Drug utilization and prescribing pattern of antibiotics in a tertiary care setups; trends and practices

Huma Ali[1], Farya Zafar[2], Shazia Alam[3], Anwar Ejaz Beg[3], Rabia Bushra[4], Ammara Manzoor[5], Ghazala R Naqvi[6], Riffat Yasmeen[4], Yousra Shafiq[1], Anum Tariq[3], Saba Zubair[3] and Saima Saleem[7]

[1]Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan
[2]Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan
[3]Department of Pharmaceutics, Faculty of Pharmacy, Ziauddin University, Karachi, Pakistan
[4]Department of Pharmaceutics, Dow College of Pharmacy, DUHS, Karachi, Pakistan
[5]Department of Medical Oncology, Jinnah Post Graduate Medical Centre [JPMC} Karachi, Pakistan
[6]Department of Pharmaceutics, Faculty of Pharmacy, Federal Urdu University of Arts, Science and Technology, Karachi, Pakistan
[7]Department of Pharmaceutical Services, NICVD, Karachi, Pakistan

Abstract: Irrational, over and misuse of antibiotics arise as global concern in both hospital and community settings and lead to adverse events including antimicrobial resistance, associated health problems, amplified hospitalization stay and cost. Hence, Drug Utilization Evaluation (DUE) studies are designed to evaluate and improve the prescribing, administration and the rational use of medications. The present study was designed to assess the pattern of antimicrobial drug utilization in in-patients cohort of tertiary care setup in Karachi, Pakistan. This cross sectional observational study was conducted in retrospective manner. World health organization (WHO) guidelines and criteria are considered to evaluate the appropriateness of drug use in various disease conditions. ATC/DDD system was applied to determine the study outcome. High frequency of antibiotics utilization found in respiratory tract infections of both lower (LRTI) 16.8% (n=42) and upper (UTI) 13.2% (n=33). The estimated total number of drug units administered per month was greater with cefixime (46) and ciprofloxacin (45) both. DDD/100 bed days drug utilization of antibiotics was higher with ciprofloxacin, cefexime and meropenem (47, 46 and 29.25) correspondingly. In conclusion, the current investigation signifies extensive scope for progress in prescribing trend. Drug adherence to customary guidelines of disease management and constraint policies to endorse judicious drug use may be considered vital in healthcare setup.

Keywords: Drug Utilization Evaluation, ATC/DDD system, retrospective, compliance, WHO guidelines.

INTRODUCTION

Drug utilization (DU) is defined by WHO as the marketing, distribution, prescription and the use of drugs in society with particular focus on medical, social and economic consequences (Patel *et al*., 2013)**.** Antibiotic offers enormous benefits with infectious diseases among hospitalized patients and remains as post discharge treatment but inappropriate use may cause serious risk of health complications without any therapeutic effects. Health care providers may decrease potential harm by implementing formal trainings, identification of interventions and screening of individual drugs to develop best practice in prescribing antibiotics to treat inpatients (Collins, 2008). Drug utilization reviews reassure the quality care and sustainability of drug therapy by determining drug usage data in health management. DU analysis are generally conducted to improve the clinical outcomes, prevention from misuse of antibiotics, guideline compliance towards medical standards and to avoid drug -drug interactions (WHO guidelines 2003; Khavane *et al*., 2010). Poor prescribing habit of antibiotics may significantly affect hospitalized patients. Worldwide, approximately half of prescribed antibiotics are reported irrational and 50% of patients had poor compliance. Main reasons found towards the consequences of mortality and morbidity and prolong hospitalization primarily the lack of health care educational programs, diagnostic error and antibiotic resistance (Khan *et al*., 2013). A study evaluated most widely used antibiotics such as 12% amino penicillin, 20% macrolides, 25% quinolones, tetracycline and cephalosporin and 85.43% of drugs prescribed by their brand names (Shapiro *et al*., 2013; Kotwani *et al*., 2014)**.** The rate of antibiotics has increased 115% in children than 86% in adults. In case of pneumonia, antibiotics are potentially prescribed. However, in Germany, prescriptions for antibiotics are found to be reduced up to 41% even in patients who are supposed to have pneumonia. More precisely, use of narrow spectrum antibiotics was higher than broad spectrum in Germany than France (Harbarth *et al*., 2002)**.** In Malaysia, antibiotics are commonly prescribed by primary care providers and most frequently prescribed for people with respiratory tract infections (Teng *et al*., 2011; Teng *et al*., 2006; Mohd and Kamaliah, 2013)**.** There are several well-differentiated methods to establish the extent of irrational

**Corresponding author:* e-mail: humaali80@live.com

use. Ample medicine utilization data can be applied to mark out costly products of minor efficacy, Anatomical Therapeutic Classification system (ATC)/Defined Daily Dose (DDD) to compute the drug consumption amongst institution or regions. Furthermore, indicators of WHO drug use including prescribing, patient care, facility, complementary drug use indicators may also be used to calculate rationality and utilization trends of medicines (Henry, 2006; Mohanraj *et al*., 2015; WHO,2003). Therefore, current study was planned to investigate the prescribing trends and aptness of antibiotics utilization in tertiary care setting.

MATERIALS AND METHODS

Study design

This cross sectional observational study was conducted in retrospective manner to assess the antimicrobial drugs utilization and prescribing trends of antibiotics. World health organization (WHO) guidelines and criteria are considered to evaluate the appropriateness of drug use in various disease conditions. ATC/DDD system was applied to determine the study outcome. Data of patients admitted in medical wards diagnosed with acute infections for which antibiotics were prescribed were included in this study. The presented investigation was carried out in two tertiary care units in Karachi, Pakistan. The healthcare setup was composed of 300 bed capacities with various dedicated services in pediatrics, gynecology, surgery, family and internal medicine etc. Data collection period was carried out between January to December 2016.

Data Collection Procedure

The data was extracted from the patient medical records through trained pharmacy professionals using the validated data collection form. Validation of data collection format for its reliability and consistency was performed by calculating the spearman coefficient correlation & Cronbach's α (p = 0.916 & α = 0.902). During the study medical records were reviewed. All the related information was gathered by thorough reviewing and recording prescription orders submitted to pharmacy department of each and also by documenting the medication chart in each of the participating unit. In case of any query during the analysis of any information and to develop a consensus on that issue, a team was composed of pharmacologist, doctors, clinical pharmacists and data collection personnel's. A formal permission was obtained from hospitals administration. Secrecy of the information was maintained throughout the period of the study. All the records of the patients including demographic, disease and medical profile were kept fully confidential.

Inclusion and exclusion criteria

Prescriptions composed of antibiotic with other drugs were incorporated and related information was extracted with reference to the indication, period, frequency and dose. All prescriptions with deficient records were excluded.

Sample size

The sample size was calculated in accordance of the Joint Commission on the Accreditation of Health Care Organization (JCAHO) standard. Approximately, an average of 1000 prescriptions was identified with antibiotic indications on quarterly basis from participating units, thus 250 cases of 25% population were selected in this study (Biru *et al*., 2014; Abier, 2007).

Study Outcome: Following formulas were used to compute the outcomes in term of the drug utilization amount.

$$\text{DDD} = \frac{\text{No. of issued items} \times \text{Amount of the drug per item}}{\text{WHO recommended DDD of Drug}}$$

$$\text{DDD/100 bed days} = \frac{\text{Drug consumption} \times 100}{\text{DDD (mg)} \times \text{No. of days in study period} \times \text{Total no. of beds} \times \text{Occupancy index}}$$

number of beds = 300; occupancy index=1

Data interpretation and analysis

Data processing was performed with Microsoft excel software and SPSS 20. Further interpretation and analysis was carried out in the light of WHO guidelines of drug utilization standards**.**

RESULTS

The development of drug utilization (DU) as research area made it possible to study drug prescribing and drug usage in a scientific and formal manner**.** Demographic profiles of overall 250 patients of both genders were analyzed and given in table 1. Approximately 134 male and 116 female patients were treated with antimicrobials. In present investigation, majority of patients 29.6% (n=74) had mean age ranges of 36-50 years, among them 19.2% (n=23) of male whereas 10.4% (n=26) were females. However, antimicrobial treatment found lesser in patients approximately 11.6% (n=29) of age group 18-25 and above 60 years (table 1). Fig. 1 demonstrated the monthly frequency of medications prescribed in various infections. Table 2 described the gender base frequency of infections including common infections against which prescriptions contain antibiotics. In present study, the incidence of typhoid was lesser in male (2.4%) than females (7.2%) (table 2, fig. 1). Table 3 summarizes the drug utilization data of antibiotics such as ciprofloxacin, meropenem, ceftrioxone, cefixime, doxycyclin, amikacin, azithromycin and levofloxacin with their generic or brand names. The classification of antibiotic utilization and disease association are mention in table 4 along with values of WHO defined daily dose (DDD) and anatomical therapeutic chemical classification (ATC) codes. Table 5 showed the prescribing pattern of antibiotics.

Table 1: Demographic details of patients treated with antimicrobials

Age (years)	Number of patients (250)	Male (n=134)	Female (n=116)
18-25	29(11.6%)	16(6.4%)	13(5.2%)
26-35	58(23.2%)	26(10.4%)	32(12.8%)
36-50	74(29.6%)	48(19.2%)	26(10.4%)
50-60	51(20.4%)	23(9.2%)	28(11.2%)
60 above	38(15.2%)	21(8.4%)	17(6.8%)

Table 2: Gender-based frequency of infections

Infections	Frequency (%)		
	Male	Female	Total
UTI	42 (16.8%)	20 (8%)	62 (24.8%)
LRTI	33 (13.2%)	24 (9.6%)	57 (22.8%)
Typhoid	06 (2.4%)	18 (7.2%)	24 (9.6%)
COPD	19 (7.6%)	26 (10.4%)	45 (18%)
GI infection	18 (7.2%)	16 (6.4%)	34 (13.6%)
Pneumonia	16 (6.4%)	12 (4.8%)	28 (11.2%)

Table 3: Drug utilization data of antibiotics

Drugs	Dose (mg)	Generic/Brand	Total number of units administered (one month)	Total amount used in one month (gms)
Ciprofloxacin	200mg	Ciproxin	45	32.5
	500mg	Quinoflox	37	
	500mg	Cycin	10	
Meropenem	500mg	Penro	34	58.5
	1000mg	Penro	19	
		Meronem	22	
	2000mg	Meronem	31	
Ceftriaxone	1000mg	Rocephin	27	27.0
Cefexime	400mg	Cefspan	46	18.4
Doxycyclin	100mg	Vibramycin	24	2.40
Amikacin	25-50mg	Amkay	37	1.85
Azithromycin	500mg	Zithrax	14	7.00
levofloxacin	500mg	Leflox	19	9.5

The compliance of antibiotics recorded through dose, duration of therapy and the frequency (table 6). The usual route of administration for prescribed antibiotics was oral, I/V and I/M and the dose ranges minimum of 40 mg to maximum 750 mg and 1g to 2g twice (BID) or three times a day (TID). WHO DDD for upper respiratory tract infections ranges from 0.2g- 0.5g, for lower respiratory tract infections ranges from 0.4g -1 g, for treatment of typhoid DDD ranges from 0.4g – 4g. DDD ranges from 0.1 g- 3 g in case of COPD whereas 0.4g- 1g and 0.5g- 4g for tuberculosis and pneumonia correspondingly (table 4). Approximately 31.6% of prescriptions contain 7 to 9 antibiotics at a time and about 11.6% prescriptions consist of poly antibiotics of more than 12 (table 5). Almost 93.2% and 91.2% prescription verified with appropriate duration and accurate dose. Similarly the frequency observed was 87.6% almost. All these are clearly given in table 6. Evaluation of DDD and routine prescribing dose (RPD) are mentioned and compared in table 7. The estimated drug utilization of antibiotics and DDD/100 bed days are given in table 8.

DISCUSSION

Routine measurement and display of consumption information to prescribers and policy-makers are a first step in increasing the awareness and importance of careful antibiotic use. Several DU researches and systemic reviews evidently reveal the high and regular consumption of antibiotics for treatment of numerous infections (*Truter, 2008*). In present study high frequency of antibiotics utilization was found in respiratory tract infections of both lower (LRTI) 16.8% (n=42) and upper (UTI) 13.2% (n=33) in male compared to low drug utilization in female to treat infections Whereas COPD was widespread among female 10.4% (n=26) than male 7.6% (n=19). Similarly the incidence of typhoid 2.4% (n=6) in male and 4.8% (n=12) in female was very less. Pneumonia was associated with female (7.2%) in contrast to male (2.4%). The similar observation about typhoid fever has been made by a study in Islamabad i.e. 37% male and 63% females. Moreover, comparable data reported through a study done in Khyber Pakhtunkhaw (Ayub *et al*., 2015; *Kalsoom et al.,* 2014*).*

Table 4: Classification of antibiotics utilization in their respective disease and also their values of WHO DDD and ATC Codes

MEDICINE	DOSE	ROA	DDD (WHO)	ATC CODES
Urinary Tract Infections (UTI)				
Ciprofloxacin	500mg BID	Oral	0.5gm	J01MA02
Nitrofurantine	50-100mg QID	Oral	0.2gm	J01XE01
Lower Respiratory Tract Infection (LRTI)				
Moxifloxacin	400mg OD	I/V, Oral	0.4gm	J01MA14
Levofloxacin	500mg OD	I/V, Oral	0.5gm	J01MA12
Amoxycillin	250-500mg TID	Oral	1gm	J01CR02
Clindamycin	600mg TID	I/V		
Typhoid				
Ceftriaxone	1-2gm BID	I/V	2gm	J01DD04
Cefexime	400mg OD	Oral	0.4gm	J01DD08
Cefotaxime	1gm BID	I/V	4 gm	J01DD01
Chloramphenicol	50-100mg QID	I/V, Oral	3gm	J01BA01
Chronic Obstructive Pulmonary Disease COPD				
Azithromycin	500mg OD	Oral, I/V	0.3-0.5gm	J01FA10
Clarithromycin	250-500mg BID	Oral, I/V	0.5-1gm	J01FA09
Cefuroxime	750mg TID	Oral, I/V	0.5-3gm	J01DC02
Doxycycline	100mg TID	Oral, I/V	0.1gm	A01AB22
Tuberculosis				
Levofloxacin	250-500mg BD	Oral, I/V	0.5gm	J01MA12
Amikacin	500-750mg OD	I/V	1gm	J01GB06
Moxifloxacin	400mg OD	Oral, I/V	0.4gm	J01MA14
Pneumonia				
Merpenem	1g BID or TID	I/V	2gm	J01DH02
Ertapenem	1gm OD	I/V	1gm	J01DH03
Ceftazidime	1g BID or TID	I/V	4gm	J01DD02
Linezolid	600mg BID	I/V, Oral	1.2gm	J01XX08
Gentamycin	40-80mg BID or TID	I/V, I/M	0.24gm	J01GB03
Clarithromycin	250-500mg BID	I/V, Oral	0.5-1gm	J01FA09

Table 5: Prescription Pattern of Medicines

S. N.	Quantity of drugs per prescription	Frequency of patients
1	1-3	25(10%)
2	4-6	67(26.8%)
3	7-9	79(31.6%)
4	10-12	50(20%)
5	Above 12	29(11.6%)

Table 6: Therapy Course Compliance of Antibiotics

Parameters	Variable	Prevalence
Dose	Accurate	228 (91.2%)
	Sub-therapeutic	9 (3.6%)
	Over medicated	13 (5.2%)
	Total	250 (100%)
Duration	Appropriate	233 (93.2%)
	Inappropriate (long and short)	17 (6.8%)
	Total	250 (100%)
Frequency	Correct	219 (87.6%)
	Inapt	31 (12.4%)
	Total	250 (100%)

Table 7: Evaluation of Defined Daily Doses (DDD) and Routine Prescription Doses (RPD)

Drugs	RPD	DDD	UNITS
Ciprofloxacin IV	0.4	0.5	gm
Moxifloxacin	0.4	0.4	gm
Nitrofurantine	0.2	0.2	gm
Levofloxacin	0.5	0.5	gm
Ceftriaxone	2	2	gm
Cefexime	0.4	0.4	gm
Cefotaxime	2	4	gm
Ceftriaxone	2	2	gm
Amikacin	0.5	1	gm
Merpenem	2	2	gm
Ertapenem	1	1	gm
Ceftazidime	2-3	4	gm
Linezolid	1.2	1.2	gm

Table 8: Drug utilization of antibiotic in DDD/100 bed days

Drugs	Dose (gm)	Drug utilization (DDD)	DDD/100 bed days
Ciprofloxacin	0.2gm	18	0.00011
	0.5 gm	47	0.00076
Meropenem	0.5-2gm	29.25	0.00022
Ceftriaxone	1gm	13.5	0.00022
Cefexime	0.4 gm	46	0.00044
Doxycyclin	0.1gm	24	0.11111
Amikacin	0.025-0.050gm	1.85	0.00111
Azithromycin	0.5gm	14	0.000055
Levofloxacin	0.5gm	19	0.000056

A variety of analyses documented the use of cephalosporin and ceftriaxone commonly encountered in hospital setup with highest rate of prescription as noticed in a trial (Forough *et al*., 2015)**.** In our study, the estimated total number of drug units administered per month was greater with cefixime (46) and ciprofloxacin (45) both. Consequently, the dimension of meropenem and ciprofloxacin were the main interventions that utilized with significant amount (grams) in one month i.e. 58.5 g and 32.5 g respectively while ceftrioxone was third most widely used medicine (table 3). Moreover, per month consumption in grams was smaller with doxycyclin (2.40) and amikacin (1.85). Likewise, various trials have been performed to evaluate the prescribing patterns of antibiotics for RTIs and approximately 50-90% of adults receive antibiotics (Gonzales *et al*., 1997; Meropol *et al*., 2009; Almeman *et al*., 2014)**.** A DU analysis reported high frequency of ceftriaxone in association of azithromycin for 5 to 6 days for lower respiratory tract infection (LRTI) and pneumonia (Naik *et al*., 2013). Similarly, cephalosporins considered as the choice of antibiotic for pneumococcal pneumonia by 33% pediatric residents (Smart *et al*., 2006)**.**

Majority of hospital pharmacies recorded the data of dispensed drugs through ATC/DDD system. The objective of ATC/DDD system is to serve as tool for DU research, to favor improvement in drug use. Similarly general units for antibiotic consumption include DDD per 1000 inhabitant-days for out-patient data and DDD per 100 bed-days in hospitals (Hutchinson *et al*., 2004; WHO guidelines, 2014)**.** Furthermore, 76% and 91.33% of cephalosporin prescribed for correct diagnosis prior to and later than implementation of guidelines by the clinicians (Shekar *et al*., 2013)**.** However, current findings also suggested ceftrioxne 1-2 g BID I/V to treat typhoid (table 4). A study declared that ceftriaxone (64.54%) was the most widely used antibiotics in the treatment of hospitalized adult typhoid patients in a hospital in Indonesia (*Anggraini et al., 2014*)**.**Again ceftazidime is a third generation cephalosporin had more consumption against pneumonia. The prescribed dose is1g BID or TID I/V and WHO DDD is 4 g as described in table 4. A data obtained from a systemic utilization of antibiotics estimated 34% amoxicillin and 6% erythromycin utilization (Pottegard *et al*., 2015).

Special methods of forecasting compliance were developed and utilized in several studies. Frequency of doses and duration of treatment were observed as the key factor influencing compliance (Sclar *et al*., 1994)**.** Superior compliance rates were reported for regimens shorter than 7 days period compared with longer period treatments (Reyes *et al*., 1997). Valuable evaluations of

the quality of drug prescribing in routine health care are difficult to perform. Both DDD and RPD found almost equivalent with most of antibiotics except ciprofloxacin IV, amikacin and ceftazidime (table 7).

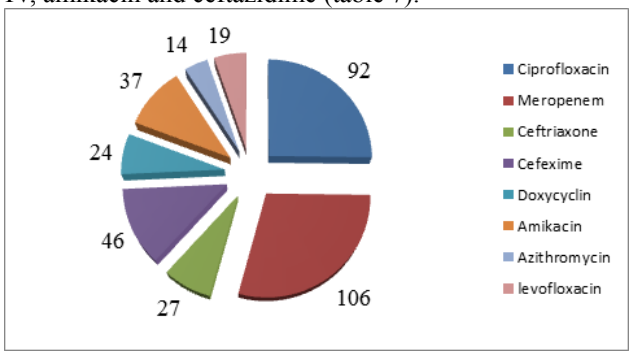

Fig. 1: Frequency of Medication Units Prescribed For Inpatient Units (One Month)

The minimum dose in grams and drug utilization has been noticed for amikacin. However, highest dose recorded 1 g for ceftrioxone and drug utilization with ciprofloxacin 0.5 g and cefexime 0.4 g respectively. DDD/100 bed days drug utilization of antibiotics was higher with ciprofloxacin, cefexime and meropenem (47, 46 and 29.25) correspondingly (table 8). In 2006, the general use of ceftriaxone in the hospital was 24.627 DDD/100 bed for all cases of disease (Ratnaningsih, 2006*).* The findings of a recent study found 13.5 DDD/100 bed for ceftriaxone. Beside this, prescribing rate of broad-spectrum antibacterial drugs particularly turned down from 3.8 to 2.9 prescriptions/1000 adults both in US and UK (Roumie *et al*., 2005)**.**Rationale prescribing pattern is necessary in local settings followed by updated hospital formulary to reduce the inadequate use of antibiotics in non-infectious patients. DU studies using ATC/DDD system need to be promoted and carried out as ongoing process. Such assessments are important for rational use of drugs.

CONCLUSION

In developing countries where antibiotic-management systems hardly exist, contrasting situations become more complex which provides the undeniable evidence of the need for more-rational use of antibiotics. Optimal therapy designs can be suggested through DUE studies by predicting the clinical success rates. Furthermore, in critically ill patients safer doses with least toxic potential can also reduce the undesirable consequences of therapy, which intern enhance the conscientiousness and accountability in the medicine use.

REFERENCES

Abier H (2009). Determination of sample size for drug use evaluation, 2007. Available at http://www.Pharmacorner.com/default.asp/ action=particle and ID+136.

Almeman AA, Izham M, Ibrahim M and Rasool S (2014). Cost analysis of medications used in upper respiratory tract infections and prescribing patterns in University, Sans Malaysia, Penang, Malaysia. *Trop. J. Pharm Res.,* **13**(4): 621-626.

Anggraini AB, Opitasari C and Aini Q (2014). The use of antibiotics in hospitalized adult typhoid patients in an Indonesian hospital. *Health Sci. J. Indonesia.,* **5**(1): 40-43.

Ayub U, Khattak AA, Saleem A, Javed F, Siddiqui N, Hussain N and Hayat A (2015). Incidence of typhoid fever in Islamabad, Pakistan. *American Eur. J. Toxicological Sci.,* **7**(4): 220-223.

Biru TT, Defersha AD, Gelaw BK and Tegegne GT (2014). Drug utilization review of ciprofloxacin in the outpatient department of Boru Meda Hospital, South Wollo Zone, Amhara Region, Ethiopia. *Int. J. Basic Clin. Pharmacol.,* **3**: 171-178.

Collins AS (2008) Preventing Health Care-Associated Infections. *In*: Hughes RG, editor. Patient Safety and Quality: An Evidence-Based Handbook for Nurses. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008 Apr. Chapter 41.

Forough AS, Hosseini SR and JabbariS (2015). Antibiotic utilization evaluation of inpatient and outpatient prescriptions in a rural general hospital in Iran. *Int. J. Basic Clin. Pharmacol.,* **4**(3): 531-536.

Gonzales R, Steiner JF and Sande MA (1997). Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA.,* **278**(11): 901-904.

Harbarth S, Albrich W and Buisson CB (2002). Outpatient antibiotic use and prevalence of antibiotic-resistant Pneumococci in France and Germany: A Sociocultural Perspective. *Emerg Infect Dis.,* **8**(12): 1460-1467.

Henry FC (2006). General considerations of antimicrobial therapy. Laurence B Burtol, Jones L, Keithl Parker, editors. *In*: Goodman and Gilman's pharmacologic basis of therapeutics. 11th Edn. McGraw-Hill, New York, pp.1095-1119.

Hutchinson JM, Patrick DM, Marra F, Bowie WR, Heule L and Muscat M *et al*. (2004). Measurement of antibiotic consumption: A practical guide to the use of the Anatomical Thgerapeutic Chemical classification and Definied Daily Dose system methodology in Canada. *Can. J. Infect Dis.,* **15**(1): 29-35.

Kalsoom F, Akbar M, Younus U, Tasneem M, Suleman SS and Ali S (2014). Prevalence of typhoid fever in five southern districts of Khyber Pakhtunkhaw, Pakistan. A preliminary study. *Inter J. Biosciences.,* **4**(1): 325-30

Khan S, Shehzad A, Shehzad O and Al-Suhaimi EA (2013). Inpatient antibiotics pharmacology and physiological use in Hayatabad medical complex. Pakistan. *Int. J. Physiol. Pathophysiol. Pharmacol.,* **5**(2): 120-127.

Khavane K, Addepalli V, Bhusare K, Payghan SA, Patweakar S and Kate V (2010). Prescribing patterns of antibiotics and sensitivity patterns of micro-organisms towards different antibiotics in multidisciplinary health care hospital. *Inter. J. Pharm. Biol. Archives.,* **1**(2): 115-122.

Kotwani A and Holloway K (2014). Antibiotic prescribing practice for acute, uncomplicated respiratory tract infections in primary care settings in New Delhi, *India. Trop Med. Int. Health,* **19**(7): 761-768.

Meropol SB, Chen Z and Metlay JP (2009). Reduced antibiotic prescribing for acute respiratory infections in adults and children. *Br. J. Gen. Pract.,* **59**: 56-57.

Mohanraj R, Suvarchala S, Ramkesava R and Yiragamreddy PR (2015). Drug Use Evaluation of Antimicrobials in Healthcare Resource Limited Settings of India. *Indian J. Pharmacy Practice,* **8**(4): 191-195.

Mohd FK and Kamaliah MN (2013). The effect of profiling report on antibiotic prescription for upper respiratory tract infection. *Malays Fam Physician*, **8**(2): 26-31.

Naik HG, Khanwelkar CC, Kolur A, Desai R and Gidamudi S (2013). Drug Utilization Study on Antibiotics Use in Lower Respiratory Tract Infection. *Natl. J. Med. Res.,* **3**(4): 324-327.

Patel MK, Barvaliya MJ, Patel TK and Tripathi CB (2013). Drug utilization pattern in critical care unit in a tertiary care teaching hospital in India. *International J Critical Illness Injury Sci.,* **3**(4): 250-255.

Pottegård A, Broe A, Aabenhus R, Bjerrum L, Hallas J and Damkier P (2015). Use of antibiotics in children: A Danish nationwide drug utilization study. *Pediatr. Infect Dis. J.,* **34**(2): 16-22.

Ratnaningsih U (2006). Analysis of antibiotic use in hospitalized patients based on hospital formulary 2005 and 2006 with ATC/DDD method in Indonesian Red Cross hospital, Bogor. Depok: Universitas Indonesia; Indonesian.

Reyes H, Guiscafre H, Munoz O, Perez-Cuevas R, Martinez H and Gutierrez G (1997). Antibiotic noncompliance and waste in upper respiratory infections and acute diarrhea. *J. Clinical Epidemiology,* **5**: 1297-304.

Roumie CL, Halasa NB, Grijalva CG, Edwards KM, Zhu Y and Dittus RS and Griffin MR (2005). Trends in Antibiotic Prescribing for Adults in the United States-1995 to 2002. *J. Gen Intern Med.,* **20**(8): 697-702.

Sclar DA, Tartaglione TA and Fine MJ (1994). Overview of issues related to medical compliance with implications for outpatient management of infectious diseases. *Infect Agents Dis.,* **3**: 266-273.

Shapiro DJ, Hicks LA, Pavia AT and Hersh AL (2007). Antibiotic prescribing for adults in ambulatory care in the USA. *J. Antimic. Chemo Adv.,* **69**(1): 234-240.

Shekar HS, Chandrashekhar HR, Govindaraju M and Venugopalreddy P (2013). Drug utilization and evaluation of cephalosporin at tertiary care teaching hospital, Bangalor. *Intern J. Res. Pharma. Biochem. Sci.,* **4**(4): 1338-1343.

Smart K, Lemay JF and Kellner JD (2006). Antibiotic choices by paediatric residents and recently graduated paediatricians for typical infectious disease problems in children. *Paediatr Child Health,* **11**(10): 647-653.

Teng CL, Nik-Sherina HCJ, Chia YC and Atiya AS (2006). Antibiotic prescribing for childhood febrile illness by primary care doctors in Malaysia. *J. Paediatr. Child Health,* **42**(10): 612-617.

Teng CL, Tong SF, Khoo EM, Lee V, Zailinawati AH, Mimi O, Chen WS and Nordin S (2011). Antibiotics for URTI and UTI prescribing in Malaysian primary care settings. *Aust. Fam. Physician.,* **40**(5): 325-329.

Truter I (2008). A review of drug utilization studies and methodologies. *Jordan J. Pharm. Sci.,* **1**(2): 91-104.

World Health Organization (2003). Introduction to drug utilization research. Oslo, Norway.

World Health Organization (2013). Collaborating centre for drug statistics methodology, Guidelines for ATC/DDD classification and DDD assignment 2014, Oslo, Norway.