Pattern and determinants of antibiotic mal-prescription by family physicians in primary health care facilities of Iran

Gholamali Karimi
Alborz University of Medical Sciences

Hosein Azizi (azizlepid@gmail.com)
Tabriz University of Medical Sciences https://orcid.org/0000-0002-4163-6158

Kourosh Kabir
Alborz University of Medical Sciences

Babak Farrokhi
Tehran University of Medical Sciences

Ali Delpisheh
Ilam University of Medical Sciences

Effat Abbaszadeh
Alborz University of Medical Sciences

Elham Davtalab Esmaeili
Tabriz University of Medical Sciences

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Abstract

Background: Mal-prescription of antibiotics is a major and ongoing global public health problem both in developing and developed countries. Family physicians are the most important and dominant health services providers in Iran their prescription pattern is poorly understood. This study aimed to assess the pattern and factors affecting antibiotic prescribing by family physicians in primary health care (PHC).

Methods: In this descriptive-analytical study, 1068 prescriptions of family physicians in PHC were assessed in Alborz province health facilities. Prescriptions were selected by simple random sampling. The mal-prescribing was assessed based on four criteria including dose per consumption, dose per day, correct duration of therapy and possible interaction with other drugs. Logistic regression was used to estimate the odds ratio and 95% confidence interval for the association between antibiotic prescription and the affecting factors.

Results: The average number of antibiotics was found 1.27 per prescription and 56.8% of the prescriptions had at least one antibiotic. There was a statistically significant relationship between age, gender, type of health insurance, work experience of physician, seasons of the year and receiving antibiotics (P<0.05). In 59.31% of antibiotic prescriptions at least one of the scientific criteria was not satisfied.

Conclusion: The number of prescribed antibiotics and the mal-prescription percentage were high among family physicians. Strong political commitment and altering physicians’ training curricula especially promoting a preventive approach and developing a registration system for identifying adverse drug reactions, antibiotic use patterns and control of mal-prescription are imperative at the grass-root level.

Introduction

Irrational use and mal-prescription of drugs are a major and ongoing global public health problem both in developing and developed countries that deserves more attention by health systems and policymakers [1, 2]. Rational and appropriate usage of drugs were defined as reasonable and appropriate use of drugs at an advisable time so that they have had beneficial effects on patients in terms of the virtue of strength, dose and duration of therapy [3]. Rational use of drugs depends on pursuing the process of prescription which includes identification of patients’ problem (diagnosis), effective and safe therapy (therapy with drugs or non-drugs options), selecting suitable drugs, dosage, and duration, writing a good prescription, providing enough information to the patient and planning to evaluate treatment responses [4].

Self-medication by patients and the prompt and constant spread of antimicrobial-resistant organisms are major threats to our ability to successfully treat most of the contagious diseases. In the lack of development of new generations of antibiotic drugs, appropriate use of current antibiotics is required to guarantee the long-term availability of effective therapy for microbial infections [2, 5-7].

In Iran, the Primary Health Care (PHC) is the first, nearest and comprehensive line of basic and essential health services which is provided by family physicians and some other health workers in all cities and villages across the country. Some evidence indicate that the inappropriate prescription of antibiotics and the prevalence of self-medication are the main causes of antibiotic resistance and side effects in Iran [8, 9]. It is reported that the antibiotics are used as common drugs in Iran and almost half of the patients receive at least one antibiotic during doctor-patient encounters. It is also estimated that more than 8% of hospital admissions in Iran occur due to adverse drug reactions [5, 10, 11]. Accordingly, rational and appropriate drug prescription, especially the antibiotics, will decrease antibiotics resistance, adverse drug reactions, toxicity risks, healthcare expenditure and household costs, and duration of therapy at the global level [11, 12].

Among PHC family physicians, the pattern and the associated factors of mal-prescription are poorly understood and very limited studies have been performed in this regard, especially after implementation of rural health insurance and family physician plan. The present study aimed to determine the prescription pattern of antibiotics for outpatients in health centers of the Alborz province, Iran and also to identify the effective factors on this pattern.
Methods

Study design

In this descriptive-analytical study, 1068 prescriptions by 48 family physicians in PHC were selected among total 90115 prescriptions from total of 8 rural, 8 urban and 3 urban-rural health centers (sampling frame) from September 2012 to September 2013 in Savojbolagh, Alborz province, Iran.

We selected 1068 prescriptions by simple random sampling and the equal proportion in the all seasons (267 prescriptions in each season). Due to different distribution (coverage) of health insurances in Iran and also the study area, the prescriptions (samples) were selected proportional to the size of population under coverage of each health insurance. Therefore, after estimating the total sample size, the samples were selected as social security health insurance 534 (50%), rural health insurance 428 (40%), therapeutic insurance 83 (8%), and armed forces health insurance 23 (2%).

We had all antibiotic prescriptions list, therefore in the sampling process, the unreadable or prescriptions with poor information were excluded and the next prescriptions were replaced. The sample size was estimated in 1068 by considering the prevalence of antibiotic prescription by family physician (P=0.4), type I error (α=0.05), and the precision (d=0.03) by Cochran formula.

Data collection

Incorrect or mal-prescription of antibiotics was assessed based on four scientific criteria including a) dose per consumption, b) dose per day, c) duration of therapy and d) possible interaction with other antibiotics or drugs. The incorrect prescription was defined if at least one of the items above is not satisfied. Assessment of the prescriptions was performed by a high expert pharmacist (more than 10 years’ experience) who was not involved in the study or analysis of the outcome measure. The assessment was based on Martindale: The Complete Drug Reference. For this purpose, firstly the symptoms and prescribed antibiotics according to the type of diagnosis (severity of the disease) were extracted from the prescriptions and health records by the clinician and the pharmacist.

Based on the standard guidelines, each drug and disease has a standard dose per day, duration of therapy, interaction with other drugs or antibiotics in accordance with various ages, genders, weight and disease. The appropriateness of antibiotic prescriptions were assessed regarding the related guideline and the mentioned four criteria, then the incorrect prescriptions were identified for each prescription.

Same number of prescriptions were selected in each season of the year. The dose of all drugs and antibiotics per each consumption, day, duration, possible interaction based on the type of disease stage, and diagnosis were determined by the Complete Drug Reference. The dose of antibiotics (different format) calculated according to Milligram (mg) for edible (oral) drugs (such as tablet, capsule) and Milliliter (ml) for suspension, ampoule and infusion drugs. The number of drops and the speed of liquid infusion was calculated with this formula: . The drop factor was special for each drug.

A checklist was used for data collection. Variables and information such as age, gender of physicians and patients, number and total price of drug items and the name and type of the prescribed antibiotic, form and usage method of drug, consumption way based on amount of use for each time, duration of treatment course, times of use each day, possible interaction with antibiotics or drugs, rate of combination therapy, type of physicians’ graduation (private or government universities) and also the status of occupation and the working experience (years) were extracted from prescriptions and personnel files.

The government medical universities are classified in 3 levels based on annual scientific report of Iranian Ministry of Health and Medical Education.

Data analysis

SPSS software (version 18.0, Chicago, IL, USA) was used for data analysis. For checking data normality, the Kolmogorov-Smirnov test was used. Chi-square test was used for binary variables and Independent Samples T-test was used for normal
quantitative variables. Logistic regression was used to estimate the odds ratio and 95% confidence interval for the possible association between antibiotic prescription and the affecting factors. P-value <0.05 was considered significant in all of the tests.

**Results**

Table 1 indicates the socioeconomic status and their relationship between antibiotics prescription and effective factors by family physicians in PHC in Alborz province, Iran. Of the total prescriptions (3704 items of drugs) assessed, 607 (56.8%) prescription had at least one item of antibiotic. Moreover, out of the 3704 items of prescribed drugs among all prescriptions, 772 (20.8%) items were antibiotics. It was found a significant difference between antibiotic prescribing and different seasons of the year. Regarding the seasons, 112 (41.9%) prescriptions in the summer and 177 (66.3%) in the winter had at least one antibiotic (P<0.05).

Among all assessed prescriptions of drugs, 640 (59.9%) of them were related to female genders, while the proportion of received antibiotic was more in males than females (63.3% versus 52.5%). Moreover, according to the type of health insurance among 1068 assessed prescriptions, patients who had social security health insurance booklet had the majority of prescriptions (more than 50%). This study showed that there was a relation between physicians’ experience and the antibiotic prescription so that the low experience of family physicians increased the likelihood of antibiotic prescribing (P=0.008).

The average age of studied outpatients was 32.4±21.4 years. There was a statistically significant difference between patients who had received antibiotics (26.07±19.3) with those who didn’t (40.7±21.2) (table 1). Also, the mean age of outpatients was reported as lowest in the winter and highest in the summer (figure 1).

Average drug items and price per prescription were 3.47±1.3 and 59034 Rls, respectively. Likewise, prescriptions involved antibiotics was reported 3.67±1.22 and 35065 Rls, respectively. A relationship was observed between price, drug items and prescriptions with antibiotic (Table 2).

Table 3 demonstrates the distribution of prescribed antibiotics based on name, form of drug and consumption way. Among all prescribed antibiotics the Amoxicillin capsule 500mg (10.2%), among drug forms the pill (24.7%), and in terms of consumption method the oral method (70.59%) had the highest frequency of prescribed antibiotics.

Table 4 indicates the proportion and distribution of incorrect prescriptions (with and without antibiotics) among all 1068 assessed prescriptions of the family physicians. As the table shows, among the four criteria of assessing the prescriptions, the incorrect prescription was higher in the dose per day criteria with 34.06% errors in prescriptions with antibiotics and 38.71% errors in those without antibiotics.

**Discussion**

This study investigated the pattern of antibiotic prescription and its affecting factors and also the mal-prescription situation among family physicians in Iranian PHC system. Family physicians are the most important and the major healthcare providers in PHC of Iran. Modification of the antibiotic mal-prescription pattern among these providers can play a major role in reducing the burden of microbial resistance and health expenditures in Iran and global health systems. Furthermore, previous studies had examined mostly the prescribing of antibiotics in general practitioners, specialists or dentists [13, 14]. This study is one of the few studies that focused on family physicians in Iran.

The proportion of prescriptions with antibiotic in this study (56.8%) is similar to the result of an Indian study that reported 55%, [15] but this portion was reported 45% in a study in Sabzevar, Iran [16]. It is a high rate of antibiotic prescription in this study. The reasons of this high and irrational prescription of antibiotics by family physicians may include beliefs, different social and cultural factors among patients, high rate of environmental pollutants in accordance to the industrial zone, especially the air pollution, due to neighboring to the capital city of Tehran and the Karaj metropolis, and being suspicious to infectious diseases.
such as sinusitis and pharyngitis. Likewise, it may occur due to easy access to medications and drugs and the low price of
drugs in comparison to other countries.

Yet, the rate of antibiotic prescription in our study was less than a study conducted from Tehran metropolis (62.39%) [17],
which supports the effect of accessibility factor and the role of environmental pollutants that causes more infections. Tehran,
the Capital of Iran, is a highly crowded city with high air pollution at the global level. In Tehran, it is easy access to prescribed
antibiotics by family physicians. The low experience of family physicians (newly graduated), the high proportion of specialists
(almost 70% of all specialists of the country), self-medication, and the habit and cultural factors of the people altogether
encourage them to refer to physicians who prescribe many antibiotics particularly in injected forms.

The average rate of prescribed drug items in this study was 3.47 per prescription, this finding is almost in agreement with
Iranian protocol of family physicians prescriptions that is 3.5 items [18]. However, this portion is higher than developing
countries which is between 2.2 to 3.8 and developed countries about 1.3 to 2.2 [19, 20]. This means an undesirable status of
drug prescribing in this study.

Another related factor to the antibiotic prescribing in the present study was the impact of the seasons so that the number of
antibiotic prescriptions increased as the cold season came. This finding is in agreement with national studies [11, 21].

One of the most important criteria for evaluating the correct and rational prescribing of antibiotics is compliance with
international valid guidelines and up-to-date medical science. Our findings showed that a large volume of antibiotics
prescribed in our study area did not follow the correct scientific method. This defect may be a major determinant of the
development of antibiotic resistance and maybe a threat to human life.

In this study, incorrect and unscientific antibiotic prescriptions were assessed based on four criteria including antibiotic
dosage per consumption, daily doses, duration of therapy and interaction with other antibiotics or drugs. Our findings showed
that prescription of the antibiotics by family physicians were unscientific or incorrect in most cases. This finding has been
observed in other studies in Iran and other countries [22-26]. But this issue in our study was reported slightly high. Therefore,
reducing the number of antibiotics in each prescription and inappropriate and unscientific prescribing of antibiotics are major
concerns for drug resistance and it is a challenge for the country's health system that deserves prompt attention to improve
and modify it.

In the present study injecting form of antibiotics was prescribed more than other forms with 22.27%. Although this amount
was reported 49% in a study in Urmia city of Iran [27] that is higher than our study but the injection form was reported less than
our study in the Bhopal zone of India with 13.8% [28]. Therefore, a high percentage of injectable antibiotics are prescribed by
family physicians shows an irregular form of injecting antibiotics by them. It may have resulted from cultural-social factors
and believing the high effect of injecting form of drugs by the patients which, besides being expensive in regard to oral form,
sometimes are dangerous for patients [29]. Another reason maybe the existence of injecting section in most of therapeutic and
health centers and following the desire of patients to receive whole services from the place of their refer [11, 17]. Amoxicillin
and Penicillin were the most commonly prescribed drug in our study and also a study of Dong and et al. in China [30].

The price of antibiotics in proportion to total price of drugs of each prescription was 33.7% and to the prescriptions that
included antibiotics was 56.4%. This is a high number in comparison to the results of the study from Urmia, Iran with 35% [27]
and the finding from other countries such as France with 34.7% and USA with 33% [31, 32]. This high rate of antibiotic
prescription imposes more economic load on families and the health system of the country. A previous study stated that up to
$3500 can be saved by limiting the antibiotic prescribing [33]. Anyway the average price of prescriptions in this study which
was 59034 RIs in comparison to the U.S, that was $75 in 2006, was a low number that shows the lower price of the drugs and
unreal cost of it in the country [34].

**Conclusion**
Our findings indicated that antibiotic prescription rate and its mal-prescription were high among family physicians and need intervention by health care system. Findings of this study can be useful about the antibiotic prescribing pattern and mal-prescribing of drugs in Iranian PHC by family physicians. Our study results may assist program managers and policymakers to develop effective plans to improve irrational antibiotic prescribing patterns and health expenditure in Iranian PHC and also worldwide health systems.

Developing a registration system for identifying adverse drug reactions, antibiotic use patterns, and inappropriate prescriptions, revising the treatment protocols and family physicians service package, development of targeted and effective training programs at different levels are suggested.

**Abbreviations**

PHC: Primary Health Care

**Declarations**

**Ethics approval and consent to participate**

Protocol of this study was reviewed and approved by the Students’ Research Committee and the institutional review board which is the Ethic Committee of the Ilam University of Medical Sciences with code IR.MEDILAM.REC.1391.87. Data collection included the drug prescriptions by family physicians in the records.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The dataset generated and analyzed during this study are not public but can be accessed if sufficient request is made to the corresponding author.

**Competing interests**

The authors have no conflicts of interest to declare for this study.

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**Authors’ contributions**

HA, GK: Developed the original idea, protocol development and interpretation, data analysis, and data collection and drafted all sections of the manuscript. Data collection, Data extraction, contributed to the development of the protocol: AD, KK, BF, EA and EDE. All the authors approved the final manuscript.

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Tables

**Table 1.** Selected socio-economic status and factors affecting antibiotic prescription by family physicians in primary health care, Savojbolagh, Alborz province, Iran
| Variables                  | Prescription (1068) | OR (95% CI) | p-value |
|---------------------------|--------------------|-------------|---------|
|                           | With antibiotic N=607 | Without antibiotic N=461 |         |
| Age of patients           | 32.4±21.4          | 26.07±19.3  | 40.7±21.2 | 4.47 (2.58-8.89) | 0.001 |
| Gender of patients        |                    |             |         |
| Male                      | 271(44.6%)         | 157(34.1%)  | 1.56 (1.22-2.01) | 0.001 |
| Female                    | 336(55.4%)         | 304(65.9%)  | 1.06 (0.81-1.38) | 0.688 |
| Gender of physicians      |                    |             |         |
| Male                      | 174(28.7%)         | 127(27.5%)  | 1.06 (0.81-1.38) | 0.688 |
| Female                    | 433(71.3%)         | 334(72.5%)  | 1.06 (0.81-1.38) | 0.688 |
| Seasons of year           |                    |             |         |
| Autumn                    | 172(28.3%)         | 95(20.6%)   | 1.74 (1.07-4.88) | 0.042 |
| Winter                    | 177(29.2%)         | 90(19.5%)   |         |         |
| Spring                    | 146(24.1%)         | 121(26.2%)  |         |         |
| Summer                    | 112(18.5%)         | 155(33.6%)  |         |         |
| Type of insurance booklet | Rural and tribes   | 216(35.4%)  | 212(46.4%) | 4.12 (1.67-14.39) | 0.002 |
|                          | insurance social security | 333(55%) | 201(43.8%) |         |         |
|                          | therapeutic services | 46(7.6%)   | 37(7.4%)   |         |         |
|                          | armed forces        | 12(2%)      | 11(2.4%)   |         |         |
| Employment statues of Physicians | Regular Hiring | 44(7.2%) | 39(8.5%) | 1.02 (0.33-1.54) | 0.898 |
|                          | Contractual Hiring | 20(3.3%) | 15(3.3%) |         |         |
|                          | Family physician’s contract | 410(67.5%) | 310(67.2%) |         |         |
|                          | Plan bill           | 133(21.9%) | 97(21%) |         |         |
| Experience of the physicians | <2 years           | 317(60.96%) | 203(39.03%) | 1.38 (1.08-1.77) | 0.008 |
|                          | ≥2 years            | 290(52.91%) | 258(47.08%) |         |         |
| Graduation university    | Governmental university | 392(64.6%) | 317(68.8%) | 0.83 (0.64-1.07) | 0.152 |
|                          | Private university  | 215(35.4%) | 144(31.2%) |         |         |
| Type of university*      | Type I              | 256(65.3%) | 205(64.7%) | 0.78 (0.76-1.12) | 0.188 |
|                          | Type II             | 118(30.1%) | 105(33.1%) |         |         |
|                          | Type III            | 18(4.6%)   | 7(2.2%)   |         |         |
| Type of health center    | Rural               | 243(40%)   | 201(43.6%) | 0.86 (0.46-1.39) | 0.259 |
|                          | Urban               | 49(8.1%)   | 27(5.6%)   |         |         |
|                          | Rural-Urban         | 315(51.9%) | 233(50.5%) |         |         |

* Scientific rank

**Table 2.** The average and difference mean of number and price of total drug items and antibiotic items among prescriptions with and without antibiotic.
| Variables                          | Prescription with antibiotic | Prescription without antibiotic | Mean ± SD | p-value | Mean difference | 95% Confidence Interval |
|-----------------------------------|------------------------------|---------------------------------|-----------|---------|----------------|------------------------|
|                                  |                              |                                 |           |         |                | Lower Bound | Upper Bound |           |         |
| Total of drug items              | 2229                         | 1475                            | 3.47±1.3  | 0.001   | 0.47           | 0.31       | 0.62       |           |         |
| Total of antibiotic items        | 772                          | 0                               | 1.27±76   | -       | -              | -          | -          |           |         |
| Overall price or prescriptions   | 37,719.35                    | 25,329.21                       | 59034.23  | ±9161.65| 0.018          | 7196.55    | 1260       | 13132     |         |
| Price of antibiotics per prescriptio | 21,284.95                     | 0                               | 35065.19  | ±4172.86| -              | -          | -          | -         |         |

*Rls

**Table 3.** Frequency of prescribed antibiotics based on name, the form of drug and consumption method by family physicians

| Rank | Name                                | Percentage | Form of Drug | Percentage | Method | Percentage |
|------|-------------------------------------|------------|--------------|------------|--------|------------|
| I    | Amoxicillin 500 mil.g (cap)         | 10.23%     | Tablet       | 24.7%      | Oral   | 70.59%     |
| II   | Penicillin 1,200,000 u.v (vial)     | 9.06%      | Capsule      | 23.05%     | Injection | 22.27%     |
| III  | Azithromycin 250 mil.g (cap)        | 8.03%      | Suspension   | 22.7%      | Local  | 7.12%      |
| IV   | Penicillin 6.3.3 u.v (vial)         | 6.9%       | Vail         | 21.3%      |         |            |
| V    | Cefixime 100(susp)                  | 5.8%       | Ointment     | 4.2%       |         |            |
| VI   | Cefixime 400 mil.g (tab)            | 5.6%       | Drop         | 2.7%       |         |            |
| VII  | Co-amoxyclov 312 (susp)             | 5.5%       | Ampoule      | 0.9%       |         |            |
| VIII | Other antibiotics                   | 48.88%     |              |            |        |            |

**Table 4.** Distribution of incorrect prescriptions with and without antibiotics by family physicians in primary health care
| Type of incorrect prescription | With Antibiotic prescription | Without Antibiotic prescription | Total incorrect prescriptions |
|--------------------------------|-------------------------------|---------------------------------|------------------------------|
| Dose per consumption           | 10.23%                        | 12.52%                          | 21.9%                        |
| Doses per day                  | 34.06%                        | 38.71%                          | 67.72%                       |
| Duration of treatment          | 15.02%                        | 17.13%                          | 29.97%                       |
| Interaction with other antibiotics | 23.22%                        | 17.41%                          | 40.63%                       |

**Figures**

**Figure 1**

Comparison of the difference in the average of patients’ age based on seasons.