Original Article

Wealth-related Inequality in Utilization of Antihypertensive Medicines in Iran: an Ecological Study on Population Level Data

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Abstract

Background: We aim to evaluate the trend of national and sub-national (provincial) utilization pattern of antihypertensive medicines in the Iranian population in the past decade and evaluate whether there is any wealth-related inequality in utilization of these medicines among different provinces.

Method: Either fixed effect or random effect linear panel data model was used to check the effect of wealth index on utilization of all antihypertensive medicines and each class, adjusting for other covariates including years of schooling, urbanization, mean age, and food type of provinces. The principal component analysis was applied to make summery measures for covariates using available national datasets.

Results: The effect of wealth category on the utilization of all antihypertensive medicines among Iranian provinces was positive and significant (0.84; 95% CI: 0.09, 1.59). Accordingly as subgroup analysis, in BBs and CCBs classes, the effects of wealth category on utilization of medicines were positive and significant (0.36; 95% CI: 0.12, 0.60 and 0.27; 95% CI: 0.07, 0.40, respectively). However in ACEIs and Diuretics classes, the effects of wealth category were positive but not significant. In ARBs class, the effect of wealth on utilization was negative and not significant (-0.04; 95% CI: -0.27, 0.18).

Conclusion: According to this study, an inequality could be observed in Iran related to wealth category in utilization of total antihypertensive medicines between provinces.

Keyword: Antihypertensive; inequality, Iran, utilization

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Introduction

Cardiovascular diseases are among the most prevalent chronic and non-communicable diseases (NCDs) and a leading cause of death in Iran and the world.[1,2] The attributable burden of cardiovascular and circulatory diseases in the world has been estimated at 4,282 (95% CI: 3963, 4493) DALYs per 100,000 population in 2010.[3] Hypertension is the most important risk factor of CVDs before diabetes and obesity.[4] According to the report of the World Health Organization (WHO) in 2013, not only the prevalence of hypertension is higher in low and middle income countries but also the number of undiagnosed or untreated people is more in these regions compared with developed nations.[5] The high prevalence of hypertension in developing countries might be related to increasing urbanization, population aging pattern and inadequate access to health services.[6] According to a study on metabolic risk factors of mortality in Iran, high systolic blood pressure (SBP) was estimated to cause 41,000 and 39,000 deaths in 2005 in men and women, respectively and by reducing SBP to the optimal level, life expectancy would be increased by 3.2 and 4.1 years.[7]

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The effectiveness of treatment

The effective role of antihypertensive medicines in hypertension control has been proved in many studies[8,9] and is suggested in therapeutic guidelines.[10,11] In a study, it has been estimated that using a multidrug regimen (including a statin, aspirin and two antihypertensive medicines) for high risk patients over a 10-year period can prevent 17.9 million cardiovascular deaths in low and middle income countries.[12] Also, in an updated version of this study for Iranian patients, it was estimated that using this Polypill strategy can prevent 28,500 (95% CI: 21700, 34100) ischemic heart disease deaths and 12,700 (95% CI: 8800, 15900) stroke deaths in the Iranian population.[13]

The equality of treatment utilization

Regarding these supporting evidences, availability and affordability of antihypertensive medicines for all patients, regardless of their income and other socioeconomic and geographic factors, can help to avoid more complicated and costly health states among the population. Monitoring the current utilization and prescription pattern of antihypertensive medicines at national and sub-national levels is very useful for at least two purposes: first, to monitor the inter-regional variation inside the country and check for disparity and inequality issues[14]; and second, to evaluate the consistency of current strategies compared with international and domestic clinical evidences.[15] In the current ecologic study, we aim to evaluate the trend of national and sub-national (provincial) utilization pattern of antihypertensive medicines in the Iranian population in the past decade and evaluate whether there is any wealth-related inequality in utilization of these medicines among different provinces.

Materials and Methods

This is an ecological utilization study using national and subnational population level data of Iran. In this study, the utilization trend of different antihypertensive classes and the inequality of utilization were assessed using panel data models.

Data sources and data preparation

Medicine utilization data source

The annual pharmaceutical market database of Iran's food and drug administration (IR FDA) was used to extract the sales data of antihypertensive medicines as a proxy for utilization. This database is constructed from monthly and annual sales reports (value and volume) of pharmaceutical distribution companies to pharmacies at district-level.[16]

We extracted the districts-level sales data of antihypertensive medicines in their different strengths and dosage forms for years 2002–2011. Given the uncertainty on validity and accuracy of this district-level sales data, we aggregated them at province level according to the new 31-province structure of the country at the time of study. As access to district-level data was not possible for after 2011, we could not update our data anymore. The sales volume of each medicine was transformed to Defined Daily Dose (DDD) according to WHO guidelines[17]; therefore, all dosage forms and strengths of a medicine were unified.

The utilization trend of antihypertensive medicines was assessed totally and also in five major pharmacologic classes including beta blockers (BBs), angiotensin converting enzyme inhibitors (ACEIs), calcium channel blockers (CCBs), angiotensin II receptor blockers (ARBs), and diuretics. The utilization of all antihypertensive medicines and utilization of each class was calculated based on DDDs per 1000 inhabitants per day.[17] As hypertension is rarely observed before the age of 30, and also to exclude the effect of differences in population age group distribution between provinces, people aged over 30 years were only considered in calculation of per capita utilization.

Wealth data source and index measurement

To include the wealth level of each province, we used the results of national household expenditure survey that is run annually by the Iran statistics center. In one part of this survey, sampled households in all provinces are asked about their current particular assets (for example, house, car, motorcycle, carpet, refrigerator, etc.). Using the individual-level data of the household expenditure survey and performing a principal component analysis on the asset-related variables, a measure was made as wealth index for each province-year. Such an approach for constructing socioeconomic indices has been reported in literature.[18,19]

Covariates

A list of covariates including years of schooling, urbanization, the mean age, and food type were also used in this study as explanatory variables. The mean years of schooling of inhabitants of each province in each year were calculated from the national census data and used in the model as a potential factor affecting medical utilization.[20–22] The urbanization was also included as a covariate, given its impact on healthcare access and utilization.[23,24] The proportion of urbanization and the mean age of each province were also calculated using census data. For food type covariate, the household expenditure national survey data was applied.[25] One section of this survey is about food and drinks utilization, from which we constructed 14 food classes, based on Iran national and subnational burden of disease (NASBOD)[26] and global burden of disease (GBD) projects[27]; then, we created food type measure using principal component analysis (PCA). Finally, four principal components (ft1-ft4) were included in the model. According to the results of PCA on food items, Ft1 mostly explains regimens containing fruits, vegetables, and seafood; Ft2 explains grains, oil crops and animal products regimens; Ft3 explains animal products and Ft4 explains tree nuts and fruits containing regimens.

Principal Component Analysis (PCA)

PCA is a statistical method for reducing the number of variables in a dataset. In other words, PCA transforms inter-correlated variables to a small number of linearly uncorrelated components (called principal components).[28] The extracted components totally account for the variance in the dataset while the first component explains the largest possible amount of variation.[29] This process was followed on asset related variables of household expenditure questionnaire and the first principal component was extracted as our «wealth index» covariate. The identified component for wealth index could explain 22% of the total variance of all items. For constructing food type measures, four principal components were used with cumulative 23% of total variance.

Inequality Assessment Analysis

The provinces were categorized in five quintiles according to their wealth index level. Then, the average utilization of different antihypertensive classes was plotted against the wealth quintiles to test the hypothesis of existing significant trend of difference between utilization among provinces of different wealth index level. Means and confidence intervals of utilization were evaluated for each quintile to check the 95% statistical significance of different utilization amount in different quintiles.

In the next step, fixed effect and random effect linear panel data models were used to check the effect of wealth index on utilization, adjusting for other covariates including years of schooling, urbanization, mean age, and food type of provinces. The fixed effect and random effect models were applied to exclude the effect of all time-invariant unobserved variables on the response variable (medical utilization). The Hausman specification test was applied to choose between these two models.[30] In this test, the null hypothesis is that random effect is the appropriate model. The general equation for fixed effect and random effect panel data model in our study is:

$$\begin{aligned} \textit{Medicines utilization} &= \beta_0 + \beta_1.WI_{it} - \beta_2.Yos_{it} - \beta_3.Urb_{it} - \beta_4.Age_{it} + \beta_5.ft1_{it} + \beta_6.ft2_{it} \\ &- \beta_7.ft3_{it} + \beta_8.ft4_{it} + U_{(i)} + e_{it} \end{aligned}$$

Where *WI*: wealth index category; *Yos*: years of schooling; *Urb*: urbanization proportion; *ft*: food type; *U*: fixed effect or random effect; age: mean age; i: province; t: time (year)

The model was then estimated separately for all five antihypertensive classes. We used both R statistical software[31] and STATA 11[32] to conduct above mentioned analysis of this study.

Results

The result of this study showed that the national per capita utilization of total antihypertensive medicines and also all classes had an increasing trend during the investigated years. As shown in Figure 1, the BBs and diuretic classes show the most utilization among antihypertensive classes in 2011.

The correlation between wealth and utilization

Figure 2 indicates the utilization of total antihypertensive medicines in 2002 and 2011 by maps. There are considerable differences between provinces in utilization of total antihypertensive medicines. In addition, the utilization level of provinces shows some variation in 2011 compared with 2002.

The trend of utilization in different wealth level quintiles is shown Figure 3. In these error bars, the confidence interval is shown and the differences are not significant in the overlapping cases. As it shows, there might be a relationship between wealth category and per capita utilization of provinces in total antihypertensive medicines and in all classes. The differences in the utilization of total antihypertensive medicines between quintiles

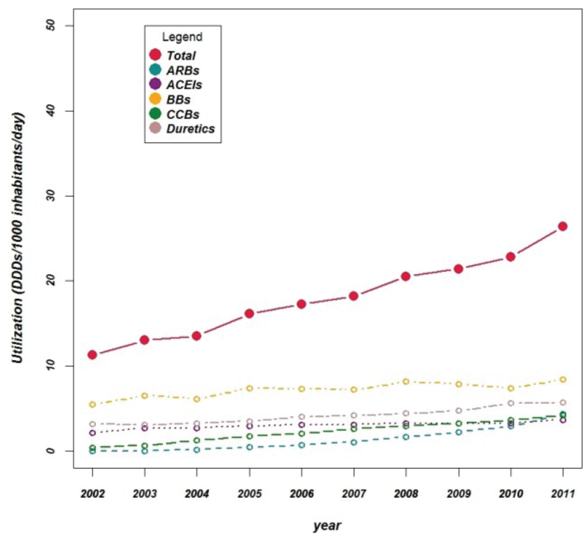


Figure 1. National utilization trend of different antihypertensive classes in 2002-2011.

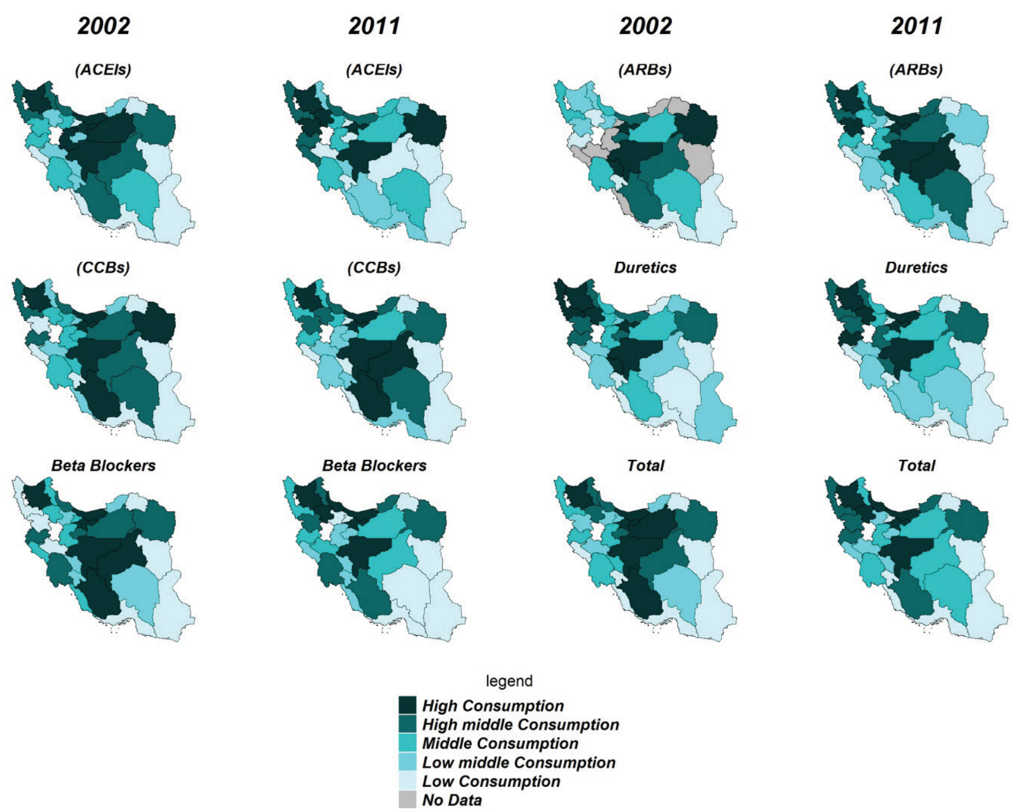
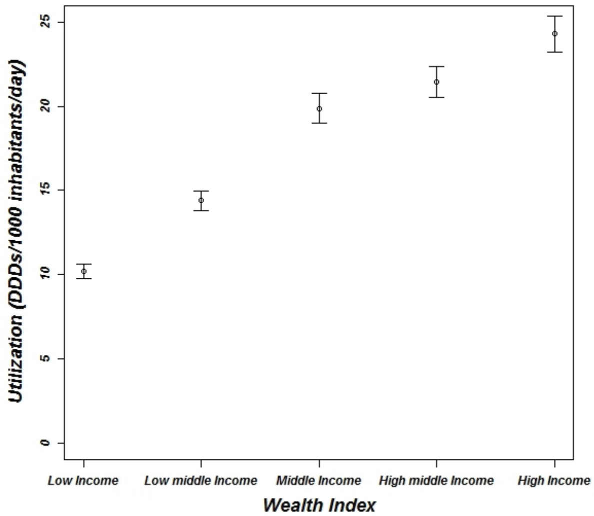
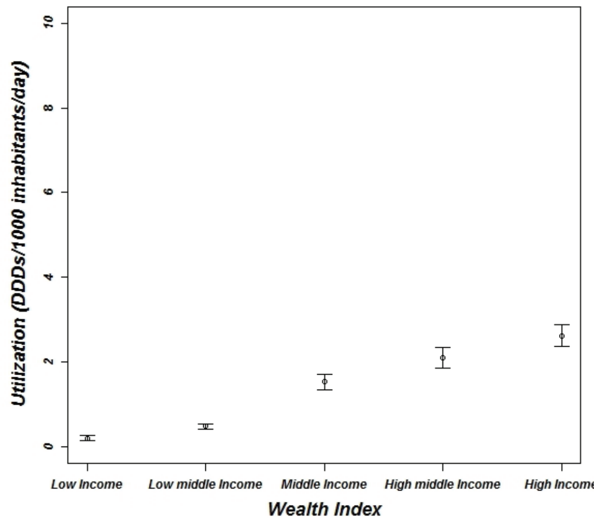


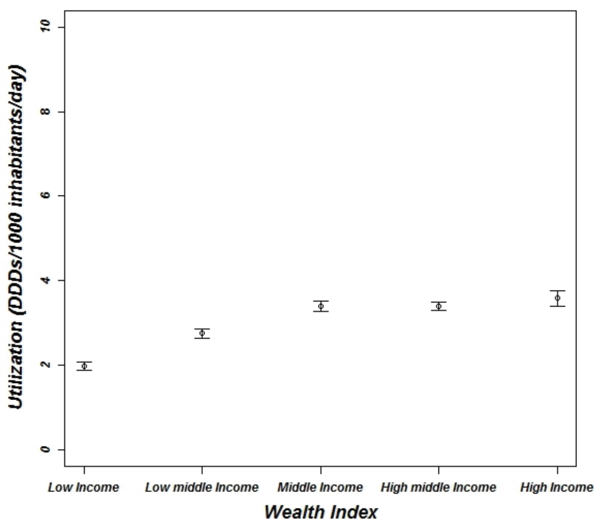
Figure 2. Utilization pattern of total antihypertensive medicines in different provinces in 2002 and 2011.



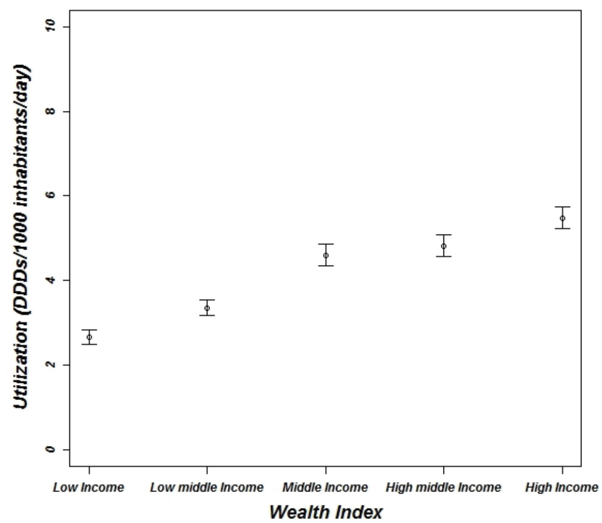
3.a. Total antihypertensive medicines.



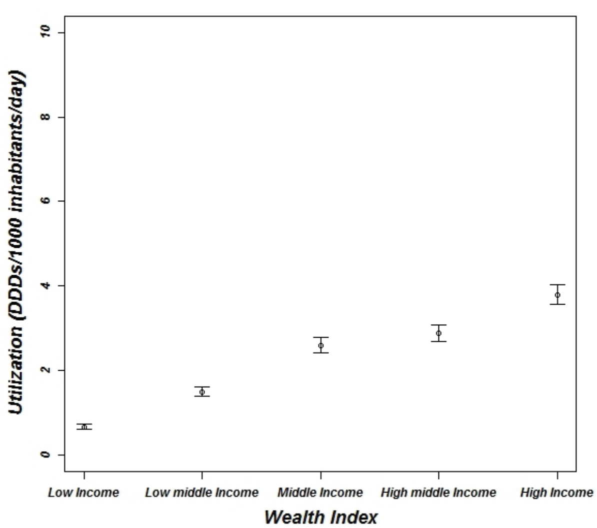
3.b. Angiotensin receptor blockers



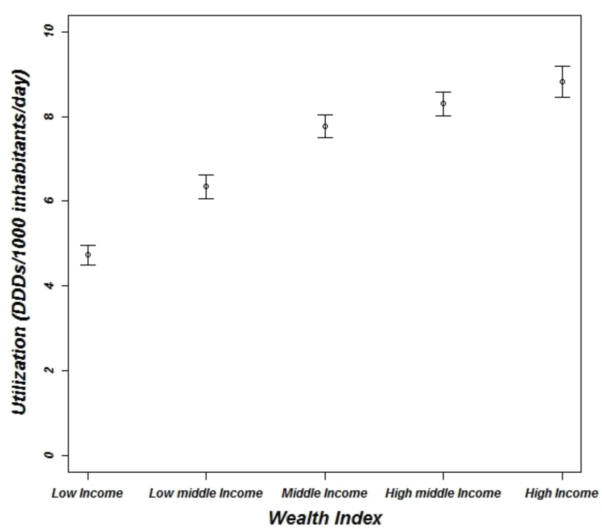
3.c. Angiotensin converting enzyme inhibitors



3.d. Diuretics



3.e. Calcium channel blockers



3.f. Beta blockers

Figure 3. Per capita utilization of antihypertensive medicines in different wealth related quintiles

Table 1. Result of fixed effect model in total antihypertensive medicine utilization.

	Coefficient	Std Err	t	*P>t*	[95% Conf. Interval]
Wealth category	0.845	0.382	2.21	0.028	0.092, 1.598
Years of schooling	6.139	0.968	6.34	0.000	4.231, 8.046
Urbanization	45.820	28.744	1.59	0.112	-10.77, 102.411
Food type 1	1.136	1.012	1.12	0.263	-0.857, 3.130
Food type 2	-2.974	2.047	-1.45	0.148	-7.005, 1.057
Food type 3	-4.728	2.127	-2.22	0.027	-8.917, -0.538
Food type 4	0.101	2.427	0.04	0.967	-4.677, 4.881
Mean age	8.018	1.273	6.30	0.000	5.510, 10.525
Constant	-422.532	59.880	-7.06	0.000	-840.422, -304.642

Std Err = standard error; Conf. Interval = confidence interval

Table 2. Summary result of fixed effect model in each of 5 antihypertensive classes utilization.

	BBs		ACEIs		ARBs		CCBs		Diuretics	
	Coef.	*P>t*	Coef.	*P>t*	Coef.	*P>t*	Coef.	*P>t*	Coef.	*P>t*
Wealth category	0.367	0.003	0.105	0.122	-0.043	0.709	0.272	0.006	0.210	0.076
Years of schooling	0.693	0.012	0.323	0.032	2.635	0.000	1.896	0.000	0.996	0.001
Urbanization	2.403	0.433	1.144	0.408	-10.232	0.273	-3.521	0.635	30.919	0.001
Food type 1	0.475	0.119	-0.084	0.612	0.476	0.133	0.187	0.474	0.132	0.673
Food type 2	-1.156	0.056	-0.552	0.090	-1.845	0.004	-0.448	0.396	0.352	0.578
Food type 3	-0.056	0.646	-0.662	0.045	-2.992	0.000	-0.561	0.306	-1.036	0.116
Ft4 4	-0.994	0.171	-1.206	0.002	2.413	0.002	-0.322	0.606	0.322	0.668
Mean age	0.904	0.004	0.274	0.078	3.929	0.000	1.838	0.000	1.113	0.005
Constant	-41.548	0.005	-12.643	0.087	-189.6	0.000	-92.342	0.000	-74.152	0.000

BBs = beta blockers; ACEIs = angiotensin converting enzyme inhibitors; ARBs = angiotensin receptor blockers, Calcium channel blockers; Coef = coefficient; the models of BBs and ACEIs are random effect and the models of ARBs, CCBs, and diuretics are fixed effect.

are significant. In all antihypertensive classes, the difference of utilization is also significant in favor of wealthier provinces.

The panel data regression model

After controlling for urbanization pattern, years of schooling, mean age, and food types using a fixed effect panel data regression model (Hausman test: $P = 0.001$), the effect of wealth category on the utilization of total antihypertensive medicines among Iranian provinces remained significant (0.84; 95% CI: 0.09, 1.59). In addition, years of schooling (6.139; 95% CI: 4.23, 8.04), mean age (8.01; 95% CI: 5.51, 10.52), and food type 3 (-4.72; 95% CI: -8.91, -0.53) variables also significantly affected utilization (see Table 1).

The same approach was followed for each antihypertensive class using fixed effect model for ARBs, CCBs and diuretics classes and random effect model for BBs and ACEIs classes based on the results of Hausman test. Accordingly, in BBs and CCBs classes, the effect of wealth category on utilization of medicines remained positive and significant (0.36; 95% CI: 0.12, 0.60 and 0.27; 95% CI: 0.078, 0.40, respectively) but in ACEIs and Diuretics classes, the effect of wealth category were not significant anymore (P = 0.12, and 0.07, respectively). In ARBs, the effect of wealth on utilization was negative but not significant (-0.04; 95% CI: -0.27, 0.18). Furthermore, the impact of education (years of schooling) and mean age on utilization was significant in all classes. The urbanization did not show any significant effect on utilization of antihypertensive classes except for diuretics ($P < 0.001$). More details about the result of models in each class are presented in Table 2.

Discussion

There are a few studies about the utilization pattern of medicines in Iran but most of them have assessed the rational prescription and use of medicines. Only in one study by Sarayani *et al.*, it was found that in spite of low price, the utilization of diabetes medicines in Iran is lower than in OECD countries (33). Also, there is no study evaluating wealth related inequality in medicine utilization in Iran; however, the income related health inequality has been assessed during the last years. For instance, Hosseinpoor *et al.,* indicated in their study that the socioeconomic status has the greatest contribution to inequality of infant mortality.[34] In the current study, for the first time we evaluated the sub-national wealth related inequality of utilization in antihypertensive medicine classes in Iran. We used several national level data sources for including different parameters in the models.

The result of this study could raise concern about inequality issues in access to medical services in low income population of the country. The differences in utilization of antihypertensive medicines could be caused by several factors including more undiagnosed cases in lower income areas or inefficient medication after diagnosis. Farzadfar *et al.,* estimated that about only half of patients with hypertension are diagnosed (57.9% in urban and 49.8% in rural areas) and only 39% of patients receive treatment (38.1% in urban, 31.1% in rural areas).[35] The inequality of utilization could also be related to differences in prevalence of hypertension in different geographic regions in Iran.[36] Ebrahimi *et al.*, in their study on the relationship between hypertension prevalence, treatment and control with socioeconomic factors, indicated that human development index of provinces could be related to the prevalence of hypertension but they could not find any relationship between income and hypertension prevalence.[37] Although according to the latest WHO study on pharmaceutical pricing and affordability in Iran, the medicines have been considered as affordable,[38] taking other health related costs into consideration, we should pay attention that medicine price is not the only factor determining the adequate affordability and access of people to medicines and healthcare services. The result of our study is consistent with some studies about the catastrophic health expenditure in Iran.[39,40] One other reason could be the wealth related differences in accessible to well informed physicians or the differences in prescribing pattern of hypertension in provinces of Iran. There is neither such study in Iran about the access to physicians or the prescription pattern of antihypertensive medicines in Iran and their inter-province differences.

The result of this study is also consistent with international evidences. In a household level utilization study on OECD countries, a pro-rich inequality has been observed in physician visit, in spite of equal distribution of physicians.[41] Also, the results of our study are consistent with the results of two studies in Denmark and China on income-related inequality in utilization of health services, in which the medicine consumption of lower income groups was observed to be lower than advantaged groups.[42,43]

This study was faced with some limitations both related to data and estimations. The validity and accuracy of data was the first limitation. This issue was more serious in pharmaceutical sales data because they are reported by distribution companies to the Iran food and drug organization and they might be motivated to underestimate the sales in their report. However, this underestimation would seem to cause a random error rather than a systematic error in favor of wealthier or poorer provinces. Furthermore, there is no incentive for these companies to report accurate data, especially at district level. For example, the sales data of a medicine in a district might be reported in the sales data of a neighboring strict located in the same province. To solve at least part of this issue, we transformed district level pharmaceutical sale data to province level data to make them more accurate and reliable. The data of other variables, extracted from national surveys of the Statistical Center of Iran, were more valid and reliable because of lack of conflict of interest by this independent organization.

The limitation of the model was due to probable existence of some unobserved variables causing the differences in the level of medical utilization between provinces in Iran. This unobserved variable bias is a type of endogeneity that could cause inconsistency of coefficients. Although the applied fixed or random effect model could cancel out the effect of time-invariant factors in the analysis, there is no way to solve the issue of other probable confounders. In addition, ecological fallacy is the most important limitation of ecologic studies.[44] Ecological fallacy arises when we make causality inference for individuals based on the observed relationship for groups. In this study, for example, it could not be concluded that less wealthy people utilize lower antihypertensive medicines, given the existence of such relationship at province level.

In spite of these limitations, the results of this study could be used by policy makers to pay more attention to less wealthy communities in the country for assuring their access to and utilization of needed medical services. Considering the existing utilization inequality in setting appropriate pricing and reimbursement policies for pharmaceuticals could be a good option.[45,46]

In conclusion, according to this study, an inequality related to wealth category in utilization of total antihypertensive medicines between provinces could be observed in Iran, after controlling for education, urbanization and food type. However, the wealth related inequality is statistically significant only in BBs and CCBs classes, separately.

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