ijlpr 2020; doi 10.22376/ijpbs/lpr.2021.11.4.P49-57

International Journal of Life science and Pharma Research

Research Article

Pharmacy Practice

# Antibiotic Prescribing Practice in Chronic Kidney Disease Patients in a Tertiary Care Teaching Hospital: Analysis Based on 2019 WHO AWaRe Classification

**Juveriya Mahin[1#], Mounika Peddireddy[1#], Venkataramana Mangalapalli[2], and Satyanarayana SV Padi[1*]**

[1]*Department of Pharmacy Practice, Care College of Pharmacy, Warangal, 506001, Telangana, India*

[2]*Department of Nephrology, SVR Multispecialty Hospital, Warangal, 506001, Telangana, India*

[#]*Equally contributing authors*

**Abstract:** Chronic kidney disease (CKD) patients are prone to infections and inevitably require antibiotics. Antimicrobial resistance (AMR) is a global threat to humans. Indeed, the most important cause for spread of AMR is irrational use of antibiotics. Therefore, the present study evaluates prescribing practice of antibiotics in CKD patients. A cross-sectional study was carried out in 382 CKD in-patients prescribed with antibiotics. The data were analysed using the WHO prescribing indicators and the WHO Access, Watch, and Reserve (AWaRe) classification. The average number of drugs prescribed per encounter was 3.1. Antibiotics prescribed by generic name and prescribed from the Essential Medicines List were 52.9% and 47.1%, respectively. % Encounters with antibiotics and parenteral antibiotics were 59.2% and 77.4%, respectively. Third generation cephalosporins (76.9%), particularly cefoperazone (40%) and ceftriaxone (21.2%), were the most commonly prescribed antibiotics. A total of 19 specific antibiotics (Access 5, Watch 13, Reserve 1, and Not Recommended 0) were prescribed. According to WHO AWaRe classification, 10.6%, 89%, and 0.4% of antibiotics prescribed were from the 'Access', 'Watch', 'Reserve' categories, respectively. 'Watch' category antibiotics, particularly cephalosporins (98%), were prescribed in high rate. The most commonly prescribed 'Access' and 'Watch' category antibiotics were amikacin (37%) and cefoperazone (44.9%), respectively. Amoxicillin index was 1.6 and 'Access-to-Watch' index was 0.1, which were below the priority values. Prescription pattern of antibiotics observed in this study was not fully met the WHO recommendations. Additionally, 'Watch' category antibiotics, particularly cephalosporins, were prescribed frequently. Changes in prescription pattern and monitoring of antibiotic use are essential to preserve effectiveness and promote rational use of antibiotics, and to overcome AMR.

**Keywords:** Antibiotics, Antimicrobial resistance, Cephalosporins, Chronic kidney disease, Prescribing pattern, Prescribing practice, AWaRe classification.

***Corresponding Author**

**Satyanarayana SV Padi , Department of Pharmacy Practice, Care College of Pharmacy, Warangal, 506001, Telangana, India**

**Received On** **17 July, 2021**
**Revised On** **24 July, 2021**
**Accepted On** **25 July, 2021**
**Published On** **29 July, 2021**

**Funding** This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

**Citation** Juveriya Mahin, Mounika Peddireddy, Venkataramana Mangalapalli, Satyanarayana SV Padi , Antibiotic Prescribing Practice in Chronic Kidney Disease Patients in a Tertiary Care Teaching Hospital: Analysis Based on 2019 WHO AWaRe Classification.(2021).Int. J. Life Sci. Pharma Res.11(4), P49-57 http://dx.doi.org/10.22376/ijpbs/lpr.2021.11.4.P49-57

# 1. INTRODUCTION

Antimicrobial resistance (AMR) is the ability of microbes to evolve and render the antimicrobials ineffective. There is an increase in the prevalence of drug-resistant infections as well as emergence and persistence of multidrug-resistant bacteria (MDR) or 'superbugs'.[1,2] Globally, extensive and inappropriate use of antibiotics in primary care and hospital settings is a major contributing factor to the spread of AMR. It is a serious threat to public health and has a significant economic impact globally, especially developing nations like India.[2,3] It is estimated that AMR could cause 10 million deaths a year worldwide and two million deaths are projected to occur in India by 2050.[3,4] Moreover, human antibiotic consumption in India is among the highest in the world and sales continue to surge rapidly even though the prevalence of infectious diseases remained stagnant whereas the morbidity and mortality due to infectious diseases decreased.[5,6] A recent study on antibiotic consumption and its trend over time revealed a remarkable increase between 2000 and 2015 in low- and middle-income countries (LMICs) wherein antibiotic use in India alone increased by 103%, which is more than in any other country, due to overall increased access to antibiotics and irrational use.[6,7]Chronic kidney disease (CKD) is highly prevalent worldwide wherein India (115·1 million) along with China (132·3 million) had almost a third of all cases of CKD globally. CKD patients are more susceptible to infections, which remain one of the major non-cardiovascular causes of hospitalization and mortality, and CKD was the 12th leading cause of death worldwide in 2017.[8] Nephrologists empirically prescribe antibiotics for prophylaxis and treatment in severely ill and immunocompromised CKD patients. Nevertheless, the selection of antibiotic is a challenge for the treatment of CKD patients with infections and it increases the cost of treatment, especially in those receiving dialysis.[9,10] Among antibiotics, cephalosporins are highly preferred over other classes of antibiotics due to broad spectrum of action and lower hypersensitivity reactions; however, AMR is slowly emerging due to extended spectrum beta-lactamases (ESBLs).[10,11] Thus, appropriate antibiotic selection and preserving antibiogram are important to ensure favourable therapeutic outcomes. To preserve the effectiveness and rationalize antibiotics use, WHO prescribing indicators have been used for drug utilization evaluation and antibiotic stewardship programs in different healthcare settings.[12-14] Recently, the WHO developed the Access, Watch, and Reserve (AWaRe) antibiotic categories. The 'Access' category consists of first and second choices of antibiotics for the empirical treatment of the most common infections, that are available at all times, and affordable with assured quality. The 'Watch' category consists of most of the "highest-priority critically important antibiotics", though these are associated with toxicity concerns and/or resistance potential and are recommended only for specific indications. The 'Reserve' category includes antibiotics of last resort for MDR infections when all other antibiotics have failed.[15] The WHO AWaRe categories can help clinicians to minimize harms by selecting the right antibiotic, rationalizing prescribing without compromising on therapeutic outcomes, and thereby reducing the spread of AMR. Recently, few studies adopted this index and reported a global trend of increased sales and consumption of antibiotics.[7,16,17] Nevertheless, such analyses were based on pharmaceuticals sales and consumption data, thus revealing limited information regarding antibiotic prescription practices and patterns. To the best of our knowledge, there is no such study using the AWaRe categories and indices has been conducted in India and accordingly, the current status of prescribing cephalosporins is unknown. Therefore, the present study evaluates prescribing practice and pattern of antibiotics in CKD patients using the WHO core prescribing indicators and the AWaRe classification.

# 2. METHODOLOGY

## *2.1. Study design*

A prospective, observational, cross-sectional study was conducted in the department of nephrology at the SVR Multispecialty Hospital, a tertiary care teaching hospital in Warangal for a period of three months i.e., from 1 August, 2019 to 31 October, 2019. The study was approved by the Institutional Ethics Committee of the Care College of Pharmacy, India (PDPW/CCP/201920-07-005). The permission was obtained and individual patient consent was taken to collect the data.

## *2.2. Data collection procedure*

The legible and complete prescriptions collected from CKD patients, who were admitted during the study period, were included. Patients who visited the nephrology department for second opinion, and prescriptions that were incomplete and not written during the study period were excluded. After individual data extraction, information was compared, the responsible healthcare practitioner was asked for clarifications if any crucial data were unclear, and reached a consensus of inclusion or exclusion for each patient.

# 3. STATISTICAL ANALYSES

Descriptive statistics were applied to the collected data using Microsoft Excel and the results are expressed as frequencies, averages, and percentages. A total of 382 eligible prescriptions were analysed for socio-demographic and co-morbid characteristics of CKD patients, and general prescription pattern and distribution of antibiotics. The WHO prescribing indicators with their standard values were utilized to measure rational use of drugs and antibiotics with due focus on cephalosporins prescribing pattern.[12] ICD-10-CM was used to code appropriate co-morbid condition(s).[18] Antibiotics were reported by chemical class (the third and fourth level) and drug names according to the fifth level WHO ATC classification system., and their inclusion in the 21st WHO Essential Medicines List (EML).[19,20] The prescribing patterns of antibiotics emphasizing on cephalosporins were described according to the 2019 WHO AWaRe antibiotic classification.[15] The data were further analysed for three AWaRe index metrics: the percentage of amoxicillin (Amoxicillin index), the percentage of 'Access' antibiotics, and the ratio of 'Access to Watch' antibiotics prescribed (Access-to-Watch index) to examine prescription pattern as well as prioritizing rationalise use of antibiotics.[17]

# 4. RESULTS

## *4.1. Patient characteristics*

Only one prescription from the eligible patients was collected and a total of 382 prescriptions that met the inclusion criteria were finally selected to analyse the general prescription pattern of drugs. Out of 382 in-patient encounters, 226 (59.2%) received at least one antibiotic, of which 159 were male (70.4%) and 67 were female (29.6%). On the other hand, the highest rate of prescriptions was seen in the 46 - 60 years (40.7%) age group. The most common co-morbidity in CKD patients was hypertension (92, 40.7%) followed by both hypertension and type-2 diabetes (51, 22.6%) (Table 1).

**Table 1: Socio-demographic and clinical characteristics of the study population**

| Patient characteristics | Any drug (382) n (%) | Any antibiotic (226) n (%) |
|---|---|---|
| **a) Gender** | | |
| Male | 261 (68.3) | 159 (70.4) |
| Female | 121 (31.7) | 67 (29.6) |
| **b) Age (years)** | | |
| 0 - 15 | 2 (0.5) | 2 (0.9) |
| 16 - 30 | 24 (6.3) | 17 (7.5) |
| 31 - 45 | 53 (13.9) | 35 (15.5) |
| 46 - 60 | 154 (40.3) | 92 (40.7) |
| > 60 | 149 (39.0) | 80 (35.4) |
| **c) Co-morbidities** | | |
| Hypertension (I12.9) | 162 (42.4) | 92 (40.7) |
| Hypertension (I12.9) and Diabetes mellitus Type 2 (E11.22) | 90 (23.6) | 51 (22.6) |
| Diabetes mellitus Type 2 (E11.22) | 60 (15.7) | 36 (15.9) |
| Anaemia (D63.1) | 40 (10.5) | 26 (11.5) |
| Coronary artery disease (I25.9, N18.1) | 15 (3.9) | 10 (4.4) |
| Heart failure (I13.0, N18.1) | 8 (2.1) | 6 (2.7) |
| Stroke (G46.4, N18.9) | 7 (1.8) | 5 (2.2) |

### *4.2.* General prescription pattern of antibiotics and cephalosporins

Out of 382 in-patients, 226 (59.2%) received at least one antibiotic, wherein 200 patients were prescribed with only one (52.4%) antibiotic and the remaining 26 encounters had two (23, 6%) and three (3, 0.8%) antibiotics. None of the patients was prescribed four antibiotics. Further, 200 encounters had at least one (52.4%) cephalosporin which constitutes 88.5% of 226 prescriptions with at least one antibiotic indicating the most frequently prescribed antibiotics belong to cephalosporins. However, none of the patients was prescribed two cephalosporins (Table 2). These 382 prescriptions accounted for a total of 1210 drug regimens, with 21.1 % (255) antibiotics (J01) and the remaining 78.9% (955) non-antibiotics (other than antibiotics). Overall, 16.5% of the total drugs prescribed were cephalosporins (J01D; 200) and 4.5% drugs were antibiotics (55) other than cephalosporins (Table 3). Of 255 prescribed antibiotic (J01) regimens, 78.5% (200) were cephalosporins (J01D) and 21.5% were antibiotics (55) other than cephalosporins. Cefuroxime (1.6%) was the only prescribed second generation cephalosporins (J01DC; 4) whereas cefoperazone was the most frequently (40%, 102) prescribed from the third generation cephalosporins (J01DD; 196) (Table 4).

**Table 2: Prescription pattern of antibiotics (N = 382)**

| Pattern descriptor | Number of encounters, n (%) |
|---|---|
| Without antibiotic | 156 (40.8) |
| With antibiotic | 226 (59.2) |
| One antibiotic | 200 (52.4) |
| Two antibiotics | 23 (6.0) |
| Three antibiotics | 3 (0.8) |
| At least one cephalosporin | 200 (52.4) |
| At least one cephalosporin[1] | 200 (N = 226, 88.5) |

*[1]at least one cephalosporin among 226 antibiotic encounters*

**Table 3: Distribution of prescribed drugs (N = 1210)**

| Class of drugs | ATC code | Frequency, n (%) |
|---|---|---|
| (1) Non-antibiotics | | 955 (78.9) |
| (2) Antibiotics (J01) | | 255 (21.1) |
| (i) Cephalosporins | J01D | 200 (16.5) |
| (ii) Other than Cephalosporins | | 55 (4.5) |
| Penicillins | J01C | 16 (1.3) |
| Quinolones | J01M | 15 (1.2) |
| Aminoglycosides | J01G | 10 (0.8) |
| Tetracyclines | J01A | 4 (0.3) |
| Glycopeptides | J01XA | 3 (0.2) |
| Macrolides | J01FA | 2 (0.2) |
| Carbapenems | J01DH | 2 (0.2) |
| Imidazoles | J01XD | 2 (0.2) |
| Monobactams | J01DF | 1 (0.1) |

**Table 4: Distribution of cephalosporins among total antibiotics prescribed (N = 255)**

| Class of antibiotics | Frequency, n (%) |
|---|---|
| (1) Other than cephalosporins | 55 (21.5) |
| (2) Cephalosporins (J01D) | 200 (78.5) |
| (i) Second generation (J01DC) | 4 (1.6) |
| Cefuroxime | 4 (1.6) |
| (ii) Third generation (J01DD) | 196 (76.9) |
| Cefoperazone | 102 (40.0) |
| Ceftriaxone | 54 (21.1) |
| Cefixime | 18 (7.0) |
| Cefpodoxime | 17 (6.6) |
| Cefotaxime | 5 (2.0) |

### 4.3. *Prescribing pattern of drugs and antibiotics based on WHO prescribing indicators*

A total of 1210 drug regimens were prescribed in the 382 prescriptions with an average number of drugs per encounter found to be 3.1. The total number of encounters prescribed with antibiotics and parenteral drugs were 59.2% and 81.4%, respectively. About 29.9% of the drugs were prescribed by their generic name and 72.8% prescribed drugs were from the EML (Table 5). Among 226 antibiotic prescriptions, the average number of antibiotics and cephalosporins per encounter were 1.1 and 0.9, respectively. Percentage of encounters with an antibiotic and cephalosporins was 100 and 88.5, respectively. Percentage of antibiotics prescribed by generic name, percentage of encounters with parenteral antibiotics, and percentage of antibiotics prescribed from EML were 52.9, 69.5, and 47.1, respectively whereas that of cephalosporins were 45.1, 77.4, and. 43.1, respectively (Table 6).

**Table 5: Prescribing pattern of drugs based on WHO prescribing indicators**

| WHO prescribing indicator | Number | WHO standard |
|---|---|---|
| Average number of drugs per encounter | 3.1 | 1.6 – 1.8 |
| Percentage of encounters with an antibiotic prescribed | 59.2 | 20 – 26.8 |
| Percentage of drugs prescribed by generic name | 29.9 | 100 |
| Percentage of encounters with parenteral drug prescribed | 81.4 | 13.4 – 24.1 |
| Percentage of drugs prescribed from EML | 72.8 | 100 |

**Table 6: Prescribing pattern of antibiotics based on WHO prescribing indicators**

| WHO prescribing indicator | Number |
|---|---|
| Average number of antibiotics per encounter | 1.1 |
| Average number of cephalosporins per encounter | 0.9 |
| Percentage of encounters with a antibiotic prescribed | 100 |
| Percentage of encounters with a cephalosporin prescribed | 88.5 |
| Percentage of antibiotic prescribed by generic name | 52.9 |
| Percentage of cephalosporins prescribed by generic name | 45.1 |
| Percentage of encounters with parenteral antibiotic prescribed | 77.4 |
| Percentage of encounters with parenteral cephalosporin prescribed | 69.5 |

| | |
|---|---|
| Percentage of antibiotics prescribed from EML | 47.1 |
| Percentage of cephalosporins prescribed from EML | 43.1 |

### 4.4. *Prescription pattern of antibiotics based on* **WHO AWaRe** *classification*

A total of 255 antibiotic regimens from 226 prescriptions were systematically classified into Access, Watch, and Reserve (AWaRe) antibiotic categories. Of 255, 10.6% antibiotic regimens (27) and 2% cephalosporins (4) were from the 'Access' category. Most importantly, 89% of the antibiotic regimens (227 out of 255) and 98% cephalosporin regimens (196 out of 200) were from the 'Watch' category indicating a higher prescription rate. Conversely, only 1 out of 255 antibiotics (0.4%) were from the "Reserve' category. None of the cephalosporins prescribed were from the 'Reserve' antibiotics. None of the antibiotics including cephalosporins prescribed were from the 'Not Recommended' category (Table 7). The percentage of amoxicillin prescribed was very less (1.6%), the percentage of 'Access' antibiotics was also less (10.6%; Recommended value more than 60%), and the ratio of 'Access to Watch' antibiotics (Access-to-Watch index) was 0.1, which was less (Priority value 1.5) indicating the prescription pattern of antibiotics was yet to meet the WHO recommendations (Table 8).

**Table 7: Prescription pattern of antibiotics based on WHO AWaRe classification**

| WHO AWaRe category | All antibiotics (255) | Cephalosporins (200) |
|---|---|---|
| | n (%) | n (%) |
| Access | 27 (10.6) | 4 (2.0) |
| Watch | 227 (89.0) | 196 (98.0) |
| Reserve | 1 (0.4) | 0 (0) |

**Table 8: Prescription pattern of antibiotics based on AWaRe Index metrics**

| AWaRe Index Metrics | Observed value (%) | Priority value |
|---|---|---|
| Amoxicillin index | 1.6 | > any antibiotic **(%)** |
| Access antibiotics index | 10.6 | > 60% |
| Access-to-Watch index | 0.1 | 1.5 |

**Table 9: Distribution of prescribed antibiotics by WHO AWaRe classification (N = 255)**

| WHO AWaRe Category | ATC code | n (%) | Listed in EML |
|---|---|---|---|
| **Access (27)** | | | |
| Amikacin | J01GB06 | 10 (37.0) | Yes |
| Amoxicillin/clavulanic acid | J01CR02 | 7 (25.9) | Yes |
| Amoxicillin | J01CA04 | 4 (14.8) | Yes |
| Doxycycline | J01AA02 | 4 (14.8) | Yes |
| Metronidazole | J01XD01 | 2 (7.4) | Yes |
| **Watch (227)** | | | |
| Cefoperazone | J01DD12 | 102 (44.9) | No |
| Ceftriaxone | J01DD04 | 54 (23.7) | Yes |
| Cefixime | J01DD08 | 18 (7.9) | Yes |
| Cefpodoxime | J01DD13 | 17 (7.4) | No |
| Ofloxacin | J01MA01 | 8 (3.5) | No |
| Cefotaxime | J01DD01 | 5 (2.2) | Yes |
| Piperacillin/tazobactam | J01CR05 | 5 (2.2) | Yes |
| Levofloxacin | J01MA12 | 5 (2.2) | No |
| Cefuroxime | J01DC02 | 4 (1.7) | Yes |
| Vancomycin | J01XA01 | 3 (1.3) | Yes |
| Meropenem | J01DH02 | 2 (0.8) | Yes |
| Moxifloxacin | J01MA14 | 2 (0.8) | No |
| Azithromycin | J01FA10 | 2 (0.8) | Yes |
| **Reserve (1)** | | | |
| Aztreonam | J01DF01 | 1 (100) | No |

### 4.5 *Distribution of prescribed antibiotics by* **WHO AWaRe** *classification*

A total of 19 specific antibiotics were frequently prescribed in 226 encounters accounted to 255 antibiotic regimens that were examined for their listing in the 2019 WHO-EML. Of 19 specific antibiotics, 13 antibiotics were listed and the remaining 6 antibiotics were not listed. Out of 19, 5 specific antibiotics were from the 'Access' category and all are listed. The most frequently prescribed 'Access' antibiotic was amikacin (10, 37%) followed by amoxicillin/clavulanic acid (7, 25.9%). Notably, 'Watch' antibiotics were commonly prescribed (227 out of 255). Among 19 frequently prescribed specific antibiotics, 13 were from the 'Watch' category, of which only 8 antibiotics are listed. The most frequently prescribed 'Watch' antibiotics was cefoperazone

(102, 44.9%) followed by ceftriaxone (54, 23.7%). 'Reserve' antibiotics were uncommon, and included aztreonam, a monobactam, which was prescribed only once and was not listed in the EML (Table 9).

## 5. DISCUSSION

In the present study, 59.2% prescriptions contained at least one antibiotic, which is similar to previous studies including those conducted in India.[12-14,21,22] Numerous studies reported prescription rates of antibiotics ranging from low (18.5%) in the higher income countries like Saudi Arabia to very high 71.1% and 81.3% reported in Nigeria and Sudan, respectively, which are poor economies.[6,13,16,23,24] The reasons could be socioeconomic status, poor primary and secondary healthcare facilities accompanied by poor hygiene and sporadic occurrences of infections. In our study, males constituted a larger number of in-patients who received antibiotics. Contrary to our study, more females with urinary tract infections were prescribed with antibiotics including cephalosporins than males.[25,26] Moreover, the highest antibiotic exposure was in the age group 46-60 years indicating the risk of infection in CKD is high. While the least antibiotic exposure was observed in paediatric patients indicating reduced risk of dysbiosis and its associated several distinct health conditions with childhood onset including asthma, food allergies, obesity, and psychiatric disorders.[27,28] In most cases, the co-morbid conditions observed in this study has similar trend to a previous study which reported mortality rate in CKD patients with hypertension, followed by type-2 diabetes mellitus, and other causes.[5,8] It is observed that the prescribed antibiotics including cephalosporins were without any undesirable side effects and well tolerated in patients with diverse infectious disease along with other comorbid conditions that justifies appropriate selection of antibiotics with respect to patient compliance. In this study, antibiotics prescribed are belongs to eight different pharmacological classes with broad-spectrum of activity and cephalosporins were prescribed in more percentage. Our results are parallel to previous studies which reported a higher prescription and use of third generation of cephalosporins. [4,14,22,29,30] On the contrary, few studies reported high prescription of penicillins over cephalosporins while both the classes of antibiotics were prescribed almost equally in few studies.[13,26] Intriguingly, monotherapy (52.4 %) was preferred over combination therapy because most of the antibiotics, chiefly cephalosporins (88.5% of all antibiotic encounters), were used empirically which requires single antibiotic. Predominantly, cefoperazone was prescribed in high rate; however, ceftriaxone was reportedly the most commonly prescribed third generation cephalosporin in few studies.[21,26,30] This might be due to regional variation in bacterial susceptibility and resistance, prescribing habits and the difference in prevalence of infectious diseases in different countries.[1,3] Moreover, third generation cephalosporins have enhanced activity against many microorganisms and good tolerability, therefore, these are generally prescribed in high rate which further supports the empirical evidence.[11] Notwithstanding to this, one of the growing concerns is the development of resistance to third generation cephalosporins due to ESBLs, which confer resistance to all β-lactams except cephamycins and carbapenems.[1,3,31] This kind of emergence of resistance warrants necessary action to reduce over prescription and to preserve effectiveness of antibiotic, particularly cephalosporins in healthcare facilities. According to the WHO prescribing indicators, the average number of drugs per encounter was 3.1 and percentage of antibiotics per prescription was 59.2%, which is much higher than the recommended value (20-26.8). The results were similar to previous studies wherein polypharmacy, high percent of antibiotics, and more than two antibiotics per encounter were reported.[12-14,30,32,33] It is possible that these studies investigated outpatients, which sole rely on oral antibiotics whereas studies conducted on hospitalized patients reported both oral and parenteral antibiotics. Conversely, these values vary with nature of underlying infection, status of renal function, and associated comorbid conditions in CKD patients, which require treatment with drugs other than antibiotics. Of particular interest, the number of antibiotics per encounter with at least one antibiotic was within the recommended range whereas that of cephalosporin was less than one, which is desirable. Many studies reported varying numbers of drugs with more than one antibiotic per encounter.[33-35] The lower the number of antibiotics prescribed per encounter, which is almost one, is a positive sign of good prescribing practice. It reduces polypharmacy, minimizes disease complication due to drug-drug interactions, and adverse drug reaction including AMR and MDR owing to reduction in evolutionary and antibiotic selective pressure.[12,14,21,36] It is observed that the percentage of antibiotics including cephalosporins prescribed by generic names was low as opposed to the WHO recommended value of 100. This may be due to medication procurement policy, non-availability of generic version in time, and affordability of medications by in-patients influence the choice of brand or generic products. Percentage of parenteral antibiotics prescribed was found to be high exceeding the WHO standard limit. Globally, there were variations, however, the highest prescription and consumption of injectables compared to oral formulations was reported in LMICs including China and India.[14,21,34,37] Parenteral route was most commonly used route of administration which may be because the study was conducted in the in-patient departments to achieve better bioavailability and faster onset of action and recovery, which could reduce the duration of hospital stay. Moreover, in-patient setting, prevailing disease condition, and patient compliance preclude oral antibiotic preparations in a tertiary hospital. Herein, the percentage of antibiotics prescribed from the latest EML was found to be low. The WHO recommends updated national EML, which is pivotal for drug availability and access locally and regionally. However, in a typical tertiary hospital involving in-patients, where the antibiotic options may not be limited to the national EML and physicians and surgeons may manage treatment of diseases based on expertise and empirical knowledge. Though the present study results showed a high level of adherence, better results still can be achieved. It is well known that amoxicillin is one of the most commonly used first-line and narrow spectrum antibiotics to treat a wide variety of bacterial infections and predominantly highly prescribed "Access' antibiotic.[17,37-40] In the present study, amoxicillin alone and in combination with clavulanic acid was also prescribed less frequently. Accumulating data indicated that the percentage of use accounted for amoxicillin is highly variable even in countries with high access percentages owing to highly variable health-care systems and income classification.[7,14,17,37] In the present study, out of all the prescriptions encountered, most of the frequently prescribed antibiotics including cephalosporins were from the 'Watch' category indicating their use was high. The frequent prescription of 'Access' antibiotics including first generation cephalosporins was low against the WHO recommended value of 60%. Notably, the 'Access-to-Watch' index of the prescribed antibiotics was 0.1, which was well below the priority limit of 1.5 that substantiates the very less prescription rate of relatively safer and narrow spectrum antibiotics. The most striking finding in this study was that the prescription of reserve group antibiotics was almost negligible that supports rational use of "Reserve' antibiotics. Antibiotics in the 'Access' category have a key role in treating infectious diseases globally, however, there is a substantial global and regional variation in the proportion of AWaRe antibiotics used in hospitalised paediatric and adult patients. The 'Access' use was highest and the 'Watch' use was lowest in Oceania whereas the 'Access' use was lowest in Oceania and the 'Watch' use was highest in West and Central Asia.[37,38,40] In addition, there were large differences in AWaRe prescribing at country level with 'Watch' antibiotics use was high in few LMIC countries like China, India, and Iran.[17,22,32,39] One reason could be the lack of availability of narrow-spectrum antibiotics belongs to 'Access' category and easy availability of 'Watch' antibiotics such as second and third generation cephalosporins.[14,41] The existing unfavourable condition of frequent prescription and availability of 'Watch' over 'Access' antibiotics can be improved by focussing on change in the prescribing practice and hospital antibiotic policies to limit their excess use. With direct recommendation from the WHO, 60% of all antibiotics consumed must come from the 'Access' category, the antibiotics at lowest risk of resistance, by 2023. Evidence exists that there is a gradual decline in overall antibiotics use, particularly from 'Watch' category, and increase in the prescription and consumption of 'Access' antibiotics over many years because of continuous surveillance and implementation of National Action Plan.[42,43] Thus, regional and national guidelines can use this AWaRe classification in antibiotic surveillance framework as part of their WHO National Action Plan. Over and above, it is the highest priority national goal for preserving critical antibiotics by increasing use of 'Access' antibiotics and reducing higher risk of AMR by limiting use of 'Watch' and 'Reserve' antibiotics at the same time.

## 6. CONCLUSION

The study gives insight into prescription patterns of antibiotics, particularly cephalosporins, based on the WHO core indicators and AWaRe classification**.** The third generation cephalosporins, particularly cefoperazone and ceftriaxone, are the most frequently prescribed antibiotics. Very few antibiotics listed in the EML were prescribed. Most of the antibiotics including cephalosporins were from the 'Watch' category indicating a higher prescription rate over 'Access' antibiotics. Monitoring of antibiotic prescription by promoting antibiotic policies and implementation of the WHO 'National Action Plan' are essential to curtail AMR in the post-antibiotic era.

### *6.1 Limitations*

There are certain limitations for this study. First, the study was short duration. Second, the study had not included patients who reported to the triage area after 5 PM owing to time limits of healthcare personnel. Third, these data evaluated antibiotics prescribed rather than consumed. Fourth, the study was conducted at one site in one city and thus, it would not be possible to generalize the findings.

## 7. AUTHOR CONTRIBUTION STATEMENT

Conceptualization: Juveriya Mahin, Mounika Peddireddy, Satyanarayana SV Padi Methodology: Juveriya Mahin, Mounika Peddireddy, Venkataramana Mangalapalli, Satyanarayana SV Padi; Investigation: Juveriya Mahin, Mounika Peddireddy, Satyanarayana SV Padi; Data analysis: Juveriya Mahin, Satyanarayana SV Padi; Validation: Juveriya Mahin, Venkataramana Mangalapalli, Satyanarayana SV Padi; Writing-original draft: Juveriya Mahin, Mounika Peddireddy; Writing-review and editing: Juveriya Mahin, Satyanarayana SV Padi. All authors take responsibility for appropriate content, critically revised the manuscript, and approved the version of the manuscript to be published. All the authors read and approved the final version of the manuscript.

## 8. ACKNOWLEDGEMENTS

We thank all the healthcare professionals of the Department of Nephrology, SVR Multispecialty Hospital for helping in completion of the study.

## 9. CONFLICT OF INTEREST

Conflict of interest declared none.

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