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Inequality in Prescribing Anti-dementia Medications in Iran: Evidence From Social Security Insurance Claim Data

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ABSTRACT

Background: The prescribed doses of medications used for chronic diseases can be a good index for assessing inequality in healthcare services employment in communities. This study aimed to evaluate inequality in the prescribed dose of anti-dementia medications from 2012 to 2015 in the claim data, in Iran.

Methods: This study used the data on the prescribed dose of anti-dementia medications registered by the Social Security Organization (SSO) of Iran. The data on wealth index and educational attainment were extracted from Household, Income, and Expenditure Surveys (HIES) and merged into the claim data. Univariate and multivariable ordinal logistic regression models were applied to evaluate the factors associated with the prescribed dose of anti-dementia medications. DASP Stata package was used to calculate Gini and concentration indices.

Results: In multivariable models, prescription year, age, and educational attainment were related to the prescribed dose of anti-dementia medications. From 2012 to 2015, Gini indices of the prescribed dose of donepezil and rivastigmine were decreased. Gini indices in wealthier subjects were smaller than that in poorer individuals. Furthermore, with increasing the subjects' age up to the age of 80 years, Gini indices were decreased. Concentration indices were positive about rivastigmine, donepezil and memantine.

Conclusion: Different levels of inequality in the prescribed doses of donepezil and rivastigmine were observed among various wealth and education quintiles. Inequality in the prescribed doses of both mentioned medications was reduced from 2012 to 2015 among individuals under the SSO coverage in Iran.

Keywords: Healthcare; Socioeconomic factors; Dementia; Disparities; Iran

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1. Introduction

Dementia is a disabling disease, i.e., most prevalent among the elderly population [1-3]. This disease presents a progressive course that finally leads to severe cognitive impairments. Furthermore, older adults are more susceptible to inequality in receiving health services in developing countries. This is because of the variability in functional status and socioeconomic capability among older adults [4, 5].

Cholinesterase inhibitors and memantine are the only cognition-enhancing medications used for treating Alzheimer's Disease (AD) and some other types of dementia. These medications are approved by the Food and Drug Administration (FDA) of the United States and recommended by the National Institute for Health and Clinical Excellence (NICE) [6, 7]. Some studies revealed that cholinesterase inhibitors and memantine presented a significant positive effect on cognitive and functional status in subjects with dementia [4].

The daily prescribed doses of medications are dependent on the pharmacokinetics and pharmacodynamics of medications; each may be influenced by age, gender, liberation, absorption, and the volume of distribution of medications [8]. The severity of diseases is another characteristic that may be affected the daily prescribed dose [7]. Moreover, adherence to prescribed medication is another characteristic that can modify the annual prescribed dose of medications for chronic diseases. Additionally, socioeconomic factors, such as education and the ability to afford the medications [9] may be related to the annual prescribed dose.

The data of medications' prescribed dose in subjects with chronic diseases could be used for estimating inequality across different socioeconomic groups [10, 11]. Poorer individuals may be at higher risks of receiving an insufficient dose of medications [12]. This could be attributed to their lower access to physicians' visits or financial barriers to medication adherence [13, 14]. In other words, policies that lead to a decrease in patients' out-of-pocket payments for medications (increment the reimbursement rate by insurance organizations or decreased the total price of medications) may help to increase medication use and patients' adherence to pharmacotherapy [15].

In Iran, medications are usually accessible. Besides, because of the subsidy that the government pays for the production of medications, almost all medications are affordable [16]. Furthermore, all medical insurance included the Social Security Organization (SSO) in Iran pays about 70% of the cost of most of the medications, including anti-AD drugs. Despite the rational price of medication and compensation of the SSO for the expenditure of medications in Iran, there might be residual inequality in the prescribed dose of anti-AD medications through aggregated wealth index of the provinces, i.e., addressed in this study. Moreover, we assessed inequality between the annual dose of the treatment of patients with AD between provinces according to aggregated wealth index of the population of the provinces based on age groups and gender. Moreover, we evaluated the trend of inequality in the prescribed dose of anti-AD medications in 4 years. The present study results could assist the policymakers and researchers to identify the effects of socioeconomic factors on the prescribed doses of anti-AD medications. These results also could signify an inequality trend in using anti-ADs drugs in the subjects undercover of the Iranian Health Insurance Organization (IHIO).

2. Methods

The prescriptions of SSO from 2012 to 2015 that contained at least one anti-AD medication were considered for analysis. We only considered the SSO data, because some basic insurance claim data were inaccessible. Furthermore, the data of IHIO were incomplete and lacked essential items for analysis, like the prescription dose. SSO is an insurance organization, i.e., the second-largest health service provider in Iran, covering approximately 39 million Iranians [17]. Anti-AD medications were under the coverage of the SSO from 2012 to 2015 [18]. We used the data of socioeconomic status and educational attainment for gender-age groups in provinces per year. This information was obtained from the data of the Household Expenditure Surveys that were carried out annually (conducted and published by the Statistical Center of Iran).

The required data were prepared by merging two data sets. The annual prescribed dose of anti-AD medications, i.e., calculated as per the below formula:

Annual prescribed dose= $\sum_{n}^{1}$ *total prescribed dose for all patients (in the prescriptions) in each year/n.* In this formula, n is the number of patients that anti-AD medication was prescribed for them annually. Defined Daily Dose (DDD) was estimated by dividing the annual prescribed dose by 365.25 (days). In other words, DDD= ∑prescribed dose for all patients/(N_p×365.25), where N_p represents the number of patients in a defined year.

Wealth index data were calculated using Principal Component Analysis (PCA). PCA was performed on different variables to construct wealth index, including the home's area, the number of rooms in the home, the type of the materials used for the construction of the home, the type of fuels used for the home heating, owning laundry machine, freezer, vacuum cleaner, personal computer, cell phone, telephone, and car, as well as kitchen, bathroom, and access to gas pipelines. The standardized values were applied for constructing wealth index because we attempted to consider similar weight for all variables. The population was categorized into 5 groups according to the distribution of the years of schooling. The data of wealth and education of the provinces were merged into the clam data.

Routinely, 4 medications; donepezil, rivastigmine, galantamine, and memantine are prescribed for treating AD and other dementia types in Iran. Data on the consumption of galantamine was excluded from the analysis because only a few subjects consumed it. All these medications were under the SSO coverage from 2012 to 2015.

The therapeutic agents used for treating cognitive disorders in the explored subjects with AD were relatively specified; thus, we applied a simple algorithm for assigning AD diagnosis to subjects who consumed medications. If there were ≥1 prescription over these 4 years that contained ≥1 anti-AD medication and per prescription, there were ≥28 tablets (one blister), we assumed that this subject presented AD. The validity of this algorithm was approved by a panel of neurologists, psychiatrists, and pharmacists.

We assumed that the patients did not buy the anti-AD medications without using their insurance. Of note, the relatively high price of anti-AD medications and the ruled of the minister of health of Iran that the pharmacies are not right to sell these medications without physician orders, this assumption seemed to be correct.

The prescribed doses of anti-AD medications were categorized according to 5 percentiles. Totally, 16 groups were formed (instead of 20 groups, i.e., because some groups had similar fifth percentiles). We used the univariate Ordinal Logistic Regression (OLR) model and odds ratios to demonstrate the relationship between sociodemographic factors and the prescribed dose of anti-AD medications. A multivariable OLR model was used to adjust the results based on the years of schooling, the time of prescription, age group, and the wealth index.

Inequality analyses were performed using Stata 12 and DASP Stata module [19]. Lorenz curve is a cumulative dose of prescribed anti-AD medications total, i.e., that was plotted against the cumulative percentage of the population [20]. Inequalities were revealed using a Gini coefficient. The Gini coefficient is a ratio of the areas under the Lorenz curve and calculated by the Formula 1:

$$1.\ G = 1-2\int_0^1 L(X)d(X)$$

In this formula, the G= Gini coefficient and Y= L(X) function represent the Lorenz curve [20]. The concentration index was defined as twice the area between the concentration curve and equality line (the 45-degree line).

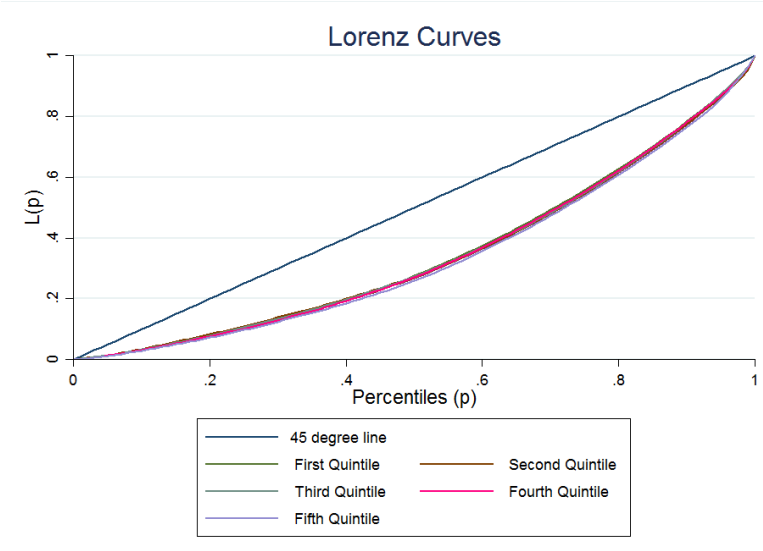

Figure 1. The Lorenz curve of the annual prescribed dose of anti-dementia medications on the quintiles of wealth index

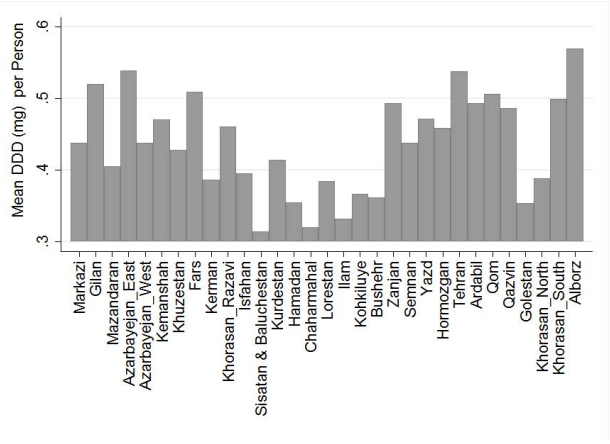

Figure 2. Mean dose of prescription Rivastigmine

The claim data of SSO were used without any individual identifiers. This study was approved by the Ethics Committee of the Endocrine and Metabolism Research Institute (Code: EC00295).

3. Results

Four-year data of the SSO prescriptions were analyzed (from 2012 to 2015). The total number of prescriptions, i.e., recorded the name of ≥1 of anti-AD medications into them equaled 98128. These prescriptions belonged to 44595 patients. Of total prescriptions, in 64.6% donepezil, in 71% rivastigmine, and only in 1% of them, memantine was prescribed. The mean annual prescribed doses per individual of donepezil, rivastigmine and memantine were measured as 423mg, 174mg, and 776mg, respectively. The DDD of donepezil was calculated as 1.16mg/d, rivastigmine as 0.48mg/d, and memantine as 2.13mg/d (Table 1). The least DDD of donepezil was prescribed in Kerman Province (0.86 SD: 0.52mg) and the highest DDD of donepezil was prescribed in Markazi Province (Figure 1). The least DDD of rivatigmine was calculated in Sistan and Baluchistan Province and the highest belonged to Alborz Province (Figure 2). The highest mean dose per subject of Memantine was prescribed in Kurdestan Province and the lowest mean dose of memantine was prescribed in Ilam province (Figure 3).

The association between the daily prescribed dose of anti-AD medications and wealth index was assessed using OLR. Based on the univariate analyses results, the annual prescribed doses of donepezil and rivastigmine were associated with the quintiles of wealth index. With improved wealth status, there was an increase in the odds of prescription of higher doses of anti-AD medications (odds ratios were 1.08 in the second to 1.41 in the fifth quintile) (Figure 1). Moreover, with the increased rank of years of schooling, there was an elevation in the odds of prescribing higher doses of anti-AD medications (odds ratio increased from 0.97 to 1.4 in second to fifth quintiles). The prescribed doses of anti-AD medications were not related to gender and age groups in univariate analyses; however, they were related to the years of prescription. Prescribed doses increased from 2012

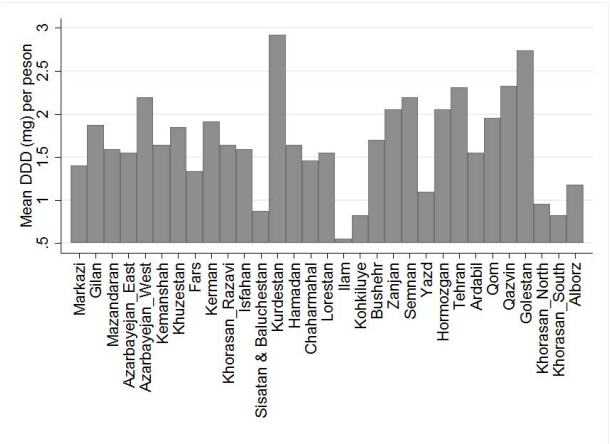

Figure 3. Mean dose prescription of Memantin by provinces

Table 1. Description of the data used in this study

Medications	The Total Amount of Prescribed Medication (mg*)	Total Number of Subjects	Mean±SD The Dose Prescribed per Individual Annually (mg)
Donepezil	1.99×10^7	28788	423.74±287.830
Revastigmine	1.05×10^7	31680	174.33±139.40
Memantine	0.039×10^7	460	776.99±533.73

* Milligram.

Table 2. Odds ratios and 95% Confidence Interval (CI) for the determinants of anti-dementia medications' annual prescribed dose

Variables		Odds Ratio (95% CI OR) Crude	Odds Ratio (95% CI OR) Adjusted*
Wealth index	1st Quintile	Reference group	
	2nd Quintile	1.08 (1.04-1.13)	1.04 (0.97-1.11)
	3rd Quintile	1.20 (1.15-1.25)	1.09 (1.01-1.18)
	4th Quintile	1.25 (1.20-1.31)	1.08 (0.99-1.18)
	5th Quintile	1.41 (1.35-1.48)	0.95 (0.86-1.06)
Gender**	Female	Reference group	
	Male	0.98 (0.95-1.00)	-
Year	2012	Reference group	
	2013	1.17 (1.11-1.22)	1.13 (1.05-1.21)
	2014	1.39 (1.33-1.45)	1.38 (1.29-1.47)
	2015	1.54 (1.47-1.61)	1.53 (1.44-1.63)
Age groups, y	30-49	Reference group	
	50-59	1.00 (0.94-1.06)	1.35 (1.21-1.50)
	60-69	1.06 (1.01-1.12)	1.60 (1.43-1.80)
	70-79	1.00 (0.94-1.05)	2.05 (1.79-2.34)
	80+	0.91 (0.86-0.95)	1.89 (1.65-2.16)
Years of schooling	1st Quintile	Reference group	
	2nd Quintile	0.97 (0.92-1.03)	0.93 (0.87-1.00)
	3rd Quintile	1.20 (1.13-1.28)	1.34 (1.22-1.47)
	4th Quintile	1.27 (1.20-1.35)	1.44 (1.29-1.60)
	5th Quintile	1.38 (1.30-1.47)	2.17 (1.88-2.51)

*Adjusted for other variables in the Table; **Gender was omitted from multivariable analysis because of collinearity.

Table 3. The Gini index of the annual prescribed dose of anti-dementia medications

Variables		Donepezil Gini Index	Rivastigmine Gini Index	Memantine Gini Index
Wealth index	1st Quintile	0.170809	0.217672	0.306322
	2nd Quintile	0.164177	0.151227	0.292270
	3rd Quintile	0.178663	0.179610	0.281455
	4th Quintile	0.155710	0.188019	0.303902
	5th Quintile	0.157013	0.185259	0.244356
Year of schooling	1st Quintile	0.171468	0.215352	0.279338
	2nd Quintile	0.161706	0.144239	0.314990
	3rd Quintile	0.172271	0.191441	0.274045
	4th Quintile	0.157824	0.180188	0.312036
	5th Quintile	0.164352	0.191351	0.234734
Gender	Female	0.175269	0.196058	0.275339
	Male	0.160984	0.176544	0.281916
Time	2012	0.206815	0.209325	0.286235
	2013	0.178692	0.182320	0.230431
	2014	0.146201	0.174955	0.286820
	2015	0.136292	0.173543	0.302018
Age groups, y	30-49	0.189505	0.223395	0.256295
	50-59	0.185126	0.207488	0.285047
	60-69	0.160551	0.168820	0.327021
	70-79	0.137525	0.159275	0.222378
	80+	0.160537	0.162876	0.266795

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to 2015. In the multivariable ordinal analysis, no relationship was observed between the prescribed doses of anti-AD medications and the wealth index. Contrarily, a strong relationship was observed between prescribed doses and age also years of schooling in the multivariable models (Table 2).

The Gini coefficients of the prescribed dose of donepezil and rivastigmine decreased from 2012 to 2015. Furthermore, the wealthiest groups presented lower Gini indices, compared to the poorest groups. The Gini indices of donepezil and rivastigmine prescribed doses were lower in males than females; however, the Gini index of memantine was higher in males, compared to females. Moreover, the Gini indices of donepezil and rivastigmine decreased with the aging of the population up to 80 years (Table 3). Concentration indices were significantly positive for donepezil, rivastigmine, and memantine prescribed dose across the quintiles of wealth index. Thus, for wealthier subjects, a higher dose of anti-AD medications was prescribed (Table 4).

4. Discussion

This study assessed inequality in the prescribed dose of anti-AD medications in claim data registered by the SSO in Iran. We found a slight inequality in the prescribed dose of anti-AD medications across the ranks of the wealth index. It was revealed that the prescribed dose of anti-AD medications increased with the increment of the years of schooling rank. Additionally, with

Table 4. The concentration index of annual prescribed dose based on the wealth index

Medication	CI*	Lower Band CI	Upper Band CI
Donepezil	0.042	0.037	0.046
Rivastigmine	0.036	0.030	0.041
Memantine	0.042	0.008	0.077

*Concentration Index.

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increased age, the odds of prescribing higher doses of anti-AD medications were enhanced.

Moreover, inequality demonstrated by Gini indices was lower in wealthier groups than poorer ones. These findings were consistent with those of a study in the UK; it reported the most privileged subjects were 25% more prone to prescribing anti-AD medications, compared to the most deprived group [4]. According to our findings, inequality decreased from 2012 to 2015 concerning the prescribed dose of donepezil and rivastigmine, but not memantine.

We observed a decrease in inequality in the prescribed doses of donepezil and rivastigmine with the aging of the population of up to 80 years; however, the prescribed doses of these medications increased again among the population of >80 years. Additionally, inequality in the prescribed dose of these two medications was slightly more prominent in females than males. Cooper et al. reported inequality between different age groups. Furthermore, they observed that lower doses of anti-AD medications were prescribed for females [4].

Studies reported that severe dementia was more prevalent in older individuals than younger subjects [21]. Thus, that the prescribed dose of anti-AD medications is higher and close to the maximum dose in severe cases, compared to the mild to moderate cases of AD. Accordingly, it caused a variation in the prescribed dose of these medications that decreased with aging, i.e., found in our study [22].

We observed that the odds of prescribing higher doses of anti-AD medications in the highest educated quintile was two times greater than the least educated groups. Similarly, in 2015, the probability of prescribing higher doses of anti-AD medications was approximately 1.5 times higher than that in 2012. Furthermore, inequality between the prescribed doses of anti-AD medications continuously decreased from 2012 to 2015. The justification of our finding of the effect of educational levels on inequality in prescribed dose may be attributed to greater adherence to pharmacotherapy among higher educated subjects, compared to the lesser educated individuals [23]. We considered two explanations for increasing the prescribed doses of anti-AD medications and decreased inequality in these years. First, an increase in individuals' access to donepezil and rivastigmine in Iran. This was due to the increased production of such medications in domestic pharmaceutical companies at this time [19]. Moreover, with the decrease in sanctions against Iran, the import of the medications has been facilitated, recently [24]. Another rationale concerned the raising awareness of the patients and their caregivers on the significance of treating AD that improved compliance to these medications.

We reported a positive concentration index about all types of anti-AD medications prescribed dose. In other words, the prescribed dose was higher in the wealthier than poorer groups. This result could be because of lesser access to these medications or different cultural factors, like lower compliance in poorer populations than wealthier subjects [4].

As a limitation of this study, we overlooked individual-level data about the socioeconomic status of the study participants. Accordingly, we used the socioeconomic data, such as the wealth index and the years of schooling of the general population per age group and province to calculate inequality. It might have led us to an ecological fallacy. Another limitation of this study was that the number of the subjects consuming memantine was far lower than that of the patients consuming the other anti-AD medications; we expected that the prescribed rate of memantine is close to donepezil and rivastigmine. These results may be due to the higher price of memantine than the other 2 medications. Moreover, we disregarded the coverage of SSO per province in our calculation. This is because we could not access these data (due to the SSO intra-organization policies). However, we divided the prescribed dose by the same size, and the SSO coverage might have not seriously confounded the mean prescribe dose.

To our knowledge, this was the first study on inequality in the prescribed doses of medication use for chronic disease in Iran. Moreover, as another strength of our study, we used the total claim data of SSO prescribed for treating AD in 4 years. Therefore, we have evaluated the data of prescriptions in about half of the subjects with AD in Iran.

5. Conclusion

There was an inequality in the prescribed doses of anti-AD medications in the subjects across the wealth index quintiles among those under the coverage of SSO, and females, in Iran. We also found that the prescribed doses of anti-AD medications continuously increased from 2012 to 2015. We recommend conducting further studies at an individual level about inequality in chronic disease. Such investigations are particularly suggested on individuals with AD. This is because this population is at higher risks of inequality in receiving health services, including the dose of consumed medication. The present research results indicated that policymakers and healthcare system providers should pay more attention to improve the diagnosis rate of AD and the promotion of the patients' access to integrated healthcare services.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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