ORIGINAL ARTICLE

SOCIODEMOGRAPHIC FACTORS' INFLUENCE ON ADHERENCE TO ANTIHYPERTENSIVE MEDICATION

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Abstract

Non-adherence to antihypertensive medication is commonly associated with suboptimal clinic outcomes but is nonetheless a common behaviour. This observational study investigated medication adherence of hypertensive Romanian patients using the Morisky-Green-Levine questionnaire. 22.2% of patients had low adherence, 51.3% of patients had moderate adherence and 26.5% had high adherence. Investigating the influence of age, sex, education, medication regimen complexity, comorbidities and information about medicines offered by the pharmacist to the patient on adherence levels, the most important positive predictor of adherence was the educational level. For patients having finished secondary school and patients with primary school, odd ratios to be in a higher category of adherence, compared to university graduates, were 0.62 and 0.53 respectively. Another significant predictor of adherence was the drug regimen, the increasing number of daily medicines and nutritive supplements reducing adherence.

Rezumat

Non-aderența la medicația antihipertensivă este frecvent asociată cu rezultate clinice suboptimale, și totuși este un comportament des întâlnit. Prezentul studiu observațional a determinat gradul de aderență la medicație al pacienților hipertensivi români, evaluat cu ajutorul chestionarului Morisky-Green-Levine. 22,2% dintre pacienți au avut o aderență scăzută, 51,3% dintre pacienți au avut o aderență moderată și 26,5% au avut o aderență ridicată. Studiul a investigat influența vârstei, sexului, nivelului de educație, regimului medicamentos, comorbidităților și tipului de informații despre medicament furnizate de farmacist asupra aderenței. Cel mai important predictor al aderenței înalte a fost nivelul de școlarizare. Șansele ca pacienții absolvenți de liceu să fie într-o categorie superioară de aderență, comparativ cu un absolvent de facultate sunt 0,62, iar cele ale pacienților care au terminat doar gimnaziul sunt 0,53. Alt predictor semnificativ al aderenței a fost regimul medicamentos, aderența scăzând cu creșterea numărului de pastile administrate zilnic.

Keywords: antihypertensive medication adherence, sex, age, education, drug regimen

Introduction

In Romania, cardiovascular diseases are the first cause of mortality, being responsible for 62% of all deaths [4]. High blood pressure (HBP) is the most important risk factor for cardiovascular morbidity and mortality, and, despite the availability of efficacious medicines, a large percent of hypertensive Romanian patients has their HBP uncontrolled.

Medication adherence is defined as "the extent to which a person's behaviour with regard to taking medication corresponds with agreed recommendations from a health care provider" [25]. Even if current antihypertensive medication is effective [6, 11], the percent of hypertensive population who do not reach their arterial pressure target is still high [3]. Low adherence to medication is a strong predictor of not controlling high blood pressure [14].

Current guidelines for the management of arterial hypertension emphasise the importance of detecting low adherent patients and of implementing measures for improving adherence [23].

Materials and Methods

We conceived a questionnaire addressed to patients on antihypertensive medication, in order to collect sociodemographic data (sex, age, education level), information about comorbidities, medicines and nutritive supplements used. The type of information provided by pharmacists about drugs utilizations was also assessed (doses, how to use the medication, how long to take the medication, adverse events). In order to investigate the adherence to medication we used the 4-items scale proposed by Morisky, Green and Levine (MGL) in 1986. The MGL scale consists of 4 questions: "Do you ever forget to take your medicine?"; "Are you careless at times about taking your medicine?"; "When you feel better do you sometimes stop taking your medicine?"; "Sometimes if you feel worse when

you take your medicine, do you stop taking it?". The answer "Yes" was rated 0 and "no" was rated 1; hence, the total score ranged between 0 and 4, 0 meaning very low adherence and 4 the highest. We further used a Likert Scale proposed by the original authors, where low adherence corresponded to a total score of 0 or 1, moderate adherence to 2 or 3 and high adherence to 4. MGL scale evaluating medication adherence has a moderate internal consistency (Cronbach's alpha 0.61) [16].

Pharmacists residents were trained to apply the surveys. They identified appropriated patients addressing the community pharmacies in Bucharest and completed the interviews.

Compliance with ethical standards
Participants' informed consent was obtained. Research and publications ethical standards were observed. The procedures that we used were in accordance with the national ethical standards of clinical studies and with the Declaration of Helsinki (1975), as revised in 2000.

Statistical analysis
Statistical analysis was performed using IBM SPSS Statistics 23 for Windows and Microsoft Excel for Mac, version 16.27, at a significance level of $p < 0.05$. Descriptive statistics were run for the target variable;

means, medians, standard deviations were computed for continuous data, while frequency analysis was performed for categorical ones.

Kolmogorov-Smirnov analysis was employed in order to investigate normality of data distribution. For non-normally distributed data, Mann-Whitney U test was used to investigate differences between 2 groups, while Kruskal-Wallis test was used to explore differences between 3 or more groups. Differences in percentages was assessed using χ^2 test.

A logistical regression was run in order to determine the odd ratios of being in a higher category of adherence to medications, depending on various factors.

Results and Discussion

1208 questionnaires were collected and analysed. We pooled data from people aging 21 to 97 years; age mean was 60.7 ± 15.09 years (CI 95%, 59.88 to 62.38); age values were significantly deviated from a normal distribution ($p = 0.001$ in Kolmogorov-Smirnov test). The baseline sociodemographic of the study participants is presented in Table I. Median of age was 61 years. 528 patients were male (43.71%) and 680 were women (56.29%).

Table I

Baseline sociodemographic of the study participants

Variable	Total n = 1208		Male n = 528	Female n = 680	p value*
Age (years)					
Means ± SD	60.7 ± 15.09		61.13 ± 14.62	60.37 ± 15.48	
	n	**%**	**%**	**%**	
< 30 years	54	4.5	37.04	62.09	0.0096
31 - 40 years	69	5.7	43.48	56.52	
41 - 50 years	166	13.7	37.35	62.65	< 0.0001
51 - 60 years	289	23.9	48.10	51.90	
61 - 70 years	296	24.5	45.27	54.73	0.0215
71 - 80 years	230	19.0	44.35	55.65	0.0155
81 - 90 years	93	7.7	36.56	63.44	0.0003
> 91 years	11	0.9	63.64	36.36	
Educational grade					
	n	%	%	%	
Primary school	278	23.0	42.1	57.9	0.0002
Secondary school	522	43.2	44.6	55.4	0.0005
University graduate	386	31.9	44.0	56.0	0.0009
Not specified	22				

* displayed only when p < 0.05

Almost half of our respondents had finished secondary education (43.2%) and a third were university graduates (31.9%). On the same levels of education there were significantly more women than men, but that reflected the general structure of our sample.

Data showed an increasing number of conditions affecting patients as they became older, as presented in Figure 1 and Figure 2. In almost all age categories, diabetes and hyperlipidaemias were the most present comorbidities, amplifying the consequences of hypertension.
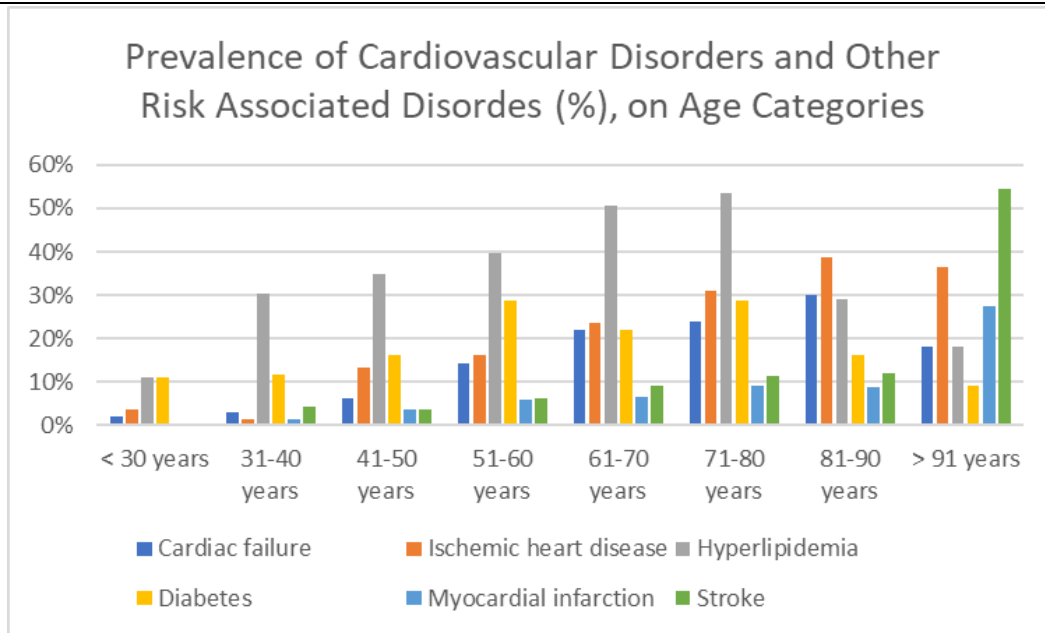
Figure 1.

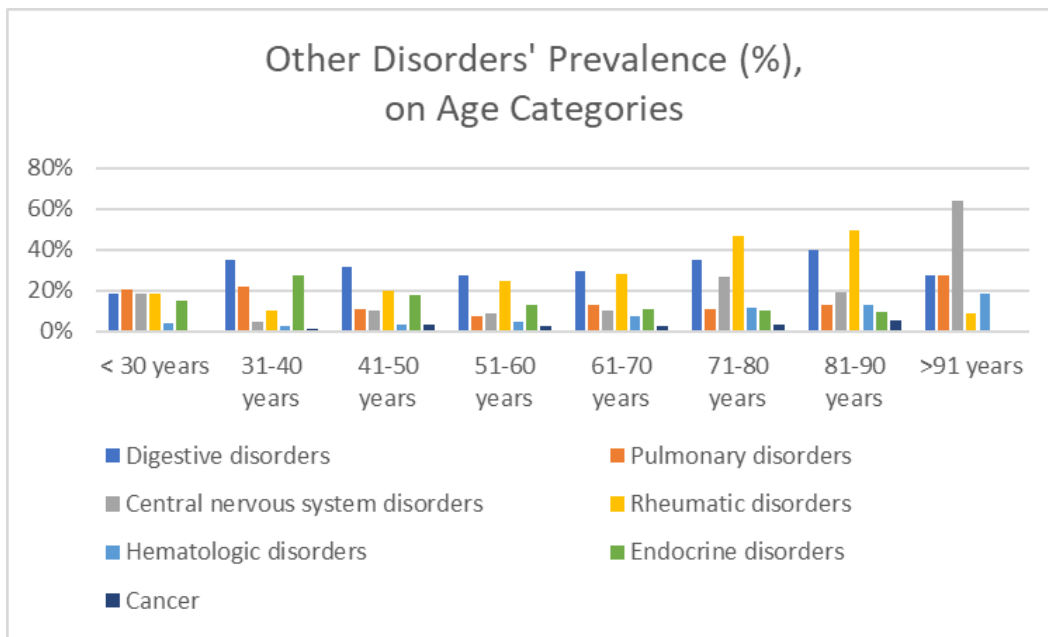Prevalence of cardiovascular disorders and other risk associated disorders

Figure 2.

Prevalence of other disorders

Digestive and rheumatic disorders were other very frequent pathologies affecting the patients; all these numerous comorbidities commonly required a large number of medicines, thus complicating the medication regimens (Table II).

As people aged and had more comorbidities, the number of daily drugs and nutritive supplements increased. When nutritive supplements were concerned, women took more of them than men, on each age category, except the youngest one. When it came to medicines, we didn't observe the same uniformity. Data showed that while a large number of patients were counselled by pharmacists regarding doses and mode of administration, only around half received information about how long to take the medicines and about adverse effects of drugs.

Table II

Medication regimen (number of daily drugs and nutritive supplements) and drug information provided by pharmacists

Variable	Total n = 1208	Male n = 528	Female n = 680
No. of daily drugs			
	Means ± SD	Means ± SD	Means ± SD
< 30 years	1.78 ± 0.95	1.9 ± 1.17	1.71 ± 0.80
31 - 40 years	2.20 ± 1.13	2.13 ± 1.23	2.26 ± 1.07
41 - 50 years	3.08 ± 1.93	3.53 ± 1.99	2.97 ± 1.90
51 - 60 years	3.93 ± 2.35	4.29 ± 2.62	3.60 ± 2.02
61 - 70 years	4.61 ± 2.16	4.43 ± 2.12	4.77 ± 2.19
71 - 80 years	5.69 ± 2.20	5.27 ± 1.93	6.03 ± 2.34
81 - 90 years	6.01 ± 2.84	5.44 ± 2.72	6.34 ± 2.88
> 91 years	5.73 ± 3.10	5.86 ± 3.93	5.00 ± 1
No. of daily food supplements			
	Means ± SD	Means ± SD	Means ± SD
< 30 years	0.69 ± 0.89	1 ± 0.86	0.5 ± 0.82
31 - 40 years	0.90 ± 0.83	0.70 ± 0.7	1.05 ± 0.89
41 - 50 years	0.93 ± 1.00	0.73 ± 0.85	1.06 ± 1.07
51 - 60 years	1.09 ± 1.19	0.99 ± 1.02	1.19 ± 1.32
61 - 70 years	1.15 ± 1.24	0.96 ± 1.03	1.31 ± 1.37
71 - 80 years	1.37 ± 1.47	1.29 ± 1.7	1.43 ± 1.27
81 - 90 years	1.12 ± 1.11	0.82 ± 0.94	1.23 ± 1.18
> 91 years	1.27 ± 1.19	0.86 ± 0.90	2 ± 1.41
Patients receiving drugs information from pharmacist at dispensing			
	n	%	%	%
Posology	997	82.5	81	84
Method of administration	1103	91.3	91	92
Length of treatment	618	51.2	51	51
Adverse effects	586	48.5	48	49

Mean of adherence MGL score was 2.48 ± 1.23. Median adherence MGL score was 3. Distribution of adherence MGL score was a non-parametric one (p < 0.001 in Kolmogorov-Smirnov test). 22.2% of patients had low adherence, 51.3% of patients had moderate adherence and 26.5% had high adherence (Table III).

Table III

Adherence MGL score in different categories of patients

Adherence score	Means ± SD	Medians	% of patient		
			High adherence	Moderate adherence	Low adherence
Men	2.48 ± 1.23	3	25.9	53.1	21
Women	2.46 ± 1.26	3	26.9	50	23.1
< 30 years	2.15 ± 1.35	2	33.3	42.6	24.1
31 - 40 years	2.49 ± 1.28	3	27.5	50.7	21.7
41 - 50 years	2.62 ± 1.22	3	29.5	53.6	16.9
51 - 60 years	2.55 ± 1.22	3	29.8	49.1	21.1
61 - 70 years	2.60 ± 1.21	3	28.7	53.7	17.6
71 - 80 years	2.30 ± 1.25	3	20.0	53.0	27.0
81 - 90 years	2.18 ± 1.34	3	20.4	50.5	29.0
> 91 years	2.36 ± 1.36	3	27.3	27.3	45.5
Primary school	2.28 ± 1.27	2	20.1	52.9	27.0
Secondary school	2.40 ± 1.22	2	22.6	54.4	23.0
University graduate	2.69 ± 1.24	3	35.8	46.1	18.1

Globally, women had a lower adherence score than men, without statistically significance. For both men and women, almost half had medium adherence. In patients with medium adherence, men were more prone to sometimes forget to take the medication than women (54.3% *versus* 47.1%, p = 0.074) but more women than men stopped the drugs administration if they felt worse (43.2% *versus* 33.2%, p = 0.01).

In different categories of age, scores of adherence varied. Adherence increased through fifth, sixth and

seventh decades of life, then decreased. The percentage of patients having high adherence varied accordingly. Extreme ages made exceptions (largest percent of high adherent patients in those less than 30 years old and large percent of high adherent patients in those more than 91 years old), possibly due to the small number of patients in those categories of age.

Important difference in adherence was observed in patients having different level of education. Distribution of adherence MGL scores differed statistically significant across patients with different level of education (p < 0.05, Kruskal Wallis test). University graduates had the highest adherence score (2.69), followed by patients having secondary school (2.40). The least adherent patients, judged by MGL score, were those having only primary school (2.28). The percentage

of patients highly adherent reached a maximum in university graduates.

Logistical regression provided the following results. The odds of women to be in a higher category of adherence to medications was similar to that of men (OR = 0.99, 95% CI, 0.797 to 1.230), Wald $\chi^2(1) = 0.008$, p = 0.927 (Figure 3).

An increase in age was associated with a small increase in the odds of being a more adherent patient, not statistically significant (OR = 1.002, 95% CI, 0.994 to 1.011).

The number of medicine information provided by pharmacist when dispensing the drugs was associated with a small increase in the odds of one patient to be more adherent (OR = 1.008, 95% CI, 0.913 to 1.112), also not statistically significant.
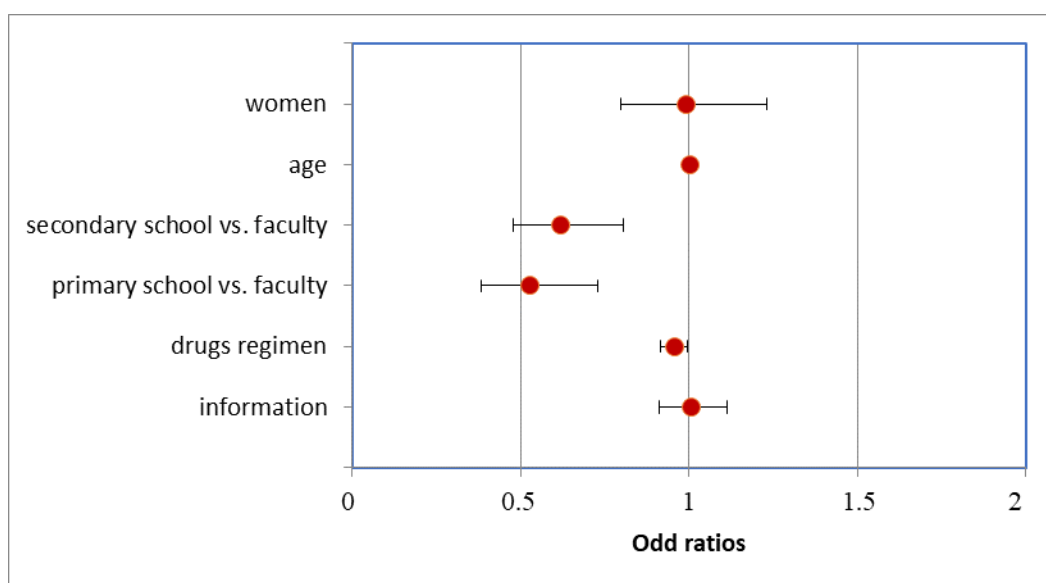

Figure 3.
Factors associated with odds of being more adherent

The education level has a statistically significant effect on the prediction of a patient being more adherent to medication (Wald $\chi^2(3) = 19.906$, p < 0.001).

The odds of a patient who had finished secondary school to be in a higher category of adherence was 0.620 (95% CI, 0.478 to 0.805) times that of a university graduate, a statistically significant effect (Wald $\chi^2(1) = 12.931$, p < 0.001).

The odds of a patient who had finished primary school to be in a higher category of adherence was 0.528 (95% CI, 0.382 to 0.730) times that of a university graduate, a statistically significant effect (Wald $\chi^2(1) = 14.925$, p < 0.001).

The number of daily medicines and nutritive supplements is a statistically significant predictor of a patient being in a higher category of adherence. An increase of medication regimen complexity (expresses as number of daily medicines or nutritive supplements) was associated with a decrease of the odds that the patient being more adherent (OR = 0.956, 95% CI, 0.917 to

0.996), a statistically significant effect (Wald $\chi^2(1) = 4669$, p = 0.031).

In one cross-sectional 48-month retrospective study realized in primary medical care in Romania regarding treatment adherence among adult hypertensive patients, 69.8% of patients had high adherence, 20.3% had medium adherence and 9.9% had low adherence. Levels of adherence were computed starting from percentage of time covered by medication possession, as observed investigating pharmacy databases [23]. The difference in adherence levels between our study, which found that 22.2% of patients had low adherence, 51.3% of patients had moderate adherence and 26.5% had high adherence, and the cited one could come from different methods of assessing adherence to medication. Similar to us, the study conducted by Tilea showed that older age was positively associated with higher adherence to medication. While we didn't find significant differences between men and women regarding adherence to medication, Tilea and colleagues reported

women being more adherent than men; conversely, Tilea and colleagues found no influence of the level of education on adherence, while we found that the more education accomplished, the more adherent to education the patients were [23].

Leaving aside comparison with the study regarding Romanian hypertensive patients realized by Tilea and colleagues and going more globally the following remarks about influence of sociodemographic factors, medication regimen and drugs information provided by pharmacists on adherence could be made.

One Canadian study found no difference in adherence depending on sex; the study, which assessed adherence to antihypertensive medication following stroke, revealed that only 61.8% to 75.8% of patients were highly adherent to medication [8]. Low level of adherence even in the first year after stroke was associated with higher risk of death (odds ratio 1.75, p = 0.025) [8]. Knowing that adherence decreased with time [2], mortality and morbidity burdens associated to non-adherence could only rise in time.

In another meta-analysis of 51 articles reporting clinical studies evaluating adherence to statin therapy, women were at increased risk for nonadherence. Rates of nonadherence were 53% in woman and 50% in men, with 10% higher odds of nonadherence for women compared to men [10]. Meta-analysis' authors conjectured that the belief that women are at less cardiovascular risk, as much as their frequent role of caregiver, could make them and the clinicians to underestimate the importance of primary cardiovascular prevention, hence a lower medication adherence.

Conversely, a systematic review on adherence to anti-hypertensive medication in low-and middle-income countries reported that being a woman is correlated with higher adherence levels [17].

The previously cited systematic review on adherence to antihypertensive medication in low-and middle-income countries showed that older age was slightly associated with better adherence [17].

Frequently the relation age-adherence to antihyper-tensive therapy is illustrated as a concave curve, adherence to medication increasing as age increases, reaching a maximum in the sixth and seventh decades of life and afterwards declining [20].

The Cohort Study of Medication Adherence in Older Adults (CoSMO) that enrolled older patients (mean age 75 years) reported lower medication adherence and more frequent uncontrolled HBP in patients less than 75 years old [9].

Our results were similar to others studies, showing a marginally increase in adherence as age increases.

Educational level is another factor pertaining to the patient that could influence medication adherence, but present evidence is inconclusive.

Some studies reported that lower educational levels are associated with lower adherence to therapy [19],

while higher education positively influence medication adherence [13].

There are also studies that found no relation between educational level and medication adherence [5, 26]. Our results matched the conclusions of SEPHAR II survey, a national representative cross-sectional study aiming to evaluate the prevalence, treatment and control of hypertension in Romania. According to SEPHAR II, the level of education had an important role in treatment adherence. SEPHAR II' authors put the increase in controlled blood pressure from about 20% of those with no education to roughly 40% of those with higher education, on behalf of increased awareness of hypertension-related risks, healthier life-styles and better adherence to medications [4].

A greater number of comorbid illnesses was associated with poor adherence [7]. Complex medication regimens were commonly associated with medication errors. Preventing medication errors should be an essential activity for pharmacist, which could improve adherence to medication; thus, implementing a risk management plan for preventing such errors could be a strategy for increasing adherence [18]. Frequently, the number of comorbidities increases as patients get older, as well as the number of drugs and nutritive supplements taken. For example, one study found that in UK, 50.5% of patients ageing 65 to 84 years took at least 3 daily chronically prescribed medication [15]. It is considered that each additional daily dose is followed by a 10% decrease in adherence [2].

The results of our study fit well with other authors, which found that almost half of patients older than 65 years took 4 to 6 daily medicines, and almost 40% took more than 7 daily drugs [12]. The logistic regression showed that an increase in the number of daily medicines or nutritive supplements was associated with a decrease of the odds of the patient being more adherent.

Knowledge about the purpose of medications, how to use them and what to expect are essential for the proper use of medications and better clinical outcomes [1]. Information about medication could dismiss false beliefs about medications (e.g., no need of medication, distrust in medication efficacy), could engage the patient in his therapeutic process and could prepare patients to manage potential adverse events, mitigating their consequences [2].

Despite critical importance of instructing the patient about medication, a study evaluating clinicians' communication with patients about newly prescribed medications found that the purpose of the medication was exposed in 87% of interactions, but adverse effects was addressed only for 35% of medications. Only 34% of the encounters physicians specified how long medicines should be taken. The timing and frequency of administration were explained in 58% of the interactions [22]. These data stress the importance of the pharmacist. When dispensing the medications,

pharmacist should reinforce important information, provide information skipped by the physician or forgotten by the patient and check the accuracy of drugs information owned by the patient. All of these are of paramount importance when it comes to HBP, which is often asymptomatic and demands pharmacological intervention sometimes across entire lifespan in order to prevent cardiovascular fatal or near-fatal events.

Pharmacist-patient communication is sometimes deficient [21], so it could damage medication adherence. Unfortunately, our study showed similar disparities in communications between pharmacists and patients. Just around a half of patients received information about length of treatment and drugs adverse effects. These could be important leverages of improving pharmaceutical services and thus promoting better clinical outcomes.

Study limitations

The most important limitation of our study is the lack of representability regarding Romanian hypertensive patients. Since we collected data only in a metropole, our results are generalizable just for urban population living in well developed areas. Further investigations are needed in order to cover rural areas and less economically developed areas, because in low- and middle-income regions, social and economic factors have a higher impact on medication adherence than in high-income regions [25].

Another caveat is that MGL Scale does not finely discriminate between reasons for medication non-adherence. However, it is a useful tool for appreciating the degree of adherence to medication. Further studies should shed more light on patients' beliefs and behaviours leading to non-adherence.

Conclusions

Improving adherence to medication could be an important step in improving hypertensive control. Knowing what factors favours low adherence could help more frequently identify non-adherent patient in order to apply intervention to increase adherence, because even a small increase in adherence could be clinically meaningful.

Conflict of interest

The authors declare no conflict of interest.

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