopaedics (Fracture)	Chronic Kidney Disease	Heart Problems	Surgical Procedures	Gastric Problems		Anaemia	Gynaecology/Obstetrics
Children	83 (12.1)	7 (1)	41 (6)	21 (3)	0 (0)	20 (2.9)	0 (0)	2 (0.2)	7 (1)	11 (1.6)	20 (2.9)	0 (0)	217 (31.7)
Teenager	2 (0.2)	10 (1.4)	0 (0)	6 (0.8)	0 (0)	20 (2.9)	1 (0.1)	0 (0)	11 (1.6)	7 (1)	1 (0.1)	4 (0.5)	65 (9.5)
Adults	11 (1.6)	70 (10.2)	0 (0)	58 (8.4)	19 (2.8)	52 (7.5)	22 (3.2)	22 (3.2)	28 (4)	16 (2.3)	0 (0)	99 (14.4)	403 (58.8)
Total	96 (14)	87 (12.7)	41 (6)	85 (12.4)	19 (2.8)	92 (13.4)	23 (3.4)	24 (3.5)	46 (6.7)	34 (5)	21 (3.1)	103 (15)	685 (100)

Table 3: Association of age and availability of cultural sensitivity report

Age Category	Availability Of Culture Sensitivity In No. (%)		Total
	Yes	No	
Children	70 (10.2)	147 (12.4)	217 (31.7)
Teenager	12 (1.75)	53 (7.7)	65 (9.5)
Adults	91 (13.2)	312 (45.5)	403 (58.8)
Total	173 (25.3)	512 (74.7)	685 (100)

N = 685 Values are expressed in n (%)

Table 4: Association of age with type of specimen for cultural sensitivity report

Age Category	Specimen n (%)							Total	
	Blood	Blood & urine	URINE	PUS	HVS	CSF	SPUTUM		SWAB
Children	49 (28.8)	0 (0)	7 (4)	2 (1.1)	0 (0)	2 (1.1)	5 (2.8)	5 (2.8)	70(40.4)
Teenager	11 (6.3)	0 (0)	1 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	12(6.9)
Adults	19 (10.9)	3 (1.7)	39 (22.5)	22 (12.7)	5 (2.8)	0 (0)	1 (0.5)	2 (2.8)	91(52)
TOTAL	79(45.6)	3(1.73)	47(27.1)	24(13.8)	5(0.2)	2(1.1)	6(3.4)	7(4)	173(100)

N = 173 Values are expressed in n (%)

Table 5: Pathogen found in culture sensitivity report

Age Category	Pathogen Found From Culture Sensitivity Report In No.(%)												Total
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>B. cereus</i>	<i>B. subtilis</i>	<i>H. influenza</i>	<i>Klebsiella spp.</i>	<i>L. monocytogens</i>	<i>S. pneumoniae</i>	<i>E. histolytica</i>	<i>N. gonorrhoea</i>	Others	
Children	40 (23.1)	1 (0.5)	3 (1.7)	0 (0)	1 (0.5)	2 (1.1)	10 (5.7)	1 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)	62(35.8)
Teenager	11 (6.3)	10(5.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	21(12.1)
Adults	50 (28.9)	18(10.4)	5 (2.8)	1 (0.5)	0 (0)	0 (0)	6 (3.4)	0 (0)	0 (0)	0 (0)	0 (0)	10 (5.7)	90(52)
Total	101 (58.7)	29 (16.7)	8 (4.6)	1 (0.1)	1 (0.1)	2 (0.3)	16 (9.3)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	11 (6.3)	173(100)

N=173 values are expressed in n (%)

adults 99 (14.1%) followed by teenagers 4 (0.5%). Urinary tract infections were found to third common diagnosis that showed highest percentage in adults 70 (10.2%) followed by teenager 10 (1.4%) and children 7 (1%). Meningitis was the fourth commonly observed diagnosis solely found in children 41 (6%) of the total while other diagnosis shows variable percentages as below.

Association of age of the patient and availability of cultural sensitivity report

Table 3 depict that only 173 (25.3%) out of 685 patients have their cultural sensitivity report in which adults were 91 (13.2%), children were 70 (10.2%) and teenagers were 12 (1.75%), whereas 512 (74.7%) patients were prescribed antibiotics without any cultural sensitivity test.

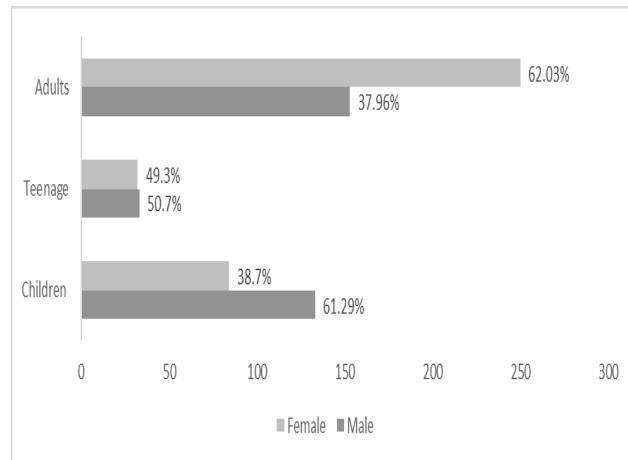


Fig. 1: Number of patients in each age category

Association of age with type of specimen for cultural sensitivity report

Table 4 show the type of specimen taken from patients (n=173) for cultural sensitivity report. Blood was found to be the most common specimen withdrawn from patients 79 (45.6%), among them children 49 (28.8%) were the most frequent age category followed by adults 19 (10.9%) and teenagers 11 (6.3%). The second common specimen was urine 47(27.1%) that showed adults 39 (22.9%), children 7 (4%) and teenagers 1 (0.5%) while other specimens show variable percentages as shown below.

Association of age with pathogen found in cultural sensitivity report

Table 5revealed that the most common pathogen found is *E. coli* 101 (58.7%). them adults were 50 (28.9%), children were 40 (23.1%) and teenagers were 11 (6.3%). The second most pathogen was found to be *Pseudomonas aeruginosa* with 29 (16.7%) followed by adults 18 (10.4%) followed by teenagers 10 (5.7%) and children 1 (0.5%). The third organism *Klebsiella spp.* with total 16 (9.3%) is found most commonly in children 10 (5.7%) followed by adults 6 (3.4%) while other organisms shows variable percentages.

DISCUSSION

The present investigation was carried out to give a sight for the use of broad spectrum cephalosporin in different age groups of hospitalized patients. The focused areas were the prophylactic use, availability of culture sensitivity, type of infection, specimen and pathogen. Among N=685 studied patients 403 were adults, 217 were children and 65 were belonged to teenage group (fig. 1).

In developing countries where policies are not implemented and practiced, they are using excessive amount of cephalosporin in hospitalized patients (Soman *et al.*, 2019). Broad spectrum antibiotics are highly prescribed in hospitals, the excessive exposure and constant use resulted the development of resistance mechanisms in the Gram-Negative bacteria. The global dissemination of extended spectrum beta lactamases (ESBLs) is related to third generation or extended spectrum cephalosporin(Livermore *et al.*, 2013, Daoud *et al.*, 2014), the restricted use can decrease these incidences (Aldeyab *et al.*, 2012).

Third generation cephalosporin are highly prescribed in various regions of world (Abou-Shaabab *et al.*, 2016, Chang *et al.*, 2019, Krasniqi *et al.*, 2019) and highly associated with consumption of other broad spectrum antibiotics due to resistance development (Muller *et al.*, 2018).The utilization of cephalosporin was found 37.2% (255/685) among total studied population (table 1), 32.6 % (223/685) were prescribed by cephalosporin with combination whereas, out of 685 patients 91 and 72 were

prescribed with penicillin and quinolones respectively. Similar pattern was observed in previous study from Pakistan have reported high rate of prescribed cephalosporin in hospitals, followed by penicillin and quinolones (Atif *et al.*, 2016, Khan *et al.*, 2019b, Nadeem *et al.*, 2020).

The utilization and consumption of cephalosporin was increased in last 5 years from Pakistan and majority of the studies reported prophylactic use (Malik and Figueras, 2019). The inappropriate consumption was reported from Pakistan and extensively prescribed antibiotic was cephalosporin (Saleem *et al.*, 2019). Developed countries are establishing various policies and stewardship trainings which impacted as reduced uses of third generation cephalosporin in outpatients and inpatients (Taylor *et al.*, 2020, Kato *et al.*, 2020, Borde *et al.*, 2015).

In adults and children, the prescribing of cephalosporin was found to be 119 (46.6%) and 118 (46.27%) respectively. The utilization of broad spectrum antibiotics such as cephalosporin in children is increasing resistance among them and the developed resistance can limit the use during the lifespan (Labi *et al.*, 2018). The prescribing pattern of cephalosporin in children must be rationale and such broad spectrum antibiotics must be prescribed only on basis of culture sensitivity, the continuous exposure to broad spectrum cephalosporin lead serious consequences related to resistance mechanism. Inappropriate use of third generation cephalosporin to children under age of 5 years have been reported (Wacharachaisurapol *et al.*, 2020).

In children most of the prescribed antibiotics was found in patient with respiratory tract infections, gastrointestinal infections and meningitis (table 2). The leading death rate in children under age of 5 years associated with pneumonia and diarrhea according to WHO (Hoan *et al.*, 2009). In developing countries, the major causes of morbidity and mortality are related to Diarrheal diseases and respiratory illness (Organization, 2005). A Previously published study indicated that major illness rate of children under five years were diarrheal diseases and acute respiratory tract infections (Kotloff *et al.*, 2013).

The prophylactic use of antibiotics in developing countries has increased in hospitals because hospitals are main source of infections due to unsuitable hygiene (Weinstein, 2001), Furthermore in underdeveloped countries extra causes are crowding and absence of hospital contamination control (Istúriz and Carbon, 2000). To evade chances of nosocomial infections due to opened wound in body tissues, the higher utilization of antibiotics is associated with surgical procedures involved in gynecology and obstetrics ward in 103 out of 685 patients admitted for surgical procedure related to child birth deliveries and other complications, whereas in 92 and 46 patients were in orthopedics and surgery wards. A study

reported higher consumption of cephalosporin in patients with surgical procedures (Soman *et al.*, 2019). Various studies have conducted to evaluate the impact of appropriate usage of cephalosporin as prophylaxis in surgical procedures (Ierano *et al.*, 2020, Mirzaei *et al.*, 2019), the stewardship impact on reduction of third generation cephalosporin (Abubakar *et al.*, 2019).

Only 25% (173/685) have been screened for culture sensitivity and rest of the cases were treated empirically or prophylactically (table 3). In countries where health care facilities are not easily afforded by the patients, diagnostic tests for infectious diseases is lower in developing countries due to inadequate diagnostic facilities (Berkley *et al.*, 2001) additionally these tests are expensive to afford by the patients (Laxminarayan and Heymann, 2012). A previous study reported that 44% of antibiotics were used prophylactically and 78.4% antibiotics were as empiric treatment in Turkey (Usluer *et al.*, 2005), 95% of lower respiratory tract infections were treated empirically in Egypt (Ahmed *et al.*, 2016).

The most of antibiotic treatment is related to Gram-Negative bacteria of family *Enterobacteriaceae* (*Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella spp.*) recovered from blood and urine specimens (n=173) (table 4 & 5). The consumption of broad spectrum cephalosporin is associated with extended spectrum beta lactamase production in *E. coli* and *Klebsiella pneumoniae* (Nielsen *et al.*, 2015). Further studies are suggested to evaluate the appropriate consumption of broad spectrum cephalosporin and impact on reduced incidence of ESBL resistance mechanism in GNB related to family *Enterobacteriaceae*. The overall consumption can be controlled by developing policies and antibiotic stewardship trainings programme to avoid resistance mechanisms and improve patient outcome.

Limitation of the study

The study has some limitation. First the study was single centered and observational and has limited sample size based on the availability of medical records during the study period. Secondly an important aspect of bacterial resistance was not assessed because the objectives were to analyzed the prescribing trends of cephalosporin among children.

CONCLUSION

The study concluded that high incidence of prescribed and utilized broad spectrum cephalosporin for children in tertiary care hospital setup. The culture sensitivity was performed in limited number of patients and most of the prescribed antibiotics were used prophylactically or empirically. The overall medical cost and burden to the patient can be improved and reduced by antibiotic stewardship training programme for physicians and practitioners. The studies must be published based on pre

and post training impact on appropriate and rationale prescribing of antibiotics in children from developing countries.

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