doi.org/10.36721/PJPS.2020.33.4.SUP.1879-1888.1

Antibiotic prescribing trends in patients with upper respiratory tract infections reporting to tertiary care hospitals of Lahore

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Abstract: To estimate the antibiotic utilization and treatment compliance in URTIs reported to tertiary care hospitals of Lahore. A cross-sectional study was conducted by including 423 prescription files from public and private hospitals of Lahore. Descriptive statistics were used to estimate percentage frequencies. The reporting frequency of URTIs, tonsillitis, pharyngitis and otitis media, was higher in public hospitals (JH; 27.4%, LGH; 25.8%) compared to private (NHMC;16.3%, DHMC;15.1%) hospitals in patients aged 21–40 years. Patients aged 18–40 years (59%) received most antibiotics. Broad spectrum antibiotics (95%) were prescribed in both public (JH; 27.4%, LGH;25.9%) and private hospitals (NHMC;16.3%, DHMC;14.8%) - co-amoxiclave (30%) in penicillin class, ceftriaxone (15.4%) and cefixime (11.6%) in cephalosporin class, levofloxacin (11.3%) in quinolone class and clarithromycin (10.4%) in macrolide class, in tonsillitis, pharyngitis and otitis media. The diagnosis that received most antibiotics included tonsillitis (30%), pharyngitis (29.1%) and otitis media (11.1%). Superior treatment compliance was observed in public hospitals compared to private hospitals. The highest treatment non-compliance was observed in laryngitis (36.4%), otitis media (34%) and pharyngitis (26%). 1st line and over all treatment compliance was superior in public hospitals - sore throat, tonsillitis, sinusitis, otitis media and pharyngitis received the most appropriate choices.

Keywords: URTIs, antibiotic consumption, cephalosporin, quinolones, macrolides, co-amoxiclave, Lahore, tertiary hospitals.

INTRODUCTION

In a clinical setting, respiratory tract infections (RTIs) are the most common reasons of health care consultations worldwide (Godman *et al.,* 2020). It's an undeniable fact that antibiotics have been widely used by humans over the past 55 years, either as prophylaxis or as therapeutics conferring tremendous benefits to humans against various infections (Chem *et al.,* 2018). However, irrational use of antibiotics can pose a major challenge to public health in terms of increase in antimicrobial resistance, patient's morbidity and mortality, soaring costs and use related adverse drug reactions (Atif *et al.,* 2016). Studies have also demonstrated direct relationship between the use of antibiotics and antimicrobial resistance (Wushouer *et al.,* 2018). Recently, it has been reported that the global antibiotic consumption, in term of defined daily doses (DDDs), increased from 21.1 to 34.8 billion DDDs, demonstrating an increase of 65% from 2000 to 2015 (Klein *et al.,* 2018). This surge in global antibiotic consumption was chiefly driven by increased consumption of antibiotics in low middle-income countries (LMICs), including Pakistan. In this context, between 2000 and 2015, the highest increase in antibiotic consumption was evident among LMICs, i-e., 79% in China, 103% in India and 65% in Pakistan (Klein *et al.,* 2018). Besides this increase antibiotic consumption in Pakistan, bacteria isolated from various infections obtained from different hospitals of Pakistan are gradually becoming resistant to conventional antibiotics (Kaleem *et al.,* 2010).

Among others, prescribing pattern and attitudes have been shown to have a greater impact on the treatment outcomes (Chem *et al.,* 2018). Presumably, prescribing an antibiotic is a very intricate decision influenced by a host of inter-connected and inter-dependent factors, but not limited to, including physician's training and education, default beliefs and attitudes, patient age, co-morbidities, sign and symptoms, socio-economic and cultural impediments, non-availability of culture sensitivity testing and un-due patient's expectations (Godman *et al.,* 2017). Besides, a combined report from Saudi Arabia and Malaysia suggested that the junior doctors tend to prescribe antibiotics more frequently compared to specialists (Rezal *et al.,* 2015). In this context, antibiotics are frequently prescribed in URTIs without knowing the need of antibiotics and causative agent (Saleem *et al.,* 2019). In Iran, almost 35% of the total antibiotics consumed are being prescribed in URTIs a much higher value compared to UK (15%)(Hashemi *et al.,* 2013). A study from North West Cameron suggested that antibiotics were even prescribed to malaria patients at primary care facilities (Chem *et al.,* 2018). Additionally, studies from Pakistan clearly suggested that hospitals in Pakistan do have list of essential medicines but do not have standard treatment guidelines in place for infectious diseases (Atif *et al.,* 2017). We have also reported previously that out of total

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antibiotic prescriptions, 27.2% of these were generated for patients with respiratory tract infections, and out these 27.2% antibiotic prescriptions, 62.8% had inappropriate antibiotic choices (Saleem *et al.,* 2019).

In Pakistan, unpublished or published data suggest that in tertiary care hospitals junior doctor tend to follow the prescriptions of senior or specialist doctors, yet for them standard treatment guidelines are non-existent to guide clinical decisions (Atif *et al.,* 2017, Butt *et al.,* 2019, Saleem *et al.,* 2019). In order to develop national antibiotic policy or infection control policy, data on antibiotic prescribing patterns in various infections reporting to different tertiary care public and private hospitals are need-fully required. Thus, we aimed at conducting the study to estimate the recent antibiotic prescribing or consumption trends in upper respiratory infections reporting to various public and private tertiary care hospitals of Lahore, Pakistan.

MATERIALS AND METHODS

Study Design

A descriptive cross-sectional study was conducted by including 1200 prescription files enlisted in hospital's health information system (HIS), generated for URTIs to out-patient department (OPD), medicine and ENT, out which only 423 were considered for final analysis as per the study inclusion criteria. The data were collected for a period of 6-month; June 2018 to Dec 2018. Out of total 423, 268 (63.4%) prescriptions were from public hospitals, i-e., 43 from Mayo hospital, 116 from Jinnah hospital & 109 from Lahore general hospital, while 155 (36.6%) patient's prescriptions were from the private hospitals, i-e., 69 from National hospital & medical center, 64 from Doctors hospital & medical center and 22 from Hameed latif hospital. Data obtained was sectioned into three sections, i-e., demographics (age, gender), clinical diagnosis and antibiotic utilization. Prescribed antibiotics were classified by generic names and according to WHO Anatomical Therapeutic Chemical Classification (ATCC)

Study Settings

The data was collected from tertiary care hospitals, public and private, of Lahore, Pakistan. Details of the public and private hospitals included in the study are as follows; -

Public health facilities

Mayo Hospital (MH): established in 1871 with 2399 beds capacity located in Lahore encompassing 54.6 acers of land. MH provides, clinical (in-patient & out-patient), diagnostic and emergency services (Hospital, 1871).

Jinnha Hospital (JH): established in 1996, 1250 bedded teaching hospital located in Lahore and spread over 105 acers. JH is involved in all the services, i-e., clinical (out-patient & in-patient), diagnostic and emergency (AIMC, 2012).

Lahore General Hospital (LGH); established in 1959, 1200 bedded teaching hospital located in Lahore over an area of one sqaure and seven acers. LGH provides clinical (in-patient & out-patient), diagnostic, emergency and disaster management services (Hospital, 1959).

Private health facilities

National hospital & medcial center (NHMC); started operating in early 1990s with capacity of 250 beds and providing clinical (in-patient & out-patient), diagnostic and emergency services (Center, 1996).

Doctors hospital & medcial center (DHMC); founded in 2000, 250 bedded hospital located in Lahore that provides clinical (in-patient & out-patient), diagnostic and emergency services (Center, 2000).

Hameed latif hospital (HLH); established in 1992, 325 bedded hospital located in Lahore that provides clinical (in-patient & out-patient) and diagnostic services (Hospital, 1992).

Study Population

A total of 1200 patient's prescription files, out-patient, with confirmed upper respiratory tract infections (URTIs) were enrolled from specialized tertiary care, public and private, hospitals of Lahore, Pakistan. Out of total, only 530 met the study inclusion criteria, while in 243 prescrption files antibiotics were not prescribed. Out of 530, in 47 prescriptions antibiotics were also prescribed for concomitant infections other than URTIs and 60 prescriptions had no mention of antibiotics, thus, 423 patient's prescriptions, 244 males (57.6%) and 179 (42.3%) females, were included in the study for data collection and further analysis. The patient's prescription were included based on the following criteria

Inclusion criteria

All prescriptions for patients age 1 to 80 years, having confirmed diagnosis of URTIs, not more than two concomitant infection or diseases, irrespective of gender, disease duration, and consented to participate were included in the study.

Exclusion criteria

Patient's prescription files with unconfirmed diagnosis, more than two concomitant diseases, illegible written prescriptions and patient's not willing to participate were excluded from study.

Ethical Approval

The study was approved by the Ethical Committee on Human Research, University of Balochistan, Pakistan, ref #.2002/UB-2016/R-376 and Institutional Review Board (IRB), ref# 5330 of the hospital.

Table 1: Gender and age specific distribution of upper respiratory tract infections (URTIs)

Gender	Gender specific distribution of URTIs, *n* (%)								Total
	Tonsillitis	Pharyngitis	Sinusitis	Otitis Media	Laryngitis	Common Cold & Flu	Rhinitis	Sore Throat	
Males	77 (18.2)	71 (16.8)	18 (4.3)	21 (5)	6 (1.4)	9 (2.1)	22 (5.2)	20 (4.7)	244 (57.6)
Females	50 (11.8)	52 (12.3)	15 (3.1)	26 (6.1)	5 (1.2)	6 (1.4)	12 (2.8)	12 (2.8)	179 (42.3)
Total	27 (30)	123 (29.1)	33 (7.8)	47 (11.1)	11 (2.6)	15 (3.5)	34 (8)	33 (7.8)	423 (100)
Age (*yrs*)	Age specific distribution of URTIs, *n* (%)								
1-5	19 (4.5)	7 (1.7)	0 (0)	2 (0.5)	0 (0)	3 (0.7)	0 (0)	4 (0.9)	35 (8.3)
6-10	13 (3.1)	8 (1.9)	1 (0.2)	2 (0.5)	0 (0)	0 (0)	2 (0.5)	1 (0.2)	27 (6.4)
11-15	17 (4)	11 (2.6)	1 (0.2)	1 (0.2)	0 (0)	1 (0.2)	3 (0.7)	2 (0.5)	36 (8.5)
16-20	15 (3.1)	11 (2.6)	6 (1.4)	4 (0.9)	0 (0)	1 (0.2)	2 (0.5)	7 (1.7)	46 (10.9)
21-30	31 (7.3)	43 (10.2)	10 (2.4)	18 (4.3)	5 (1.2)	6 (1.4)	11 (2.6)	10 (2.4)	134 (31.7)
31-40	18 (4.3)	24 (5.7)	8 (1.9)	4 (0.9)	3 (0.7)	2 (0.5)	6 (1.4)	4 (0.9)	69 (16.3)
41-50	6 (1.4)	13 (3.1)	5 (1.2)	10 (2.4)	1 (0.2)	0 (0)	5 (1.2)	2 (0.5)	42 (9.9)
51-60	6 (1.4)	6 (1.4)	2 (0.5)	4 (0.9)	1 (0.2)	2 (0.5)	2 (0.5)	2 (0.5)	25 (5.9)
61-70	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)	0 (0)	3 (0.7)
≥ 80	1 (0.2)	0 (0)	0 (0)	2 (0.5)	1 (0.2)	0 (0)	1 (0.2)	1 (0.2)	6 (1.4)
Total	127 (33.6)	123(29.1)	33 (7.8)	47 (11.1)	11 (2.6)	15 (3.1)	34 (8)	33 (7.8)	423 (100)

Table 2: Frequency distribution of URTIs in public and private hospitals of Lahore

Hospitals		Diagnosis specific distribution of URTIs in hospitals, *n* (%)								Total
		Tonsillitis	Pharyngitis	Sinusitis	Otitis Media	Laryngitis	Common Cold & Flu	Rhinitis	Sore Throat	
Public Hospitals	Mayo hospital *(MH)*	13 (3.1)	7 (1.7)	7 (1.7)	3 (0.7)	3 (0.7)	2 (0.5)	3 (0.7)	5 (1.2)	43 (10.2)
	Jinnah hospital *(JH)*	30 (7.1)	37 (8.7)	8 (1.9)	20 (4.7)	1 (0.2)	1 (0.2)	11 (2.6)	8 (1.9)	116 (27.4)
	Lahore general hospital *(LGH)*	41 (9.7)	35 (8.3)	12 (2.8)	6 (1.4)	1 (0.2)	1 (0.2)	6 (1.4)	7 (1.7)	109 (25.8)
Private Hospitals	National hospital & medical center *(NHMC)*	10 (2.4)	12 (2.8)	3 (0.7)	15 (3.1)	2 (0.5)	11 (2.6)	9 (2.1)	7 (1.7)	69 (16.3)
	Doctor hospital & medical center *(DHMC)*	22 (5.2)	26 (6.1)	1 (0.2)	2 (0.5)	4 (0.9)	0 (0)	3 (0.7)	6 (1.4)	64 (15.1)
	Hameed latif hospital *(HLH)*	11 (2.6)	6 (1.4)	2 (0.5)	1 (0.2)	0 (0)	0 (0)	2 (0.5)	0 (0)	22 (5.2)
Total		127 (30)	123 (29.1)	33 (7.8)	47 (11.1)	11 (2.6)	15 (3.1)	34 (8)	33 (7.8)	423 (100)

Data collection

Data was collected using a questionnaire/form designed after careful literature review taking into account the study objectives (Iftikhar *et al*., 2019, Yimenu *et al*., 2019, Atif *et al*., 2016). Later, the questionnaire was sent to subject experts/academicians for content validation and the expert opinion was incorporated to make the questionnaire more simple and objective driven. Data was recorded from the prescription papers in medical record files. A framed checklist from WHO and relevant literature reports were utilized to customize the documetation procedure acocording to study needs (Organization, 1988, Atif *et al*., 2016). The checklist mechanism was adopted to assess the validity of the prescription papers, paitent's information and drug related information. Information included patient's age and gender, types of diagnosis, antibiotics prescribed and type of health facility.

Antibiotic therapy comlpiance

Antibiotic therapy compliance in URTIs was estaimted considering Center for Disease Control (CDC) (Rosenfeld *et al*., 2015) and National Instititute for Health and Care Excellence (NICE) adult treatment guidelines for URTIs (NICE, 2020), since these hospitals did not have their own therapy guidlines. Treatmement compliance was assessed for 1st line, 2nd line and 3rd line treatment options with regards to the antibiotc choice and dose. Any prescription that failed to me*et al*l three treatment options, i-e., 1st, 2nd and 3rd with regards to antibiotic choice and dose was documented as non-compliant. Generally, antibiotics in penicillin class was considered 1st line while cephalosporin/macrolides (clarythromycin or Azithromycin) were considered 2nd & 3rd line, respectively, for treating all kind of bacterial URTIs, except for sinusitis and rhinitis in which Levofloxacin & Moxifloxacin was considered 2nd line agents and cephalosporins/macrolides (azithromycin) were considered 3rd line choices – dealt on case to case basis as per clinical diagnosis.

Table 3: Gender and age specific utilization of antibiotics in URTIs

Gender	Gender specific utilization of antibiotics, *n*=423 (%)													
	Penicillin (*ATC code*)			Cephalosporins (*ATC code*)					Quinolones (*ATC code*)			Macrolides (*ATC code*)		
	AMX (J01CA04)	AMC (J01CR02)	AMP (J01CA01)	RAD (J01DB09)	CEC (J01DC04)	CXM (J01DD08)	CRO (J01DD04)	CFM (J01DD01)	CIP (J01MA02)	LVX (J01MA12)	MXF (J01MA14)	ERY (J01FA01)	CLR (J01FA09)	AZM (J01FA10)
Males	3 (0.7)	79 (18.6)	4 (0.9)	1 (0.2)	1 (0.2)	1 (0.2)	36 (8.5)	29 (6.9)	14 (3.3)	26 (6.1)	9 (2.1)	1 (0.2)	26 (6.1)	13 (3.1)
Females	7 (1.7)	48 (11.3)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0)	29 (6.9)	20 (4.7)	15 (3.1)	21 (5)	5 (1.2)	1 (0.2)	18 (4.3)	11 (2.6)
Age *(Yrs)*	Age specific utilization of antibiotics, *n* (%)													
1-5	2 (0.5)	13 (3.1)	0 (0)	1 (0.2)	1 (0.2)	1 (0.2)	10 (2.4)	5 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)	0 (0)
6-10	0 (0)	14 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1.2)	5 (1.2)	1 (0.2)	1 (0.2)	0 (0)	0 (0)	0 (0)	1 (0.2)
11-15	1 (0.2)	13 (3.1)	2 (0.5)	0 (0)	0 (0)	0 (0)	8 (1.9)	1 (0.2)	1 (0.2)	4 (0.9)	0 (0)	0 (0)	5 (1.2)	1 (0.2)
16-20	1 (0.2)	12 (2.8)	0 (0)	0 (0)	0 (0)	0 (0)	6 (1.4)	6 (1.4)	1 (0.2)	5 (1.2)	1 (0.2)	1 (0.2)	6 (1.4)	8 (1.9)
21-30	3 (0.7)	33 (7.8)	2 (0.5)	0 (0)	0 (0)	0 (0)	10 (2.4)	20 (4.7)	12 (2.8)	21 (5)	5 (1.2)	1 (0.2)	17 (4)	10 (2.4)
31-40	1 (0.2)	23 (5.4)	0 (0)	1 (0.2)	0 (0)	0 (0)	11 (2.6)	4 (0.9)	4 (0.9)	9 (2.1)	4 (0.9)	0 (0)	9 (2.1)	1 (0.2)
41-50	1 (0.2)	11 (2.6)	1 (0.2)	0 (0)	1 (0.2)	0 (0)	4 (0.9)	4 (0.9)	6 (1.4)	4 (0.9)	3 (0.7)	0 (0)	4 (0.9)	3 (0.7)
51-60	0 (0)	6 (1.4)	0 (0)	0 (0)	0(0)	0 (0)	9 (2.1)	4 (0.9)	2 (0.5)	3 (0.7)	1 (0.2)	0 (0)	0 (0)	0 (0)
61-70	1 (0.2)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
≥ 80	0 (0)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)	0 (0)	1 (0.2)	1 (0.2)	0 (0)	0 (0)	1 (0.2)	0 (0)
Total	10 (2.4)	127 (30)	5 (1.2)	2 (0.5)	2 (0.5)	1 (0.2)	65 (15.4)	49 (11.6)	29 (6.9)	48 (11.3)	14 (3.3)	2 (0.5)	44 (10.4)	24 (5.7)

Table 4: Diagnosis specific utilization of antibiotics in URTIs

Antibiotics (*ATC code*)	Diagnosis specific utilization of antibiotics, *n*=423 (%)								
	Tonsillitis	Pharyngitis	Sinusitis	Otitis Media	Laryngitis	Common Cold & Flu	Rhinitis	Sore Throat	Total
Penicillin *AMX* (*J01CA04*)	3 (0.7)	3 (0.7)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.7)	10 (2.4)
AMC (*J01CR02*)	47 (11.1)	31 (7.3)	10 (2.4)	15 (3.1)	2 (0.5)	2 (0.5)	9 (2.1)	11 (2.6)	127 (30)
AMP (*J01CA01*)	1 (0.2)	3 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.2)	0 (0)	5 (1.2)
Cephalosporin *RAD* (*J01DB09*)	1 (0.2)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)
CEC (*J01DC04*)	2 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)
CXM (*J01DD08*)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.2)	1 (0.2)
CRO (*J01DD04*)	28 (6.6)	9 (2.1)	4 (0.9)	7 (1.7)	2 (0.5)	3 (0.7)	2 (0.5)	10 (2.4)	65 (15.4)
CFM (*J01DD01*)	10 (2.4)	12 (2.8)	4 (0.9)	6 (1.4)	1 (0.2)	5 (1.2)	7 (1.7)	4 (0.9)	49 (11.6)
Quinolones *CIP* (*J01MA02*)	5 (1.2)	6 (1.4)	2 (0.5)	10 (2.4)	1 (0.2)	1 (0.2)	3 (0.7)	1 (0.2)	29 (6.9)
LVX (*J01MA12*)	8 (1.9)	18 (4.3)	6 (1.4)	6 (1.4)	2 (0.5)	2 (0.5)	4 (0.9)	2 (0.5)	48 (11.3)
MXF (*J01MA14*)	4 (0.9)	8 (1.9)	1 (0.2)	0 (0)	1 (0.2)	0 (0)	0 (0)	0 (0)	14 (3.3)
Macrolides *ERY* (*J01FA01*)	2 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)
CLR (*J01FA09*)	11 (2.6)	24 (5.7)	2 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	4 (0.9)	0 (0)	43 (10.2)
AZM (*J01FA10*)	5 (1.2)	8 (1.9)	3 (0.7)	2 (0.5)	1 (0.2)	1 (0.2)	3 (0.7)	1 (0.2)	24 (5.7)
Total	127 (30)	123 (29.1)	33 (7.8)	47 (11.1)	11 (2.6)	15 (3.5)	34 (8)	33 (7.8)	423 (100)

Abbreviations: AMX; amoxicillin, AMC; co-amoxiclave AMP;ampicillin, RAD ;cephradine, CEC; cefaclor, CXM;cefixime, CRO; ceftriaxone, CFM; cefotaxime, CIP; ciprofloxacin, LVC; levofloxacin, MXF, moxifloxacin, ERY; erythromycin, CLR; clarithromycin, AZM; azithromycin

Table 5: Hospitals specific consumption of antibiotics in URTIs

Antibiotics (*ATC code*)	Hospital specific consumption of antibiotics, *n*=423 (%)						
	Public Hospitals			*Private Hospitals*			Total
	Mayo Hospital	Jinnah Hospital	Lahore General Hospital	National Hospital	Doctor Hospital	Hameed Latif Hospital	
Penicillin *AMX* (*J01CA04*)	2 (0.5)	2 (0.5)	0 (0)	2 (0.5)	3 (0.7)	1 (0.2)	10 (2.4)
AMC (*J01CR02*)	10 (2.4)	48 (11.3)	41 (9.7)	7 (1.7)	18 (4.3)	3 (0.7)	127 (30)
AMP(*J01CA01*)	0 (0)	4 (0.9)	1 (0.2)	0 (0)	0 (0)	0 (0)	5 (1.2)
Cephalosporin *RAD* (*J01DB09*)	1 (0.2)	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.5)
CEC (*J01DC04*)	0 (0)	1 (0.2)	0 (0)	1 (0.2)	0 (0)	0 (0)	2 (0.5)
CXM (*J01DD08*)	1 (0.2)	0 (0)	0 (0)	1 (0.2)	0 (0)	0 (0)	2 (0.5)
CRO (*J01DD04*)	18 (4.3)	4 (0.9)	14 (3.3)	13 (3.1)	14 (3.3)	2 (0.5)	65 (15.4)
CFM(*J01DD01*)	1 (0.2)	6 (1.4)	3 (0.7)	28 (6.6)	5 (1.2)	6 (1.4)	49 (11.6)
Quinolones *CIP* (*J01MA02*)	0 (0)	10 (2.4)	7 (1.7)	7 (1.7)	4 (0.9)	1 (0.2)	29 (6.9)
LVX (*J01MA12*)	1 (0.2)	13 (3.1)	17 (4)	6 (1.4)	9 (2.1)	2 (0.5)	48 (11.3)
MXF (*J01MA14*)	3 (0.7)	0 (0)	7 (1.7)	0 (0)	2 (0.5)	2 (0.5)	14 (3.3)
Macrolides *ERY* (*J01FA01*)	0 (0)	1 (0.2)	0 (0)	0 (0)	1 (0.2)	0 (0)	2 (0.5)
CLR(*J01FA09*)	2 (0.5)	14 (3.3)	18 (4.3)	3 (0.7)	6 (1.4)	1 (0.2)	44 (10.4)
AZM(*J01FA10*)	4 (0.9)	12 (2.8)	2 (0.5)	1 (0.2)	1 (0.2)	4 (0.9)	24 (5.7)
Total	43 (10.1)	116 (27.4)	110 (25.9)	69 (16.3)	63 (14.83)	22 (5.17)	423 (100)

Abbreviations:AMX; amoxicillin, AMC; co-amoxiclaveAMP;ampicillin, RAD;cephradine, CEC;cefaclor, CXM;cefixime, CRO; ceftriaxone, CFM;cefotaxime, CIP; ciprofloxacin, LVC; levofloxacin, MXF,moxifloxacin, ERY; erythromycin, CLR; clarithromycin, AZM; azithromycin

Table 6: Hospitals and the diagnosis specific treatment compliance to standard treatment guidelines (STGs)

Hospitals		Compliance with standard treatment guidelines *n*=423 (%) (*choice + dose*)			
		1st line compliance	*2nd line compliance*	*3rd line compliance*	*Non-compliance*
Public hospitals	Mayo hospital *(MH)*	12 (27.9)	20 (46.5)	8 (18.6)	3 (7)
	Jinnah hospital *(JH)*	54 (46.6)	11 (9.5)	30 (25.9)	21 (18.1)
	Lahore general hospital *(LGH)*	41 (37.8)	17 (15.6)	24 (22)	27 (24.8)
Private hospitals	National hospital and medical center *(NHMC)*	9 (13)	43 (62.3)	4 (5.8)	13 (18.8)
	Doctor hospital and medical center *(DHMC)*	21 (32.8)	19 (29.7)	10 (15.6)	14 (21.9)
	Hameed latif hospital *(HLH)*	4 (18.2)	9 (40.9)	4 (18.2)	5 (22.7)
Upper respiratory tract infections	Tonsillitis	50 (39.4)	41 (32.3)	19 (15)	17 (13.4)
	Pharyngitis	37 (30.1)	21 (17.1)	33 (26.8)	32 (26)
	Sinusitis	11 (33.3)	8 (24.2)	11 (33.3)	3 (9.1)
	Otitis Media	15 (31.9)	13 (27.7)	3 (6.4)	16 (34)
	Laryngitis	2 (18.2)	3 (27.3)	2 (18.2)	4 (36.4)
	Common Cold & Flu	2 (13.3)	8 (53.3)	2 (13.3)	3 (20)
	Rhinitis	10 (29.4)	10 (29.4)	9 (26.5)	5 (17.7)
	Sore Throat	14 (42.4)	15 (45.5)	1 (3)	3 (9.1)
Total		141 (33.3)	119 (28.1)	80 (18.9)	83 (19.3)

STATISTICAL ANALYSIS

The data were analyzed using SPSS (IBM, version 22), unless otherwise stated. The percentages and frequencies were estimated using descriptive statistics. The frequency distrubution of clinical diagnosis and antibiotic utilization was estimated according to patinet's age, gender, types of diagnosis and types of health care facility, i.e., public and private hospitals.

RESULTS

Age and gender specific distribution of upper respiratory tract infections (URTIs)

Data suggested that in both males (57.6%) and females (42.3%), tonsillitis (M; 18.2%, F; 11.2%) and pharyngitis (M;16.8%, F; 12.3%) remained the most frequent URTIs infections reported to both private and public sector hospitals of Lahore, followed by otitis media (M; 5%, F; 6.1%), sore throat (M; 4.7%, F; 2.8%) and sinusitis (M; 4.3%, F; 3.1%) (table 1). The frequency of URTIs were higher in subjects aged between 21-30 years (31.7%), followed by 31-40 years (16.3%), 16-21 years (10.9%) and 41-50 years (9.9%). Among URTIs, pharyngitis was most common in subjects between 21-31 years of age (10.2%), followed by tonsillitis (7.3%) and otitis media (4.3%) (table 1). Similar trend was observed in patients between 31 – 40 years of age (table 1).

Frequency distribution of URTIs in public and private hospitals

Overall, among various hospitals, highest number of URTIs cases were reported in JH (27.4%), followed by LGH (25.8%), NHMC (16.3%) and DHMC (15.1%). In public sector hospitals, tonsillitis was the most common URTIs followed by pharyngitis, otitis media, sinusitis, rhinitis and sore throat (table 2). In private hospitals again pharyngitis was the most common URTI followed by tonsillitis, otitis media, common cold & flu, rhinitis and sore throat (table 2).

Age and gender specific utilization of antibiotics in URTIs

As shown in table 3, in both males and females; co-amoxiclave was the most frequently used antibiotic (M; 18.6%, F; 11.5%) in penicillin class, followed by ceftriaxone (M; 8.5%, F; 6.9%) in cephalosporin class, levofloxacin (M; 6.1%, F; 5%) in quinolone class and clarithromycin (M; 6.1%, F; 4.3%) in macrolide class of antibiotics. In age group, 1-5 years, maximum consumption was observed for co-amoxiclave (3.1%), followed by ceftriaxone (2.4%) and cefixime (1.2%) (table 3).

Diagnosis specific utilization of antibiotics

Overall, co-amoxiclave (30%) was the most frequently prescribed antibiotic among all the classes and also in penicillin class, followed by ceftriaxone (15.4%) and cefixime (11.6%) in cephalosporin class and levofloxacin (11.3%) in quinolone class (table 4). In penicillin class, co-amoxiclave was the most frequently prescribed antibiotic in tonsillitis (11.1%) followed by pharyngitis (7.3%), otitis media (3.1%), sore throat (2.6%), sinusitis (2.4%) and rhinitis (2.1%). In cephalosporin class, ceftriaxone (CRO) and cefxime (CFM) were the most frequently prescribed antibiotics in tonsillitis (CRO; 6.6%, CFM; 2.4%), pharyngitis (CRO; 2.1%, CFM; 2.8%), otitis media (CRO; 1.7%, CFM; 1.4%), sore throat (CRO; 2.4%) and rhinitis (CFM; 1.7%). In quinolone class, levofloxacin (LVX) was the most frequently prescribed antibiotic in pharyngitis (4.3%) followed by tonsillitis (1.9%), sinusitis (1.4%) and otitis media (1.4%). In macrolide class, clarithromycin (CLR) followed and azithromycin (AZM) were most prescribed antibiotics in pharyngitis (CLR; 5.7%, AZM; 1,9%) and tonsillitis (CLR;2.6%, AZM; 1.2%) (table 4).

Hospital specific consumption of antibiotics

As shown in table 5., in penicillin class co-amoxiclave was the most frequently used antibiotic in both public and private hospitals (30%), with highest consumption in Jinnah hospital (JH; 11.3%) followed by Lahore general hospital (LGH; 9.7%) and Doctors hospital and medical center (DHMC; 4.3%). In cephalosporin class, highest rate of consumption was of ceftriaxone (15.4%) followed by cefixime (11.6%) in both public and private hospitals. The consumption of CRO was more frequent in Mayo hospital (MH; 4.3%) and JH (3.3%) belonging to public sector, while in public sector, it was more frequent in DHMC (3.3%) and National hospital and medical center (NHMC; 3.1%). While the frequency of CFM consumption was higher in private hospitals – NHMC (6.6%), DHMC (1.2%) and Hameed latif hospital (HLH; 1.4%). In quinolone class of antibiotics, the consumption of LVX and CIP was higher in public sector hospitals compared to private hospitals (table 5). Lastly, in macrolide class of antibiotics, only CLR was frequently consumed by private hospitals, while in private hospital only 1.4% patients consumed CLR while consumption of other antibiotics was even less than 1% (table 5).

Hospital and diagnosis specific antibiotic therapy adherence to standard treatment guidelines (STGs) in URTIs

Data revealed that in public sector hospitals, 1st line treatment compliance was better in Jinnah hospital (JH; 46.6%) and Lahore general hospital (LGH; 37.8%) in comparison to Mayo hospital (MH); having better compliance to 2nd line (MH; 46.5%) treatments (table 6). Among private hospitals, 32.8% prescription from doctor hospital and medical center (DHMC) demonstrated adherence to 1st line treatment, while 62.3% from National Hospital and Medical Center (NHMC) and 40.9% from Hameed Latif Hospital (HLH) showed

adherence to 2nd line treatment. Besides, compared to public hospitals, all private hospitals exhibited some percentage of non-adherence, i.e., 22.7% in HLH, 21.9% in DHMC and 18.8 in NHMC (table 6).

Based on clinical diagnosis, 39.4% prescriptions generated for tonsillitis were adherent to 1stline followed by 33.3% for sinusitis, 31.9% for otitis media and30.1% for pharyngitis. Additionally, 53.3% prescription generated for common cold & flu were adherent to 2nd line treatments followed by 33.3% for tonsillitis, 27.7% for otitis media and 27.3% for laryngitis. Mixed trends were observed for both rhinitis and sinusitis. The highest number of prescriptions that did not adhere with any guideline options included those generated for laryngitis (36.4%), otitis media (34%), pharyngitis (26%) and common cold & flu (20%) (table 6).

DISCUSSION

The growing injudicious and unreasonable antibiotic prescribing has led to the surge in antibiotic resistance, health care finances, adverse effects and poor disease outcomes (Mboya *et al.,* 2018) (Butt *et al.,* 2017), requiring health facility specific assessment of antibiotic patterns. In the present study, we found that in public and private hospitals of Lahore, broad spectrum antibiotics were frequently prescribed in URTIs, tonsillitis, pharyngitis and otitis media, among males and females, aged 21 – 40 years. The notable antibiotics included, co-amoxiclave, ceftriaxone, cefixime, levofloxacin, clarithromycin and ciprofloxacin. Similar antibiotic prescribing trend was observed in both public and private hospitals of Lahore, yet with superior treatment compliance in public hospitals compared to private hospitals.

Numerous literature evidences, even from Pakistan, suggested that, irrespective of gender, tonsillitis, pharyngitis and otitis media are the most frequently diagnosed URTIs in patients aged between 21-40 years (Saliba-Gustafsson *et al.,* 2019). We also observed a similar trend, i-e., tonsillitis was the most frequent URTI followed by pharyngitis and otitis media in both male and female patients aged between 21-40 years (>46%) in both public and private hospitals though the reporting frequencies were higher in public hospitals. No literature evidences from Pakistan were available to compare these findings. Nonetheless, a study from Karachi, the largest metropolitan city of Pakistan, reported that overall antibiotic prescribing frequency was higher in public health facilities (67.9%) compared to public sector (51.59%) (Asghar *et al.,* 2017, Saleem *et al.,* 2019) yet, contrary to that, another study from the same city, though on pediatric population, suggested that antibiotics prescribing frequency was higher in private sector health facilities (77.7%) in comparison to public (65.6%) (Baig *et al*., 2017). These differences can be explainable by differences in the study population and also due to differences in study objectives and methods; former report studied only prescribing behavior using WHO indicators, while later report evaluated irrational prescribing using culture sensitivity reports (CSR) and by assessing the choice and dose of antibiotics.

Furthermore, we observed that the rate of antibiotic consumption in URTIs, tonsillitis, pharyngitis and otitis media, was higher in patients aged between 21-40 years, and major antibiotics consumed were co-amoxiclave in penicillin class, ceftriaxone in cephalosporin class, levofloxacin in quinolone class and clarithromycin in macrolides class. Similar to our findings, studies have shown that in URTIs, antibiotic are consumed more frequently in patients aged between 20-40 years (Ab Rahman *et al.,* 2016), (Akkerman *et al.,* 2004), yet, surprisingly not a single study was found from Pakistan for direct comparison. Literature is replete with evidences that among all the possible indications asserting antibiotic prescriptions, by far, URTIs are the most isochronous indication affirming antibiotic prescribing (Ab Rahman *et al.,* 2016, Chem *et al.,* 2018). In this context, previous reports suggest that the consumption of antibiotics in low middle income countries (LMICs), including Pakistan, proffered considerable portion of increase in global antibiotic consumption an upsurge of 103% in India, 79% in China and 65% in Pakistan (Butt *et al.,* 2019, Saleem *et al.,* 2019, Klein *et al.,* 2018).

As reported previously that in Pakistan, overall antibiotic consumption, not specifically in URTIs, is higher in public sector hospitals in comparison to private (Asghar *et al.,* 2017), but to our knowledge, there are very limited or no literature reports that compared health facility specific, public vs private, antibiotic prescribing patterns and treatment compliance to STGs in URTIs. Our data is in complete agreement with previously published report (Asghar *et al.,* 2017), suggesting that the consumption of broad spectrum antibiotics was higher in two main public teaching hospitals (JH and LGH) compared to private hospitals (NHMC and DHMC). In this regard, the most frequently prescribed antibiotics were co-amoxiclave in penicillin class, ceftriaxone and cefixime in cephalosporin class, levofloxacin in quinolone class and clarithromycin in macrolide class, in both public and private hospitals. A similar antibiotic prescribing trends, but not specific to URTIs, have been reported previously from Pakistan (Saleem *et al.,* 2019) and United Arab Emirates (UAE) (John *et al.,* 2014), and also to some extent from Malaysia (Ab Rahman *et al*., 2016) and India (Sharma *et al.,* 2012). Another report from Attock district of Pakistan, comparing prescribing practices between private and public health care providers, demonstrated that at least one antibiotic was prescribed in 62% of the prescriptions generated by private sector providers compared to 54% by

public sector providers–with most prescriptions in acute respiratory tract infections (Siddiqi *et al.,* 2002). However, according to one report from Pakistan (Saleem *et al.,* 2019), in the emergency department of a tertiary care hospital of Bahawalpur, one of the major city of Pakistan, cephalosporin consumption was 81.5% and in this class ceftriaxone (71.8%) was the most frequently prescribed antibiotic (Atif *et al.,* 2016). These data corroborated one major trend, that there is imprudent surge in the prescribing of broad spectrum antibiotics coupled with arduous non-compliance to STGs. In this respect, we found that 1st line therapy compliance was much better in public sector hospitals of Lahore compared to private hospitals, observing 2nd line compliance and higher overall the non-compliance to STGs. Besides, the foremost non-compliance, based on clinical diagnosis, was observed for laryngitis followed by otitis media and pharyngitis. Thus, in Pakistan, a very precise workup on antibiotic prescribing practices and compliance to STGs in URTIs is almost tenuous, yet the overall prescribing frequency seems to be higher, particularly for the broad-spectrum antibiotics.

Clinical implications and policy recommendations

In Pakistan, majority of people with URTIs report to public hospitals in comparison to private hospitals, the sole reason of preference could be the affordability, since private hospitals, mostly not regulated by the health department, charge hefty bills even for limited services. Nonetheless, it's encouraging to see superior compliance to STGs in public hospitals compared to private hospitals. The higher non-compliance in private sector is more of a patient's factor, probably because of patient's education and loaded finances, not only because patients assume antibiotics as panacea but also due to patient's tendency to shift to another session, thus the prescribers, mostly specialist, are conscripted to prescribe antibiotics – an attempt to become more responsive towards patient's expectations. In public hospitals, prescriber decision is merely influenced by a patient, but diagnostic uncertainties exist due to non-functional cash strapped laboratories that posolutely effect antibiotic prescription. However, in public hospitals, the prescriptions generated by a Professor are followed by juniors that may add to prescription rationality. Nevertheless, almost 90% public sector specialists are working as private consultants in private sector hospitals, though with significant shifts in responses towards the patients.

As a policy recommendation, there should be more stringent, yet uniformly managed single regulatory policy for both private and public sector hospitals of Pakistan. There should be antibiotic stewardship, quality assessment and continuous education programs under the auspices of drugs and therapeutic committee (DTC) for the prescribers targeting the most deficient prescribing practices. The DTC must perform periodic antibiotic reviews and devise quality assurance mechanisms, such as quality assessment checklists to assure rationale prescribing. Several in-house supervisory checks can be primed utilizing the services of a clinical pharmacist.

Study limitations

The cross-sectional designs of the study preclude the long term assessment of antibiotic prescribing patterns, particularly seasonal impacts. Prescribing patterns in hospitals of Lahore in no way can predict the prescribing practices in other cities, districts and provinces of Pakistan. Due to cross-sectional design and reliance on prescription files, the authenticity of the available data cannot be cross-checked. A very few literature reports were available from Pakistan, with regards to public and private hospitals antibiotic prescribing trends in adult URTIs, to present a direct comparison of our study.

CONCLUSION

These data suggested that in both public and private hospitals of Lahore, broad spectrum antibiotics were frequently consumed in URTIs, pharyngitis, tonsillitis and otitis media, in both males and females, aged between 21-40 years. The major antibiotics consumed were co-amoxiclave, ceftriaxone and cefixime, levofloxacin and clarithromycin. Significant differences exist among the selection of 1st, 2nd and 3rd line treatment choices between public and private hospitals. Overall, public hospitals demonstrated improved treatment compliance in comparison to private hospitals.

ACKNOWLEDGEMENTS

Authors are highly thankful to the patients for their willingness to share their culture sensitivity reports and the kind cooperation of hospital laboratory staff.

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