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RESEARCH

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WHO/INRUD prescribing indicators with a focus on antibiotics utilization patterns at outpatient department of Adigrat general hospital, Tigrai, Ethiopia: a retrospective cross-sectional study

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Abstract

Background The World Health Organization (WHO) defines rational use of drug as a state in which medications are received by patients appropriately according to their clinical needs and individual requirement, for adequate period and at the right cost. More than 50% of all medicines are prescribed, dispensed, or sold inappropriately worldwide. This study aimed to evaluate the prescribing patterns in Adigrat general hospital, Tigrai, Ethiopia.

Methods A retrospective cross-sectional study was done to evaluate prescription patterns. A systematic random sampling technique was used to select 600 prescriptions and the prescriptions were reviewed using WHO/International Network of Rational Use of Drugs prescribing indicators. Data was collected from prescriptions dispensed from 01 March 2023 to 30 March 2024 at outpatient pharmacy of Adigrat general hospital. Data was analyzed using SPSS version 21 and a p-value < 0.05 was declared statistically significant.

Results A total of 1088 medicines were prescribed in 600 prescription encounters, giving an average number of 1.8 (± 0.83) medicines per encounter. The percentage of medicines prescribed by generic name was 91.5% while 98.7% of the medicines were prescribed from essential medicine list (EML). Besides, the percentages of encounters containing at least one antibiotic and one injection were 44.5% and 7.2%, respectively. A total of 340 antibiotics were prescribed in 267 encounters. Penicillins (34.4%), macrolides (23.8%) and fluoroquinolones (17.1%) were the most prevalent antibiotics classes. The "Access" and "Watch" groups covered 54.4% and 45.6% of the total antibiotics prescribed, respectively. Being under 18 years old [Adjusted Odds Ratio (AOR): 9.830, CI: 4.062–23.786], being prescribed with three medicines (AOR: 3.247, CI: 1.571–6.708) and certain diagnosis like diseases of the respiratory system (AOR: 3.750, CI: 2.136–6.584) were significantly associated with antibiotic prescribing.

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Conclusion This study showed deviations of prescribing patterns from WHO standards. The percentage of prescriptions with antibiotic was far from WHO optimal value. The use of antibiotics from "Access" group was below WHO standard. The percentage of medicines prescribed by generic name and the percentage of encounters with injection also deviated from WHO standard. Antibiotics prescribing showed significantly association with age, number of medicines and certain diseases.

Keywords Antibiotics prescribing, AWaRe, WHO/INRUD prescribing indicators

Background

Medicines in the last decades have displayed a greater impact to improve quality of life, reduce disease burden and mortality than ever [1]. The rational use of medicines is an integral component of any health facility to optimize the quality of healthcare for individual patients and the population at large [2–4]. The World Health Organization (WHO) defines rational use of drugs when the right medicines are given to the right patients, in the right doses, for the right period of time and at the right cost to them and their community [5]. Despite this definition, irrational use of medicine is a major health problem observed worldwide [2, 4, 6, 7], which is argued to be more common in developing countries [8]. According to the WHO worldwide estimation, more than half of all medicines are prescribed, dispensed, or sold inappropriately while half of the patients fail to comply with their appropriate treatment regimens, resulting in a broad range of health problems. Besides, about one-third of the world's population lacks access to essential medicines [5].

The frequently encountered types of irrational medicines use include the use of too many medicines per patient (polypharmacy), inappropriate use of antibiotics (use of antibiotics for non-bacterial infections, inadequate dosages of antibiotics, using wrong antibiotics), overuse of injectable medicines when oral formulations would be more appropriate, failure to adhere clinical guidelines to prescribe, self-medication including prescription only medicines [2, 9–12].

The inappropriate use of medicines leads to increased morbidity and mortality, wastage of resources, increased cost, increased adverse drug effects, increased drug- drug interactions, and the emergence of antimicrobial resistance (AMR) [8]. It has been indicated that hundreds of thousands of deaths per year are attributable to AMR worldwide. In 2019, there were an estimated 1.27 million deaths directly attributable to bacterial AMR and 4.95 million deaths associated with bacterial AMR globally [13]. But, according to the Review on Antimicrobial Resistance argument, the global burden of deaths from AMR is projected to be 10 million per year in 2050 with a cumulative cost of 100 trillion USD unless urgently acted [14].

To limit the irrational use of medicines, WHO in collaboration with the International Network of Rational Use of Drugs (WHO/INRUD) developed a set of core drug use indicators in three general areas namely, prescribing indicators, patient care indicators and healthcare facility indicators [15]. The prescribing indicators measure the performance of healthcare providers in five key areas related to the appropriate use of medicines in individual or groups of health facility [6].

To assist the development of antibiotics stewardship programmes, WHO developed a new classification of antibiotics in 2017 (revised in 2019, 2021 and 2023) classifying antibiotics as the Access, Watch and Reserve (**AWaRe**) groups. These categories were developed to give emphasize on AMR and their appropriate use [16, 17]. WHO also launched the "**AWaRe**" antibiotics book, which provides guidance for the use of 39 antibiotics to treat 35 infections in primary healthcare and hospital facilities [18]. Antibiotics in the "Access" group are essential antibiotics that should be widely available and affordable. The "Watch" group antibiotics are mainly indicated for more severe conditions. On the other hand, the "Reserve" groups are last-resort antibiotics indicated for severe infections caused by multidrug-resistant pathogens [19, 20].

Studying the drug prescribing patterns in a health facility is a crucial activity to provide a baseline data for the health practitioners and for further assessment with an ultimate goal to promote rational use of medicines and to improve the quality of health of the community. There are limited studies in Ethiopia in general and in Tigrai region of Ethiopia in particular that have published prescribing indicators in health facilities. So, this study aimed to evaluate the prescribing patterns using the WHO/INRUD prescribing indicators in outpatient setting of Adigrat general hospital, Tigrai, north Ethiopia.

Methods

Study area and period

Tigrai region is one of the national regional states in Ethiopia, with its capital city of Mekelle. The region has seven administrative zones viz. Eastern Tigrai, Southern Tigrai, Central Tigrai, Western Tigrai, Southeast Tigrai, Northwest Tigrai and Mekelle zone. Adigrat town is a major administrative town in the Eastern zone of Tigrai located 120 km away from Mekelle, and 900 km away from Addis Ababa (the capital city of Ethiopia). In Adigrat town, only one governmental hospital, and two private hospitals are currently present. Adigrat general hospital is the governmental hospital which provides health services for nearly one million people in its catchment area through its major wards such as pediatric, surgical, medical and obstetrics/ gynecology wards; two major operation rooms and one central emergency clinic, and different outpatient services including central outpatient pharmacy. Data was collected from 01 June 2024 to 30 June 2024 retrospectively from the prescriptions encounters kept in the central outpatient pharmacy of the hospital.

Study design

Hospital based retrospective cross-sectional study was conducted to investigate the overall prescribing practices in the outpatient department of Adigrat general hospital using the WHO/INRUD prescribing indicators.

Eligibility criteria

All prescription encounters dispensed for the patients attending at the outpatient department of Adigrat general hospital and whose prescription was kept in the central outpatient pharmacy from 01 April 2023 to 31 March 2024 were included in the study. On the other hand, outpatient prescriptions that contained only medical supplies like glove, and syringe; those prescriptions without clear diagnosis, prescriptions which were found to be illegible and prescriptions which were brought from outside of the hospital were excluded from the study.

Operational definitions and outcome measures

The following five WHO/INRUD prescribing indicators were evaluated in this study in comparison to WHO optimal values as shown below [5].

Average number of medicines per encounter

It measures the degree of polypharmacy. This is calculated by dividing the total number of medicines prescribed by the number of prescriptions (WHO optimal value: 1.6–1.8).

Percentage of medicines prescribed by generic name

It measures the tendency to prescribe by generic name and is calculated by dividing the total number of generic medicines prescribed by the total number of medicines prescribed and multiplied by 100 (WHO optimal value: 100%).

Percentage of patient (prescription) encounters with antibiotic prescribed

This measures the overall use of antibiotics which can be calculated by dividing the total number of encounters prescribed with one or more antibiotic by the total number of encounters and multiplied by 100 (WHO optimal value: 20–26.8%).

Percentage of prescriptions (encounters) with injection prescribed

It measures the overall use of injection. It is calculated by dividing the total number of encounters prescribed with one or more injection by the total number of encounters and multiplied by 100 (WHO optimal value: 13.4–24.1%).

Percentage of medicines prescribed from essential medicine list

It measures the degree to which practices conform to a national drug policy. This is calculated by dividing the total number of medicines in essential medicines list (EML) by the total number of medicines prescribed and multiplied by 100 (WHO optimal value: 100%).

Antibiotics

The WHO definition of antibiotics was used in this study, which includes penicillins and other antibacterials, antiinfective dermatological drugs, antiinfective ophthalmological agents, antidiarrheal drugs with streptomycin, neomycin, nifuroxazide, or combinations (6, 15). Besides, the 2023 update of the "**AWaRe**" classification was employed in the current study (17).

Sample size determination and sampling technique

The WHO recommends that at least 600 encounters should be included in a cross-sectional study in order to determine the core prescribing indicators in health facility or a group of health facilities [15]. Accordingly, the sample size for this study was determined to be 600 prescriptions encounters collected retrospectively from annually dispensed prescriptions. The prescriptions dispensed in each month were sorted according to their chronological order. Then, the prescriptions from each month were selected using a systematic random sampling technique so as to minimize bias due to disease spread associated with seasonal variations as well as variation in medicines availabilities across the year. Based on the number of dispensed prescriptions in each month, a varying sampling interval was then used for each month to attain the desired total sample (600 encounters).

Data collection tool, procedure and management

The data collection was carried out by three trained pharmacists under the supervision of the principal investigator. Data collection tool developed based on the five prescribing indicators set by WHO was used. The tool was modified by reviewing related previous studies [4, 15, 21–24]. The data collection tool had two sections; the first section assessed sex, age and the diagnosis of the patients. In the second section of the tool, information pertaining prescribing indicators, that is, the number of medicines per encounter, number of medicines prescribed by generic name, number of medicines prescribed

Table 1 Socio-demographic and clinical data of the study population (*n* = 600)

Variables	Categories	Frequency (*n*)	Percent (%)
Sex	Male	281	46.8%
	Female	319	53.2%
Age category (years)	< 18	145	24.2%
	18 to 64	383	63.8%
	≥ 65	72	12.0%
	Median (IRQ)	31 (18–51)	-
Number of disease per encounter	1disease	513	85.5%
	≥ 2 diseases	87	11.5%

from EML, presence of antibiotics in an encounter, presence of injectable medicines in an encounter as well as specific type of antibiotics prescribed were collected.

For the sake of standardization and avoiding ambiguities, internationally agreed classification systems were employed. Accordingly, the International Classification of Diseases version 10 (ICD-10) [25], and the Anatomical Therapeutic Chemical classification (ATC) were used to categorize medical conditions and medicines, respectively [26]. In measuring the proportion of medicines prescribed with generic names and from EML, the Ethiopian EML 6th edition was used as a reference [27].

Data analysis

Data was entered into and analyzed using Statistical Package for Social Sciences (IBM SPSS statistics version 21). Binary logistic regression analysis was applied to identify the association of independent variables with the antibiotics prescribing. The dependent variable entered statistical analysis was antibiotics prescribing. The independent variables included in the analysis were age, gender, number of disease per encounter, number of medicines prescribed per encounter and different diseases conditions based on ICD-10 classification of diseases. The association between the top seven prevalent diseases and antibiotics prescribing was investigated. The disease of the genitourinary system (N00-N99), the fifth prevalent disease, was not included in the statistical analysis as all of the patients with this diagnosis had received antibiotics [28]. Multivariable binary logistic regression analysis was used to assess the degree of association of the independent variables with antibiotics prescribing for variables having a p-value of <0.25 in the bivariate analysis. A p-value of <0.05 was declared statistically significant. Descriptive statistics on patients' socio-demographic, disease conditions and WHO/INRUD prescribing indicators were summarized using frequency, percentage, interquartile range, median, mean and standard deviation (SD) appropriately. The results are presented in tables and bar graphs.

Table 2 Prevalence of diseases based on ICD-10 classification of diseases (*n* = 669)

ICD-10 classification of diseases (ICD-10 code)	Frequency (%)
Diseases of the respiratory system (J00–J99)	146 (21.8%)
Infectious and parasitic diseases (A00–B99)	113 (16.9%)
Endocrine, nutritional and metabolic diseases (E00–E90)	77 (11.5%)
Diseases of the circulatory system (I00–I99)	62 (9.3%)
Diseases of the genitourinary system (N00–N99)	50 (7.5%)
Diseases of the nervous system (G00–G99)	35 (5.2%)
Mental and behavioral disorders (F00–F99)	35 (5.2%)
Diseases of the musculo-skeletal system and connective tissue (M00–M99)	33 (4.9%)
Diseases of the skin and subcutaneous tissue (L00–L99)	29 (4.3%)
Pregnancy, childbirth and the puerperium (O00–O99)	27 (4.0%)
Diseases of the digestive system (K00–K93)	21 (3.1%)
Others	41 (6.1%)

Others: includes certain conditions originating in the perinatal period (P00-P96), diseases of the eye and adnexa (H00-H5), dseases of the ear and mastoid process (H60-H95) etc

Results

Socio-demographic and clinical information

Out of the 600 prescription encounters we analyzed, 319 (53.2%) prescriptions belonged to female patients. Almost two third (63.8%) of the prescriptions were for the patients in the age category of 18 to 64 years [median: 31; interquartile range (IQR): 18–51] (Table 1).

As per the WHO-ICD-10 classification of diseases, a total of 669 diseases were identified. Diseases of the respiratory system (J00–J99) was the most prevalent diagnosis (21.8%) followed by infectious and parasitic diseases [A00–B99 (16.9%)] and endocrine, nutritional and metabolic diseases [E00–E90 (11.5%)] (Table 2).

WHO/INRUD prescribing indicators

The current study revealed that a total of 1088 medicines were prescribed in all the 600 encounters (prescriptions). Accordingly, the average number of medicines per encounter was 1.8 and SD of ±0.83. On the other hand, 91.5% of the total medicines were prescribed by their generic name. The percentage of medicines prescribed from EML was 98.7%. The percentage of encounters with at least one antibiotic and the percentage of encounters with at least one injectable medicine prescribed were 44.5% and 7.2%, respectively (Table 3). The number of medicines per prescription varied from 1 to 7 medicines. As shown in Figs. 1, 43.2% of the prescriptions contained two medicines per prescription and 60.2% of the prescriptions contained 2 or more medicines (43.2%+14.0%+3.0% = 60.2%).

Table 3 WHO/INRUD prescribing indicators in the outpatient department of Adigrat general hospital ($n = 600$)

Prescribing indicators	Total medicines or encounters	Observed value	WHO optimal value (4,15)	WHO African regional value (22)
Average number of medicines per encounter	1088	1.8 ± 0.83*	1.6–1.8	2.6
% Medicines prescribed by generic name	995	91.5%	100%	65.1%
% Encounters with antibiotics prescribed	267	44.5%	20.0–26.8%	45.9%
% Encounters with injection prescribed	43	7.2%	13.4–24.1%	28.4%
% Medicines from the essential medicine list	1074	98.7%	100%	89.0%

±0.83*: standard deviation

Patterns of antibiotic prescribing and the "AWaRe" classification

A total of 340 antibiotics were prescribed in 267 prescriptions. As per the ATC classification system, the *beta* lactam penicillin (J01C) antibiotics were the most prevalent (34.4%) antibiotics class followed by macrolides (J01F) (23.8%) and fluoroquinolones (J01M) 17.1%. These three antibiotic classes accounted for 75.3% of the total antibiotics prescribed. At single antibiotic level, the top five frequently prescribed were amoxicillin (22.4%), azithromycin (19.4%), ciprofloxacin (13.8%), metronidazole (9.4%) and amoxicillin-clavulanic (8.2%) (Table 4).

The WHO "**AWaRe**" classification of antibiotics showed that 54.4% antibiotics prescribed were from the "Access" group, while antibiotics in the"Watch" group accounted for 45.6% of the total antibiotics prescribed. The most commonly prescribed antibiotics were still amoxicillin (41.1%) and azithromycin (42.6%) in the "Access" and "Watch" groups, respectively. However; no antibiotic was prescribed from the "Reserve" group (Table 5).

This study documented a total of 278 primary infectious conditions for which the antibiotics were prescribed. From these, lower respiratory tract infection (pneumonia) accounted for almost one third (33.1%). Moreover, urinary tract infection, gastro-intestinal inefction (dominantly acute gastroenteritis; AGE) and upper respiratory tract infection (including pharyngitis and tonsillitis) consisted of 16.9%, 12.9% and 11.2% of the total infectious diseases, respectively (Fig. 2).

Predictors of antibiotic prescribing

Multicollinearity was checked among predictor variables using the Variance Inflation Factor (VIF) and Tolerance test. The VIF value for all predictor variables was < 10 (mean VIF = 1.23) and the minimum Tolerance value was 0.69, indicating there was no multicollinearity problem. We performed a model fitness test in order to confirm

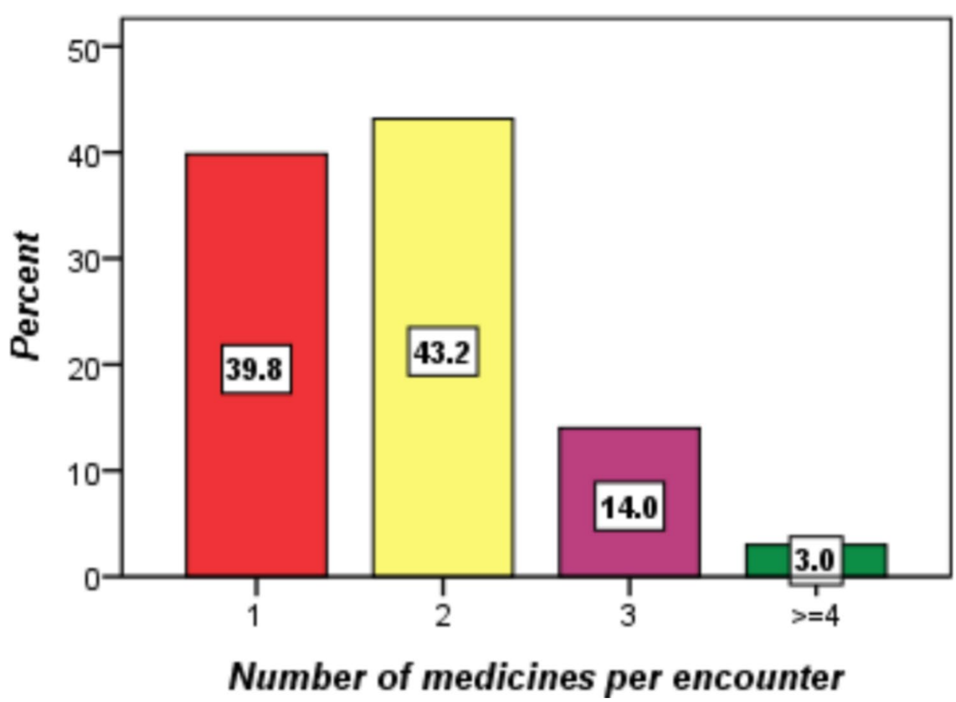

Fig. 1 Percentage of prescriptions according to the number of drugs per prescription ($n = 600$)

Table 4 Classification of the antibiotics types using the Anatomical Therapeutic Chemical (ATC) classification system (*n* = 340)

ATC code	Antibiotic chemical classes /subgroups	Specific antibiotic	Frequency (%)
J01CA04	Penicillins with extended spectrum	Amoxicillin	76 (22.4%)
J01CR02	Combination of penicillins	Amoxicillin-clavulanic acid	28 (8.2%)
J01CF02	Beta-lactamase resistant penicillins	Cloxacillin	12 (3.5%)
J01CE08	Beta-lactamase sensitive penicillins	Benzathine penicillin	1 (0. 3%)
J01C	**Beta lactam penicillins, total**	-	**117 (34.4%)**
J01FA10	Macrolides	Azithromycin	66 (19.4%)
J01FA01	Macrolides	Erythromycin	8 (2.4%)
J01FA09	Macrolides	Clarithromycin	7 (2.1%)
J01F	**Macrolides, total**	-	**81 (23.8%)**
J01MA02	Fluoroquinolones	Ciprofloxacin	52 (15.3%)
J01MA06	Fluoroquinolones	Norfloxacin	6 (1.8%)
J01M	**Quinolones (fluoroquinolones), total**	-	**58 (17.1%)**
J01XD01	Imidazole derivatives	Metronidazole	32 (9.4%)
J01X	**Other antibacterials, total**	-	**32 (9.4%)**
J01DD08	Third generation cephalosporins	Cefixime	12 (3.5%)
J01DB01	First-generation cephalosporins	Cefalexin	5 (1.5%)
J01DD04	Third generation cephalosporins	Ceftriaxone	4 (1.2%)
J01D	**Beta lactam cephalosporins, total**	-	**21 (6.2%)**
J01EE01	Combinations of sulfonamides- trimethoprim	Sulfamethoxazole-trimethoprim	17 (5.0%)
J01E	**Sulfonamides and trimethoprim, total**	-	**17 (5.0%)**
J01AA02	Tetracyclines	Doxycycline	8 (2.4%)
J01AA07	Tetracyclines	Tetracycline	4 (1.2%)
J01A	**Tetracyclines, total**		**12 (3.6%)**
J01GB03	Aminoglycoside	Gentamicin	2 (0.6%)
J01G	**Aminoglycosides, total**	-	**2 (0.6%)**

suitability of the model using the Hosmer-Lemeshow goodness-of-fit. The Hosmer-Lemeshow test showed that the model was fit to differentiate between the encounters prescribed with antibiotics and encounters not prescribed with antibiotics [$X^2 = 4.480$, (df) = 8, $P = 0.811$]. The model accurately identified 80.0% of those with antibiotics prescribed and explained between 41.4% (Cox and Snell *R* squared) and 55.4% (Nagelkerke *R* squared) of the variance in prescribing of antibiotics. The percentage of the groups with antibiotics prescribed that the model accurately identified (sensitivity test of the model) and the percentage of the groups without antibiotics prescribed that the model accurately identified (specificity test of the model) were 79.4% and 80.4%, respectively.

Table 5 Classification of the antibiotics using the WHO "**AWaRe**" grouping system [17] (*n* = 340)

"Access" (*n* = 185; 54.4%)		**"Watch" (*n* = 155; 45.6%)**		**"Reserve" (*n* = 0)**
Specific antibiotic	Percent (%)*	Specific antibiotic	Percent (%)**	
Amoxicillin	41.1%	Azithromycin	42.6%	-
Metronidazole	17.3%	Ciprofloxacin	33.5%	
Amoxicillin-clavulanic acid	15.1%	Cefixime	7.7%	
Sulfamethoxazole-trimethoprim	9.2%	Erythromycin	5.2%	
Cloxacillin	6.5%	Clarithromycin	4.5%	
Doxycycline	4.3%	Norfloxacin	3.9%	
Cefalexin	2.7%	Ceftriaxone	2.6%	
Tetracycline	2.2%			
Gentamicin	1.1%			
Benzathine penicillin	0.5%			

*: the percent was calculated within the "Access" group; **: the percent was calculated within the "Watch" group

Bivariate analysis showed that age ($P<0.001$), number of diseases ($P=0.017$), number of medicines per encounter ($P<0.001$), infectious and parasitic diseases (A00–B99) ($P<0.001$) and diseases of the respiratory system (J00–J99) ($P<0.001$) were significantly associated with antibiotics prescribing. Conversely, conditions such as endocrine, nutritional and metabolic diseases (E00–E90) ($P<0.001$), diseases of the nervous system (G00–G99) ($P<0.001$), mental and behavioral disorders (F00–F99) ($P<0.001$) and diseases of the circulatory system (I00–I99) ($P<0.001$) showed significant protective effect against antibiotics prescribing (Table 6).

In the multivariate logistic regression, the infectious and parasitic diseases ($P=0.42$) and number of diseases ($P=0.220$) were retained as confounders. Multivariate analyses showed that subjects who were less than 18 years of age ($P<0.001$), subjects with 2 medicines ($P<0.001$) and diseases of the respiratory system ($P<0.001$) remained significant predictors of antibiotics prescribing. Hence, individuals under 18 years old had almost 10-fold higher chance of being prescribed with antibiotics than those ≥ 65 years old [Adjusted Odds Ratio (AOR): 9.830, CI: 4.062–23.786]. Besides, subjects prescribed with 2 medicines had about 3 times higher probability to be prescribed with antibiotics compared to those having one medicine only (AOR: 2.690, CI: 1.625–4.453). Similarly,

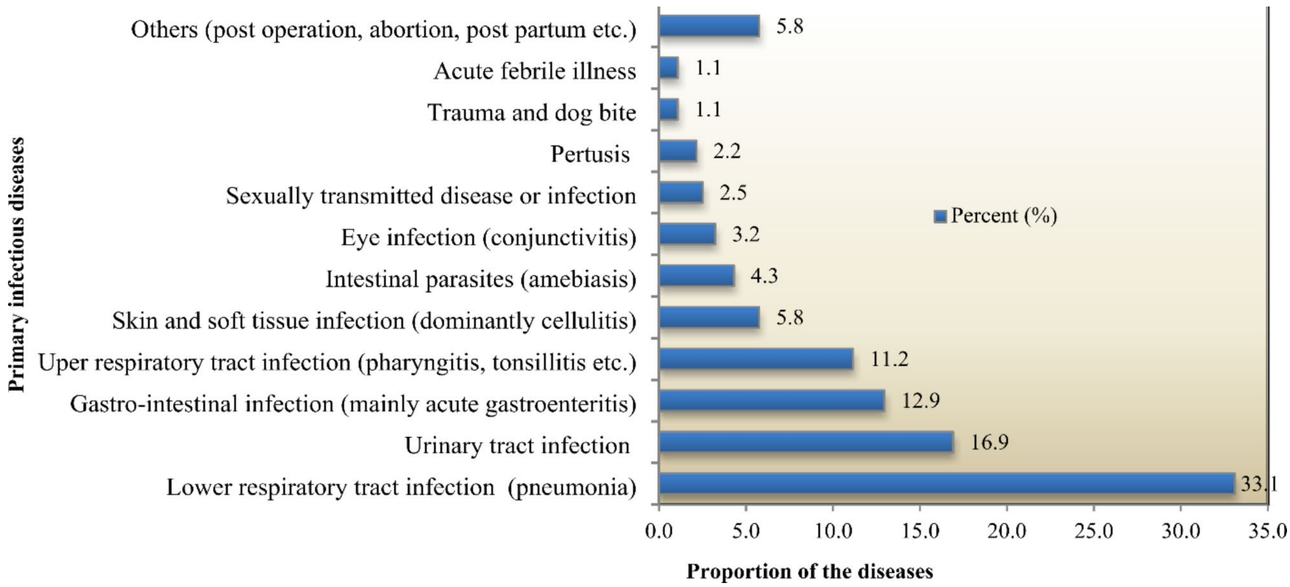

Fig. 2 Primary infectious conditions for which antibiotics were prescribed ($n = 278$)

the odds of antibiotics prescribing with diagnosis of diseases of the respiratory system increased almost by 3.8 times compared when there was no diagnosis of this disease (AOR: 3.750, CI: 2.136–6.584) (Table 6).

As in the bivariate analysis, some of the ICD-10 diseases were protective against antibiotics prescribing in the multivariate analysis. So, subjects without endocrine, nutritional and metabolic diseases were about16 times more likely to receive antibiotics (AOR: 16.452, CI: 5.413–50.010). Absence of diseases of the nervous system (AOR: 16.693, CI: 3.461–80.522), mental and behavioral disorders (AOR: 14.124, CI: 2.710 −73.610) and diseases of the circulatory system (AOR: 8.681, CI: 3.094–24.362) also increased odds of antibiotics prescribing (Table 6).

Discussion

WHO/INRUD prescribing indicators

In the present study, a total of 600 prescriptions representing 600 patients were assessed in outpatient setting. This study showed the existing prescribing practices of the study hospital compared to WHO/INRUD prescribing indicators. The five prescribing indicators namely: average number of medicines per encounter, percentage of medicines prescribed by generic name, percentage of encounters with antibiotics, percentage of encounters with injection and percentage of medicines prescribed from EML were evaluated against the WHO optimal values.

The results of this study revealed that a total of 1088 medicines were prescribed, giving an average number of 1.8 (SD: ±0.83) medicines per prescription. This is within the upper limit of the WHO optimal value (1.6–1.8), which is encouraged. But, this might not be the case. A study conducted on the impact of war on the health system of Tigrai, Ethiopia, showed that only 27.5% of the hospitals and 17.5% of health centers were functional six months after the onset of Tigrai war [29]. So, low medicines supply chain attributed to the long-lasting effet of war crisis in the study area might have influenced prescribing practice of the clinicians in the hospital. First, clinicians may not prescribe for the medicines unavailable in their hospital. Second, clinicians may hesitate to prescribe drugs for fear of unaffordability of the patients, particularly for the drugs to be obtained from private pharmacies. Our finding on average number of medicines per encounter is comparable to the study finding from Eritrea [30] and slightly higher compared to the study elsewhere from Ethiopia [23] where it was 1.76 and 1.69, respectively. But, studies done in eastern Ethiopia [3], Pakistan [12], Saudi Arabia [2] and Sri Lanka [4] reported higher average number of medicines per prescription than ours, which varied from 2.17 to 3.1. As polypharmacy is a main risk factor for drug interactions [31, 32] and adverse drug reactions [33], prescribers are encouraged to restrict the number of medicines they prescribe as few as possible.

WHO recommends that all medicines should be prescribed by generic name, as generic name is much simpler and cheaper than medicines prescribed with brand names [21]. Besides, generic name prescribing promotes better communication among health care providers, which is good for the safety of the patients [2]. In this study, the percentage of drugs prescribed by generic name was 91.5%, a value below the WHO standard value of 100%. This result is very similar to a systematic review done in Ethiopia, which was 91.6% [34]. But, higher

Table 6 Predictors of antibiotics prescribing

Variables	Category	Odds ratio (95% CI)			
		COR	*P*-value	AOR	*P*-value
Age (years)	< 18	15.200 (7.553–30.589)	**< 0.001**	9.830 (4.062–23.786)	**< 0.001**
	18 to 64	2.092 (1.141–3.836)	**0.017**	1.475 (0.698–3.119)	0.309
	≥ 65	1 (ref.)	-	1 (ref.)	-
Sex	Male	1 (ref.)	-	1 (ref.)	-
	Female	1.244 (0.900-1.719)	0.186	1.369 (0.857–2.185)	0.188
Number of diseases	1 disease	1 (ref.)	-	1 (ref.)	-
	> 1diseases	1.745(1.103–2.760	**0.017**	1.514 (0.781–2.935)	0.220
Number of drugs per encounter	1 drug	1 (ref.)	-	1 (ref.)	-
	2 drugs	2.523 (1.750–3.638)	**< 0.001**	2.690 (1.625–4.453)	**< 0.001**
	3 drugs	2.596 (1.561–4.318)	**< 0.001**	3.247 (1.571–6.708)	**0.001**
	≥ 4 drugs	0.825 (0.284–2.397)	0.724	2.232 (0.465–10.724)	0.316
Infectious and parasitic diseases (A00–B99)	Absent	1 (ref.)	-	1 (ref.)	-
	Present	2.747(1.794–4.207)	**< 0.001**	1.258 (0.717–2.206)	0.423
Diseases of the respiratory system (J00–J99)	Absent	1 (ref.)	-	1 (ref.)	-
	Present	8.627(5.466–13.613)	**< 0.001**	3.750 (2.136–6.584)	**< 0.001**
Diseases of the nervous system (G00–G99)	Absent	14.575 (3.464–61.321)	**< 0.001**	16.693 (3.461–80.522)	**< 0.001**
	Present	1 (ref.)	**-**	1 (ref.)	**-**
Diseases of the circulatory system (I00–I99)	Absent	10.822 (4.271–27.418)	**< 0.001**	8.681 (3.094–24.362)	**< 0.001**
	Present	1 (ref.)	**-**	1 (ref.)	**-**
Mental and behavioral disorders (F00–F99)	Absent	14.575 (3.464–61.321)	**< 0.001**	14.124 (2.710–73.610)	**0.002**
	Present	1 (ref.)	**-**	1 (ref.)	**-**
Endocrine, nutritional and metabolic diseases (E00-E90)	Absent	18.461 (6.650-51.244)	**< 0.001**	16.452 (5.413–50.010)	**< 0.001**
	Present	1 (ref.)	-	1 (ref.)	-

Bold values indicate that there was statistically significant association between independent variables and antibiotics prescribing

generic prescribing was reported from studies in Jordan (100.0%) [7] and north Ethiopia (97.5%) [23] while lower levels were reported from studies in Pakistan (56.6%) [9] and Sri Lanka (35.5%) [4].

In this study, only 43 (7.2%) prescription encounters included injectable medicine (s), a value much lower than the WHO standard (13.4–24.1%). The finding was also lower compared to studies from various parts of Ethiopia including 13.5% in Dire Dawa [35], 15.9% in Mekelle [23], 26.5% in eastern Ethiopia [3] and 44.77% in Dire Dawa [36]. The current study was conducted in outpatient setting where injections are reasonably expected to be low. This may be one possible reason for low prescribing rate of injection in this study. Inpatient pharmacy of Adigrat general hospital had been either partially or totally out of service for the last three years due to the war crisis in Tigari, making it difficult to retrieve prescription information. Overuse of injectable medicine may lead to a higher probability of transmission of hepatitis, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and other blood borne diseases [5].

Regarding essential medicine prescription, the percentage of medicines prescribed from the Ethiopian EML was relatively frequent (98.7%). Although this value did not meet the WHO optimal value (100%), it is higher than the WHO African regional value of 89.0% [22]. Similar findings to our result were reported as 98.8% in Pakistan [9] and 99.2% in Dire Dawa, Ethiopia [35]. In contrast to our finding, some previous studies carried out in Jordan [7], Sri Lanka [4] and Ghana [28] showed lower values (54.1 – 88.1%). Prescribing medicines from the EML is a crucial step to provide safe, efficacious and cost effective medicines to the individual patient and to the community at large [1, 21]. In resource limited health facilities like in our study area, prescribing medicines from the EML is particularly important for the patients as far as the cost of medicines is concerned. The relatively high practice of prescribing medicines from EML observed in this study is, therefore, quite promising, which needs further encouragement.

In this study, a total of 340 antibiotics were prescribed. The percentage of prescriptions with least one antibiotic prescribed was 44.5%. This is almost twice the average WHO standard value of 20–26.2%. The current finding is also higher than the result of studies done in different parts of Ethiopia, which was 24.85% in southwest Ethiopia [37], 27.62% in Dire Dawa [36], 32.05% in Mizan-Tepi [38], 32% in north Ethiopia [39] and 37.5% in Gondar [40]. But, our finding is close to previous findings reported from Dire Dawa [35] and from systematic review of 11 African countries [22], where percentage of prescriptions with antibiotics were 47.8% and 46.8%, respectively. On the other hand, inconsistent with our result, higher percentage of encounters with antibiotics were reported from different parts of the world as; 88.0% in Tanzania [41], 52.4% in Pakistan [12], 59.9% in Ghana [28], 58.2% in Mekelle, Ethiopia [23] and 78% in Bangladesh [42].

The discrepancy in the rate of antibiotics prescriptions could be due to potential differences between our study and the contrasted studies in terms of level of vigilance of prescribers, epidemiology of the infectious diseases, the sample size, number of health facilities included, prescribing guidelines and socio-demographics of the study populations. Unlike to our study, some of the aforementioned studies included more than one health facility [23, 28, 37, 41], while the other studies used sample size either <600 prescription encounters [36, 38, 39, 42] or >600 prescription encounters [12]. These could contribute for the observed differences in patterns of antibiotics prescription.

Penicillins (J01C) (34.4%), macrolides (J01F) (23.8%) and fluoroquinolones (J01M) (17.1%) were the most commonly prescribed antibiotics classes in the present study, which combinely covered 75.5% of the total antibiotics prescribed. Moreover, amoxicillin (22.4%), azithromycin (19.4%) and ciprofloxacin (13.8%) were the top three frequently prescribed at single antibiotic level. Consistent with our finding, previous studies from southwest Ethiopia [24], Tanzania [43], Botswana [44] and Addis Ababa [45] reported that penicillins were the first commonly prescribed classes of antibiotics (32.7 –**5**1.9%). In contrast, previous study found that cephalosporins as a class and ceftriaxone at drug level covered 81.5% and 71.8% of the antibiotic prescriptions, respectively [12]. On the other hand, the most commonly prescribed drug was amoxicillin in both the studies from Botswana (28.4%) [44] and Addis Ababa (44.8%) [45]. This is similar to our finding. Besides, ciprofloxacin (21.1%), amoxicillin (11.8%) and azithromycin (10.6%) were the top three frequently prescribed in previous study [24], which is similar to our finding despite the order of these three drugs.

The current study indicates that almost three-fourth (75.5%) of the antibiotics prescription was covered only by three classes of antibiotics, namely, penicillins, macrolides and fluoroquinolones. Besides, amoxicillin, azithromycin and ciprofloxacin combinely accounted for more than half (55.6%) of the total antibiotic prescriptions. Such excesive use of antibiotics only from few types of antibiotics can worsen the emergence of resistant bacteria against these antibiotics in our setting.

Clinicians' practice to prescribe antibiotics merely based on assessment of patient's symptoms is a common cause for over prescription of antibiotics, especially in resource limited countries. This is, in part, due to scarcities of modern diagnostic tests to confirm infectious diseases [14]. Use of antibiotics for self-limiting diseases is also other factor for over prescription of antibiotics [11]. The perception of both health professionals and the public as antibiotics are powerful medicines may also contribute to the over-prescription of antibiotics [28].

But in context of our study, the high rate of antibiotics prescription may also indicate the high burden of infectious diseases in Tigrai, Ethiopia. So, the results should be interpreted carefully. Neverthless, indiscriminate use of antibiotics is a key driver for the emergence of AMR, which obligates us to sake new drugs. Unfortunately, a truly new class of antibiotics has not been discovered in the last decades, and there are still commercial challenges to develop new antibiotics [11, 46]. The excessive use of antibiotics may aggravate the rapidly emerging AMR in Ethiopia [47], including in Tigrai region of Ethiopia [48]. So, the prescribers herein the study area should adhere antibiotics guidelines and be vigilant that antibiotic prescriptions should be supported by up-to-date surveillance.

"AWaRe" classification of antibiotics

In the current study, the "Access" group covered 54.4% of the antibiotics, whereas the "Watch" group accounted for the rest 45.6% of the total antibiotics prescription as per the "**AWaRe**" classification. No antibiotic was prescribed from the "Reserve" group. This result is close to a study done in eastern Ethiopia which found that 55.3% and 43.1% of the antibiotics were from the "Access" and Watch" groups, respectively [35]. Higher proportion of antibiotics in the "Access" group was reported in some African countries (73.9 – 90%) [44, 45, 49, 50], which is inconsistent with our finding. However, no antibiotic was in the "Reserve" group in all these studies, which is similar to the current study. The use of antibiotics in the "Watch" category was 50.69% in a study from southwest Ethiopia [24], which is higher than our result.

The "Access" antibiotics have narrow spectrum of activity with lower potential for antimicrobial resistance. Whenever appropriate, antibiotics in the "Access" group should be preferred over "Watch" groups concerning the spread of antibiotic resistance [51, 52]. The "Watch" group antibiotics, on the other hand, have higher resistance potential and hence, they should be prioritized as key targets of antibiotics stewardship programmes and monitoring to prevent their overuse [16]. The use of "Watch" antibiotics should be discouraged unless clearly clinically required [18]. Hence, the WHO recommends that at least 60% of all antibiotics use should be from the "Access" group to contain trising AMR and make antibiotic use more effective [11, 52].

The current study showed that the use of "Watch" group antibiotics in the study hospital was relatively high. This may be an alarm for clinicians to focus on the evidence based use of these very crucial antibiotics found in the "Watch" group. Besides, ciprofloxacin and azithromycin accounted for 33.5% and 42.6% of total antibiotics in the “Watch” group, respectively. This may indicate that the appropriate use these drugs should be closely monitored in the outpatient setting of the hospital.

Predictors of antibiotic prescribing

Our analysis using multivariate logistic regression showed that age of patients was significantly associated with antibiotics prescribing ($P < 0.001$). In individuals under 18 years old, the odds ratio of antibiotics prescribing increased by almost 10 times compared to those $\geq$ 65 years old. This is in line with the studies from Addis Ababa [45], Dire Dawa, Ethiopia [35], Eritrea [30] and Ghana [28]. In these studies, antibiotics prescribing pattern decreased significantly with increase in patient’s age, which is consistent with our finding. The high level of antibiotics prescribing in this age group (in our study) could be partly due to the high burden of lower respiratory tract infection in the pediatric patients in Ethiopia [53]. This is further supported by our finding that this disease showed significant association with antibiotics prescribing. But, unlike to our result, patient’s age did not show statistically significant association with antibiotics prescribing in previous studies [41, 54]. Apart from the risk of AMR, children are more vulnerable for adverse drug reactions than adult patients due to that they can react differently to drugs than adult populations attributed to pharmacokinetics differences [55]. So, the clinicians in our study area should remain vigilant especially when prescribing antibiotics to the pediatrics age group.

In previous similar studies, gender was significantly associated with antibiotics prescribing [41, 50], which is inconsistent with our study. The current study showed that prescribing two medicines per prescription had significant association with antibiotics prescribing. Accordingly, the odds ratio of prescribing antibiotics was increased by almost 3 times in subjects with two medicines prescribed compared to those having only one medicine. This is similar to previous studies done in Eritrea [30] and elsewhere in Ethiopia [35] where the odds of antibiotics prescribing was significantly inceased as the number of medicines per prescription increased.

In the present study, being diagnosed with diseases of the respiratory system (J00–J99) increased the odds of prescribing antibiotics by almost 3.8-fold (AOR: 3.75, CI: 2.136–6.584) compared when there was no diagnosis of this disease. In previous study, individuals diagnosed with respiratory tract infection had increased odds of antibiotics prescribing by about 7.3 (AOR: 7.27, CI: 1.86, 11.99) compared to those with no diagnosis of respiratory tract infection, which is in line with the finding of the present study. In the current study, lower respiratory tract infection (pneumonia) was the most prevalent disease for which antibiotics were prescribed. This could be attributable to the high level of antibiotics prescribing for diseases of the respiratory system. But, inappropriate use of antibiotics to treat self-limiting upper respiratory tract infections like otitis media could be other reason, as our analysis was done to determine the association between antibiotics prescribing and diseases of the respiratory system in general [11].

On the other hand, some of the ICD-10 diseases were protective against antibiotics prescribing in our study. Subjects with no diagnosis of endocrine, nutritional and metabolic diseases were about 16 times more likely to receive antibiotics. There was also increased odds of prescribing antibiotics with the absence of diseases of the nervous system (AOR: 16.693, CI: 3.461–80.522), mental and behavioral disorders (AOR: 14.124, CI: 2.710 −73.610) and diseases of the circulatory system (AOR: 8.681, CI: 3.094–24.362).

Strengths and limitations

To our best knowledge, this is the first study conducted to determine the prescription patterns using WHO/INRUD prescribing indicators in Adigrat general hospital of Tigrai, north Ethiopia. But, the study has certain limitations that need to be considered when interpreting the findings. First, patient care indicators and healthcare facility indicators were not assessed. Second, the retrospective nature of our study may not provide sufficient evidences about the patient profile as we might have missed unrecorded data. Besides, our study was conducted only in one health facility, which makes it difficult to compare with other health facilities present in the study surroundings. Nevertheless, the study highlighted some important characteristics of WHO/ INRUD prescribing indicators in Adigrat general hospital including the WHO “**AWaRe**” classification of antibiotics. Therefore, this study can serve as a baseline for the clinicians working herein and for future comprehensive studies on drug utilization pattern in the hospital.

Conclusion

Our study showed that the prescription indicators in Adigrat general hospital of Tigrai, north Ethiopia showed deviations from WHO recommendations. The percentage of prescriptions with antibiotic was 44.5%, which is far from the WHO standard (20–26.8%). Only 54.4% of the antibiotics prescribed were from “Access” group, a value below the WHO standard (at least 60%) while the “Watch” group covered 45.6% of the total antibiotics prescription. The excesive use of antibiotics from few types of antibiotics and from the “Watch” group may worsen the emergence of AMR. The percentage of medicines prescribed by generic name was also below WHO optimal value of 100%. The percentage of prescriptions with injection was lower than WHO standard value

(13.4–24.1%). But, the average number of medicines per prescription was within the WHO standard value and the percentage of medicine from EML was almost within the WHO standards. Antibiotic prescribing was significantly associated with age and number of medicines per encounter as well as with certain diseases like diseases of the respiratory system. To meet the WHO recommendations given for the core prescribing indicators as well as for "**AWaRe**" classifications, the clinicians working in the hospital should comply with WHO Guidelines, National Standard Treatment Guidelines and other standard guidelines. The hospital administrators should foster the diagnostic protocols to confirm infectious diseases so as to reduce overuse of antibiotics. The establishment of antibiotics stewardship programmes in the hospital further helps to promote appropriate use of the antibiotics and to contain spread of AMR.

Abbreviations

AMR	Antimicrobial resistance
ATC	Anatomical Therapeutic Chemical classification
AWaRe	Access, Watch and Reserve groups
EML	Essential Medicines List
ICD-10	International Classification of Diseases version 10
INRUD	International Network of Rational Use of Drugs
SD	Standard deviation
WHO	World Health Organization

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Author contributions
GGH conceptualized and developed research methodology of the study. MGW and SAG developed the study proposal and collected data. BGW and GGH performed the statistical analysis and prepared the manuscript. All authors read and approved final version of the manuscript.

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Data availability
All the data used to support findings of this study are available from the corresponding authorwhen reasonable requests come from concerned body.

Declarations

Ethics approval and consent to participate
An ethical approval was obtained from the Research and Community Service Office of the College of Medicine and Health Sciences of Adigrat University, with a registration number of AGU/CMHS/RCSH/0017/24. Permission was, then, obtained from the respective hospital administrators of Adigrat general hospital before commencement of the study. Informed consent was not obtained from the patients as this was retrospective cross-sectional study where secondary data was collected from the patients' prescription paper after the patients had already been discharged. However, confidentiality of patients and health professionals was ensured accordingly where data was anonymously used.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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