

Determination of Barriers in Medication Adherence for Secondary Prevention in Stroke Patients

Sivakumar Velusamy, Kanishya Varatharaj, Rasika Kathirvel, Pavithra Venkatesan, Leah Jayan Varghese*

Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, Tamil Nadu, INDIA.

ABSTRACT

Background: It is a challenge for healthcare professionals to ensure that patients adhere to their medications. Although medications are more effective in reducing the risk of recurrent strokes, adherence to long-term treatment is low. The identification of barriers preventing medication adherence is therefore necessary to ensure optimal treatment. Our study aims to determine the barriers in medication adherence for secondary prevention in patients with ischemic stroke. **Materials and Methods:** A prospective study done in the Department of Neurology, PSG Hospitals, Coimbatore, India. 132 patients who received secondary prevention treatment for ischemic stroke were included in the study. **Results:** The patients were grouped into high, medium and low adherent categories. None of them had low adherence, 9.09% showed medium adherence and 90.9% of them fell into the high adherence category despite experiencing barriers. The following factors significantly reduced the medication adherence: worry about taking medication for a long time (52.3%, $p=0.001$), stopping medicines when feeling better (38.6%, $p=0.000$), stopping medicines intentionally (34.1%, $p=0.000$), white coat adherence (11.4%, $p=0.000$), forgetfulness (43.2%, $p=0.000$), frequency (9.1%, $p=0.000$), confusion in taking medicines (9.1%, $p=0.000$), number of medications (31.8%, $p=0.000$), difficulty to access hospital (36.4%, $p=0.004$) and difficulty in understanding the doctor (2.3%, $p=0.000$). **Conclusion:** It is important to identify the barriers to medication adherence and to resolve them at the earliest to avoid recurrent stroke. Among the significant barriers, the most important one was worrying about taking medications for a long time. Therefore, healthcare professionals, caregivers, and patients should work together to enhance medication adherence.

Key words: Recurrent stroke, Barriers, Medication adherence, Secondary prevention.

INTRODUCTION

Stroke is a medical condition in which there is insufficient blood flow to the brain, resulting in cell death. It is a global health problem and is the second leading cause of death worldwide.¹ The most prevalent type of stroke is ischemic stroke. Following an ischemic stroke, secondary prevention strategies and interventions are crucial in preventing recurrence. According to studies, the cumulative probability of recurrence stroke in the first five years after a stroke is estimated to be 26%.² As a result, long term prevention is believed to be associated with an improved outcome and a reduced risk of death.^{3,4}

Medication adherence is a challenge for healthcare professionals. Non adherence varies among individuals, gender, age, personality and economic status. Studies have found that 50% of stroke patients fail to comply with their medications because of polypharmacy and co-morbidities.^{5,6} In addition, there are other barriers such as difficulty taking medications, fear, lack of knowledge, intentional withdrawal, neglect from caregivers, drug interactions, and forgetting to take medications.⁷⁻⁹ Poor adherence to secondary prevention treatment further adds on to the risk of recurrence and mortality in patients with stroke.¹⁰

DOI: 10.5530/ijopp.15.2.16

Address for correspondence:

Miss. Leah Jayan Varghese, PharmD Intern, Department of Pharmacy Practice PSG College of Pharmacy, Coimbatore, Tamil Nadu, INDIA.
Email id: team5project2020@gmail.com



www.ijopp.org

Achieving patient compliance to medications is dependent on identifying and addressing the barriers to adherence.^{7,11} Therefore, the current study investigated the barriers to medication adherence in stroke patients receiving secondary prevention treatment.

MATERIALS AND METHODS

Study site and subjects

This prospective study was conducted in the Department of Neurology, PSG hospitals, Coimbatore, Tamil Nadu, India. The study was approved by PSG Institutional Human Ethics Committee and was conducted over a period of 6 months (February 2020 – July 2020). Patients aged >18 years and post ischemic stroke patients receiving secondary prevention treatment for more than 6 months were included in the study. Patients who were not willing to participate, those who had any mental disability, aphasia, terminal illness and cognitive impairment were excluded. Sample size was calculated based upon the number of inpatient and outpatient hospital admissions. A sample size of 132 patients was calculated using Rao software sample size calculator, with 5% margin of error, 95% confidence interval, 50% response distribution.

Barrier and Adherence assessment

The barrier and adherence assessment questionnaire was developed based on the common problems faced by patients in the local setting. The quality and accuracy of the questionnaire was assessed using the EQIP tool. Informed consent was obtained from the patient before the interview. The duration of the interview was 15 min. The questionnaire consisted of 2 parts, the first (a) to assess the barriers and the second (b) to assess the adherence level of the patient. The second part of the questionnaire was scored as YES = 1 indicating that barriers had an effect on the adherence (non-adherent) and NO = 0 indicating that barriers did not have an effect on the adherence (adherent). Barriers were identified based on their responses, and an adherence score was calculated. The score ranges from 0-31, where the score 0 is low adherence and 31 is high adherence. The higher the number, the lower the amount of adherence, and vice versa. The study participants were categorized as low adherent (21-31), medium adherent (11-20) and high adherent (0- 10) based on their scores.

Demographic details

Details like age, sex, education, occupation, social habits, number of drugs being taken, medication administration, co-morbidities and occurrence of previous stroke were all collected from the patients.

Statistical analysis

Statistical analysis was carried out using SPSS version 20. One-Way ANOVA was used to analyze the patient demographics with adherence level. The Chi-Square was used to examine the association between barriers and adherence level. A level of significance was accepted as two tailed *P* value <0.05 with a confidence interval of 95%.

RESULTS

Patient Demographics

Table 1 shows the demographic characteristics of the study participants as well as their level of adherence. The average age observed was 55 years, with male patients (84.0%) outnumbering female patients. The majority (56.8%) of the patients were employed. Majority of the study participants had completed high school (65.9%). Approximately 62.3% were discovered to be non-smokers and non-drinkers.

The co-morbidities observed among the participants were hypertension (26.5%), diabetes mellitus (23.4%), dyslipidemia (18.9%), coronary artery disease (12.1%), chronic kidney disease (6.8%), anemia (5.3%), seizure (4.5%), diabetic neuropathy (3.0%), chronic obstructive pulmonary disease (3.0%) and other comorbidities were osteoarthritis, homocysteinemia, hypothyroidism, depression and Parkinsonism (5.3%). Five to eight drugs were prescribed to 70.4% of the patients. Around 47.7% of patients take their medications on their own. Approximately 61.30% of the patients had a prior stroke within the preceding 1 to 3 years. Patients' age, number of medicines taken, and number of co-morbidities all differed considerably between the high and medium adherence groups.

Assessment of barriers and its effect on patient adherence

Among the eight main categories of barriers, five of them were further classified into subtypes and a total of 24 barriers were obtained. They are listed in Table 2.

The maximum number of barriers found among the study participants were 14 however this constituted only a small part of the population and is represented in Figure 1. In comparison 18.18% of the patients were found to have an average of 8 barriers. Figure 2 shows the additional categorization of patients into high, medium and low adherent categories with 90.9% of them falling into the high adherent category despite experiencing some barriers.

Table 1: Demographic characteristics.

Characteristics	Overall (n=132)	High Adherence (n=120)	Medium Adherence (n=12)	P - value
1. Age				
Mean age	55	53.4	65.5	0.000*
2. Gender				
Male	111(84.0%)	99(75.0%)	12(9.0%)	0.116
Female	21(15.9%)	21(15.9%)	0	
3. Education				
School	87(65.9%)	81(62.3%)	6(4.5%)	0.889
College	21(15.9%)	18(13.6%)	3(2.2%)	
Uneducated	24(18.1%)	21(15.9%)	3(2.2%)	
4. Work				
Working	75(56.8%)	69(52.2%)	6(4.5%)	0.620
Non-working	57(43.1%)	51(38.6%)	6(4.5%)	
5. Social Habits				
No social habits	81(62.3%)	75(56.8%)	8(6.0%)	0.245
Smoking	12(9.0%)	12(9.0%)	0	
Alcohol	15(11.3%)	12(9.0%)	3(2.2%)	
Both smoking and alcohol	24(18.1%)	21(15.9%)	3(2.2%)	
6. No. of comorbidities				
< 5	123(93.2%)	117(88.6%)	6(4.5%)	0.000*
> 5	9(6.8%)	3(2.2%)	6(4.5%)	
7. No. of drugs				
< 5	9(6.8%)	9(6.8%)	0	0.000*
5-8	93(70.4%)	90(68.1%)	3(2.2%)	
>8	30(22.7%)	21(15.9%)	9(6.8%)	
8. Occurrence of previous stroke				
<1 year	30(22.7%)	27(20.4%)	3 (2.2%)	0.289
1-3 years	81(61.3%)	72(54.5%)	9 (6.8%)	
>3 years	21(15.9%)	21(15.9%)	0	
9. Medicine administration				
Family	63(47.7%)	58(43.9%)	5(3.7%)	0.662
Self	69(52.2%)	62(46.7%)	7(5.3%)	

P-value <0.05 indicates significant difference

Table 3 shows the patient's level of adherence to each barrier. The barriers that showed a significant difference between the high and medium adherent groups were found to be worry about taking medication for long time (52.3%), stopping medicines when they feel better (38.6%), stopping medicines intentionally (34.1%), white coat adherence (11.4%), forgetfulness (43.2%), frequency (9.1%), confusion in taking medicines (9.1%), number of medications (31.8%), difficulty to access hospital (36.4%) and difficulty in understanding the doctor (2.3%) indicating that they contribute predominantly to the patients' adherence level.

DISCUSSION

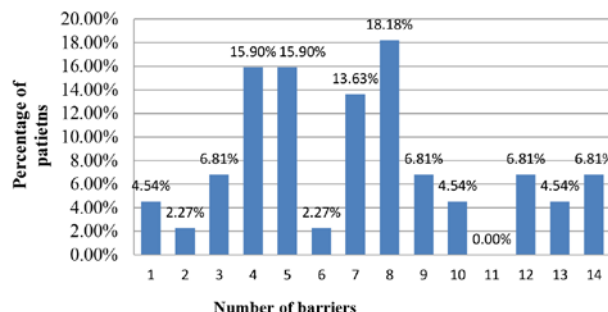
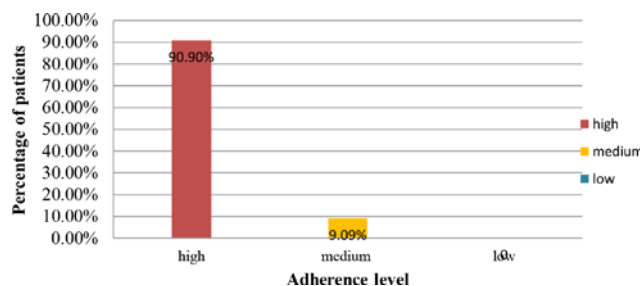
The average age of the study participants was 55 years and the majority of them were men (84.0%). Our study participants were predominantly from the working class. Majority of them received school level education. Most of them administered medications by themselves. Majority of the study participants (70.4%) took five to eight drugs

in a day and were found to have less than five comorbid conditions (93.2%).

Our findings were relatively similar to a study done by Ian M. Kronish *et al.* where 600 stroke patients were interviewed through MMAQ and BMQ and it was found that increased concern about medication such as worry about medications, long term consequences and medication dependence were significant barriers among their study participants.¹¹ A similar report was also seen in the article by Caroline Souter *et al.*, done with 30 patients diagnosed with stroke through a one-on-one interview in 2012, which showed that strong negative beliefs regarding medicines were enough for patients to stop taking their medications.¹² In our study, worry about taking medications for a long time was found to be a major concern among patients. Most of them believed that they had become better and stopped their medications. An open-ended and collaborative approach between the health care provider and the patient is an effective way to address these challenges for specific patients.^{13,14}

Table 2: List of barriers.

1. Lack of knowledge on drug and disease
2. Concern and Beliefs
 - Stop medicines when they felt better
 - Worry about taking medications for long time
 - Believes natural remedies are better
 - Life being dependant on medications
 - Taking natural/herbal remedies
 - Not feeling good after taking medicines
 - Fear
3. Forgetfulness
4. Intentional Withdrawal
 - Stop medicines intentionally
 - White coat adherence
5. Difficulty to access healthcare
 - Difficulty in accessing hospital
 - Difficulty in accessing pharmacy
6. Medication related barriers
 - Cost
 - Monitoring tests
 - Frequency
 - Side effects
 - Number of medicines
 - Confusion in taking medications
7. Caretaker related barriers
 - Dependent on caretaker
 - Relationship changed with family
8. Healthcare professional related barriers
 - Increased waiting time
 - Difficulty in understanding the doctor properly
 - Health care professional not spending adequate time

**Figure 1: Percentage of patients Vs Number of barriers.****Figure 2: Percentage of patients based on the adherence level.**

Another key contributing factor to the patients' adherence level in our study was medicine related barriers. Patients often found it difficult to adhere to medicines when they had frequent dosing and an increasing number of

medicines, while some patients reported having confusion regarding the tablet name, appearance, and time of administration.

A study conducted by Zullig LL *et al.* in a primary care setting reported that medication adherence was lower in patients taking more than two tablets a day.¹⁵ Simplifying medication routines and treatment regimens through measures such as fixed dose combinations and reduction of daily dosing contributes to reducing the patients' burden of taking several tablets in a day. Provision of blister packs and pill boxes also resulted in fewer instances of confusion among patients while taking their medications.^{8,16}

A major proportion of our study participants reported that they forgot to take their medicines while traveling and going out to work. Not remembering to take antihypertensive medications was the most commonly reported barrier in a study done by Lamuel Vawter *et al.* among US adults through a health style survey questionnaire in 2008.¹⁷ SMS-based interventions reminding patients to take their medications have shown significant improvement in adherence levels.¹⁸

Intentional withdrawal was another significant barrier reported among the patients. This included both withdrawing medicines intentionally as well as white coat adherence. White coat adherence is a situation wherein a patient remains adherent to their medications for a short time just before and after consultation with the doctor.¹⁶

Lack of proximity to healthcare was also one of the problems faced by the patients. They reported that traveling a long distance made it difficult for them to access the hospital for their follow-up appointments. Some of them also had difficulty understanding the doctor properly. This may be due to shorter consultation times, which may be contrary to the patient's expectations. Findings similar to our study were also reported by Kirsi Kvarnstrom *et al.*¹⁹

Healthcare professionals should ensure that the patient always has a clear understanding of their disease and treatment. Patients should be involved in the decision-making process regarding their treatment plan. Patients should be aware of their medications at all times and, if possible, keep reminders and acquire the needed support from their families for timely administration of medicines. Our findings can be used to create personalized treatments for each patient in order to enhance drug adherence.

Table 3: Patients level of adherence for each barrier.

Barrier	Total	High adherent group	Medium adherent group	P-value
01. Lack of knowledge on drug and disease				
Yes	120(90.9%)	108 (81.2%)	12 (9.1%)	0.251
No	12(9.1%)	12 (9.1%)	0	
02. Stop medicines when they felt better				
Yes	51 (38.6%)	39 (29.5%)	12 (9.1%)	0.000*
No	81 (61.4%)	81 (61.4%)	0	
03. Worry about taking medications for a long time				
Yes	69 (52.3%)	57 (43.2%)	12 (9.1%)	0.001*
No	63 (47.7%)	63 (47.7%)	0	
04. Believes natural remedies are better				
Yes	9 (6.8%)	9 (6.8%)	0	0.326
No	123(93.2%)	111 (84.1%)	12 (9.1%)	
05. Life being dependent on medications				
Yes	60 (45.5%)	51 (38.6%)	9 (6.8%)	0.031
No	72 (54.5%)	69 (52.3%)	3(2.3%)	
06. Taking natural/herbal remedies				
Yes	9 (6.8%)	9 (6.8%)	0	0.326
No	123(93.2%)	111 (84.1%)	12 (9.1%)	
07. Not feeling good after taking medicines				
Yes	3 (2.3%)	3 (2.3%)	0	0.580
No	129(97.7%)	117 (88.6%)	12 (9.1%)	
08. Fear				
Yes	33 (25%)	30 (22.7%)	3 (2.3%)	1.000
No	99 (75%)	90 (68.1%)	9 (6.8%)	
09. Forgetfulness				
Yes	57 (43.2%)	45 (34%)	12 (9.1%)	0.000*
No	75 (56.8%)	75 (56.8%)	0	
10. Stop medicines intentionally				
Yes	45 (34.1%)	33 (25%)	12 (9.1%)	0.000*
No	87 (65.9%)	87 (65.9%)	0	
11. White coat adherence				
Yes	15 (11.4%)	6 (4.5%)	9 (6.8%)	0.000*
No	117(88.6%)	114 (86.3%)	3 (2.3%)	
12. Difficulty to access hospital				
Yes	48 (36.4%)	39 (29.5%)	9 (6.8%)	0.004*
No	84 (63.6%)	81 (61.3%)	3 (2.3%)	
13. Difficulty to access pharmacy				
Yes	36 (27.3%)	24 (18.2%)	12 (9.1%)	0.087
No	96 (72.7%)	96 (72.7%)	0	
14. Cost				
Yes	90 (68.2%)	78 (59.1%)	12 (9.1%)	0.013
No	42 (31.8%)	42 (31.8%)	0	
15. Monitoring test				
Yes	12 (9.1%)	12 (9.1%)	0	0.251
No	120(90.9%)	108 (81.8%)	12 (9.1%)	
16. Frequency				
Yes	12(9.1%)	3 (2.3%)	9 (6.8%)	0.000*
No	120(90.9%)	117 (88.6%)	3 (2.3%)	
17. Side effects				
Yes	12 (9.1%)	9 (6.8%)	3 (2.3%)	0.044
No	120(90.9%)	111 (84.1%)	9 (6.8%)	
18. Number of medicines				
Yes	42(31.8%)	30 (22.7%)	12 (9.1%)	0.000*
No	90 (68.2%)	90 (68.2%)	0	
19. Confusion in taking medications				
Yes	12 (9.1%)	6 (4.5%)	6 (4.5%)	0.000*
No	120(90.9%)	114 (86.4%)	6 (4.5%)	
20. Dependent on caretaker				
Yes	48 (36.4%)	42 (31.8%)	6 (4.5%)	0.303
No	84 (63.6%)	78 (59.1%)	6 (4.5%)	
21. Relationship changed with family				
Yes	3 (2.3%)	3 (2.3%)	0	0.580
No	129(97.7%)	117 (88.6%)	12 (9.1%)	
22. Increased waiting time				
Yes	60 (45.5%)	57 (43.2%)	3 (2.3%)	0.136
No	72 (54.5%)	63 (47.7%)	9 (6.8%)	
23. Healthcare professional not spending adequate time				
Yes	3 (2.3%)	3 (2.3%)	0	0.580
No	129(97.7%)	117 (88.6%)	12 (9.1%)	
24. Difficulty in understanding the doctor				
Yes	3 (2.3%)	0	3 (2.3%)	0.000*
No	129(97.7%)	120 (90.9%)	9 (6.8%)	

P-value<0.05 indicates significant difference.

CONCLUSION

It is important to identify the barriers to medication adherence experienced by a patient and also resolve them at the earliest to avoid recurrent stroke episodes. Among the significant barriers that affected adherence, the most important one was worry about taking medications for a long time. This study suggests that healthcare professionals, caretakers, and stroke patients should have good collaboration to improve medication adherence among stroke patients. The patient's concerns about the medication should be carefully addressed. Despite facing many barriers, patients were found to remain adherent to their medications. Even though counseling strategies are a good way to improve adherence, in addition to that, mobile-based measures (medication reminders, information about drugs and diseases, motivational quotes, fixing appointments, review reminders, counseling notes) will continue to be helpful in the future.

ACKNOWLEDGEMENT

We take this opportunity to express our profound gratitude and deep regards to our respected guide, Dr. V. Sivakumar, M.Pharm., Ph.D., Professor, Department of Pharmacy Practice, PSG College of Pharmacy. His excellent guidance, unflinching inspiration, kind cooperation, and moral support have brought our dissertation into this shape, and it will be remembered always. We wish to express our sincere thanks to Dr. M. Ramanathan, M.Pharm., Ph.D., Principal, PSG College of Pharmacy, for providing us with the necessary facilities and amenities to carry out our dissertation work with great ease. We owe a debt of gratitude to Dr. R. Balakrishnan, M.D., DM.DNB, Department of Neurology, PSG hospitals, for his guidance, motivation, and constant support to complete this work. We extend our sense of gratitude to one and all who, directly or indirectly, have lent their helping hand in this venture.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

EQIP: Ensuring Quality Information for Patients; **SPSS:** Statistical Package for the Social Sciences; **ANOVA:** Analysis of variance; **MMAQ:** Morisky Medication Adherence Questionnaire; **BMQ:** Beliefs about medicines questionnaire.

SUMMARY

This prospective study aims to determine the barriers to medication adherence for secondary prevention in ischemic stroke patients in the Neurology department of a tertiary care hospital. By conducting such studies, we can understand the various barriers faced by the patients, address the patients' concerns regarding their medications, and provide effective solutions for the same, thus improving patient compliance and treatment outcome. This study also shows that healthcare providers, caregivers, and stroke patients should work together to improve medication adherence.

REFERENCES

- Katan M, Luft A. Global burden of stroke. *Semin Neurol.* 2018;38(2):208-11. doi: 10.1055/s-0038-1649503, PMID 29791947.
- Mohan KM, Wolfe CDA, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke.* 2011;42(5):1489-94. doi: 10.1161/STROKEAHA.110.602615, PMID 21454819.
- Lackland DT, Roccella EJ, Deutsch AF, Fornage M, George MG, Howard G, Kissela BM, Kittner SJ, Lichtman JH, Lisabeth LD, Schwamm LH, Smith EE, Towfighi A, American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Quality of Care and Outcomes Research, Council on Functional Genomics and Translational Biology. Factors influencing the decline in stroke mortality: a statement from the American Heart Association/American Stroke Association. *Stroke.* 2014;45(1):315-53. doi: 10.1161/01.str.0000437068.30550.cf. PMID 24309587.
- Palnum KH, Mehnert F, Andersen G, Ingeman A, Krog BR, Bartels PD, Johnsen SP. Use of secondary medical prophylaxis and clinical outcome among patients with ischemic stroke: a nationwide follow-up study. *Stroke.* 2012;43(3):802-7. doi: 10.1161/STROKEAHA.111.635342, PMID 22207506.
- Evidence for action World Health Organization; 2003 [internet]. Available from: <http://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf> [cited 26/1/2022].
- Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care Program on Medication Adherence and Persistence, Blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA.* 2006;296(21):2563-71. doi: 10.1001/jama.296.21.joc60162, PMID 17101639.
- Bauler S, Jacquin-Courtois S, Haesebaert J, Lualaba J, Coudeyre E, Feutrier C, Allenet B, Decullier E, Rode G, Janoly-Dumenil A. Barriers and facilitators for medication adherence in stroke patients: a qualitative study conducted in French neurological rehabilitation units. *Eur Neurol.* 2014;72(5-6):262-70. doi: 10.1159/000362718, PMID 25277833.
- Jamison J, Graffy J, Mullis R, Mant J, Sutton S. Barriers to medication adherence for the secondary prevention of stroke: a qualitative interview study in primary care. *Br J Gen Pract.* 2016;66(649):e568-76. doi: 10.3399/bjgp16X685609, PMID 27215572.
- Sardana V, Kiran R. Evaluation of Medication Adherence among Elderly Patients at the time of stroke Onset in Southeast Rajasthan. *Journal of the Indian Academy of Geriatrics.* 2019;15(1):5-9. doi: 10.35262/jiag.v15i1.05-09.
- Yeo SH, Toh MPHS, Lee SH, Seet RCS, Wong LY, Yau WP. Impact of medication non adherence on stroke recurrence and mortality in patients after first-ever ischemic stroke: Insights from registry data in Singapore. *Pharmacoepidemiol Drug Saf.* 2020;29(5):538-49. doi: 10.1002/pds.4981, PMID 32190948.
- Kronish IM, Diefenbach MA, Edmondson DE, Phillips LA, Fei K, Horowitz CR. Key barriers to medication adherence in survivors of strokes and transient ischemic attacks. *J Gen Intern Med.* 2013;28(5):675-82. doi: 10.1007/s11606-012-2308-x, PMID 23288379.
- Souter C, Kinnear A, Kinnear M, Mead G. Optimisation of secondary prevention of stroke: A qualitative study of stroke patients' beliefs, concerns and difficulties

- with their medicines. *Int J Pharm Pract.* 2014;22(6):424-32. doi: 10.1111/ijpp.12104, PMID 24606322.
13. Schoenthaler A, Chaplin WF, Allegrante JP, Fernandez S, Diaz-Gloster M, Tobin JN, *et al.* Provider communication effects medication adherence in hypertensive African Americans. *Patient Educ Couns.* 2009;75(2):185-91. doi: 10.1016/j.pec.2008.09.018, PMID 19013740.
14. Cutrona SL, Choudhry NK, Stedman M, Servi A, Liberman JN, Brennan T, *et al.* Physician effectiveness in interventions to improve cardiovascular medication adherence: A systematic review. *J Gen Intern Med.* 2010;25(10):1090-6. doi: 10.1007/s11606-010-1387-9, PMID 20464522.
15. Zullig LL, Stechuchak KM, Goldstein KM, Olsen MK, McCant FM, Danus S, *et al.* Patient-reported medication adherence barriers among patients with cardiovascular risk factors. *J Manag Care Spec Pharm.* 2015;21(6):479-85. doi: 10.18553/jmcp.2015.21.6.479, PMID 26011549.
16. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: Its importance in cardiovascular outcomes. *Circulation.* 2009;119(23):3028-35. doi: 10.1161/CIRCULATIONAHA.108.768986, PMID 19528344.
17. Vawter L, Tong X, Gemilyan M, Yoon PW. Barriers to antihypertensive medication adherence among adults--United States, 2005. *J Clin Hypertens (Greenwich).* 2008;10(12):922-9. doi: 10.1111/j.1751-7176.2008.00049.x. PMID 19120718.
18. Kamal AK, Shaikh Q, Pasha O, Azam I, Islam M, Memon AA, *et al.* A randomized controlled behavioral intervention trial to improve medication adherence in adult stroke patients with prescription tailored Short Messaging Service (SMS)-SMS4Stroke study. *BMC Neurol.* 2015;15(1):212. doi: 10.1186/s12883-015-0471-5, PMID 26486857.
19. Kvarnström K, Airaksinen M, Liira H. Barriers and facilitators to medication adherence: A qualitative study with general practitioners. *BMJ Open.* 2018;8(1):e015332. doi: 10.1136/bmjopen-2016-015332, PMID 29362241.