

Factors influencing antihypertensive medication compliance in Taiwan: a nationwide population-based study

Chien-Ying Lee^{1,2}, Chun-Che Huang³, Hung-Che Shih^{1,2} and Kuang-Hua Huang⁴

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Abstract

Background: Poor medication compliance with antihypertensive drugs may have a significant impact on clinical outcomes, hospitalisation and healthcare expenditure. This study aims to assess medication compliance and its underlying factors in patients receiving antihypertensive drugs in Taiwan.

Methods: This retrospective population-based study was based on data from Taiwan's Longitudinal Health Insurance Database (LHID). All patients ($n = 78,558$) were aged 30 years or more and had received at least one antihypertensive prescription between January 2004 and December 2007. We used the medication possession ratio (MPR) as an index to measure the level of medication compliance.

Results: Approximately 53% of the patients had high compliance with antihypertensive medication. Factors that were positively associated with medication compliance included patients being aged 30–44 years, higher comorbidity scores (odds ratio (OR): 1.18; 95% confidence interval (CI): 1.08–1.28), the same prescribing physician being visited and a single-drug therapy being prescribed. Female sex (OR: 0.92; 95% CI: 0.89–0.95) and higher socioeconomic status (OR: 0.91; 95% CI: 0.86–0.96) were negatively associated with drug compliance. In addition, high-compliance patients were less likely to be treated at medical centres, corporations (OR: 0.89; 95% CI: 0.84–0.93) or rural (OR: 0.88; 95% CI: 0.83–0.94) institutions.

Conclusion: Several patient- and institution-related factors may influence medication compliance. Therefore, for optimal outcomes, patients' awareness of the need for compliance with antihypertensive therapy must be enhanced, and effective intervention strategies should be developed.

Keywords

Hypertension, antihypertensive drugs, compliance, risk factors

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Introduction

Hypertension is currently a major contributory cause of disease burden (responsible for 12.8% of total deaths worldwide) and continues to be an important public health issue.¹ Uncontrolled hypertension may increase the risk of cardiovascular (CV), cerebrovascular and kidney diseases.^{1,2} Furthermore, low compliance to therapy is a primary cause of refractory hypertension. Previous studies have demonstrated that noncompliance with antihypertensive medication increases healthcare expenditure and the risk of hospitalisation, as well as morbidity and mortality.^{3,4}

A study in the United States estimated that approximately 30% of patients with hypertension took their

¹Institute of Medicine, Chung Shan Medical University, Taiwan

²Department of Pharmacy, Chung Shan Medical University Hospital, Taiwan

³Institute of Health Policy and Management, National Taiwan University, Taiwan

⁴Department of Health Service Administration, China Medical University, Taiwan

Corresponding author:

Kuang-Hua Huang, Department of Health Service Administration, China Medical University, No. 91 Hsueh-Shih Road, Taichung City 40402, Taiwan

Email: khhuang@mail.cmu.edu.tw

medication irregularly.⁵ In Europe, only 26.3% of patients receiving antihypertensive medication achieved their blood pressure (BP) goals.⁶ According to a national survey in Taiwan, only 50.4% of hypertensive patients received therapeutic treatment, despite the sufficient availability of effective medical therapy.⁷ The study indicated that the low percentage of patients with controlled hypertension could be attributed to their non-compliance in taking their medication.

Efforts to quantify antihypertensive drug compliance are necessary, and researching possible factors that may be associated with medication compliance could provide physicians, as well as policy makers, with intervention targets for improving medication-taking behaviour among hypertensive patients.^{7,8} However, to date, only a few studies have investigated the factors that affect medication compliance among hypertensive patients in Taiwan⁹ and/or the risk factors of drug compliance (e.g. patient-physician relationship, medical conditions, therapeutic complexity, socioeconomic factors and the healthcare system which are different between European and Asian countries).^{6,10–13} Population-based studies may provide data on the rates and predictors of medication compliance which would help to identify patients who are less likely to comply with treatment regimens.

The National Health Insurance (NHI) programme was implemented in March 1995, and it covered nearly all of the inhabitants of Taiwan (more than 99% of the population of 23 million at the end of 2007).¹⁴ When patients use health services and obtain prescription drugs, either directly from hospitals or clinic pharmacies, all of the medical and pharmacy claims are gathered and stored in the NHI claims database. In total, 11.8% of outpatient visits are for the treatment of hypertension, and the cost of drugs used to treat this disease amounts to the fourth greatest medical expenditure in Taiwan.¹⁴ In addition, prescribed antihypertensive medication accounted for 31% of the total outpatient pharmaceutical expenditure on western medicine in 2008.¹⁵ A national database could enable the effects of hypertension treatment to be investigated among all Taiwanese inhabitants. The aim of this study was to assess antihypertensive medication compliance among patients with hypertension and discover its associated institutional factors and patient characteristics in Taiwan.

Materials and methods

Data sources and study population

This retrospective population-based study retrieved data from the Longitudinal Health Insurance

Database (LHID) of Taiwan. In total, 1,000,000 participants from the LHID were randomly selected from the 2005 registry for beneficiaries of the NHI Research Database (NHIRD). There were no significant differences in the sex or age distribution between the patients in the LHID and the original NHIRD. Consequently, the LHID enabled the valuable assessment of institutional factors that may affect antihypertensive medication compliance. All records of antihypertensive drug prescriptions were retrieved from the LHID ambulatory care and prescription claims data, and were classified according to the NHI Pharmaceutical Subsidy Anatomical Therapeutic Chemical (ATC) classification system. The linkage of all the datasets for the relevant variables employed the use of scrambled unique personal or hospital identification numbers. To protect privacy and assure confidentiality, the Bureau of National Health Insurance (BNHI) encrypted all the data before release to ensure that no health information could be identified to an individual.

We identified 122,664 patients aged 30 years or more who received ambulatory care following a principal diagnosis of hypertension between 2004 and 2007. The diagnosis of hypertension was made according to the International Classification of Diseases, 9th version, Clinical Modification (ICD-9-CM) codes 401–405, and if the patient was receiving at least one antihypertensive drug (i.e. diuretics, α -blockers, β -blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) or other classes of antihypertensive drugs). We excluded 4783 patients who were hospitalised during the previous 12 months (from January to December 2003) for diabetes mellitus, ischaemic heart disease, pulmonary circulation diseases, other forms of heart disease (including dysrhythmia and heart failure) or other causes. We also excluded 3843 patients who only visited their clinic once (because drug compliance could be assessed only for patients who had at least two clinic visits for antihypertensive treatment), and 35,480 patients who did not have a follow-up medical visit within six months.^{9,13} Our final study population consisted of 78,558 hypertensive patients.

Measurement

Compliance was measured using the medication possession ratio (MPR) which is the commonly accepted standard for the evaluation of drug compliance using a retrospective database.¹⁶ The MPR represented the percentage of time that the patient had medication available to them during the follow-up period. We calculated the ratio of the number of days the patient was supplied with a prescription (excluding the final

prescription because the number of days taken to consume these pills was unknown) divided by the number of days between the first and last prescription for each patient, and multiplied by 100.¹² Patient compliance with antihypertensive therapy was divided into three groups: low (<50%), medium (50–79%) and high compliance ($\geq 80\%$).¹⁷ If the MPR was less than 80%, which was a reasonable adherence threshold because it implied that there were inconsecutive days without drug therapy and consequently reasonably continuous medication use, then compliance was classified as non-adherent.¹⁶ Furthermore, this threshold is commonly used in clinical trials¹¹ and had been implemented in previous similar studies.^{13,18}

The LHID ambulatory care and prescription data provided patient characteristics and clinical information on sex, age (30–44, 45–54, 55–64 and ≥ 65 years), comorbidity, medical specialty visited (family medicine, internal medicine, cardiovascular internal medicine and others), the number of prescribing physicians and the number of drugs prescribed.

The Charlson Comorbidity Index (CCI) score (from 0 to ≥ 3) was used to quantify the overall burden of comorbidities after the initial antihypertensive treatment of a patient^{19,20} and it has been used in studies to adjust for patient risk factor.^{9,13} In addition, the prescriptions of antihypertensive regimens were classified into four groups: single-drug, two-drug combination, three-drug combination and four-drug or more combination treatment.²¹ The LHID enrolment files also provide information on a patient's socioeconomic status (SES). We discovered that the NHI programme is financed by wage-based premiums for people with a clearly defined monthly salary and by fixed premiums for people without a defined monthly wage. People with defined monthly wages were divided into three levels, depending on their salary in New Taiwan dollars (NT\$): level I ($\geq \text{NT\$}40,000$), level II (NT\\$20,000–39,999) and level III (<NT\\$20,000). People with fixed premiums (i.e. no defined monthly wage) tended to be on a low income or were from vulnerable subpopulations, such as farmers and fishermen, and were classified as level IV.

The LHID medical facilities files were used to identify the characteristics of the medical institutions that were visited by the patients, including ownership (public, private and corporate), urbanicity (urban, suburban and rural area) and accreditation level. The accreditation levels of the institutions were classified into medical centres, regional hospitals, district hospitals and physician clinics on the basis of their size, service volumes, range of specialty and a comprehensive list of quality of care, as recognised and managed by the BNHI.

Statistical analysis

To analyse the basic characteristic differences of patients and institutions across different levels of medication compliance, we tested for linear trends using the Mantel–Haenszel χ^2 test for categorical variables, or linear regression models for continuous variables when appropriate. Multiple logistic regression analyses were constructed to assess the predictors of high-level compliance, using patients with medium- and low-level compliance as a reference group. All predictor variables were tested for multicollinearity using the condition indices and variance inflation factors (VIF) by linear regression. In addition, two-way interactions between independent variables were tested. Odds ratios (OR) with 95% confidence intervals (CI) were estimated. All statistical analyses were conducted using SAS 9.1 (SAS Institute, Cary, North Carolina, USA), and all *p*-values less than 0.05 were considered statistically significant.

Results

A total of 78,558 hypertensive patients aged ≥ 30 years who received antihypertensive medication were identified from a nationally representative sample of Taiwan's LHID database during 2004–2007. Of this total, 50.3% were female and over half (67.1%) of the patients were at least 55 years old, with a mean age of 61.8 years (SD = 13.6). In total, 71.2% of the patients belonged to the lower SES groups (level III and IV).

Table 1 shows the basic characteristics of hypertensive patients according to different levels of compliance with antihypertensive medication. Overall, 41,599 patients (52.9%) were classified as having a high level of compliance, whereas 20,014 and 16,945 patients (25.5% and 21.6%) exhibited medium and low levels of compliance respectively. The distribution of socioeconomic characteristics, comorbidity score and visited medical specialty varied slightly among hypertensive patients with different levels of medication compliance. In comparison to low-compliance patients, a greater proportion of high-compliance patients were visiting the same physician (78% vs 32.1%) and were receiving single-drug therapy (68.8% vs 29.4%; all *p* < 0.001). Institution characteristics (level and ownership) also influenced the medication compliance of the patient. Furthermore, condition index values ranged between 1.00 and 2.22, and the highest VIF was 1.57, indicating no sign of multicollinearity among the predictor variables.

Table 2 presents the results of both univariate and multivariate logistic regression analyses of the patient and institution factors affecting compliance. The univariate results indicate that the patient's age, SES, the

Table 1. Basic characteristics of antihypertensive medication compliance by hypertensive patients in Taiwan

	Compliance level			<i>p</i> value
	Low (<i>N</i> = 16,945)	Medium (<i>N</i> = 20,014)	High (<i>N</i> = 41,599)	
Patients (%)	21.6	25.5	52.9	
Patient characteristics				
Female (%)	51.7	51.8	49.0	<0.001
Age (years)	62.6 (12.8)	62.9 (13.2)	61.0 (14.1)	<0.001
30–44 (%)	7.9	8.5	13.3	<0.001
45–54 (%)	21.2	20.7	23.0	
55–64 (%)	25.6	24.1	21.6	
≥65 (%)	45.4	46.6	42.1	
Socioeconomic level ^a				
Level I (%)	11.8	10.2	9.8	<0.001
Level II (%)	18.3	17.8	18.7	
Level III (%)	47.6	48.8	49.0	
Level IV (%)	22.3	23.2	22.5	
CCI score				
0 (%)	79.2	76.5	78.6	0.551
I (%)	17.2	19.2	17.3	
≥2 (%)	3.6	4.3	4.1	
Medical specialty				
Family medicine (%)	28.5	29.7	26.3	<0.001
Internal medicine (%)	29.2	32.6	33.6	
Cardiovascular medicine (%)	30.2	24.7	17.6	
Others (%)	12.1	13.0	22.5	
Number of prescribing physicians				
1 (%)	32.1	31.0	72.0	<0.001
2 (%)	26.7	23.9	13.0	
≥3 (%)	41.2	45.1	5.0	
Number of drugs prescribed				
1 (%)	2.2 (1.0)	2.4 (1.2)	1.6 (1.0)	<0.001
2 (%)	29.4	27.4	68.8	
3 (%)	38.1	33.2	16.6	
≥3 (%)	32.5	39.4	14.6	
Institution characteristics				
Accreditation level				
Medical centre (%)	23.3	13.8	10.5	<0.001
Regional hospital (%)	16.7	18.2	15.2	
District hospital (%)	12.0	16.0	19.7	
Primary care clinic (%)	48.0	52.0	54.6	
Ownership				
Public (%)	26.1	23.5	19.9	<0.001
Private (%)	48.9	55.7	63.3	
Legal foundation-affiliated (%)	25.0	20.8	16.8	
Urbanicity				
Urban area (%)	75.9	75.5	74.4	0.005
Suburban area (%)	16.3	16.4	17.8	
Rural area (%)	7.8	8.1	7.8	

CCI: Charlson Comorbidity Index; NT\$: new Taiwanese dollars; data are proportions (%) and means (SD); ^aLevel I ≥ NT\$40,000; Level II: NT\$20,000–39,999; Level III < NT\$20,000; Level IV: without a well-defined monthly wage.

Table 2. Crude and adjusted odds ratios (OR) with 95% confidence interval (CI) for factors associated with high level of medication compliance in Taiwan

	High-level compliance			
	Crude OR	95% CI	Adjusted OR	95% CI
Patient characteristics				
Gender				
Male	1.00		1.00	
Female	0.90	(0.87–0.92)	0.92	(0.89–0.95)
Age (years)				
30–44	1.00		1.00	
45–54	0.68	(0.65–0.72)	0.80	(0.75–0.85)
55–64	0.54	(0.51–0.57)	0.67	(0.63–0.71)
≥65	0.57	(0.54–0.60)	0.76	(0.72–0.81)
Socioeconomic level ^a				
Level I	1.00		1.00	
Level II	1.15	(1.09–1.22)	1.16	(1.09–1.24)
Level III	1.13	(1.08–1.19)	1.37	(1.29–1.45)
Level IV	1.10	(1.04–1.15)	1.23	(1.15–1.32)
CCI score				
0	1.00		1.00	
1	0.94	(0.90–0.97)	1.12	(1.07–1.17)
≥2	1.00	(0.93–1.08)	1.18	(1.08–1.28)
Medical specialty				
Family medicine	1.00		1.00	
Internal medicine	1.20	(1.15–1.24)	1.07	(1.03–1.12)
Cardiovascular medicine	0.72	(0.69–0.75)	0.91	(0.86–0.96)
Others	1.97	(1.89–2.06)	1.52	(1.45–1.60)
Number of prescribing physicians				
1	1.00		1.00	
2	0.23	(0.22–0.24)	0.34	(0.33–0.36)
≥3	0.15	(0.15–0.16)	0.26	(0.25–0.27)
Number of drugs prescribed				
1	1.00		1.00	
2	0.19	(0.18–0.20)	0.32	(0.30–0.33)
≥3	0.17	(0.16–0.17)	0.36	(0.35–0.38)
Institution characteristics				
Accreditation level				
Medical centre	1.00		1.00	
Regional hospital	1.50	(1.42–1.58)	1.52	(1.43–1.61)
District hospital	2.41	(2.29–2.54)	2.46	(2.29–2.63)
Primary care clinic	1.88	(1.80–1.96)	1.26	(1.17–1.35)
Ownership				
Public	1.00		1.00	
Private	1.49	(1.44–1.55)	1.06	(1.01–1.12)
Legal foundation-affiliated	0.92	(0.88–0.96)	0.89	(0.84–0.93)
Urbanicity				
Urban area	1.00		1.00	
Suburban area	1.11	(1.07–1.15)	0.97	(0.92–1.01)
Rural area	1.00	(0.95–1.05)	0.88	(0.83–0.94)

CCI, Charlson Comorbidity Index; NT\$, new Taiwanese dollars; ^aLevel I ≥ NT\$40,000; Level II: NT\$20,000–39,999; Level III < NT\$20,000; Level IV: without a well-defined monthly wage; no significant interactions were seen between variables.

medical specialty visited, the number of prescribing physicians and the number of drugs were significant predictors of high-level compliance. Patients with higher compliance were more likely to be treated at private and low-level institutions (district hospitals and physician clinics). However, the urbanicity of institutions influenced compliance only slightly. The multivariate results indicate that the factors that are associated with low-level compliance are female sex (OR: 0.92; 95% CI: 0.89–0.95), age of 55–64 years (OR: 0.67; 95% CI: 0.63–0.71), high SES and treatment being provided at a cardiovascular medical centre (OR, 0.91; 95% CI, 0.86–0.96). Patients with comorbidity scores of 2 or more (OR: 1.18; 95% CI: 1.08–1.28), who were visiting the same prescribing physician and receiving single-drug therapy had a higher likelihood of medication compliance. In terms of institutional characteristics, the multiple logistic regression analysis revealed that high-compliance patients were less likely to be treated at medical centres and corporate institutions (OR: 0.89; 95% CI: 0.84–0.93). In addition, high-compliance patients treated at institutions in rural areas (OR: 0.89; 95% CI: 0.83–0.94) had a significantly lower likelihood of receiving antihypertensive therapy than in the urban area, but there were no significant differences between urban and suburban areas. However, none of the tested variables had significant interactions.

Discussion

This national population-based study assessed the factors associated with medication compliance among hypertensive patients in Taiwan. The overall mean MPR of study population was 76.4%; 52.9% of the patients had high medication compliance (MPR \geq 80%) and 21.6% of the patients had low compliance (MPR < 50%). We found that a younger age, male sex, lower SES and higher comorbidity score were positively associated with high compliance in relation to antihypertensive drugs. Furthermore, patients receiving treatment at internal medical centres or other medical specialties who were visiting the same prescribing physician and were only prescribed one drug (monotherapy) had higher medication compliance. However, patients who were treated at medical centres or corporate or rural institutions were less likely to be compliant with antihypertensive therapy. This is probably owing to the treatment preferences of patients, the patient–provider relationship and the efficacy of the antihypertensive medication.²

The high level of medication compliance in Taiwanese hypertensive patients was relatively lower than the 72.3% of US patients who were compliant and were covered by employer-sponsored insurance, and the 85.5% medication-compliant Chinese patients

from the Hong Kong Healthcare System.^{13,22} Nevertheless, other studies that have evaluated the percentage compliance rate from pharmacy claims data have ranged from 25 to 75%.^{17,23} These differences in medication compliance depend on the patient population, physicians and the treatment regimen employed. In the present analysis, we found that male patients tended to have better medication compliance than female patients, which is a finding that is consistent with the results of previous studies.^{8,12} However, conflicting data still exist regarding the rate of medication compliance between male and female patients.¹³ With regard to age, patients aged \geq 55 years were less likely to be compliant with antihypertensive therapy.

Several previous studies have reported that medication compliance increases with age.^{8,13,22} Nevertheless, in this study, we found that older patients had a lower likelihood of medication compliance than younger patients. This result was similar to another study that also reported lower compliance with antihypertensive medication in older patients.^{18,24} It is possible that these patients had low compliance because of complementary or alternative medicine use, medication side effects, poor quality of life and inadequate social support.^{10,21,25} However, older people might also be more concerned about their health than younger patients, and they usually receive the necessary and sufficient help required from healthcare providers or family members.^{5,7,10} As a result, they may be more willing to comply with the medication regimen.

Interestingly, we also found that patients who generally had a high SES were less likely to be compliant than those that had a lower SES. It is possible that the high SES patients were unable to be absent from work for therapy, and so appeared to be less compliant. A study suggested that white-collar patients have poor drug compliance because they have other routine priorities that are higher than medication-taking.²⁶ However, prior research has suggested that, contrary to our finding, patients from a low SES level tend to be less compliant.²⁵ In addition, other studies have reported that monthly income was not related to compliance level.¹⁰ However, it remains inconclusive whether this difference can be explained entirely by the different SES of the population in this study.¹² This discrepancy might be due to the difference between the healthcare systems of different countries.

Our finding was consistent with previous studies that showed that patients with multiple comorbid conditions were more likely to have high antihypertensive medication compliance.²¹ This may be explained by the fact that patients with high-risk conditions may be more willing to follow their prescribed treatment.

In addition, consistent with prior research, we found that an increasing number of prescribing physicians

and increasing number of prescribed antihypertensive drugs prescribed decreased compliance.¹² This implies that a consistent interaction between the physician and the patient has a positive effect on prescribed drug compliance for hypertension control. Previous studies have reported that a good physician–patient relationship and patient satisfaction with care were associated with an increased probability of medication compliance.^{2,10} A review of the recent literature had suggested that antihypertensive compliance proportionately decreased with the incremental dose frequency and therapeutic complexity.²

In this study, we also found that patients who received prescribed antihypertensive therapy at medical centres or corporation hospitals were less likely to be compliant than those treated at other types of medical institutions. Outpatient visits at larger institutions with increased waiting-time to see physicians, and appointments that interfered with work or social activities therefore isolating patients from their co-workers or peers, may result in poor compliance with medication and follow-up appointments.^{26,27} Moreover, lack of follow-up continuity and lack of accessibility of care may further decrease medication compliance. Therefore, the influence of institutional factors may, in part, explain the different rates of drug compliance between patients.

We evaluated the differential rate of medication compliance among hypertensive patients and assessed its relevant factors. However, there are several limitations of this study, which should be noted. First, other potential factors have been known to affect antihypertensive compliance, including the stage of hypertension, the side effects of the medication, the patient's knowledge about the medication, the patient's beliefs or attitudes and the patient's educational level but none of these could be assessed from our database.¹⁰ In addition, physical examination or clinical laboratory testing of the patients (i.e. body mass indices, levels of serum triglycerides or fasting blood glucose) were lacking because it was not allowed for the LHID database to be linked with private medical records.²¹ Second, the LHID pharmacy data may overestimate compliance because the drugs that are prescribed may not correspond to the patients' actual pill ingestion. Moreover, patients prescribed an insufficient number of pills in a given period may be considered to be non-compliant because they have not obtained enough medication to achieve a treatment goal.²⁸ Therefore, in this study, measures of refill compliance provided an upper bound for medication consumption, and this method was applied to determine partial medication compliance.^{13,28} Third and last, the LHID database does not record the motives for the switching and/or discontinuation of a prescribed antihypertensive medication

which could influence the MPR results. Future studies should include detailed clinical information concerning the patient-reported reasons for drug discontinuation and/or switching patterns.

In conclusion, several patient- and institution-related factors are associated with medication compliance which were observed in our study of hypertensive patients in Taiwan. However, there are appreciable differences between Eastern and Western countries in the factors affecting compliance which, in part, could be explained by ethnic differences. Using Taiwanese real-life data, the relatively low rate of compliance with prescribed antihypertensive medication could be improved. Hypertension can be controlled and the appearance of severe hypertensive complications can be prevented if the patient has high compliance with antihypertensive drugs. This finding emphasises the need to continually enhance patient awareness of the association between poor antihypertensive compliance and the risk of hypertension-related diseases. It is imperative to develop effective intervention strategies for patients with medium and low medication compliance.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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