

Correlation between Degree of Compliance to Antihypertensives with Severity of Stroke

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Abstract

Objective: Study was conducted to find out correlation between degree of compliance to antihypertensives with severity of stroke.

Methods: This correlational study was conducted in department of neurology, Pakistan Institute of Medical Sciences, Islamabad from December 2017 to May 2018. A total of 74 patients with clinically and radiologically confirmed diagnosis of stroke, having history of hypertension, were included in the study. According to the Modified Rankin Scale (MRS), scores were assigned from 0 to 6 in increasing order of severity. Quantitative assessment to drug compliance was calculated via Brief Adherence Rating Scale (BARS). According to BARS, scores were assigned from 1 to 4 in decreasing order of non-compliance or increasing order of compliance. Compliance was defined according to BARS as patients taking more than 76% of their prescribed dosage. Compliance of drug was checked for last 6 months. Data was finally analysed by SPSS v. 20. Appropriate statistical tests were applied.

Results: Mean age of the stroke patients was 58.8 ± 14.91 years. Total 33 patients i.e. 44.6% were compliant and 41 were noncompliant. Strong negative correlation ($r = -0.494$, p -value = 0.00008) was found between degree of compliance according to BARS scale and severity of stroke according to MRS. Regression analysis showed R^2 value of 0.41 and p -value of 0.0004. Most common cause of drug noncompliance according to patients was improper counselling followed by fear of getting used to medication, forgetting, cost, side effects, and dissatisfaction with treatment. Among other risk factors for stroke, 18.9% had positive history for smoking, 43.2% for hyperlipidaemia, 18.9% for coronary artery disease, and 5.4% for atrial fibrillation.

Conclusion: Adherence to antihypertensives can help in reducing severity of stroke which will result in better prognosis and reduced morbidity and mortality. Most important factor contributing to noncompliance is lack of awareness regarding disease and importance of antihypertensive medications.

Keywords: Stroke, hypertension, patient compliance, antihypertensives, counselling.

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Introduction

Stroke is the second leading cause of death worldwide attributing to 6.3 million deaths per year. Out of which, 3.3 million deaths resulted from is-

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chemic stroke and 3 million from haemorrhagic stroke¹. Majority of the deaths occurred in patients above 65 years. Furthermore, stroke is a leading cause of disability which results in a significant burden on health care services. Since last two decades, incidence of stroke has increased in middle and low-income countries, while decreased in high income countries². Incidence of stroke in US is 200 per 100,000 populations. In Pakistan, it is much higher³. According to Pakistan Stroke Society incidence of stroke in Pakistan is 250 per 100,000 populations³. Every year, 350,000 new cases are registered³. Among all ethnic groups in Pakistan, Pushtoons have highest prevalence rates for

stroke³. Incidence of stroke increases with increase in age. Approximately, 95% of the cases of stroke occur after age of 45².

Stroke is divided into haemorrhagic stroke and ischemic stroke according to aetiology. Nearly 80% of the strokes are ischemic. But the burden varies among different populations⁴. Most of the haemorrhages are intraparenchymal or subarachnoid. Most of the ischemic events are results of emboli lodging into blood vessels supplying the brain. Other causes may include atherosclerotic deposition in vessels, vasculitis, dissection and idiopathic causes⁴. Both haemorrhagic and ischemic strokes have similar risk factors. Hypertension is thought to be the single most important risk factor for both ischemic and haemorrhagic stroke⁴. Elevated blood pressure (BP) can cause haemorrhage of the blood vessels supplying to brain resulting in brain haemorrhage on one hand, or it could result in the dissemination of atherosclerotic plaque which could lodge in brain vessels resulting in ischemic stroke⁴.

Risk factors for stroke are complicated by fact that stroke appears in many varieties. However, hypertension, hyperlipidaemia, smoking, family history of stroke, history of diabetes, coronary artery disease, atrial fibrillation, obesity and physical inactivity are the major contributing risk factors towards stroke⁵. Males have a higher prevalence of smoking, hypertension and ischemic heart diseases, therefore have a higher risk of developing stroke than females⁵. Patients with previous history of stroke also have high risk of developing stroke again. Hyperlipidaemia increases the risk of stroke by forming atherosclerotic plaques in intracranial and extracranial vessels. Atrial fibrillation increases the risk for cardio-embolic event⁴. Physical inactivity and obesity are also independent risk factors of stroke⁵.

Symptoms of stroke vary according to the vessel involved. However, sudden onset of weakness on one side of body, loss of vision, slurring of speech, double vision and difficulty in walking are the major signs of both ischemic and haemorrhagic stroke³. Early treatment could help in improving the prognosis. Up to 25% of the patients die due to late admittance in hospital³.

Prognosis of stroke is also largely dependent upon severity of stroke at time of presentation. Increased severity at time of presentation is associated with increased morbidity and mortality. A study in Iran had shown that blood pressure and cholesterol are the most important prognostic factors for severity of stroke⁶.

One billion people are affected by hypertension worldwide. In Pakistan 12 million people have elevated blood pressure⁷. Studies have shown non-compliance to antihypertensive drugs as a measured cause of continuously increasing rate of hypertension⁷. Poor adherence to antihypertensives is a worldwide problem, with half of the patients prescribed with antihypertensives stop taking medication within 1 year. This is usually due to multiple regimen, poor awareness and need of taking lifelong medications⁸.

Rate of death and increased disability is increased with elevated blood pressure⁹. Noncompliance to antihypertensives is very common in Pakistan approaching nearly 68.14% and is more common in low status groups⁷. Different studies have been conducted on noncompliance to antihypertensives and factors affecting it. Also, studies are available on risk of stroke and compliance with antihypertensives. However, there is paucity of data regarding its impact on stroke especially in our country. Lee KB conducted study on this topic in South Korea. His results showed significant effect of noncompliance on NIHSS score¹⁰. We conducted this study to fill this gap and to find out correlation between compliance to antihypertensives and severity of stroke.

Patient and Methods

The study was conducted in Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad. Study duration was six months from December 2017 to May 2018. The study design was non-experimental correlational study design. Ethical approval from the department was taken prior to conduction of study. All the patients with clinically and radiologically confirmed diagnosis of either ischaemic or haemorrhagic stroke having history of hypertension were included in the study. Patients without hypertension were excluded. A total of 74

patients met the inclusion criterion. Consecutive sampling technique was used. Sample size was calculated from online sample size calculator for regression analysis with anticipated effect size of 1.53 calculated from R^2 value of 0.65, desired power of 0.8, probability level of 0.05 and number of predictors was 910. Minimum required sample size was 21.

Detailed history was taken regarding history of hypertension, hyperlipidaemia, diabetes, coronary artery disease, atrial fibrillation and previous stroke. Patients were asked about prescribed medication, number of medications, advised dosage, duration of illness, and intake of medication and reason for noncompliance to antihypertensives. Haemorrhagic or ischemic stroke was classified on the basis of radiological reports.

Patients were clinically assessed and were assigned scores according to Modified Rankin Scale (MRS) for the assessment of severity of stroke. According to MRS, scores were assigned from 0 to 6 in increasing order of severity. Score 0 indicates no symptom i.e. no disability. Score 1 means no significant disability, patient is able to carry out all usual activities, despite some symptoms. Score of 2 means slight disability, being able to look after own affairs without assistance, but unable to carry out all previous activities. Score 3 indicates moderate disability, requires some help, but able to walk unassisted. Score 4 shows moderately severe disability patient is unable to attend to own bodily needs without assistance, and unable to walk unassisted. Score of 5 shows severe disability, patient requires constant nursing care and attention, bedridden, incontinent. Score 6 is assigned to dead patient.

Quantitative assessment to drug compliance was calculated via Brief Adherence Rating Scale (BARS). For calculating BARS score patients were asked about the number of pills prescribed by the doctor and the number of pills taken by patient. Then percentage was calculated and scores were assigned. Compliance was defined according to BARS as patients taking more than 76% of their prescribed dosage. Scores were assigned from 1 to 4 in decreasing order of noncompliance or increasing order of compliance. Score 1 was given to the

patient who almost/always skips his/her medicine i.e. 76% to 100% of the time. Score 2 is assigned to patient who usually (51%-76%) misses his/her medicine. Score 3 is given to patient who sometimes (25%-51%) skips his/her medicine. Score 4 shows compliant patient who never/almost never (0% to 25%) misses his/her medication. Compliance of drug was checked for last 6 months.

Data was finally analysed by SPSS v. 20. Firstly, data was arranged and value labels were given. Spearman correlation was applied to check correlation. Regression analysis was done to control for confounding variables. Dispersion in quantitative data was analysed by standard deviation. Statistical significance was checked by $p > 0.05$ values.

Results

Mean age of the stroke patients was found to be 58.8 ± 14.91 years. Mean age for the compliant patients was 56.6 ± 14.43 years while mean age for the non-compliant patients was 60.4 ± 15.23 years. Majority ($n = 40$, 54.1%) of the patients were females, 34 were males. Out of 74, 45 i.e. 60.8% patients had ischemic stroke while 29 i.e. 39.2% suffered from haemorrhagic stroke.

The patients who had taken their medications regularly were 33 i.e. 44.6% of study population were compliant and 41 i.e. 55.4% were noncompliant to antihypertensive medications. Among males 44.11% were compliant while among females 45% were compliant. No significant association ($OR = 1.03$, $p\text{-value} = 0.56$) was found between gender and compliance to antihypertensives. No significant correlation ($r = -0.159$, $p\text{-value} = 0.18$) was found between age and degree of compliance. 82.4% of the patients were on monotherapy. No significant association ($OR = 0.45$, $p\text{-value} = 0.3$) was found between monotherapy and compliance.

Results of Spearman correlation showed that strongly negative correlation ($r = -0.494$, $p\text{-value} = 0.00008$) exist between degree of compliance according to BARS scale and severity of stroke according to MRS. Patients with compliance less than 50% presented with severe disability i.e. either MRS 4 or 5 (Fig. 1). Positive correlation ($r = 0.37$, p -

Table 1. Reasons for noncompliance to antihypertensive medications versus degree of non-compliance according to BARS

Reason for Noncompliance * BARS Cross tabulation count

Reason for non-compliance	BARS			Total
	1= 76-100% noncompliance	2= 51%-75% noncompliance	3= 26%-50% noncompliance	
Cost	0	0	3	3
Improper counseling	9	3	3	15
Forgetting	0	2	6	8
Fear of Getting Used to Medicines	5	4	0	9
Side Effects	2	1	0	3
Dissatisfaction with treatment	2	1	0	3
Total	18	11	12	41

value= 0.01) was also found between increase in age and severity of stroke.

Among other risk factors for stroke, 18.9% of the patients had positive history for smoking, 43.2% for hyperlipidaemia, 18.9% for coronary artery disease, and 5.4% for atrial fibrillation. 55.4% of the patients had positive history of previous stroke, while 56.8% of the patients had diabetes. Linear regression was done to control the confounding variables. Results of regression showed significant (R= 0.41, p-value= 0.0004) effect of independent variable i.e. compliance on severity of stroke. Among confounders, only diabetes brought change in predictor value by 11%, with significant change of 0.001. Other cofounders had little effect on dependent variable with change of age (4.20%), gender (0.21%), smoking (0.17%), hyperlipidaemia (2.14%), coronary artery disease (7.7%), atrial fibrillation (4.9%) and stroke (0.12%). We also applied ordinal logistic regression for checking dependence of severity MRS with degree of drug compliance (BARS) while taking BARS 4 i.e. compliance as reference one. Results showed significant effect of increased compliance with decrease in MRS. BARS 1 had estimate of 2.64 with significance of 0.00005. BARS 2 had estimate of 2.0 with significance of 0.00005. While BARS 3 has estimate of -0.07 with significance of 0.90.

Most common cause of drug noncompliance according to patients was improper counselling (36.8%) followed by fear of getting used to medication (21.9%), forgetting (19.5%), cost (7.3%), side-effects (7.3%), and dissatisfaction with treatment

(7.3%) (Fig. 2). Among patients, who regarded improper counselling as major cause had compliance rates less than 25%. While who forget taking medicines have compliance rate more than 50% (Table 1).

Discussion

Incidence of stroke is rising in our country. Pakistan has a higher stroke rate than western countries. Also, mortality and morbidity related to stroke is higher due to lack of proper healthcare facilities³. Many modifiable and unmodifiable risk factors are associated with rising incidence of stroke⁴. Controlling modifiable risk factors could help in reducing not only incidence but also severity of stroke. As prognosis of stroke is highly dependent upon its severity at time of presentation, good score at time of presentation can result in reduced morbidity and mortality⁶. Hypertension is known to be single most important modifiable risk factor for stroke⁴. Controlling hypertension can help in reducing severity of stroke there by reducing mortality and morbidity associated with it.

We used MRS scale for grading severity of stroke and BARS scale for drug adherence and found negative correlation between drug adherence and severity of stroke. Results of regression analysis and spearman correlation, both showed dependence of severity of stroke on noncompliance to antihypertensives. R² value was 0.41, r-value was -0.49, both having p-value <0.001. This shows compliance of antihypertensives to be an important factor in controlling stroke severity. Our results were in agreement with study conducted by Lee et al. on

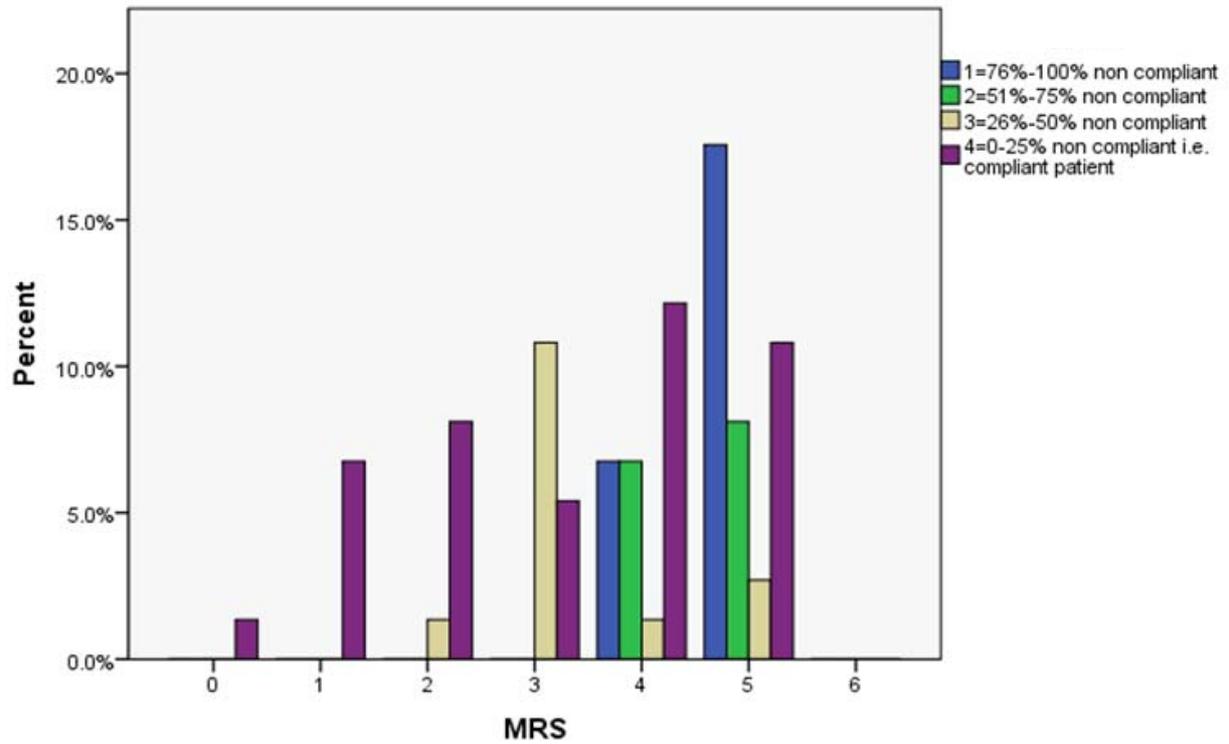


Fig. 1. Bar diagram depicting severity of stroke Modified Rankin's Scale (MRS) versus noncompliance (BARS) to antihypertensives

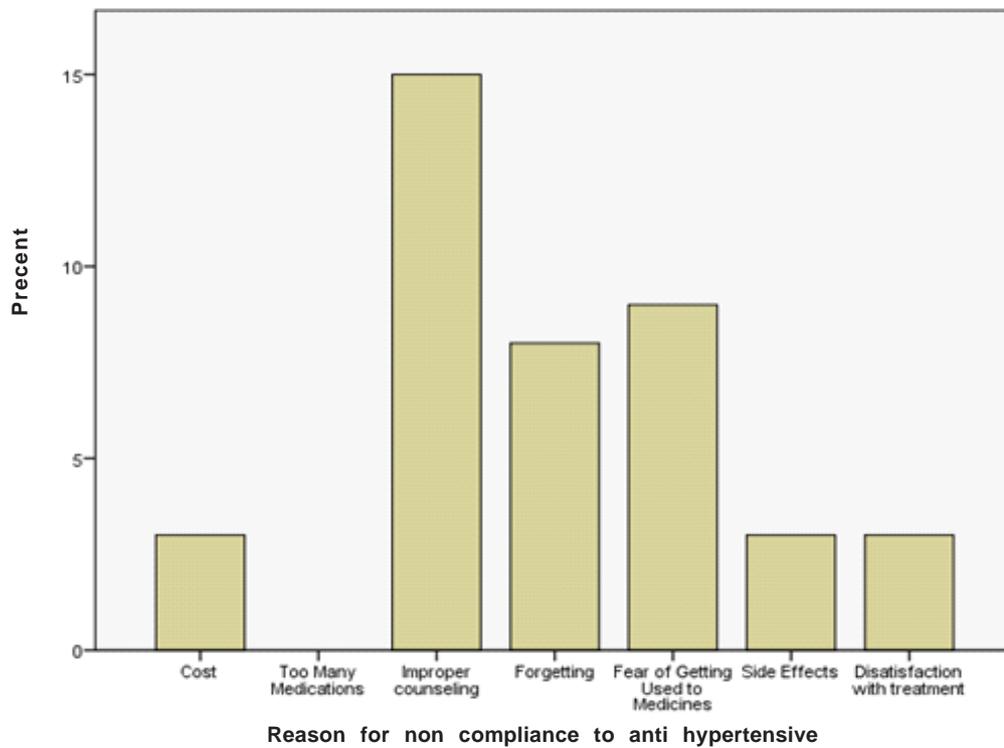


Fig. 2. Factors affecting noncompliance to antihypertensives

noncompliance of antihypertensives medication and stroke severity. They used NIHSS criterion for scoring stroke severity, their results showed increased noncompliance to antihypertensives resulted in increased severity of stroke¹⁰. Their R^2 value was 0.65.

Old age, male gender and family history of stroke are among the unmodifiable risk factors for stroke⁵. In our study mean age for stroke was 58.8 ± 14.91 years which was in concord with previous studies conducted in Pakistan. Study by Taj and colleagues showed mean age to be 57.0 ± 13.911 . Worldwide, male gender is predisposed to stroke more than females. In our study females were more commonly affected. However, this is in agreement in studies conducted in South Asian countries, which shows pattern different from the West with high prevalence among females¹². Demographic features of stroke in South Asian countries varies from the West. Also, the rate of stroke is five to ten times higher than the United States. Mostly females and young population are affected, while in the West, stroke is a disease of old age with male preponderance¹². Also, prevalence of haemorrhagic stroke is higher in South Asian countries as compared to the West¹.

Hyperlipidaemia, atrial fibrillation, smoking, diabetes, hypertension, and coronary artery diseases are established risk factors for stroke⁴. However, in our study, only a few patients had these risk factors. Among all these factors most prevalent was diabetes followed by hyperlipidaemia in the study population. Other studies conducted on risk factor of stroke in Pakistan showed these factors to be associated with stroke¹¹. All of the confounding variable have effect less than 5% on results of regression analysis except for diabetes and coronary artery disease. This was a limitation in the study. As excluding diabetic patient would have significantly reduced the sample size. Therefore, a multi-centre study on a large scale is required, excluding diabetic patients, to study the impact in more detail.

Worldwide, poor adherence to treatments remains a major hurdle in treating diseases. Majority of patients did not follow the advice of doctor⁶. Hypertensive patients usually require long life medica-

tions, therefore noncompliance to antihypertensives is common and is associated with increased risk of coronary and cerebrovascular events⁸. In Pakistan, compliance rates according to different studies are less than 50%⁷. Our results also showed compliance rate to be 44.6%. This showed that more than half of the patients with stroke had not taken their medicines regularly.

About 84% of the stroke cases have high blood pressure at time of presentation⁸. Uncontrolled hypertension is an established risk factor for stroke¹². To control hypertension, adherence to antihypertensives is necessary. Studies are available on initial BP at time of presentation and increased severity and their results showed positive correlation between them¹³. Also, literature supports that noncompliance to antihypertensives is a risk factor for stroke. Meta-analysis conducted by Xu et al. showed that 20% increment to antihypertensive adherence decreases the stroke risk by 9%¹⁴. Also, compliance to antihypertensive in patients with previous history of stroke decreases the risk of restroke¹⁵. Similar results were achieved by Jamison et al. who observed the effect of noncompliance to antihypertensives with risk of re-stroke. They found that adherence to medications effectively decreases the risk of recurrent stroke in patients with past history of stroke or transient ischemic attack¹⁶. Very few studies were conducted on correlation between drug compliance and severity of stroke. No such study is previously reported in our country. We conducted this study to fill this gap. Results of current study showed strong negative correlation between compliance with antihypertensives and stroke severity. This showed importance of drug compliance in patients with hypertension.

Studies have reported that monotherapy, young age and better awareness help in increasing compliance¹². But we did not find any association between monotherapy, gender and young age with drug adherence. In our case, majority of the patients were on monotherapy but still they were noncompliant. The most common cause of noncompliance in this study was lack of awareness. Most of the patients were unaware of the consequences associated with noncompliance to antihypertensives. Patient education regarding im-

portance of adherence and disease could help in solving the issue⁶.

Study by Polanska et al. on relationship between knowledge and medication adherence among hypertensives showed that knowledge about hypertension and its complications is an independent predictor of good adherence¹⁷. Their results showed that most common cause of nonadherence to antihypertensives is lack of knowledge regarding hypertension, its complications, and importance of drug adherence. Other reasons include, mistrust on physicians and negating the need of antihypertensives, when symptoms are not present¹⁷.

In current study, when patients were asked about the reason of noncompliance, majority of them did not know the importance of taking this medication, and the risks associated with not taking it. Patients without proper counselling tend to be less compliant than other. In our setup, proper time was not given in explaining the patients the importance of drug compliance and hazards of not taking it. Second common reason for not taking medicine was fear of getting used to it. There are so many misconceptions regarding antihypertensives and their side effects. Also, many of these patients prefer alternative medicine¹⁸. Approximately, 18.1% of the patients understood the importance of taking the medicine, but forgot to take it. They were usually less noncompliant than others. Others studies conducted in Pakistan also showed poor awareness about disease and improper counselling by physicians to be most common cause of non-adherence to antihypertensives^{19,20}.

Study was limited due to short duration and sample size. Also, we collected data from a public-sector hospital, where usually patients with low socioeconomic status and low education level reports. Due to which many patients totally negate that they had hypertension in their life, and mostly did not report in hospital unless some complication occurred. All such patients were excluded. Also lack of awareness is more common in this group. Rates of noncompliance and reason behind noncompliance in patients of private sector are expected to be different. We recommend that study should be

conducted on a large scale and should include both public and private sector hospitals.

Conclusion

Noncompliance to antihypertensives is directly associated with increased severity of stroke. Adherence to antihypertensives can help in reducing severity of stroke which will result in better prognosis and reduced morbidity and mortality. Most important factor contributing to noncompliance to antihypertensives is lack of awareness regarding disease, importance of taking antihypertensive medications regularly and consequences associated with its noncompliance. Proper counselling of patients by physicians and public awareness regarding hypertension, its complications and importance of antihypertensives could help in reducing drug noncompliance and will help in stroke prevention and stroke care.

Conflict of Interest

Authors have no conflict of interests and no grant/funding from any organisation for this study.

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References

1. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;388:1459-544. [DOI: 10.1016/S0140-6736(16)31012-1].

2. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet* 2014;383:245-54.
3. Information about Stroke [Online]. Pakistan Stroke Society. Available from: <http://www.pakstroke.com/>. Accessed on August 10, 2018.
4. Boheme AK, Eesenwa C, Elkind MS. Stroke, Risk factors, Genetics, and Prevention. *Circ Res* 2017;120:472-95. [DOI: 10.1161/CIRCRESAHA.116.308398].
5. Gan Y, Wu J, Zhang S, Li L, Yin X, Gong Y, et al. Prevalence and risk factors associated with stroke in middle-aged and older Chinese: A community-based cross-sectional study. *Sci Rep* 2017;7:9501. [DOI: 10.1038/s41598-017-09849-z].
6. Faraji F, Ghasami K, Talaie-Zanjani A, Mohammadbeigi A. Prognostic factors in acute stroke, regarding to stroke severity by Canadian Neurological Stroke Scale: A hospital-based study. *Asian J Neurosurg* 2013;8:78-82. [DOI: 10.4103/1793-5482.116378].
7. Bilal A, Riaz M, Shafiq NU, Ahmed M, Sheikh S, Rasheed S. Non-compliance to anti hypertensive medication and its associated factors among hypertensives. *J Ayub Med Coll Abbottabad* 2015;27:158-63.
8. Vrijens B, Antoniou S, Burnier M, de la Sierra A, Volpe M. Current Situation of Medication Adherence in Hypertension. *Front Pharmacol* 2017;1:100. [DOI: 10.3389/fphar.2017.00100].
9. McManus M, Liebeskind DS. Blood Pressure in Acute Ischemic Stroke. *J Clin Neurol* 2016;12:137-46. [DOI: 10.3988/jcn.2016.12.2.137].
10. Lee KB, Lee JY, Choi N, Yoon JE, Shin DW, Kim JS, et al. Association between insufficient medication of antihypertensives and the severity of acute ischemic stroke. *Clin Hypertens* 2016;22:11. [10.1186/s40885-016-0047-8].
11. Taj F, Zahid R, Syeda UE, Murtaza M, Ahmed S, Kamal AK. Risk factors of stroke in Pakistan: a dedicated stroke clinic experience. *Can J Neurol Sci* 2010;37:252-7.
12. Hörnsten C, Weidung B, Littbrand H, Carlberg B, Nordström P, Lövheim H, et al. High blood pressure as a risk factor for incident stroke among very old people: a population-based cohort study. *J Hypertens* 2016;34:2059-65. [DOI: 10.1097/HJH.0000000000001048].
13. Liu CH, Wei YC, Lin JR, Chang CH, Chang TY, Huang KL, et al. Initial blood pressure is associated with stroke severity and is predictive of admission cost and one-year outcome in different stroke subtypes: a SRICHS registry study. *BMC Neurol* 2016;16:27. [DOI: 10.1186/s12883-016-0546-y].
14. Xu T, Yu X, Ou S, Liu X, Yuan J, Tan X, et al. Adherence to antihypertensive medications and stroke risk: a dose-response meta-analysis. *J Am Heart Assoc* 2017;6:e006371. [DOI: 10.1161/JAHA.117.006371].
15. 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:e568-76. [DOI: 10.3399/bjgp16X685609].
16. Jankowska-Polaska B, Uchmanowicz I, Dudek K, Mazur G. Relationship between patients' knowledge and medication adherence among patients with hypertension. *Patient Prefer Adherence* 2016;10:2437-47. [DOI: 10.2147/PPA.S117269].
17. Hashmi M, Khan M, Wasay M. Growing Burden of Stroke in Pakistan: A Review of Progress and Limitations. *Int J Stroke* 2013;8:575-81. [DOI: 10.1111/j.1747-4949.2012.00827.x].
18. Al-Ramahi R. Adherence to medications and associated factors: A cross sectional study among Palestinian hypertensive patients. *J Epidemiol Glob Health* 2015;5:125-32. [DOI: 10.1016/j.jegh.2014.05.005].
19. Saleem F, Hassali MA, Shafie AA, Awad AG, Bashir S. Association between Knowledge and Drug Adherence in Patients with Hypertension in Quetta, Pakistan [Online]. *Trop J Pharm Res* 2011;10:125-32. Available from: <http://www.bioline.org.br/pdf?pr11018>. Accessed on September 1, 2018. [DOI: 10.4314/tjpr.v10i2.66552].
20. Mujtaba SF, Masood T, Saad M. Reasons of medical noncompliance in heart failure patients [Online]. *Pak Heart J* 2010;43:41-5. Available from: <http://www.pkheartjournal.com/index.php/pkheart/article/view/7>. Accessed on September 1, 2018.