BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers’ comments and the authors’ responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open’s open peer review process please email info.bmjopen@bmj.com
Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

| Journal          | BMJ Open               |
|------------------|------------------------|
| Manuscript ID    | bmjopen-2020-045805    |
| Article Type     | Original research      |
| Date Submitted   | 14-Oct-2020            |
| by the Author    |                       |
| Complete List of Authors | tasew, segen; Mekelle University College of Health Sciences, clinical pharmacy abraha, Haftom; Mekelle University College of Health Sciences, clinical pharmacy gidey, kidu; Mekelle University College of Health Sciences, clinical pharmacy; Gebre, Abadi; Department of Pharmacology and Toxicology, College Health Sciences, Mekelle University, Mekelle, Ethiopia, pharmacology and clinical toxicology |
| Keywords         | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, CLINICAL PHARMACOLOGY |
I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author’s Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.
Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

Segen Gebremeskel Tassew1*, Haftom Niguse Abraha1, Kidu Gidey,1 Abadi Kahsu Gebre2

1. Department of Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Ethiopia
2. Department of pharmacology and clinical toxicology, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Ethiopia

Corresponding author: kidu Gidey email: kidupharm@gmail.com

Abstract

Objective: This study aimed to assess drug use using the World Health Organization (WHO) drug use indicators in selected general hospitals in Tigray region, Ethiopia.

Materials and Methods: A cross-sectional study was conducted from March 1, 2019, to August 30, 2019, at both Mekelle and Quiha public general hospitals. A total of 1,200 randomly selected prescription papers were assessed using WHO prescribing indicators. In addition, 200 patients who visited both outpatient clinics and hospital pharmacies were interviewed and the prescriptions were evaluated using WHO patient care indicators. Moreover, the hospitals were evaluated according to WHO facility indicators. The collected data was entered into epi-info version 7 and analyzed using SPSS for Windows, version 21.

Result: The average number of medicines per prescription was 1.69 ((±0.81). Prescriptions with antibiotics and injectable were 58.15 % and 15.9 % respectively. The percentage of medicines prescribed with a generic name and those from the essential medicines list of Ethiopia were 974 (97.5%) and 970 (88.1%) in Mekelle and Quiha hospital respectively. In terms of patient care, average consultation and dispensing times were 6.56 (±3.48) minutes and 22.79 (±21.7) seconds.
respectively. The proportion of drugs actually dispensed, those correctly labeled as well as the proportion of patients knowing their dosing regimen were 81.2%, 32.7%, and 56.9% respectively. Only 77.5% of key drugs were available in stock during the study period.

**Conclusion:** In our study both prescribing and patient care indicators showed significant deviation from the World Health Organization's optimal levels indicating the presence of inappropriate medicine use in the hospitals. Strategies to improve both prescribing and dispensing practice should be implemented for promoting rational use of medicines.

Keywords: Drug use evaluation, Prescribing Indicator, Patient Care Indicators, Facility Indicators

**Strengths and limitations of this study**

- As strengths, the study used all the three WHO core drug use indicators to evaluate the drug use.
- The study included a good number of prescriptions and patients for drug use evaluation.
- The study provides alarming information for hospitals and all relevant stakeholders on the use of antibiotics which represents a very high percentage per prescription.
- The study does not examine the cause of irrational drug use and did not confirm that drug use was consistent with the diagnosis.
- The study period was short.

**Introduction**

The rational use of drugs depends on rational prescribing, correct dispensing and adherence to treatment by patients (1). According to the World Health Organization (WHO), a medicine is used rationally if patients received the appropriate medicines, in doses that meet their individual requirements, for an adequate period of time and with an affordable cost (2). The concept of
rational drug use can be summarized as the right medicine at the right dose by the right route at
the right time for the right patient (‘five rights’) (3).

On the contrary, irrational, inappropriate, improper, or incorrect use of medicines is termed to have
occurred when one or more of the above-mentioned conditions are not met (2). Irrational use of
medicines is a global challenge, especially in developing countries. Different factors are attributed
to the irrational use of medicines including patients, prescribers, workplace, supply system which
encompasses industry influences, regulation, drug information and misinformation, and
combination of these factors (4). Irrational prescribing is a major problem encountered and it is
due to lack of knowledge about medicines, unethical medicine promotions and bad prescribing
habits of clinicians (5, 6).

Medicine utilization studies are important tools to evaluate whether medicines are properly utilized
in terms of efficacy, safety, convenience and economic aspects at all levels in the chain of medicine
use (7). In order to improve medicine use practices, objective method of assessments at health
facilities is very important as it helps to improve use patterns and prescribing behaviors. WHO
core drug use indicators are developed intended for this purpose by the WHO Action Program on
Essential Drugs and International Network for Rational Use of Drugs (INRUD). These indicators
are highly standardized that do not need national adaptation and are recommended to be included
in any medicine use evaluation (8).

Prescribing indicators include average number of medicines prescribed per encounter, percentage
of those prescribed by generic name and those from national essential medicines list (EML),
percentage of encounters with antibiotics and those with injections prescribed. Patient care
indicators, on the other hand, include average consultation and dispensing times, percentage of
medicines actually dispensed and of those adequately labeled, as well as patients' knowledge of
correct dosage. Facility indicators assess the availability of copy of EML and those of key medicines available in the health facility (9).

Ethiopia has a national drug policy introduced in 1993 which aims to meet the demand for essential medicines together with appropriate use, making them affordable to the public as well as ensuring their safety, efficacy, and quality. The policy also encourages domestic manufacturing, enhancing manpower training and research and development of medicines as well as devising ways to integrate traditional medicines into conventional medicine as objectives (10). Despite these objectives’ studies conducted so far reported gaps in rational medicine use with a high percentage of encounters with antibiotics and injections prescribed (11, 12).

Considering the very large population size of Ethiopia and the diversity of geographic areas, there are very few studies on medicine use conducted so far. Therefore, this study was carried out to evaluate drug use and contribute in narrowing of the information gap in the documentation of drug use patterns in Ethiopia using WHO’s core drug use indicators.

**Methods and Materials**

**Study setting and period**

The study was conducted at Mekelle and Quiha general hospitals between March 1, 2019 and August 30, 2019. Both hospitals are located in Mekelle which is 783km from the capital city of Ethiopia.

**Study design and population**

A cross sectional study was employed. The target population of this study were all patients who were visiting outpatient department of Mekelle and Quiha hospital during the study period.
Those patients 18 years and above with a prescription recorded from 2017 to 2019 were included. Patients who were not willing to participate were excluded from the study.

**Sampling technique and procedure**

World Health Organization recommends assessments of at least 600 prescriptions and 100 patients per each hospital for assessment of prescribing, and, patient care indicators respectively. Accordingly, we had included 600 randomly selected sample prescriptions among those recorded from 1 January 2017-1 June 2019. Twenty key drugs were selected from each hospital as per WHO recommendation which is a minimum of 15 essential drugs in each health facility (9).

**Data collection instruments and process**

Three well-trained pharmacy personnel were recruited and deployed in each hospital. One of them was collecting prescribing indicators by using prescriptions and prescription registration books, while the others were collecting the patient care indicators and the facility indicators. Specific types of data necessary to measure the prescribing indicators were recorded for each prescription and entered to the prescribing indicator form.

Data on medicine use pattern was collected by using WHO's prescribing and patient care indicators. In measuring the former, the average number of medicines prescribed per encounter, the percentage of medicines prescribed with generic names and those prescribed from EML, the percentage of prescription encounters which ended up with antibiotics and those with injections prescribed were collected. In collecting data on these indicators, immunizations of children were not considered as injections. In measuring the proportion of medicines prescribed with generic names, the EML of Ethiopia was used as the main source of generic names (13).
For patient care indicators measurement, data on average consultation and dispensing times, percentages of medicines actually dispensed and of those adequately labeled as well as patients' knowledge of dosage schedule of medicines were collected. In this part of the study patients aged 18 or older were included. Consultation time and dispensing time was obtained by recording the time that the patient spent with his physician and pharmacist respectively.

In determining patients’ knowledge of their dosage regimen, patients were asked to explain what they know about the medicine dispensed for them.

Facility indicators were availability of formulary, essential drugs, standard treatment guidelines, and key drugs observed at the time of the visit.

**Operational definitions**

Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and effectiveness of a medications to improve patient care.

**Percentage of drugs prescribed by generic name:** It measures the tendency to prescribe by generic name.

**Percentage of drugs prescribed from list of essential drugs:** It measures the degree to which practices conform to a national drug policy.

**Average number of drugs per encounter:** Average number of drugs per encounter measures the degree of poly pharmacy.

**Average consultation time:** The average time that physicians spends with patients. It doesn’t include waiting time.

**Average dispensing time:** The average time that the pharmacists spend with patients while actually dispensing the medications.
Data analysis procedure

The data collected were entered to, cleaned and analyzed using Statistical Packages for Social Sciences (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were described using frequency, percentage, mean and standard deviation (SD).

Patient and Public Involvement

Patients and/or the public were not directly involved in this study.

Results

Prescribing indicators

Six hundred prescriptions from each hospital were assessed. On average, 1.69 (±0.81) drugs were prescribed and 49.7% of the prescriptions contain one drug followed by two drugs (35%) (Table 1).

Table 1: Number of drugs per prescribing encounters (degree of polypharmacy) in Mekelle and Quiha hospital March 1, 2019 – August 30, 2019 (n=1200)

| Number of drugs | QH     | MH     | Overall result | WHO   |
|-----------------|--------|--------|----------------|-------|
| One             | 306(51)| 286(47.7) | 592(49.7)     |       |
| Two             | 206 (34.3) | 214(35.7) | 420(35)      |       |
| Three           | 72 (12) | 82(13.7) | 154(12.85)    |       |
| Four            | 15 (2.5) | 17(2.8) | 32(23.5)      |       |
| Five            | 1(0.2)  | 1(0.2)  | 2(0.2)        |       |
| Average         | 1.67 (±0.8) | 1.72(±0.82) | 1.69(±0.81) ≤ 2 (1.6–1.8) |     |

QH: Quiha hospital, MH: Mekelle hospital
From the total of the prescriptions, 2028 drugs were prescribed of which 1944 (92.8%) of the drugs were prescribed in generic name. More than fifty percent (58.15%) of the prescriptions contain antibiotics while 191 (15.9%) include at least one injectable medication (Table 2).

Table 2: Percentages of encounters with generic prescription, antibiotics, and injections

| Prescribing indicators                                      | QH  | MH  | Overall result | WHO standard  |
|------------------------------------------------------------|-----|-----|----------------|--------------|
| Number of drugs prescribed                                 | 999 | 1029| 2028           |              |
| Number of drugs prescribed by generic name                 | 974 | 970 | 1944           |              |
| Percentage of drugs with generic prescription              | 97.5| 88.1| 92.8           |              |
| Total number of encounters with antibiotic                 | 392 | 306 | 698            |              |
| % of encounters with antibiotic                            | 65.3| 51  | 58.15          | <30 (20–26.8%)|
| Encounters with injections                                 | 56  | 135 | 191            | (13.4–21.1%) |
| % of encounters with injections                            | 9.3 | 22.5| 15.9           | (13.4–21.1%) |
| Percentage of drugs on essential drug list                 | 974 | 930 | 94%            | 100%         |

QH: Quiha hospital, MH: Mekelle hospital

Amongst antibiotics prescribed, 279 of them were amoxicillin or Amoxicillin / Clavulanic acid followed by Ceftriaxone (100) (Table 3).
Table 3: Antibiotics prescribed in Mekelle and Quiha hospital

| Antibiotics                        | Frequency | Overall |
|------------------------------------|-----------|---------|
|                                    | QH        | MH      |
| Acyclovir                          | 2         | -       | 2       |
| Albendazole                        | 16        | 7       | 23      |
| Amoxicillin                        | 160       | 76      | 236     |
| Ampicillin                         | 1         | 9       | 10      |
| Amoxicillin /Clavulanic acid       | 15        | 28      | 43      |
| Azitromycin                        | 19        | 16      | 35      |
| sulfamethoxazole/trimethoprim      | 13        | 11      | 24      |
| Ceftriaxone                        | 33        | 57      | 90      |
| Cephalexin                         | 20        | 35      | 55      |
| Ciprofloxacin                      | 56        | 44      | 100     |
| Clarithromycin                     | 8         | 1       | 9       |
| Clotrimazole vaginal supp.         | 3         | -       | 3       |
| Cloxacillin                        | 21        | 11      | 32      |
| Coartem                            | 2         | -       | 2       |
| Doxycycline                        | 13        | 7       | 20      |
| Acetazolamide                      | 3         | -       | 3       |
| Erythromycin                       | 2         | 2       | 4       |
| Fluconazole                        | 1         | -       | 1       |
| Gentamycin                         | 1         | 2       | 3       |
| Ketoconazole                       | 4         | -       | 4       |
| Mebendazole                        | 11        | 5       | 16      |
| Metronidazole                      | 42        | 40      | 82      |
| Norfloxacin                        | 17        | 11      | 28      |
| Praziquantal                       | 1         | -       | 1       |
| Crystalline Penicillin             | -         | 1       | 1       |
| Ceftazidime                        | -         | 2       | 2       |
| Tinidazole                         | 14        | 17      | 31      |
| Pantoprazole                       | 1         | -       |         |
Patient care indicators

On average each person spends around 7 minutes with the physician while only 22 seconds with pharmacist. 81.2% of the prescribed drugs were actually dispensed of which 32.7% of them adequately labeled and 56.9% of the patients knows about the correct dosage of their medications (Table 4).

Table 4: Percentage and average descriptions of patient care indicators

| Patient care indicators                  | QH        | MH        | Overall   | WHO standard |
|-----------------------------------------|-----------|-----------|-----------|--------------|
| Average consultation time (minute)      | 3.66±2.19 | 9.46±4.77 | 6.56±3.48 | 10 min       |
| Average dispensing time (Sec)           | 21.53±19.89 | 24.04±23.5 | 22.79±21.7 | >180 s       |
| Total number of drugs prescribed        | 189       | 171       | 360       |              |
| Total number of drugs dispensed         | 170       | 124       | 294       |              |
| Percentage of drugs actually dispensed  | 89.9      | 72.5      | 81.2      | 100%         |
| # of drugs adequately labelled          | 29        | 50        | 79        |              |
| Percentage of drugs adequately labelled | 15.4      | 50        | 32.7      |              |
| Knows dosage                           | 25(25%)   | 48 (88.8%) | 56.9      |              |

QH: Quiha hospital, MH: Mekelle hospital

Health facility indicators

Both Mekelle and Quiha hospital have their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals on average 77.5% of them were available in stock (Table 5).
Table 5: Availability of the key drugs in the hospitals

| List of key drugs          | Availability in QH | Availability in MH |
|----------------------------|--------------------|--------------------|
| Amoxicillin/clavulanic acid | ✓                  | X                  |
| Ciprofloxacin tablet       | ✓                  | ✓                  |
| Cloxacillin capsule        | ✓                  | ✓                  |
| Azitromycin               | ✓                  | X                  |
| Diclofenac injection      | ✓                  | ✓                  |
| Diclofenac tablet         | ✓                  | ✓                  |
| Tramadole                 | X                  | ✓                  |
| Metronidazole             | ✓                  | ✓                  |
| NPH                       | ✓                  | ✓                  |
| Nefidipine                | X                  | ✓                  |
| Laxis                     | X                  | ✓                  |
| Spironolactone            | X                  | ✓                  |
| Ceftriaxone               | ✓                  | X                  |
| Vancomycin                | ✓                  | ✓                  |
| Metformin                 | ✓                  | ✓                  |
| Enalapri                  | ✓                  | ✓                  |
| Cephalexin                | ✓                  | ✓                  |
| Ferrous sulfate           | ✓                  | ✓                  |
| Paracetamol syrup         | ✓                  | X                  |
| Amilodipine               | ✓                  | X                  |

QH: Quiha hospital, MH: Mekelle hospital
Discussion

In the present study among the prescribing indicators, the average number of medicines per prescription was found to be within the WHO's acceptable range of 1.6 to 1.8 (14). This figure has showed a good trend in preventing risks associated to polypharmacy. The finding was also comparable with studies done in different parts of Ethiopia including Jimma (1.59) (15), Hawassa University Teaching Referral (1.9) (11) and Bahir Dar hospital (1.8) (12). However, compared to findings from other studies in Ethiopia including Debre Tabor Hospital (2.2) (11), Hiwot Fana specialized University (2.49) (16) and Karamara general hospital (2.46)(17) as well as those done abroad like in Iran (3.03)(18), South Africa (3.2)(19) and India (2.9) (20); the figure in the present study recorded lower average number of medicines per prescription.

In terms of percentage of medicines prescribed by generic name, the result of the present study (92.8%) is lower compared to WHO's standard (100%) and it is in line with study done at Hawassa University Hospital (98.7%) (11), Hiwot Fana specialized University hospital (97.4 %) (16) as well as a finding in selected health centres of eastern Ethiopia (97 %) (21). This indicates that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution. So this cost ineffective prescribing practice will promote noncompliance. However, it is higher compared to findings of, India (13.34%)(20), South Africa (45.2%) (19), Nepal (13%) (22) and Nigeria (49.5%) (23).

The percentage of encounters with antibiotics prescribed, which is 58.15 % in the present study, is higher compared to the WHO's standard recommendation of 20 to 26.8% per prescription (8), but it is comparable with study conducted in public hospitals in Eastern Ethiopia (57.87) (17) and Hawassa teaching referral hospital (58.1) (11). However, it showed lower figure compared to a study conducted in selected health centres in Eastern Ethiopia (85.5) (24). This huge variation can
be explained due to the high prevalence of infectious disease in developing countries that may lead to prescribing of antibiotics, however high antibiotic prescribing could lead to antimicrobial resistance which is an eminent threat of global health (25).

The percentage of encounters with injection prescribed in this study was within WHO standard range, from 13.4% to 21.1%. This good practice will prevent patients from injection site related infections and injection site pain. However, there is a gap in prescribing according to essential medicine list of Ethiopia compared to the WHO standard of a 100% (8) and to that of the national assessment results of 2003 (99%) (26), but it was similar to the finding reported in Hawassa (96.6%) (11).

In this study the average consultation time that the prescribers spent with patients was approximately 7 minutes and this is comparable with findings conducted in Saudi Arabia (7.3 minutes) (27). However, it is higher in comparison with studies conducted in public hospital (4.6 minutes) (28) and health centres in eastern Ethiopia (24). The duration, however, doesn't seem to be sufficient for conducting appropriate diagnosis and provide the necessary management. High patient load could have contributed to this less than optimal duration of consultation time.

The average dispensing time recorded in the present study was approximately 23 seconds. This is very low compared to the standard WHO recommendation which is 18 minutes (14), study conducted in public hospital (276.5) (28) and health centres (162) (28) in eastern Ethiopia. The lower the dispensing time the poorer would be the understanding of the patients about their medication which this may lead to frequent encounter of drug therapy problems.

The percentage of drugs actually dispensed out of the total drugs prescribed to the patients stood at 80 % compared to the recommended 100% (6). This was due to lower than availability of
medicines as the result of frequent stock out of medicines. This is also associated to availability issues at national level as well as to medicine supply system problems.

Regarding the adequacy of labeling of medicines dispensed, only slightly over one-third of medicines were appropriately labeled which is far to the recommended level 100% (8). High patient load encountered at outpatient pharmacy department and negligence of the pharmacists together with low concern for the issue from the hospital side could be implicated to the very low level of performance in this indicator.

In this study only about half of the patients knew the dosage schedules of their medicines prescribed to them which is far below the desired 100%. The low level of awareness of patients could be attributed to the short dispensing time which hinders appropriate transfer of advice by pharmacy professionals to patients as well as the rare practice of adequate labeling of medicines.

Both of the hospitals involved in the current study have their own essential drug list and standard treatment guideline. Only 7.5% of key drugs were in stock and this is low with 100% WHO recommendation. Absence of key drugs may impair patient care and compromise patient quality of life.

Finally, our study is not without limits. The study only used two centers and it was better to use more centers. The study also does not examine the cause of irrational drug use or confirm that the drug use was consistent with the diagnosis. It was also better if the study was conducted over a longer period.

**Conclusion**

On the basis of the current findings, the prescribing practices for antibiotic use, prescribing from EDL and injection use showed a great deviation from the standards recommended by WHO. Over
use of antibiotics facilitate the emergence of antimicrobial resistance which is a major challenge for our globe. Generic prescribing showed little deviation from the standard whereas the average number of drugs per encounter lay within the range of WHO. Relatively low generic prescribing compared with WHO standard coupled with shorter consultation and dispensing time may lead to frequent encounters of drug therapy problems. Therefore, having this as a baseline data interventional strategy should be designed to reverse the existing problems (managerial, educational and regulatory) and modernize the drug utilization patterns on public hospitals.

**Abbreviation and acronyms**

DUE: Drug use evaluation, EDL: Essential drug list, WHO: World health organization, HFSUH: Hiwot Fana Specialized Hospital, QH: Quiha Hospital, MH: Mekelle Hospital, INRUD: International Networks for Rational use of medicines.

**Ethical Considerations**

The study was approved by the institutional review board of Mekelle University (reference number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health bureau. During data collection on patient care indicators, a written consent was obtained from each participant after provision of all the necessary information. In addition, the data collected in the study did not use patient identifiers and were kept strictly confidential and were used only for the purpose of the study.

**Acknowledgments**

The authors would wish to thank all the staff members of Mekelle and Qiha hospitals for their sincere cooperation and support.
Competing interests

The authors declare that they have no competing interests. The funder of this study has no any involvement in this study.

Availability of data and materials

The data of this study are available from the corresponding author on reasonable request.

Funding

This study was funded by college of health sciences, Mekelle university small scale grant with registration number of CRPO/CHS/Young/Recurrent/ 008/2011.

Patient consent for publication

Not required

Author’s contribution

SG and AK designed the study, supervising data collection, conducted data analysis, wrote the first draft of the manuscript. SG, KG, AK and HN provide critical comments, revised and finalized the manuscript. All authors read and approved the final manuscript.

Reference

1. Timmermans A, A. S. Rational use of drugs. In: United Nations High Commissioner for Refugees. Drug Management Manual. In: Refugees UNHCf, editor. 2006. p. 87-104.

2. Organization WH. The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experiences. In: organization WH, editor. 2012.

3. Mehta S, Gogtay N. From the pen to the patient: Minimising medication errors. Journal of Postgraduate Medicine. 2005;51(1):3.
4. Chaturvedi V, Mathur A, Anand A. Rational drug use–As common as common sense? Medical journal, Armed Forces India. 2012;68(3):206.

5. De Vries T, Henning RH, Hogerzeil HV, Fresle D, Policy M, Organization WH. Guide to good prescribing: a practical manual. Geneva: World Health Organization, 1994.

6. Ramsay L. Bridging the gap between clinical pharmacology and rational drug prescribing. British journal of clinical pharmacology. 1993;35(6):575.

7. Dukes MNG, Organization WH. Drug utilization studies: methods and uses: World Health Organization. Regional Office for Europe; 1993.

8. Organization WH. How to investigate drug use in health facilities: selected drug use indicators. Geneva: World Health Organization, 1993.

9. Organization WH. Promoting rational use of medicines: core components. Geneva: World Health Organization, 2002.

10. NATIONAL DRUG POLICY OF THE TRANSITIONAL GOVERNMENT OF ETHIOPIA 1993.

11. Desalegn AA. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. BMC health services research. 2013;13(1):170.

12. Desta Z, Abula T, Gebre-Yohannes A, Worku A. Drug prescribing patterns for outpatients in three hospitals in north-west Ethiopia. Ethiopian Journal of Health Development. 2002;16(2):183-9.

13. Food MaHAa, Ethiopia CAo. list of essential medicines for ethiopia. Addis Ababa.
14. Bimo H, Hogerzeil V, Choudhury A, Das A, Diwan V, Kafle K. How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators-EDM Research Series No. 007. World Health Organization. 1993;88.

15. Abdulahi M, Shiferaw T. Patterns of prescription in Jimma Hospital. The Ethiopian Journal of Health Development (EJHD). 1997;11(3).

16. Bantie L. Assessment of drug prescription practice using WHO prescribing indicators in Felege Hiwot referral hospital (FHRH) outpatient department, North Ethiopia. Int J Pharm. 2014;4(3):89-94.

17. Sisay M, Mengistu G, Molla B, Amare F, Gabriel T. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. BMC health services research. 2017;17(1):161.

18. Mosleh A, KHOSHNEVIS AS, Sorush M, Eghbalpor A, Babaeian S. Evaluation of the drug prescription status based on the WHO indices in pharmacies of health care centers affiliated to Tehran University of Medical Sciences. 2011.

19. Mohlala G, Peltzer K, Phaswana Mafuya N, Ramlagan S. Drug prescription habits in public and private health facilities in 2 provinces in South Africa. 2010.

20. Vaz F, Antao-Pereira I, Ferreira A, Kulkarni M. A study of drug prescribing practices at a Tertiary Care Hospital. Journal of Clinical and Diagnostic Research. 2010;4(2):2257-9.

21. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization’s prescribing, patient care and health facility indicators in selected health facilities in eastern Ethiopia. BMC health services research. 2016;16(1):144.
22. Ghimire S, Nepal S, Bhandari S, Nepal P, Palaian S. A prospective surveillance of drug prescribing and dispensing in a teaching hospital in western Nepal. J Pak Med Assoc. 2009;59(10):726-31. Epub 2009/10/10.

23. Tamuno I. Prescription pattern of clinicians in private health facilities in Kano, Northwestern Nigeria. Asian Pacific Journal of Tropical Disease. 2011;1:235–8.

24. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization's Prescribing, Patient Care and Health facility indicators in selected health facilities in eastern Ethiopia. BMC Health Serv Res. 2016;16:144. Epub 2016/04/24.

25. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014;5(6):229-41.

26. Organization WH. Assessment of the pharmaceutical sector in Ethiopia. Addis Ababa, Ethiopia.: Ministry of Health, 2003.

27. El Mahalli AA, Akl OA, Al-Dawood SF, Al-Nehab AA, Al-Kubaish HA, Al-Saeed S, et al. WHO/INRUD patient care and facility-specific drug use indicators at primary health care centres in Eastern province, Saudi Arabia. East Mediterr Health J. 2012;18(11):1086-90. Epub 2013/01/11.

28. Sisay M, Mengistu G, Molla B, Amare F, Gabriel T. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. BMC Health Serv Res. 2017;17(1):161. Epub 2017/02/25.
### STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

| Section/Topic          | Item # | Recommendation                                                                                     | Reported on page # |
|------------------------|--------|----------------------------------------------------------------------------------------------------|--------------------|
| **Title and abstract** | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract              | 1                  |
|                        |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 1                  |
| **Introduction**       | 2      | Explain the scientific background and rationale for the investigation being reported                | 2                  |
| **Objectives**         | 3      | State specific objectives, including any prespecified hypotheses                                   | 3                  |
| **Methods**            | 4      | Present key elements of study design early in the paper                                            | 4                  |
| Study design           | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4 and 5            |
| Setting                | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants        | 5                  |
| Participants           | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5 and 6            |
| Variables              | 8      | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 5 and 6            |
| Data sources/measurement | 9       | Describe any efforts to address potential sources of bias                                          | 5                  |
| Bias                   | 10     | Explain how the study size was arrived at                                                          | 5                  |
| Study size             | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7                  |
| Quantitative variables | 12     | (a) Describe all statistical methods, including those used to control for confounding             | 7                  |
| Statistical methods    |        | (b) Describe any methods used to examine subgroups and interactions                                | 8                  |
|                        |        | (c) Explain how missing data were addressed                                                       | --                 |
|                        |        | (d) If applicable, describe analytical methods taking account of sampling strategy                 | --                 |
|                        |        | (e) Describe any sensitivity analyses                                                             | --                 |
| **Results**            |        |                                                                                                  |                    |
| Participants | 13* | (a) Report numbers of individuals at each stage of study— eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  |
| --- | --- | --- |
| | | (b) Give reasons for non-participation at each stage  |
| | | (c) Consider use of a flow diagram |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders  |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| Outcome data | 15* | Report numbers of outcome events or summary measures  |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included  |
| | | (b) Report category boundaries when continuous variables were categorized  |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17 | Report other analyses done— eg analyses of subgroups and interactions, and sensitivity analyses |
| Discussion | 18 | Summarise key results with reference to study objectives |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results |
| Other information | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

| Journal:     | *BMJ Open*                                    |
|--------------|-----------------------------------------------|
| Manuscript ID| bmjopen-2020-045805.R1                        |
| Article Type:| Original research                             |
| Date Submitted by the Author: | 27-Apr-2021                             |
| Complete List of Authors: | tasew, segen; Mekelle University College of Health Sciences, clinical pharmacy  
                             abraha, Haftom; Mekelle University College of Health Sciences, clinical pharmacy  
                             gidey, kidu; Mekelle University College of Health Sciences, clinical pharmacy  
                             Gebre, Abadi; Department of Pharmacology and Toxicology, College Health Sciences, Mekelle University, Mekelle, Ethiopia, pharmacology and clinical toxicology |
| <b>Primary Subject Heading</b>: | Pharmacology and therapeutics |
| Secondary Subject Heading: | Pharmacology and therapeutics |
| Keywords: | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, CLINICAL PHARMACOLOGY |
I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd (“BMJ”) its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge (“APC”) for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author’s Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.
Drug use evaluation using WHO core drug use indicators in selected general hospitals in Tigray region, Ethiopia

Segen Gebremeskel Tassew1*, Haftom Niguse Abraha1, Kidu Gidey1, Abadi Kahsu Gebre2
1 Department of Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Tigray, Ethiopia
2 Department of Pharmacology and Toxicology, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Tigray, Ethiopia

*corresponding author: Segen Gebremeskel Tassew, email: segengm@gmail.com

Abstract

Objective: This study was aimed to assess drug use using the World Health Organization (WHO) drug use indicators in selected general hospitals in Tigray region, Ethiopia.

Materials and Methods: A total of 1200 randomly selected prescriptions from Mekelle and Quiha hospital that were recorded from 1 January 2017 to 1 June 2019 were cross-sectionally assessed from 1 March 2019 to 30 August 2019 using WHO prescribing indicators. Further, 100 patients from each hospital who visited both outpatient clinics and hospital pharmacies were interviewed, and prescriptions evaluated in according to WHO patient care indicators. Moreover, the hospitals were evaluated according to WHO facility indicators.

Result: The average number of medicines per prescription was 1.69 (±0.81). Prescriptions containing antibiotics and injectable were 58.2% and 15.9% respectively. The percentage of medicines prescribed with a generic name and from essential medicines list of Ethiopia were 974 (97.5%) and 970 (88.1%) in Mekelle and Quiha hospital, respectively. The patients spent an average of 6.56 (±3.48) minutes with their General Practitioner, whilst only 22.79 (±21.7) seconds with their pharmacist. Of the patients interviewed, 56.9% knew their dosing regimen and only 32.7% of them were correctly labelled.

Conclusion: The finding of this study revealed significant deviation from WHO optimal levels suggesting the need for improvement in medicine utilization in those hospitals. Understanding the factors that contributed for such gaps and implementing correct measures is required to conform with the recommended WHO standard of care.

Keywords: Drug use evaluation, Prescribing Indicator, Patient Care Indicator, Facility Indicator
Strengths and limitations of study

- The study utilized all WHO core drug use indicators to assess quality of patient care in hospital setting.
- An important evidence about rational drug use is provided in an area rarely assessed.
- The study did not try to identify the factors that contributed for the observed deviation making it difficult to propose improvement strategies.
- As diagnosis was missing in considerable number of prescriptions, we did not confirm that the drugs were prescribed for right diagnoses.

Introduction

The rational use of drugs depends on rational prescribing, correct dispensing and adherence to treatment by patients\(^1\). According to the World Health Organization (WHO), a medicine is used rationally if patients received the appropriate medicines, in doses that meet their individual requirements, for an adequate period of time and with an affordable cost\(^2\). The concept of rational drug use can be summarized as the right medicine at the right dose by the right route at the right time for the right patient (‘five rights’\(^3\)).

On the contrary, irrational use of medicines is termed to have occurred when one or more of the above-mentioned conditions are not met\(^2\) and it is a global challenge with a highest prevalence in developing countries. Patients, prescribers, workplace, supply system may attribute for irrational drug use\(^4\) because of limited knowledge about medicines, unethical medicine promotions and improper prescribing habits of clinicians\(^5\)\(^6\).

WHO drug use indicators are used to evaluate rational drug use at all levels in the chain of medicine utilization using objective assessment methods. WHO core drug use indicators, developed by WHO Action Program on Essential Drugs and International Network for Rational Use of Drugs (INRUD), are highly standardized to be used for drug use evaluations without further national validation\(^7\)\(^8\).

Prescribing indicators include average number of medicines prescribed per encounter, percentage of those prescribed by generic name and those from national essential medicines list (EML), percentage of encounters with antibiotics and those with injections prescribed. Patient care indicators, on the other hand, include average consultation and dispensing times, percentage of medicines actually dispensed and of those adequately labeled, as well as patients' knowledge of correct dosage. Facility indicators assess the availability of copy of EML and
those of key medicines available in the health facility. Ethiopia has introduced a national drug policy in 1993 with the aim of meeting the demand for essential medicines together with appropriate use, making them affordable to the public as well as ensuring their safety, efficacy, and quality. The policy also encourages domestic manufacturing, enhancing manpower training and research and development of medicines as well as devising ways to integrate traditional medicines into conventional medicine as objectives. Despite these objectives’ studies conducted so far reported gaps in rational medicine use with a high percentage of encounters with antibiotics and injections prescribed. Considering the very large population size of Ethiopia and the diversity of geographic areas, there are very few studies on medicine use conducted so far. Therefore, this study was carried out to evaluate drug use and contribute in narrowing of the information gap in the documentation of drug use patterns in Ethiopia using WHO’s core drug use indicators.

**Methods and Materials**

**Study setting and period**

The study was conducted both in Mekelle and Quiha general hospitals between 1 March 2019 and 30 August 2019. Both hospitals are located in Mekelle, the capital city of Tigray regional state, Ethiopia.

**Study design and population**

All prescriptions recorded from 1 January 2017 to 1 June 2019 were considered. Of which, randomly selected prescriptions were retrospectively for their quality using WHO prescribing indicators during the study period [1 March 2019 and 30 August 2019]. All patients who were visiting outpatient department of Mekelle and Quiha hospital during the study period were also used as a target population. Of note, patients aged less 18 or not willing to participant in the study were excluded.

**Sampling technique and procedure**

World Health Organization recommends assessments of at least 600 prescriptions and 100 patients per each hospital for drug use evaluation. Accordingly, we had included 600 randomly selected sample prescriptions recorded from 1 January 2017 to 1 June 2019 from each hospital. Twenty key drugs were selected from each hospital as per WHO recommendation which is a minimum of 15 essential drugs in each health facility.
Data collection instruments and process

Three well-trained pharmacy personnel were recruited and deployed in each hospital. One of them was collecting prescribing indicators by using prescriptions and prescription registration books, while the others were collecting the patient care indicators and the facility indicators. Specific types of data necessary to measure the prescribing indicators were recorded for each prescription and entered to the prescribing indicator form. Data on medicine use pattern was collected by using WHO's prescribing and patient care indicators. In assessing patient care indicators, the average number of medicines prescribed per encounter, the percentage of medicines prescribed with generic names and those prescribed from EML, the percentage of prescription encounters which ended up with antibiotics and those with injections prescribed were collected. However, immunizations of children were not considered as injections. In measuring the proportion of medicines prescribed with generic names, the EML of Ethiopia was used as the main source of generic names13.

For patient care indicators measurement, consultation time and dispensing time was obtained by recording the time that the patient spent with his physician and pharmacist respectively in patients aged greater than 18 years. In determining patients’ knowledge of their dosage regimen, patients were asked to explain what they know about the medicine dispensed for them. Facility indicators were availability of formulary, essential drugs, standard treatment guidelines, and key drugs at the time of the visit were assessed.

Operational definitions

Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and effectiveness of a medications to improve patient care.

**Percentage of drugs prescribed by generic name:** It measures the tendency to prescribe by generic name.

**Percentage of drugs prescribed from list of essential drugs:** It measures the degree to which practices conform to a national drug policy.

**Average number of drugs per encounter:** Average number of drugs per encounter measures the degree of poly pharmacy.

**Average consultation time:** The average time that physicians spends with patients. It doesn’t include waiting time.
**Average dispensing time:** The average time that the pharmacists spend with patients while dispensing the medications.

**Data Analysis Procedure**

The data collected were entered and analyzed using Statistical Packages for Social Sciences (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were described using frequency, percentage, mean and standard deviation (SD).

**Patient and Public Involvement**

Patient and/or the public were not directly involved in this study.

**Results**

**Prescribing indicators**

A total of 1200 prescriptions, 600 from each hospital were evaluated using WHO prescribing indicators. On average, 1.69 (±0.81) drugs were prescribed and 44.7% of the prescriptions contain one or two drugs (Table 1).

| Number of drugs | Quiha hospital | Mekelle hospital | Overall result | WHO standard 14 |
|-----------------|----------------|------------------|----------------|-----------------|
|                 | n (%)          | n (%)            | N (%)          |                  |
| One             | 306 (51)       | 286 (47.7)       | 592 (49.7)     |                 |
| Two             | 206 (34.3)     | 214 (35.7)       | 420 (35)       |                 |
| Three           | 72 (12)        | 82 (13.7)        | 154 (12.9)     |                 |
| Four            | 15 (2.5)       | 17 (2.8)         | 32 (2.3)       |                 |
| Five            | 1 (0.2)        | 1 (0.2)          | 2 (0.2)        |                 |
| Average         | 1.67 (±0.8)    | 1.72 (±0.82)     | 1.69 (±0.81)   | ≤2 (1.6-1.8)    |

From the total of 1200 prescriptions, 2028 drugs were prescribed of which 1944 (92.8%) were prescribed in generic name. More than fifty percent (58.2%) of the prescriptions contained antibiotics whilst 191 (15.9%) include at least one injectable medication (Table 2).
Table 2: Percentages of encounters with generic drugs, antibiotics, and injections in the selected general hospitals

| Prescribing indicators | Quiha hospital | Mekelle hospital | Overall result (N) | WHO standard\(^{14}\) |
|------------------------|----------------|------------------|-------------------|-------------------|
| **Generic prescription** |               |                  |                   |                   |
| Drugs prescribed, n  | 999            | 1029             | 2028              |                   |
| Drugs prescribed in generic name, n (%) | 974 (97.5) | 970 (94.3) | 1944 (95.6) |                   |
| **Antibiotics** |               |                  |                   |                   |
| Prescriptions with antibiotics, n (%) | 392 (65.3) | 306 (51) | 698 (58.2) | < 30\% (20–26.8) |
| **Injections** |               |                  |                   |                   |
| Prescriptions with injections, n (%) | 56 (9.3) | 135 (22.5) | 191 (15.9) | 13.4–21.1\% |
| **Drugs from essential drug list, n (%)** | 974 (97.5) | 930 (90.4) | 1904 (93.9) | 100\% |
Amoxicillin or Amoxicillin / Clavulanic acid, and Ceftriaxone were commonly prescribed antibiotics (Table 3).

Table 3: Antimicrobial/Antibiotics prescribed in the selected general hospitals

| Class of Antimicrobial agent | Quiha hospital | Mekelle hospital | Overall |
|------------------------------|----------------|------------------|---------|
| Amoxicillin                  | 160            | 76               | 236     |
| Ciprofloxacin                | 56             | 44               | 100     |
| Ceftriaxone                  | 33             | 57               | 90      |
| Metronidazole                | 42             | 40               | 82      |
| Cephalexin                   | 20             | 35               | 55      |
| Amoxicillin /Clavulanic acid | 15             | 28               | 43      |
| Azithromycin                 | 19             | 16               | 35      |
| Cloxacillin                  | 21             | 11               | 32      |
| Norfloxacin                  | 17             | 11               | 28      |
| Sulfamethoxazole/Trimethoprim| 13             | 11               | 24      |
| Doxycycline                  | 13             | 7                | 20      |
| Ampicillin                   | 1              | 9                | 10      |
| Clarithromycin               | 8              | 1                | 9       |
| Erythromycin                 | 2              | 2                | 4       |
| Gentamycin                   | 1              | 2                | 3       |
|                      |     |     |     |
|----------------------|-----|-----|-----|
|                      |     |     |     |
| Ceftazidime          | -   | 2   | 2   |
| Crystalline Penicillin| -   | 1   | 1   |
| Tinidazole           | 14  | 17  | 31  |
| Albendazole          | 16  | 7   | 23  |
| Mebendazole          | 11  | 5   | 17  |
| Coarthem             | 2   | -   | 2   |
| Praziquantel         | 1   | -   | 1   |
|                      |     |     |     |
| **Antiprotozoal/anthelmintics** | | | |
|                      |     |     |     |
| Ketoconazole         | 4   | -   | 4   |
| Clotrimazole vaginal supp | 3   | -   | 3   |
| Fluconazole          | 1   | -   | 1   |
|                      |     |     |     |
| **Antifungal**       |     |     |     |
|                      |     |     |     |
| Acyclovir            | 2   | -   | 2   |
Patient care indicators

On average each patient spent approximately 7 minutes with his/her General practitioner, whilst only 22 seconds with his/her pharmacist. 81.2% of the prescribed drugs were dispensed. Of which, 32.7% of them were adequately labelled. 56.9% of the patients knew about their dosage regimen of their medications (Table 4).

Table 4: Assessment of patient care using WHO patient care indicators in selected general hospitals

| Patient care indicators | Quiha hospital | Mekelle hospital | Overall | WHO standard |
|-------------------------|----------------|------------------|---------|--------------|
| Average consultation time (Minute) | 3.66±2.19 | 9.46±4.77 | 6.56±3.48 | 10 min |
| Average dispensing time (Sec) | 21.53±19.89 | 24.04±23.5 | 22.79±21.7 | >180 seconds |
| Total number of drugs prescribed | 189 | 171 | 360 | |
| Total number of drugs dispensed | 170 | 124 | 294 | |
| Percentage of drugs actually dispensed | 89.9 | 72.5 | 81.2 | 100% |
| Number of drugs adequately labelled | 29 | 50 | 79 | |
| Percentage of drugs adequately labelled | 15.4 | 50 | 32.7 | |
| Knows dosage | 25(25%) | 48 (88.8%) | 56.9 | |

Health facility indicators

Both Quiha and Mekelle hospitals have their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals on average 77.5% of them were available in stock (Table 5).
Table 5: Availability of key drugs in selected general hospitals

| List of key drugs           | Quiha hospital | Mekelle hospital |
|-----------------------------|----------------|------------------|
| Amoxicillin/clavulanic acid | ✓              | X                |
| Ciprofloxacin tablet        | ✓              | X                |
| Cloxacillin capsule         | ✓              | X                |
| Azithromycin                | ✓              | X                |
| Diclofenac injection        | ✓              | ✓                |
| Diclofenac tablet           | ✓              | ✓                |
| Tramadol                    | X              | ✓                |
| Metronidazole               | ✓              | ✓                |
| Insulin                     | ✓              | ✓                |
| Nifedipine                  | X              | ✓                |
| Lasix                       | X              | ✓                |
| Spironolactone              | X              | ✓                |
| Ceftriaxone                 | ✓              | X                |
| Vancomycin                  | ✓              | ✓                |
| Metformin                   | ✓              | ✓                |
| Enalapril                   | ✓              | ✓                |
| Cephalexin                  | ✓              | ✓                |
| Ferrous sulphate            | ✓              | ✓                |
| Paracetamol syrup           | ✓              | X                |
| Amlodipine                  | ✓              | X                |
Discussion

In this study, we have revealed within the WHO acceptable standard for average number of drugs per prescription. The finding was comparable with studies done in different parts of Ethiopia including Jimma (1.59)\textsuperscript{15}, Hawassa University Teaching Referral (1.9)\textsuperscript{11} and Bahir Dar hospital (1.8)\textsuperscript{12}. However, studies in Debre Tabor (2.2)\textsuperscript{12}, Felege Hiwot referral hospital (2.49)\textsuperscript{16} and Karamara public general hospital in Ethiopia (2.46)\textsuperscript{17} reported higher average number of drugs per prescription. Such discrepancy may be attributable to difference in the level of awareness among clinicians working in different part of the country.

In terms of percentage of medicines prescribed by generic name, the result of the present study (92.8\%) is lower compared to WHO's recommended standard value (100\%). Similar results were reported at Hawassa University Hospital (98.7\%)\textsuperscript{11}, Felege Hiwot specialized University hospital (97.4 \%)\textsuperscript{16} and selected health centres in Eastern Ethiopia (97 \%)\textsuperscript{18}. This could be due to increasing promotion of brand drugs influencing clinicians to prescribe brand names. This suggests that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution, which in turn reduce health seeking behaviour of the community\textsuperscript{19}.

The percentage of encounters with antibiotics, which is 58.2\% in the present study, is higher compared to the WHO's standard recommendation of 20 to 26.8\% per prescription (8), but it is comparable with study conducted in public hospitals in Eastern Ethiopia (57.9\%)\textsuperscript{17}, and Hawassa teaching referral hospital (58.1\%)\textsuperscript{11}. However, it lower compared to a study conducted in selected health centres in Eastern Ethiopia (85.5\%)\textsuperscript{18}. High prevalence of infectious disease in developing countries may account for such higher antibiotic prescribing than the recommended level by WHO. However, such problematic level of antibiotic prescribing may lead to antimicrobial resistance which is an eminent threat of global health\textsuperscript{20}. The percentage of encounters with injection prescribed in this study was within WHO standard range.

A deficiency was noted in terms of prescribing according to essential medicine list of Ethiopia compared to the WHO standard of a 100\% (8) and to that of the national assessment results of 2003 (99\%)\textsuperscript{21}. This may attributable to clinical condition of the patients, patient preference, clinician decision and availability of the medications.
In this study the average consultation time that the patients spent with clinicians was approximately 7 minutes which is higher in comparison with studies conducted in public hospital (4.6 minutes)\(^7\). The duration, however, doesn't seem to be sufficient for to make physical examination and select the best available treatment choices. High patient load could have contributed for such below the optimal duration of consultation time. The average dispensing time recorded in the present study was approximately 23 seconds. This is significantly lower than standard WHO recommendation which is 180 seconds\(^8\). The lower the dispensing time the poorer would be the understanding of the patients about their medication which this may lead to frequent encounter of drug therapy problems. The percentage of drugs actually dispensed out of the total drugs prescribed to the patients stood at 80 % compared to the recommended 100\(^\%\). Frequent stock out of medicines may account for such finding. Regarding the adequacy of labelling of medicines dispensed, only slightly over one-third of medicines were appropriately labeled which is far from the recommended level, 100\(^\%\). High patient load encountered at outpatient pharmacy department and negligence of the pharmacists together with poor concern and follow up from the hospital side could be implicated for such low level of performance in this indicator. Of note, only about half of the patients knew the dosage schedules of their medicines prescribed to them, which is far below the expected level, 100\(^\%\).

Both Quiha and Mekelle hospital have their own essential drug list and standard treatment guideline. Only 7.5\% of key drugs were in stock and this is low with 100 % WHO recommendation. Absence of key drugs may impair patient care and compromise patient quality of life.

The study has several strengths. Firstly, it utilized all WHO core drug use indicators to assess quality of patient care in hospital setting. Secondly, we included WHO recommended sample size. Finally, it provided an important evidence about rational drug use in a study area which is rarely assessed. The study has also limitations. The study did not try to identify the factors that contributed for the observed deviation making it difficult to propose improvement strategies. However, it can be utilized as a benchmark for further studies. As diagnosis was missing in considerable number of prescriptions, we did not confirm that prescribed drugs were consistent with the diagnoses.
Conclusion

The findings of the present study showed prescribing practices for antibiotic use, prescribing from essential drug list and injection use were not within acceptable WHO recommendations. Overuse of antibiotics facilitate the emergence of antimicrobial resistance which is a major challenge for our globe. Generic prescribing showed little deviation from the standard whereas the average number of drugs per encounter lay within the range of WHO. Poor generic prescribing coupled with shorter consultation and dispensing time may lead to frequent encounters of drug therapy problems. Future studies should look for factors attributable for the observed gaps to improve patient care in those hospitals.

Abbreviation and acronyms

DUE: Drug use evaluation, EDL: Essential drug list, WHO: World health organization, HFSUH: Hiwot Fana Specialized Hospital, QH: Quiha Hospital, MH: Mekelle Hospital, INRUD: International Networks for Rational use of medicines.

Ethical Considerations

The study was approved by the institutional review board of Mekelle University (reference number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health bureau. During data collection on patient care indicators, a written consent was obtained from each participant after provision of all the necessary information. In addition, the data collected in the study did not use patient identifiers and were kept strictly confidential and were used only for the purpose of the study. Acknowledgments The authors would wish to thank all the staff members of Mekelle and Quiha hospitals for their sincere cooperation and support.

Competing interests

The authors declare that they have no competing interests. The funder has not any involvement in this study.

Availability of data

The data of this study are available from the corresponding author up on a reasonable request.

Funding
This study was funded by college of health sciences, Mekelle university small scale grant with registration number of CRPO/CHS/Young/Recurrent/ 008/2011.

**Patient consent for publication**

Not applicable

**Author’s contribution**

SG and AKG designed the study, obtained the fund, supervising data collection, conducted data analysis, wrote the first draft of the manuscript. SG, KG, AKG and HN provide critical comments, revised and finalized the manuscript. All authors read and approved the final manuscript.
References

1. Timmermans A, Sharma A. Rational use of drugs. In: United Nations High Commissioner for Refugees. Drug Management Manual. 2006:87-104.
2. WHO. The pursuit of responsible use of medicines: sharing and learning from country experiences: 2012.
3. Mehta S, Gogtay N. From the pen to the patient: Minimising medication errors. Journal of Postgraduate Medicine 2005;51(1):3.
4. Chaturvedi V, Mathur A, Anand A. Rational drug use–As common as common sense. Medical Journal Armed Forces India 2012;68(3):206.
5. De Vries T, Henning RH, Hogerzeil HV, et al. Guide to good prescribing: a practical manual: World Health Organization, 1994.
6. Ramsay L. Bridging the gap between clinical pharmacology and rational drug prescribing. British journal of clinical pharmacology 1993;35(6):575.
7. Dukes MNG. Drug utilization studies: methods and uses: World Health Organization. Regional Office for Europe 1993.
8. WHO. How to investigate drug use in health facilities: selected drug use indicators: World Health Organization, 1993.
9. WHO. Promoting rational use of medicines: core components: World Health Organization, 2002.
10. National drug Policy of the Trational Government of Ethiopia. 1993
11. Desalegn AA. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. BMC health services research 2013;13(1):1-6.
12. Desta Z, Abula T, Gebre-Yohannes A, et al. Drug prescribing patterns for outpatients in three hospitals in north-west Ethiopia. Ethiopian Journal of Health Development 2002;16(2):183-89.
13. FMHACA. List of Essential Medicines for Ethiopia 2010
14. Isah A, Laing R, Quick J, et al. The development of reference values for the WHO health facility core prescribing indicators. West African Journal of Pharmacology and Drug Research 2001;18:6-11.
15. Abdulahi M, Shiferaw T. Patterns of prescription in Jimma Hospital. The Ethiopian Journal of Health Development 1997;11(3)
16. Laychiluh B. Assessment of drug prescription practice using WHO prescribing indicators in Felege Hiwot Referral Hospital (FHRH) outpatient department, North, Ethiopia. *International Journal of Pharmaceutics* 2014;4(3):89-94.

17. Sisay M, Mengistu G, Molla B, et al. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. *BMC health services research* 2017;17(1):1-9.

18. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization’s prescribing, patient care and health facility indicators in selected health facilities in eastern Ethiopia. *BMC health services research* 2016;16(1):1-8.

19. Shaikh BT, Hatcher J. Health seeking behaviour and health service utilization in Pakistan: challenging the policy makers. *Journal of public health* 2005;27(1):49-54.

20. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Therapeutic advances in drug safety* 2014;5(6):229-41.

21 WHO. Assessment of the pharmaceutical sector in Ethiopia: Addis Ababa, Ethiopia:. Ministry of Health, 2003.
STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

| Section/Topic                  | Item # | Recommendation                                                                                                                                                                                                                                                                                                                                 | Reported on page # |
|-------------------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Title and abstract            | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract                                                                                                                                                                                                                                                        | 1                  |
|                               |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found                                                                                                                                                                                                                                           | 1                  |
| Introduction                  |        |                                                                                                                                                                                                                                                                                                                                               |                    |
| Background/rationale          | 2      | Explain the scientific background and rationale for the investigation being reported                                                                                                                                                                                                                                                         | 2                  |
| Objectives                    | 3      | State specific objectives, including any prespecified hypotheses                                                                                                                                                                                                                                                                             | 3                  |
| Methods                       |        |                                                                                                                                                                                                                                                                                                                                               |                    |
| Study design                  | 4      | Present key elements of study design early in the paper                                                                                                                                                                                                                                                                                      | 4                  |
| Setting                       | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                                                                                                                                                                 | 4 and 5            |
| Participants                  | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants                                                                                                                                                                                                                                              | 5                  |
| Variables                     | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable                                                                                                                                                                                               | 5 and 6            |
| Data sources/measurement      | 8      | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group                                                                                                                                                  | 5 and 6            |
| Bias                          | 9      | Describe any efforts to address potential sources of bias                                                                                                                                                                                                                                                                                     | 5                  |
| Study size                    | 10     | Explain how the study size was arrived at                                                                                                                                                                                                                                                                                                      | 5                  |
| Quantitative variables        | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why                                                                                                                                                                                                                  | 7                  |
| Statistical methods           | 12     | (a) Describe all statistical methods, including those used to control for confounding                                                                                                                                                                                                                                                         | 7                  |
|                               |        | (b) Describe any methods used to examine subgroups and interactions                                                                                                                                                                                                                                                                         | 8                  |
|                               |        | (c) Explain how missing data were addressed                                                                                                                                                                                                                                                                                                  | --                 |
|                               |        | (d) If applicable, describe analytical methods taking account of sampling strategy                                                                                                                                                                                                                                                         | --                 |
|                               |        | (e) Describe any sensitivity analyses                                                                                                                                                                                                                                                                                                       | --                 |
| Results                       |        |                                                                                                                                                                                                                                                                                                                                               |                    |
Participants
(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
(b) Give reasons for non-participation at each stage
(c) Consider use of a flow diagram

Descriptive data
(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
(b) Indicate number of participants with missing data for each variable of interest

Outcome data
Report numbers of outcome events or summary measures

Main results
(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
(b) Report category boundaries when continuous variables were categorized
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses
Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results
Summarise key results with reference to study objectives

Limitations
Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Interpretation
Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Generalisability
Discuss the generalisability (external validity) of the study results

Other information

Funding
Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Assessment of drug use pattern using WHO core drug use indicators in selected general hospitals: a cross-sectional study in Tigray region, Ethiopia

| Journal: | BMJ Open |
|----------|----------|
| Manuscript ID: | bmjopen-2020-045805.R2 |
| Article Type: | Original research |
| Date Submitted by the Author: | 30-Aug-2021 |
| Complete List of Authors: | tasew, segen; Mekelle University College of Health Sciences, clinical pharmacy abraha, Haftom; Mekelle University College of Health Sciences, clinical pharmacy gidey, kidu; Mekelle University College of Health Sciences, Clinical pharmacy Gebre, Abadi; Department of Pharmacology and Toxicology, College Health Sciences, Mekelle University, Mekelle, Ethiopia, pharmacology and clinical toxicology |
| Primary Subject Heading: | Pharmacology and therapeutics |
| Secondary Subject Heading: | Pharmacology and therapeutics |
| Keywords: | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, CLINICAL PHARMACOLOGY |
I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd (“BMJ”) its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge (“APC”) for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author’s Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.
Assessment of drug use pattern using WHO core drug use indicators in selected general hospitals: a cross-sectional study in Tigray region, Ethiopia

Segen Gebremeskel Tassew¹, Haftom Niguse Abraha¹, Kidu Gidey¹, Abadi Kahsu Gebre²

¹ Department of Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Tigray, Ethiopia
² Department of Pharmacology and Toxicology, School of Pharmacy, College of Health Sciences, Mekelle University, Mekelle, Tigray, Ethiopia

*corresponding author: Segen Gebremeskel Tassew, email: segengm@gmail.com

Abstract

Objective: Inappropriate use of medicine is a global challenge with greater impact in developing countries. Assessment of drug use pattern is used to identify gaps in medicine utilization to implement strategies for promoting rational drug use. This study was aimed to assess drug use pattern using the World Health Organization (WHO) drug use indicators in selected general hospitals in Tigray region, Ethiopia.

Design: A cross-sectional study was conducted using WHO drug use indicators in two public hospitals located in Tigray.

Setting: Prescriptions recorded from January 1, 2017 to June 1, 2019 were randomly selected and participants who visited the public hospitals from March 1, 2019 to August 30, 2019 and hospital pharmacies were interviewed.

Participants: 100 patients who visited both outpatient clinics and hospital pharmacy departments of the public hospitals.

Results: The average number of medicines per prescription was 1.69 (±0.81). Prescriptions containing antibiotics and injectables were 58.2% and 15.9% respectively. The percentage of medicines prescribed with a generic name from essential medicines list of Ethiopia were 97.5% (974) and 88.1% (970) in Mekelle and Quiha hospital, respectively. The patients spent an average of 6.56 (±3.48) minutes with their General Practitioners, whilst only 22.79 (±21.7) seconds with their pharmacists. Of the patients interviewed, 56.9% knew their dosing regimen and 32.7% of them had their medication labelled.

Conclusion: The finding of the present study revealed deviation of drug use pattern from the WHO optimal levels suggesting the hospitals had limitations in appropriate utilization of medicines. Understanding the factors that attributed for the observed gaps and implementing
corrective measures are required to conform with the recommended standards of appropriate drug utilization.

Keywords: Drug use evaluation, Prescribing Indicator, Patient Care Indicator, Facility Indicator

**Strengths and limitations of study**

- The study utilized all three of the WHO core drug use indicators to assess quality of patient care in hospital setting.
- An evidence about rational drug use has been provided in an area rarely assessed.
- The study did not try to identify the factors that contributed for the observed gaps making it difficult to propose improvement strategies.
- As diagnosis was missing in considerable number of prescriptions, we did not confirm that the drugs were prescribed for right diagnoses.
Introduction

The rational use of drugs depends on rational prescribing, correct dispensing and adherence to treatment by patients\(^1\). According to the World Health Organization (WHO), a medicine is used rationally if patients received appropriate medicines, in doses that meet their individual requirements, for an adequate period of time and with an affordable cost\(^2\). The concept of rational drug use can be summarized as the right medicine at the right dose by the right route at the right time for the right patient ('five rights')\(^3\). Conversely, irrational use of medicines is termed to have occurred when one or more of the above-mentioned conditions are not met\(^2\). Irrational use of medicine is a global challenge with the highest prevalence in developing countries. Multiple stakeholders including patients, prescribers, workplace, supply system may attribute for irrational drug use\(^4\) due to many reasons such as limited knowledge about medicines, unethical medicine promotions and improper prescribing habits of clinicians\(^5\,\,6\).

WHO drug use indicators are used to evaluate rational drug use at all levels in the chain of medicine utilization (facility, clinician, pharmacist, and patient) using highly standardized indicators developed by WHO Action Program on Essential Drugs and International Network for Rational Use of Drugs (INRUD) to be used for drug use evaluations without further national validation\(^7\,\,8\). Prescribing indicators include average number of medicines prescribed per encounter, percentage of those prescribed by generic name and those from national essential medicines list, percentage of encounters with antibiotics and those with injections prescribed. Patient care indicators are used to evaluate the interaction between the patients with their clinicians and pharmacists and includes average consultation and dispensing times, percentage of medicines dispensed and those adequately labelled, as well as patients' knowledge of correct dosage. The availability of copy of essential medicine list and key medicines are assessed using facility indicators\(^9\).

Ethiopia has introduced a national drug policy in 1993 with the aim of meeting the demand for essential medicines together with appropriate use, making them affordable to the public as well as ensuring their safety, efficacy, and quality. The policy also encourages domestic manufacturing, enhancing manpower training and research and development of medicines as well as devising ways to integrate traditional medicines into conventional medicine as objectives\(^10\). Despite these policy directions’ studies conducted so far reported gaps in rational medicine use \(^11\,\,12\). Considering the very large population size of Ethiopia and the diversity of geographic areas, there are very few studies on medicine use conducted so far. Therefore, this
study was conducted to evaluate drug use and contribute to addressing the information gap in drug use pattern in Ethiopia specifically Tigray region.

**Methods and Materials**

**Study setting and period**

The study was conducted in Mekelle and Quiha general hospitals between March 1, 2019 and August 30, 2019. Both hospitals are located in Mekelle, the capital city of Tigray regional state, Ethiopia.

**Study design and population**

All prescriptions recorded from January 1, 2017 to June 1, 2019 were considered. Of which, randomly selected prescriptions were retrospectively assessed using WHO prescribing indicators during the study period [March 1, 2019 and August 30, 2019]. All patients who visited outpatient departments of Mekelle and Quiha hospitals during the study period were used as a target population. Of note, patients aged less 18 years or not willing to participant in the study were excluded.

**Sampling technique and procedure**

WHO recommends assessments of at least 600 prescriptions and 100 patients per each hospital for drug use evaluation. Accordingly, 600 randomly selected prescriptions recorded from January 1, 2017 to June 1, 2019 from each hospital were included. Twenty key drugs were also selected from each hospital as per WHO recommendation which is a minimum of 15 essential drugs for each health facility.

**Data collection instruments and process**

Three well-trained pharmacists were recruited and deployed to assess the prescriptions identified using prescription registration books, interview patients and evaluate availability of copy of essential medicine list and key medicines in the hospitals. Data on quality of prescribing was collected by using WHO's prescribing indicators. In assessing patient care indicators, the average number of medicines prescribed per encounter, the percentage of medicines prescribed with generic names and those prescribed from essential medicine list, the percentage of prescription encounters which ended up with antibiotics and those with injections prescribed were collected. However, immunizations of children were not considered as
injections. In measuring the proportion of medicines prescribed with generic names, the essential medicine list of Ethiopia was used as source for generic names. For assessment of patient care indicators, consultation time and dispensing time was obtained by recording the time that the patients spent with their physicians and pharmacists respectively. The knowledge of the patients on their dosage regimen were assessed by asking the patients to explain whether they knew about the medicine dispensed for them. Availability of formulary, essential drugs, standard treatment guidelines, and key drugs at the time of the visit were assessed to confirm whether the hospitals comply with WHO standards.

**Operational definitions**

Drug use evaluation is a systematic approach that assesses the appropriateness, safety, and effectiveness of a medications to improve patient care.

**Percentage of drugs prescribed by generic name:** It measures the tendency to prescribe by generic name.

**Percentage of drugs prescribed from list of essential drugs:** It measures the degree to which practices conform to a national drug policy.

**Average number of drugs per encounter:** Average number of drugs per encounter measures the degree of poly pharmacy.

**Average consultation time:** The average time that physicians spend with patients. It doesn’t include waiting time.

**Average dispensing time:** The average time that pharmacists spend with patient while dispensing the medications.

**Data Analysis Procedure**

The data collected were entered and analyzed using Statistical Packages for Social Sciences (SPSS) version 20. The data on prescribing indicators as well as patient care indicators were described using frequency, percentage, mean and standard deviation (SD).

**Patient and Public Involvement**

Patient and/or the public were not directly involved in this study.
Results

Prescribing indicators

A total of 1200 prescriptions, 600 from each hospital were evaluated using WHO prescribing indicators. On average, 1.69 (±0.81) drugs were prescribed and 44.7% of the prescriptions contain one or two drugs (Table 1).

| Number of drugs | Quiha hospital | Mekelle hospital | Overall result | WHO standard |
|-----------------|----------------|------------------|----------------|--------------|
|                 | n (%)          | n (%)            | N (%)          |              |
| One             | 306 (51)       | 286 (47.7)       | 592 (49.7)     |              |
| Two             | 206 (34.3)     | 214 (35.7)       | 420 (35)       |              |
| Three           | 72 (12)        | 82 (13.7)        | 154 (12.9)     |              |
| Four            | 15 (2.5)       | 17 (2.8)         | 32 (23.5)      |              |
| Five            | 1 (0.2)        | 1 (0.2)          | 2 (0.2)        |              |
| Average         | 1.67 (±0.8)    | 1.72 (±0.82)     | 1.69 (±0.81)   | ≤2 (1.6-1.8) |

A total of 2028 drugs were prescribed of which 1944 (92.8%) were prescribed in generic name. More than fifty percent (58.2%) of the prescriptions contained antibiotics and 191 (15.9%) include at least one injectable medication (Table 2). Amoxicillin was the most frequently prescribed antibiotic in both hospitals (Table 3).
Table 2: Percentages of encounters with generic drugs, antibiotics, and injections in the selected general hospitals

| Prescribing indicators          | Quiha hospital | Mekelle hospital | Overall result (N) | WHO standard$^{14}$ |
|---------------------------------|----------------|------------------|--------------------|---------------------|
| **Generic prescription**        |                |                  |                    |                     |
| Drugs prescribed, n             | 999            | 1029             | 2028               |                     |
| Drugs prescribed in generic name, n (%) | 974 (97.5)     | 970 (94.3)       | 1944 (95.6)        |                     |
| **Antibiotics**                 |                |                  |                    |                     |
| Prescriptions with antibiotics, n (%) | 392 (65.3)     | 306 (51)         | 698 (58.2)         | < 30% (20–26.8)     |
| **Injections**                  |                |                  |                    |                     |
| Prescriptions with injections, n (%) | 56 (9.3)       | 135 (22.5)       | 191 (15.9)         | 13.4–21.1%          |
| **Drugs from essential drug list, n (%)** | 974 (97.5)     | 930 (90.4)       | 1904 (93.9)        | 100%                |
### Table 3: Antimicrobial/Antibiotics prescribed in the selected general hospitals

| Class of Antimicrobial agent               | Frequency, n | Quiha hospital | Mekelle hospital | Overall |
|-------------------------------------------|--------------|----------------|------------------|---------|
| **Amoxicillin**                           |              |                |                  |         |
| Ciprofloxacin                             |              |                |                  |         |
| Ceftriaxone                               |              |                |                  |         |
| Metronidazole                             |              |                |                  |         |
| **Antibacterial agents**                  |              |                |                  |         |
| Cephalexin                                |              |                |                  |         |
| Amoxicillin /Clavulanic acid              |              |                |                  |         |
| Azithromycin                              |              |                |                  |         |
| Cloxacillin                               |              |                |                  |         |
| Norfloxacin                               |              |                |                  |         |
| Sulfamethoxazole/Trimethoprim             |              |                |                  |         |
| Doxycycline                               |              |                |                  |         |
| Ampicillin                                |              |                |                  |         |
| Clarithromycin                            |              |                |                  |         |
| Erythromycin                              |              |                |                  |         |
| Gentamycin                                |              |                |                  |         |
| Ceftazidime                               |              |                |                  |         |
| Crystalline Penicillin                    |              |                |                  |         |
| Class              | Medicine            | No. 1 | No. 7 | No. 31 |
|--------------------|---------------------|-------|-------|--------|
| Antiprotozoal/anthelmintics | Tinidazole          | 14    | 17    | 31     |
|                    | Albendazole         | 16    | 7     | 23     |
|                    | Mebendazole         | 11    | 5     | 17     |
|                    | Coarthem            | 2     | -     | 2      |
|                    | Praziquantel        | 1     | -     | 1      |
| Antifungal         | Ketoconazole        | 4     | -     | 4      |
|                    | Clotrimazole vaginal supp | 3 | - | 3 |
|                    | Fluconazole         | 1     | -     | 1      |
| Antiviral          | Acyclovir           | 2     | -     | 2      |

Amoxicillin or Amoxicillin / Clavulanic acid, and Ceftriaxone were commonly prescribed antibiotics.
Patient care indicators

On average each patient spent approximately 7 minutes with his/her General practitioner and 22 seconds with his/her pharmacist. 81.2% of the prescribed drugs were dispensed. Of which, 32.7% of them were adequately labelled. 56.9% of the patients knew about their dosage regimen of their medications (Table 4).

Table 4: Assessment of patient care using WHO patient care indicators in selected general hospitals

| Patient care indicators | Quiha hospital | Mekelle hospital | Overall | WHO standard |
|-------------------------|----------------|------------------|---------|--------------|
| Average consultation time (Minute) | 3.66±2.19 | 9.46±4.77 | 6.56±3.48 | 10 min |
| Average dispensing time (Sec) | 21.53±19.89 | 24.04±23.5 | 22.79±21.7 | >180 seconds |
| Total number of drugs prescribed | 189 | 171 | 360 |
| Total number of drugs dispensed | 170 | 124 | 294 |
| Percentage of drugs actually dispensed | 89.9 | 72.5 | 81.2 | 100% |
| Number of drugs adequately labelled | 29 | 50 | 79 |
| Percentage of drugs adequately labelled | 15.4 | 50 | 32.7 |
| Knows dosage | 25(25%) | 48 (88.8%) | 56.9 |

Health facility indicators

Both Quiha and Mekelle hospitals had their own formulary, essential drug list and standard treatment guideline. From the list of key drugs of the hospitals, on average 77.5% of them were available in stock (Table 5).
**Table 5: Availability of key drugs in selected general hospitals**

| List of key drugs         | Quiha hospital | Mekelle hospital |
|---------------------------|----------------|------------------|
| Amoxicillin/clavulanic acid | ✔️             | X                |
| Ciprofloxacin tablet      | ✔️             | X                |
| Cloxacillin capsule       | ✔️             | X                |
| Azithromycin              | ✔️             | X                |
| Diclofenac injection      | ✔️             | ✔️               |
| Diclofenac tablet         | ✔️             | ✔️               |
| Tramadol                  | X              | ✔️               |
| Metronidazole             | ✔️             | ✔️               |
| Insulin                   | ✔️             | ✔️               |
| Nifedipine                | X              | ✔️               |
| Lasix                     | X              | ✔️               |
| Spironolactone            | X              | ✔️               |
| Ceftriaxone               | ✔️             | X                |
| Vancomycin                | ✔️             | ✔️               |
| Metformin                 | ✔️             | ✔️               |
| Enalapril                 | ✔️             | ✔️               |
| Cephalexin                | ✔️             | ✔️               |
| Ferrous sulphate          | ✔️             | ✔️               |
| Paracetamol syrup         | ✔️             | X                |
| Amlodipine                | ✔️             | X                |
Discussion

In this study, the average number of drugs per prescription was within the WHO acceptable standard. The finding was comparable with studies done in different parts of Ethiopia including Jimma (1.59)\textsuperscript{15}, Hawassa University Teaching Referral (1.9)\textsuperscript{11} and Bahir Dar hospital (1.8)\textsuperscript{12}. However, studies in Debre Tabor (2.2)\textsuperscript{12}, Felege Hiwot referral hospital (2.49)\textsuperscript{16} and Karamara public general hospital in Ethiopia (2.46)\textsuperscript{17} reported higher average number of drugs per prescription. Such discrepancy may be attributable to difference in the level of awareness among clinicians working in different part of the country and lack of harmonized national prescribing guidelines.

In terms of percentage of medicines prescribed by generic name, our finding is lower than the WHO's recommended standard value. Similar results were reported in Hawassa University hospital (98.7\%)\textsuperscript{11}, Felege Hiwot specialized University hospital (97.4 \%)\textsuperscript{16} and selected health centres in eastern Ethiopia (97 \%)\textsuperscript{18}. This may be attributable to increasing promotion of brand drugs names influencing clinicians to prescribe drugs in their brand names. Of note, Workneh et al (2016) has shown the prescribing decision of clinicians working in Mekelle were influenced by promotion of medical representatives\textsuperscript{19}. This suggests that there is a gap in ensuring patients to get cost-effective medicines on the side of prescribers and the health institution, which in turn reduce health seeking behaviour of the community\textsuperscript{20}.

The percentage of encounters with antibiotics, which is 58.2\% in the present study is comparable with study conducted in public hospitals in eastern Ethiopia (57.9\%)\textsuperscript{17}, and Hawassa teaching referral hospital (58.1\%)\textsuperscript{11}. As high as 85.5\% were also reported in selected health centres in eastern Ethiopia \textsuperscript{18}. However, our finding is higher than WHO recommended standard (20\%-26.8\%). This finding should be interpreted cautiously as high prevalence of infectious disease in developing countries may partly contributed for such high antibiotic prescribing. However, overprescribing of antibiotics is problematic that need to be carefully monitored as it is associated to antimicrobial resistance which is threat of global health\textsuperscript{21}. The percentage of prescriptions encounters with injections were within WHO standard level.

WHO recommends health care professionals to adhere to national essential medicine for drug prescribing. To this end, a deficiency was noted in terms of prescribing according to essential medicine list of Ethiopia compared to the WHO standard of a 100\%\textsuperscript{8} and to that of the national assessment results of 2003 (99\%)\textsuperscript{22}. This may be attributable to patient preference, clinician decision and availability of the medications.
In this study the average consultation time that the patients spent with clinicians was approximately 7 minutes which is higher compared with studies conducted in public hospitals in eastern Ethiopia (4.6 minutes)\textsuperscript{17}. The duration, however, doesn't seem to be sufficient for to make physical examination and select the best available treatment choices. High patient load could have contributed for such below the optimal duration of consultation time. The average dispensing time recorded in the present study was approximately 23 seconds. This is significantly lower than the WHO recommendation which is 180 seconds\textsuperscript{8}. The lower the dispensing time the poorer would be the understanding of the patients about their medications which this may lead to frequent encounter of drug therapy problems. The percentage of drugs actually dispensed out of the total drugs prescribed to the patients stood at 80% compared to the recommended 100%\textsuperscript{6}. Frequent stock out of medicines may account for this finding. Regarding the adequacy of labelling of medicines dispensed, only slightly over one-third of medicines were appropriately labelled which is far from the recommended level, 100%\textsuperscript{8}. High patient load encountered at outpatient pharmacy department and negligence of the pharmacists together with poor concern and follow up from the hospital side could be implicated for such low level of performance in this indicator. Of note, only about half of the patients knew the dosage schedules of their medicines prescribed to them, which is far below the expected level, 100%.

Both Quiha and Mekelle hospital had their own essential drug list and standard treatment guideline. Only 7.5% of key drugs were in stock and this is low with 100% of the WHO recommendation. Absence of key drugs may impair patient care and compromise patient quality of life.

Conclusion

The findings of the present study showed prescribing practices of antibiotics, prescribing from essential drug list and injections were not within the acceptable WHO recommendations. Overuse of antibiotics facilitate the emergence of antimicrobial resistance which is threat for global health. There was a little deviation in terms of generic prescribing, whereas the average number of drugs per encounter was within the acceptable standard. Poor generic prescribing coupled with shorter consultation and dispensing time may lead to frequent encounters of drug therapy problems. Future studies should investigate underlying factors that contributed for the observed gaps to improve patient care in those hospitals.
Abbreviation and acronyms

EDL: Essential drug list, WHO: World health organization, QH: Quiha Hospital, MH: Mekelle Hospital, INRUD: International Networks for Rational use of medicines.

Ethical Considerations

The study was approved by the institutional review board of Mekelle University (reference number: ERC/224/2019). Based on this a letter of support was written from Tigray regional health bureau. During data collection on patient care indicators, a written consent was obtained from each participant after provision of all the necessary information. In addition, the data collected in the study did not use patient identifiers and were kept strictly confidential and were only used for the purpose of the study.

Acknowledgments

The authors would wish to thank all the staff members of Mekelle and Quiha hospitals for their sincere cooperation and support.

Competing interests

The authors declare that they have no competing interests. The funder has not any involvement in this study.

Availability of data

The data of this study are available from the corresponding author up on a reasonable request.

Funding

This study was funded by college of health sciences, Mekelle university small scale grant with registration number of CRPO/CHS/Young/Recurrent/008/2011.

Patient consent for publication

Not applicable

Author’s contribution

SG and AKG designed the study, obtained the fund, supervising data collection, conducted data analysis, wrote the first draft of the manuscript. SG, KG, AKG and HN provide critical comments, revised and finalized the manuscript. All authors read and approved the final manuscript.
References

1. Timmermans A, A. S. Rational use of drugs. In: United Nations High Commissioner for Refugees. Drug Management Manual. In: Refugees UNHCR, ed., 2006:87-104.
2. Organization WH. The pursuit of responsible use of medicines: sharing and learning from country experiences: World Health Organization, 2012.
3. Mehta S, Gogtay N. From the pen to the patient: Minimising medication errors. Journal of Postgraduate Medicine 2005;51(1):3.
4. Chaturvedi V, Mathur A, Anand A. Rational drug use–As common as common sense? Medical Journal, Armed Forces India 2012;68(3):206.
5. De Vries T, Henning RH, Hogerzeil HV, et al. Guide to good prescribing: a practical manual: World Health Organization, 1994.
6. Ramsay L. Bridging the gap between clinical pharmacology and rational drug prescribing. British journal of clinical pharmacology 1993;35(6):575.
7. Dukes MNG, WHO. Drug utilization studies: methods and uses: World Health Organization. Regional Office for Europe 1993.
8. WHO. How to investigate drug use in health facilities: selected drug use indicators: World Health Organization, 1993.
9. Organization WH. Promoting rational use of medicines: core components: World Health Organization, 2002.
10. National drug Policy of the Trational Government of Ethiopia. 1993
11. Desalegn AA. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. BMC health services research 2013;13(1):1-6.
12. Desta Z, Abula T, Gebre-Yohannes A, et al. Drug prescribing patterns for outpatients in three hospitals in north-west Ethiopia. Ethiopian Journal of Health Development 2002;16(2):183-89.
13. FMHACA. List of Essential Medicines for Ethiopia 2010
14. Isah A, Laing R, Quick J, et al. The development of reference values for the WHO health facility core prescribing indicators. West African Journal of Pharmacology and Drug Research 2001;18:6-11.
15. Abdulahi M, Shiferaw T. Patterns of prescription in Jimma Hospital. The Ethiopian Journal of Health Development 1997;11(3)
16. Laychiluh B. Assessment of drug prescription practice using WHO prescribing indicators in Felege Hiwot Referral Hospital (FHRH) outpatient department, North, Ethiopia. International Journal of Pharmaceutics 2014;4(3):89-94.
17. Sisay M, Mengistu G, Molla B, et al. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. BMC health services research 2017;17(1):1-9.
18. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization’s prescribing, patient care and health facility indicators in selected health facilities in eastern Ethiopia. BMC health services research 2016;16(1):1-8.
19. Workneh BD, Gebrehiwot MG, Bayo TA, et al. Influence of Medical Representatives on Prescribing Practices in Mekelle, Northern Ethiopia. PLOS ONE 2016;11(6):e0156795. doi: 10.1371/journal.pone.0156795
20. Shaikh BT, Hatcher J. Health seeking behaviour and health service utilization in Pakistan: challenging the policy makers. Journal of public health 2005;27(1):49-54.
21. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Therapeutic advances in drug safety 2014;5(6):229-41.
22. WHO. Assessment of the pharmaceutical sector in Ethiopia: Addis Ababa, Ethiopia.: Ministry of Health, 2003.
**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies**

| Section/Topic          | Item # | Recommendation                                                                                                                                                                                                   | Reported on page # |
|------------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Title and abstract     | 1      | *(a)* Indicate the study's design with a commonly used term in the title or the abstract                                                                                                                          | 1                  |
|                        |        | *(b)* Provide in the abstract an informative and balanced summary of what was done and what was found                                                                                                            | 1                  |
| Introduction           |        |                                                                                                                                                                                                                  |                    |
| Background/rationale   | 2      | Explain the scientific background and rationale for the investigation being reported                                                                                                                             | 2                  |
| Objectives             | 3      | State specific objectives, including any prespecified hypotheses                                                                                                                                                | 3                  |
| Methods                |        |                                                                                                                                                                                                                  |                    |
| Study design           | 4      | Present key elements of study design early in the paper                                                                                                                                                    | 4                  |
| Setting                | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                                   | 4 and 5            |
| Participants           | 6      | *(a)* Give the eligibility criteria, and the sources and methods of selection of participants                                                                                                                   | 5                  |
| Variables              | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable                                                                            | 5 and 6            |
| Data sources/measurement| 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group                                      | 5 and 6            |
| Bias                   | 9      | Describe any efforts to address potential sources of bias                                                                                                                                                    | 5                  |
| Study size             | 10     | Explain how the study size was arrived at                                                                                                                                                                       | 5                  |
| Quantitative variables | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why                                                                                     | 7                  |
| Statistical methods    | 12     | *(a)* Describe all statistical methods, including those used to control for confounding                                                                                                                         | 7                  |
|                        |        | *(b)* Describe any methods used to examine subgroups and interactions                                                                                                                                           | 8                  |
|                        |        | *(c)* Explain how missing data were addressed                                                                                                                                                                   | --                 |
|                        |        | *(d)* If applicable, describe analytical methods taking account of sampling strategy                                                                                                                            | --                 |
|                        |        | *(e)* Describe any sensitivity analyses                                                                                                                                                                        | --                 |
| Results                |        |                                                                                                                                                                                                                  |                    |
| Category            | Number(s) | Description                                                                                                                                                                                                 | Page | Note                                                                 |
|---------------------|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------------------------------------------------------------------|
| Participants        | 13*       | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed                                   | 7    |                                                                      |
|                     |           | (b) Give reasons for non-participation at each stage                                                                                                                                                       | 7    |                                                                      |
|                     |           | (c) Consider use of a flow diagram                                                                                                                                                                        | --   |                                                                      |
| Descriptive data    | 14*       | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders                                                                    | 7    |                                                                      |
|                     |           | (b) Indicate number of participants with missing data for each variable of interest                                                                                                                                                 | ---  |                                                                      |
| Outcome data        | 15*       | Report numbers of outcome events or summary measures                                                                                                                                                            | 7-11 |                                                                      |
| Main results        | 16        | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included    | ---  |                                                                      |
|                     |           | (b) Report category boundaries when continuous variables were categorized                                                                                                                                   | ---  |                                                                      |
|                     |           | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period                                                                                            | ---- |                                                                      |
| Other analyses      | 17        | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                                                                                                                 | ---  |                                                                      |
| Discussion          |           |                                                                                                                                                                                                           |      |                                                                      |
| Key results         | 18        | Summarise key results with reference to study objectives                                                                                                                                                     | 12   |                                                                      |
| Limitations         | 19        | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                          | 12   |                                                                      |
| Interpretation      | 20        | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                               | 13-14|                                                                      |
| Generalisability    | 21        | Discuss the generalisability (external validity) of the study results                                                                                                                                       | 14   |                                                                      |
| Other information   |           |                                                                                                                                                                                                           |      |                                                                      |
| Funding             | 22        | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based                                                                 | 16   |                                                                      |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.