BAOJ Cellular & Molecular Cardiology

Mohammad Zaid Hossain, et al., BAOJ Cell Mol Cardio 2016, 2: 1
1: 008

Research Article

Association of Irregular Intake of Antihypertensive Drugs and Socio Demographic Trend With Risk of Stroke

Mohammad Zaid Hossain[1*], Pratyay Hasan[2], Kazi Tuba-E Mozazfia[3], Mohammed Abaye Deen Saleh[4], Tahmeed Hussain[5] and Khan Abul Kalam Azad[6]

[1]Department of Medicine, Dhaka Medical College, Dhaka, Bangladesh

[2] Department of Cardiology, Sir Salimullah Medical College, Dhaka 1100, Bangladesh

[3] Upazilla Health Complex, Dhamrai, Dhaka, Bangladesh

[4] Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh

[5]Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[6]Department of Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh

Abstract

Background

This case control study attempted to determine the relationship between irregular intake of antihypertensive drugs and stroke among hypertensive patients. Demographic profile of the patients was analyzed thoroughly, and risk factors among those characteristics were also sought.

Materials and Methods

90 cases matched with 90 controls were included in the study. The relationship was determined employing statistical methods including Chi Square ($\chi 2$) test, binary logistic regression.

Findings

The odds of development of stroke was 4.78 times higher (95% confidence interval 2.465-9.272) in the group taking antihypertensive drugs irregularly than in the group adhering to antihypertensive medication on a regular basis. Age, sex, social-status, monthly income, educational status, irregularity in taking drugs, all were calculated as independent covariates, and development of stroke as dependent variable, one year increase in age raises the odds of developing stroke by 1.113, *p value < 0.001*, male sex has the odd's ratio = 30.029 of having stroke which is statistically significant, p value = 0.004. Similarly, a person from small business has the odd's ratio = 32.423, *p value = 0.006*, illiterate educational group has odd's ratio = 20.250, *p value = 0•016*, irregularity of taking drugs has odd's ratio = 12.174, and *p value < 0.001*.

Conclusion

Irregular intake of antihypertensive drugs is associated with stroke. Significant associations were also found with male sex, age, and small business occupation and illiteracy with development of stroke.

Keywords: Stroke; Antihypertensive Agents; Demography

Introduction

Stroke has been commented to be the most common neurological disease [1]. The importance of stroke is increasing with the advancement of time [2,3]. The American Health Association estimates that 780 000 strokes occur each year; 600,000 of these are new strokes, and 180,000 are recurrent strokes [4]. In Bangladesh, there is no adequate data on incidence and mortality from stroke [5]. According to yearbook of Department of Medicine at Dhaka Medical College Hospital (2009), 14.7% of total admission in 2009 in Medicine Department in Dhaka Medical College Hospital was due to stroke. In Bangladesh about 40-50% of beds in a neurology ward are occupied by the stroke patients [6]. A recent Bangladeshi study showed that 53% of the stroke patients had ischemic stroke, 40% intra cerebral hemorrhage and only 2% subarachnoid hemorrhage. 72% of the patients were male and 28% were female [6]. Stroke has certain recognized stroke risk factors [7]. Among the risk factors, blood pressure is the most easily and conveniently controllable condition, provided good compliance, awareness and adherence to treatment protocol, and adaptation of a healthy life style. Overall, there is an association between both systolic and diastolic BP and risk of stroke without a clear threshold even at a systolic BP of 115 mm-Hg [8]. Meta-analyses of randomized controlled trials have shown that BP lowering is associated with a 30% to 40% reduction in risk of stroke [9–11]. Risk reduction

***Corresponding author:** Mohammad Zaid Hossain, Department of Medicine, Dhaka Medical College, Dhaka, E-mail: zhvalentino@gmail.com

Sub Date: December 13, 2016, **Acc Date:** December 19, 2016, **Pub Date:** December 19, 2016.

Citation: Mohammad Zaid Hossain, Pratyay Hasan, Kazi Tuba-E Mozazfia, Mohammed Abaye Deen Saleh, Tahmeed Hussain and Khan Abul Kalam Azad (2016) Association of Irregular Intake of Antihypertensive Drugs and Socio Demographic Trend With Risk of Stroke. BAOJ Cell Mol Cardio 2: 008.

is greater with larger reductions in BP [11]. Evidence-based recommendations for BP screening and treatment of persons with hypertension are summarized in the American Stroke Association (ASA) Guidelines on the Primary Prevention of Ischemic Stroke and are detailed in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) [12,13]. Unfortunately many patients do not adhere to the treatment. What is more alarming is, not only this practice renders the patient vulnerable to the pathological effect of uncontrolled hypertension, but in actuality, clinical experiences suggest that there may be an increased risk of developing stroke, in taking antihypertensive drugs irregularly. A Bangladeshi study showed that 66% of patients were aware that they were hypertensive though only 12.9% were taking anti-hypertensive drugs regularly. 62% of the patients had suffered from stroke within five years of detection of hypertension, and 15% patients died in the hospital [14]. A British study in 1997 demonstrated that risk of stroke is clearly related to quality of control of blood pressure with treatment [15]. In routine practice consistent control of blood pressure to below 150/90 mm Hg seems to be required for optimal stroke prevention. In another Bangladeshi study [16], one hundred cases of hypertensive complications due to irregular drug-therapy were studied in medicine units of Dhaka Medical College Hospital for the period of one year from February 7, 1989 to February 6, 1990. Among those, stroke headed the list (48%). Adhering to antihypertensive drugs has been said to be of great importance for reduction of long-term consequences of hypertension [17]. The purpose of this case control study is to establish the association between irregular in-take of antihypertensive drugs and stroke and find risk factors among the demography of the patients.

Materials and Methods

It was a case-control study. The cases were selected as hypertensive patients who had sustained a non-fatal ischemic or hemorrhagic stroke. WHO definition of stroke [18], was accepted as the operational definition. A total of 90 cases were selected along with 90 controls matching with cases in respect of age. Cases and controls were selected via random sampling of stroke free, hypertensive patients, similar in age to stroke cases. Sampling technique was systematic random sampling. Place of study was Dhaka Medical College Hospital. Duration of study was 1 July 2013 to 31December 2013. Method of data collection was interviews with case record forms. Research instruments used in the study were blood pressure machine, hammer, CT scanner, pen & paper, personal computers, etc. As data analysis strategy, first, a Pearson's chi square test assessed risk association between development of stroke and irregularity of drug intake. Then a binary logistic model was created to see effects of some independent variables, age, sex, social status, income, occupation, educational status. For performing statistical tests standard statistical packages, SPSS version 22 (International Business Machines Corporation,IBM, USA) Microsoft Excel 2013 (Microsoft Corporation, Inc., USA) were used.

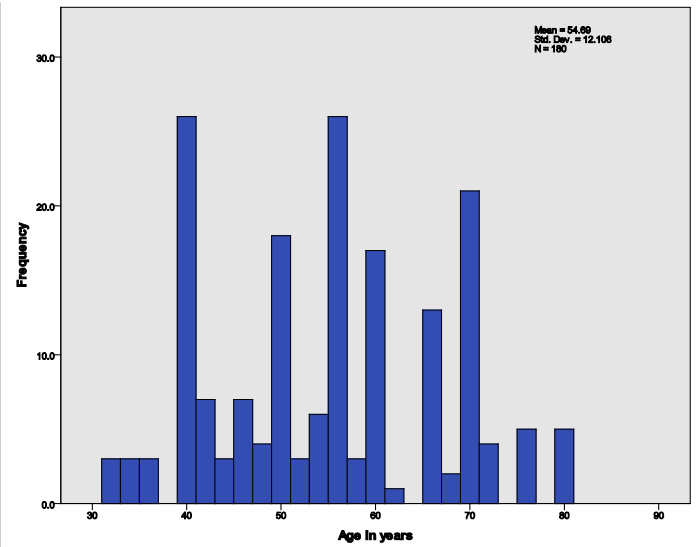

Figure 1: Age Distribution of the respondents

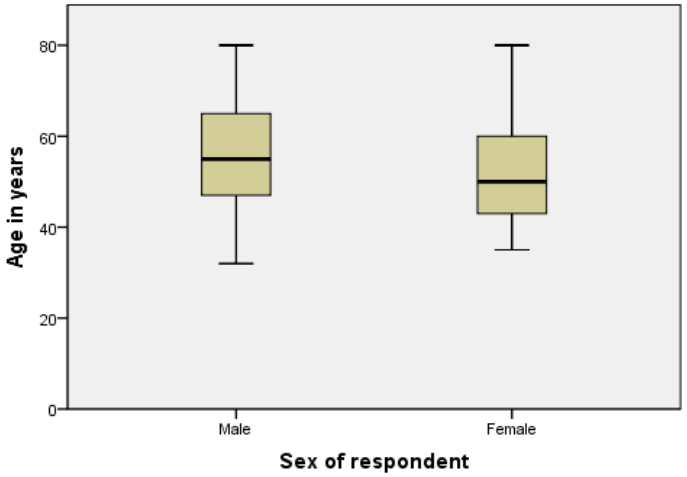

Figure 2: Age Distribution of subjects grouped by sex.

Results

A total of 180 subjects were studied (Table 1 - Age distribution of the respondents), 90 cases were taken along with 90 controls matching the case group. Among the 180 respondents, 117 (65%) were male, and 63 (35%) were female.

Mean age was 54.69 years with a standard deviation of ±12.11 years (Table 1).

The subjects were taken from diverse groups of occupations. Different occupations of the respondents are shown in (Table 2). The occupations of the cases and controls are compared side by side in (Figure 3)

The levels of education and social status and income range of the cases and controls are compared side by side in (Figure 3), (Figure 5) and (Figure 7), (Figure 9) Income of the cases and controls compared side by side, Pearson's chi square value= 8.482, $p = 0.132$. The practice of taking antihypertensive drugs regularly or

Mean	54·69 years
Standard Deviation	12·11 years
Minimum	32·00 years
Maximum	80·00 years

Table 1: Age Distribution of the Respondents

Types of occupation	Frequency	Percent
Housewife	44	24·4
Government employee	29	16·1
Non Govt· employee	20	11·1
Small business	25	13·9
Large business	5	2·8
Teacher	14	7·8
Farmer	18	10·0
Unemployed	14	7·8
Others	11	6·1
Total	180	100·0

Table 2: Occupation of the respondents

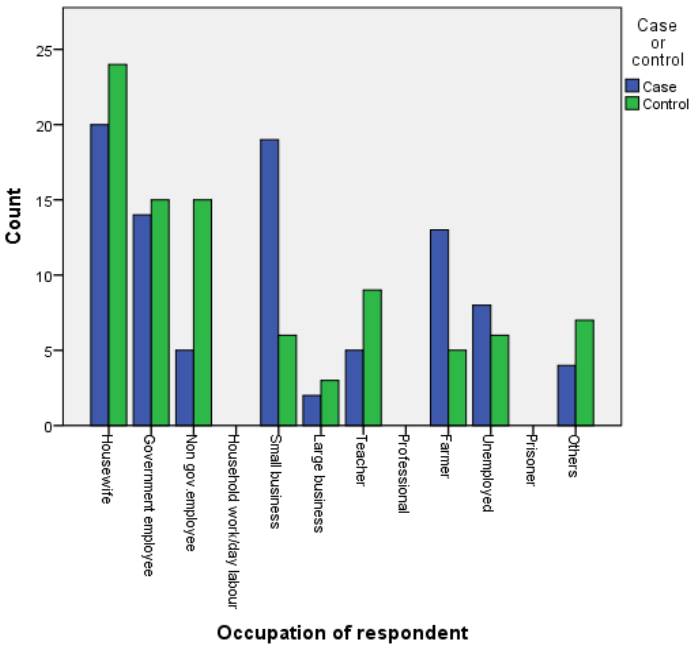

Figure 3: Occupation of the cases and controls compared side by side, pearson's chi-square value= 18.160, *P= 0.020*.

irregularly are represented on the basis of occupations, educational level, social status, and monthly income are shown by bar charts in (Figure 4), (Figure 6), (Figure 8), (Figure 10)

(Table 3) shows the association of educational level, social status, and income range with case or control status, and irregular intake of antihypertensive medication. It is evident from (Table 3). Association of educational level, social status, and income range with case or control status, and irregular intake of antihypertensive medication, that occupation, educational level, and social status all

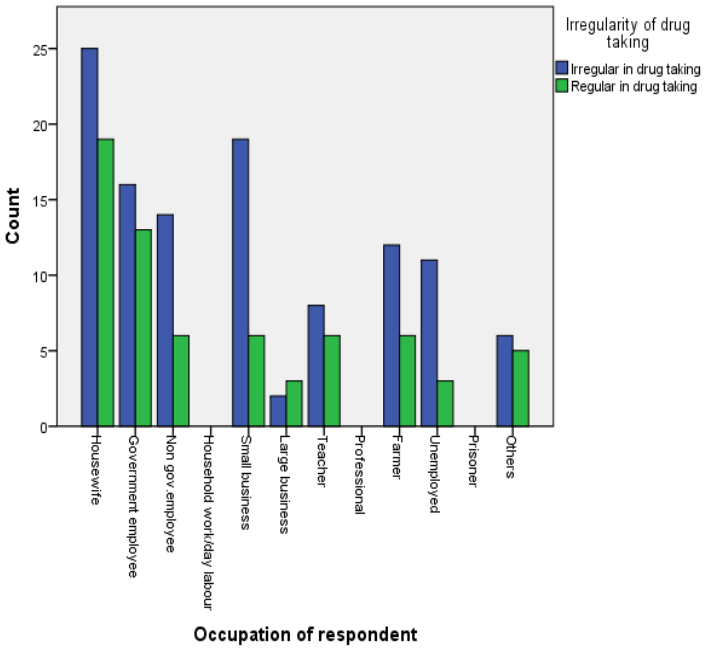

Figure 4: Practice of taking drugs regularly or irregularly represented here based on occupations, Pearson's chi-square value=6.934, *p value= 0.544*

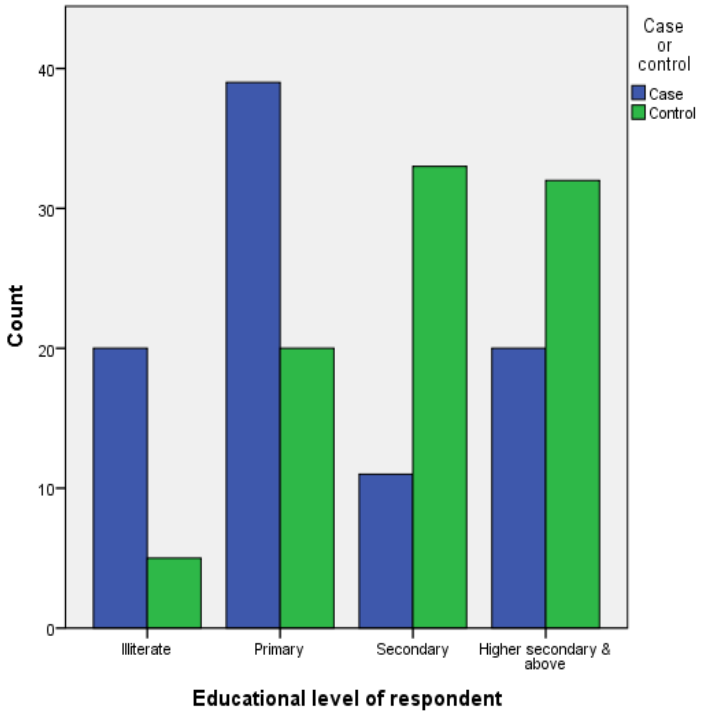

Figure 5: Educational Level of the cases and controls compared side by side. Pearson's chi-square value = 28.888, *P = <0.001*

are associated with development of stroke, whereas, educational level and social status are associated with habit of taking irregular intake of antihypertensive drugs.

Out of 90 cases (Figure 11, Table 4), 72 (80%) took antihypertensive

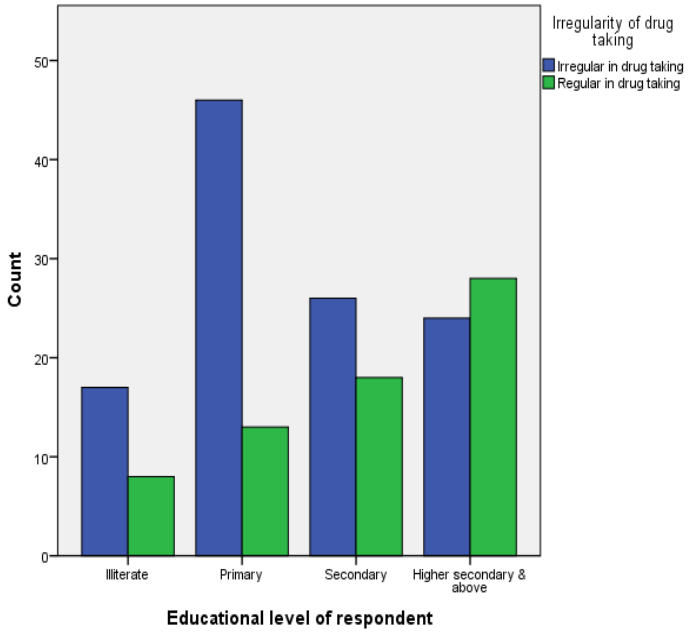

Figure 6: Practice of taking drugs regularly or irregularly represented on the basis of educational level, Pearson's chi-square value = 12.522, *P = 0.006*

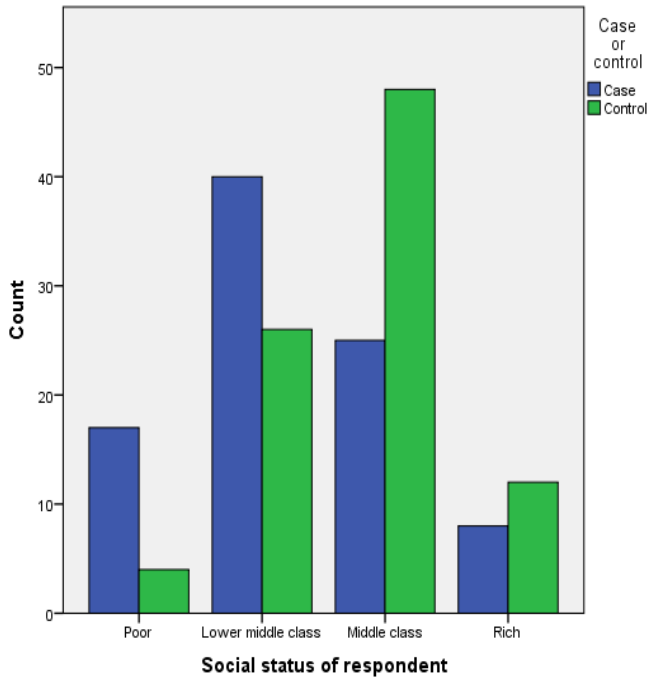

Figure 7: Social status of the cases and controls compared side by side. Pearson's chi-square value = 19.064, *P = <0.001*

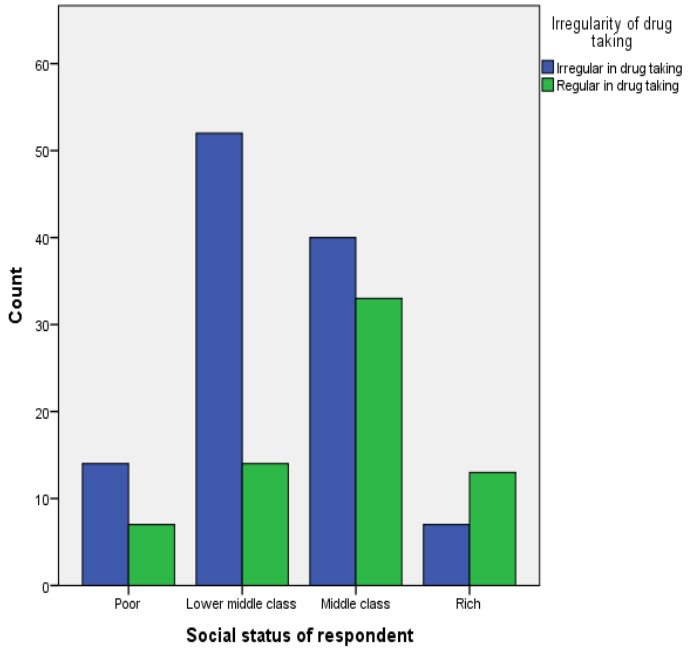

Figure 8: Practice of taking drugs regularly or irregularly represented on the basis of social status, Pearson's chi-square value = 15.971, *P = 0.001*

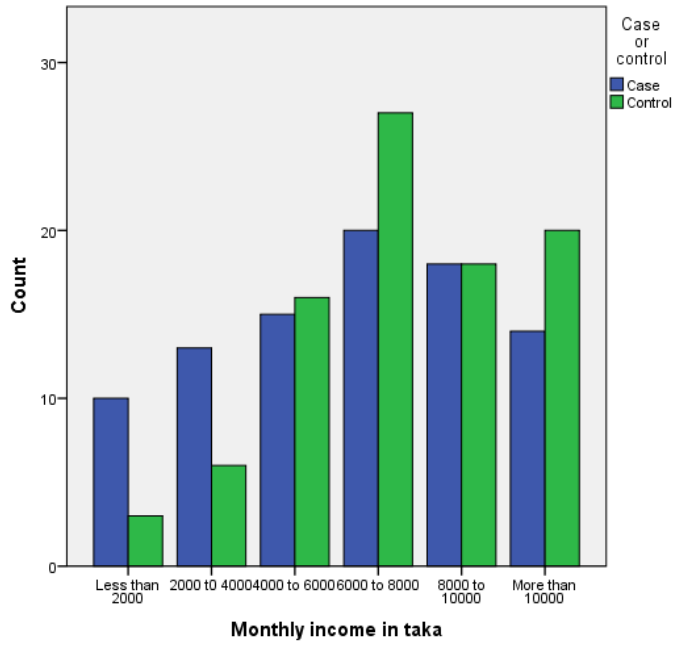

Figure 9: Income of the cases and controls compared side by side, Pearson's chi-square value = 8.482, *P = 0.132.*

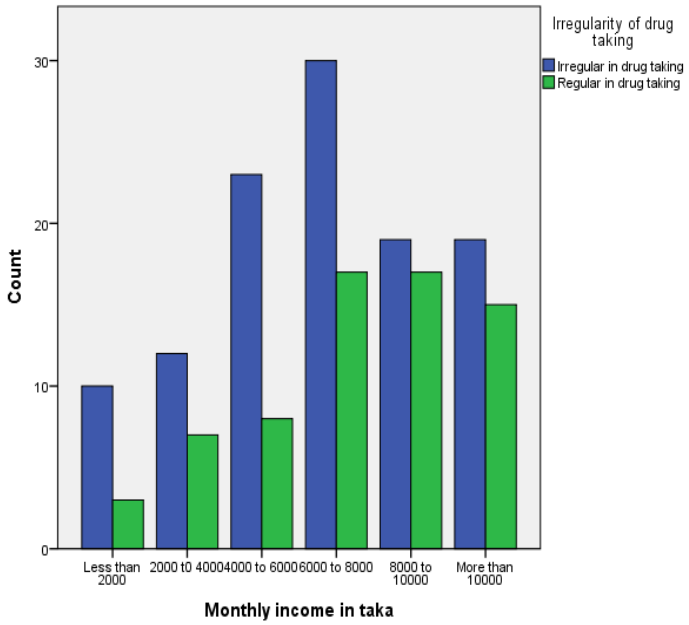

Figure 10: Practice of taking drugs regularly or irregularly represented on the basis of income, Pearson's chi-square value = 5.098, *P = 0.404*

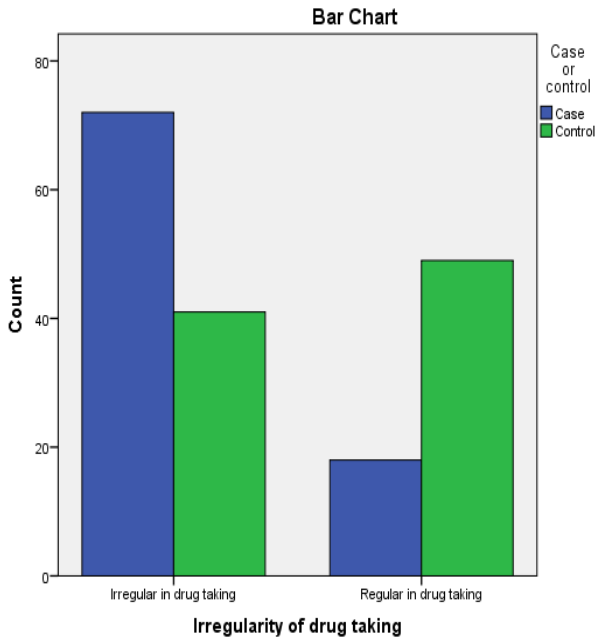

Figure 11: Irregularity of taking drugs among the cases and controls.

	Case Control		Irregular intake of drug	
	Pearson's chi-square value	P value	Pearson's chi-square value	P value
Occupation	18.160	0.020*	6.934	0.544
Educational level	28.888	<0.001*	12.522	0.006*
Social status	19.064	<0.001*	15.971	0.001*
Income	8.482	0.132	5.098	0.404

*significant at *p<0.05*

Table 3: Association of Educational level, Social Status, and income rage with case or control status, and irregular intake of antihypertensive medication

			Irregularity of drug taking		Total
			Irregular in drug taking	Regular in drug taking	
Case or control	Case	Count	72	18	90
	Control	Count	41	49	90
Total		Count	113	67	180

Table 4: Case or control by irregularity of drug taking cross tabulation

drugs irregularly, whereas only 18 (20%) took antihypertensive drugs regularly. In contrast with that out of 90 controls, 41 (45.6%) took antihypertensive drugs irregularly and 49 (54.4%) took antihypertensive drugs regularly. So case group constituted 63.7% of the group taking irregular antihypertensive drugs, whereas controls consisted 36.3%. So 113 patients out of 180 took antihypertensive drugs irregularly which is 62.8% of the total patients, and only 67 out of 180 (37.2%) took antihypertensive drugs regularly.

The number of cases and patients taking antihypertensive drugs irregularly are higher in the lower socio-economic groups, groups with low income and groups with lesser educational qualification.

A chi square test was performed and from these results there is highly significant association between irregular intake of antihypertensive and development of stroke in hypertensive adult patients, $\chi 2$ (1, N= 180) = 22.848, $p < 0.001$.

Odd's ratio is 4.78 with a 95% confidence interval (2.465 - 9.272).

Among these patients, (Figure 12) 48.9% of patients developed stroke within <15 days or 15 days of discontinuation of drugs, and 14.4% within 1 month, 18.9% within two month or more than two

		Responses		Percent of Cases
		N	Percent	
reasons for discontinuing drugs	Ignorance or lack of knowledge	37	37·8%	48·1%
	High price	14	14·3%	18·2%
	BP was normal	21	21·4%	27·3%
	Difficulty in collecting medicine	11	11·2%	14·3%
	Others	15	15·3%	19·5%
Total		98	100·0%	127·3%

Table 5: Frequency of reason for discontinue frequencies

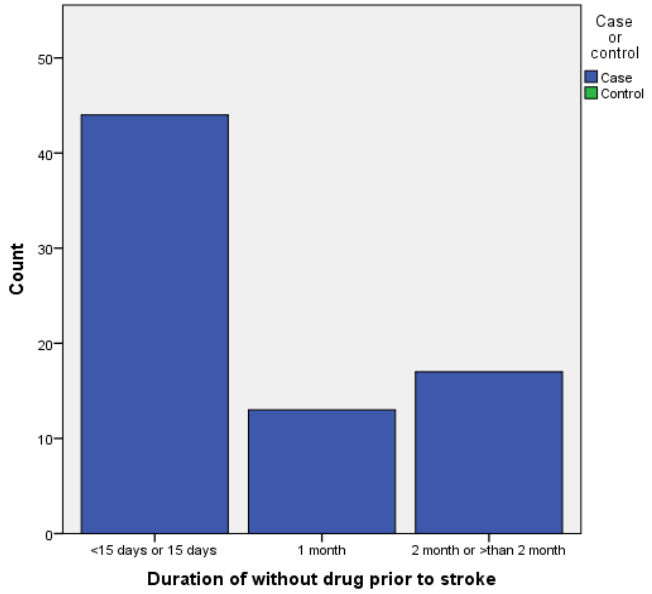

Figure 12: Duration of absence of treatment before development of stroke in bar chart Causes of discontinuation of drugs are shown in (Table 5, Figure 13).

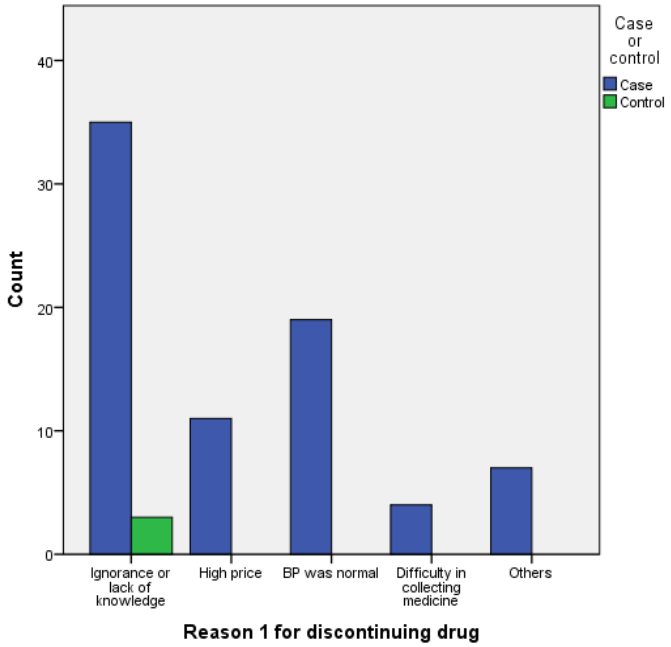

Figure 13: Reasons for discontinuation of drugs.

months of the same. 17.8% of patients' data were missing.

We performed a binary logistic regression analysis using age, sex, occupation, educational status, social status, and monthly income, intake of irregularity of drugs as independent covariates, and development of stroke as dependent variable. We found in the omnibus tests of model coefficients, the Chi Square value $\chi 2 = 120.087$ with degree of freedom, df = 22, $p < 0.001$. So, the model is statistically significant.

a. Variable(s) entered on step 1: sex, occupation, education, social-status, income (BDT monthly).

Discussion

It is clearly evident from our study, that odds of development of stroke is significantly *(p value < 0.001)*, 4.78 times higher (95% confidence interval 2.465 - 9.272) in the group taking antihypertensive drugs irregularly than in the group adhering to antihypertensive medication on a regular basis, which is similar to the opinion of Mayor, S (2013),[19][15]. According to a population based study by [20],conducted on 73 527 hypertensive patients aged 30 years or older and without pre-existing stroke or cardiovascular disease, 2144 died from stroke and 24 560 were hospitalized due to stroke during the follow-up. At the two- and ten year follow-up after the start of continuous antihypertensive medication, non-adherent patients had 3.81 [95% confidence interval (CI) 2.85–5.10] and 3.01 (95% CI: 2.37–3.83) times higher odds of stroke death when compared with the adherent patients. It is also noteworthy that poor control of HTN or non-adherence to antihypertensive medication is considered as an unrecognized risk factor in development of cardiovascular disease by many researchers including [21].

In a study by[22], in 2006 in Pakistan, it was shown that factors

		β	Standard Error.	Wald chi square value	Degree of free-dom	p value	Exp(B)	95% C.I.for EXP(B) = Odd's ratio	
								Lower	Upper
Step 1[a]	Sex (1) = Male	2.812	.927	9.208	1	.002	16.636	2.706	102.263
	Occupation			16.479	8	.036			
	occupation(1) = Housewife	2.384	1.269	3.529	1	.060	10.851	.902	130.547
	Occupation (2) = Govt. em-ployee	2.549	1.132	5.077	1	.024	12.800	1.393	117.595
	Occupation (3) = Non Govt. employee	.580	1.159	.250	1	.617	1.786	.184	17.311
	Occupation (4) = Household work / day labourer	3.275	1.164	7.911	1	.005	26.438	2.699	259.009
	Occupation (5) = Small business	.689	1.783	.149	1	.699	1.991	.060	65.599
	Occupation (6) = Large business	2.075	1.238	2.812	1	.094	7.967	.705	90.101
	Occupation (7) = Teacher	.872	1.119	.607	1	.436	2.391	.267	21.444
	Occupation (8) = Professional	.448	1.307	.117	1	.732	1.565	.121	20.277
	education			16.500	3	.001			
	Education (1) = Illiterate	3.478	1.121	9.633	1	.002	32.408	3.603	291.472
	Education (2) = Primary	1.925	.921	4.363	1	.037	6.852	1.126	41.700
	Education (3) = Secondary	-.463	.713	.422	1	.516	.629	.156	2.545
	Social status			4.507	3	.212			
	Socialst (1) = Poor	1.053	1.221	.743	1	.389	2.865	.262	31.386
	Socialst (2) = Lower middle class	-.322	1.045	.095	1	.758	.725	.093	5.618
	Socialst (3) = Middle class	-.691	.857	.650	1	.420	.501	.093	2.690
	Income			5.733	5	.333			
	Income (1) = <2000	3.270	1.757	3.464	1	.063	26.305	.841	823.195
	Income (2) = 2000 - 4000	.756	.949	.635	1	.426	2.129	.332	13.671
	Income (3) = 4000 - 6000	.168	.856	.038	1	.845	1.182	.221	6.333
	Income (4) = 6000 - 8000	.516	.758	.464	1	.496	1.675	.379	7.401
	Income (5) = 8000 - 10000	1.326	.833	2.532	1	.112	3.764	.736	19.263
	Constant	-5.119	1.430	12.817	1	.000	.006		

a. Variable(s) entered on step 1: sex, occupation, education, social-status, income (BDT monthly).

Table 6 Binary Logistic Regression analysis using sex, Occupation, Education, Income and social status as independent co-variants, and development of stroke as dependent variable.

behind noncompliance were, missing of doses due to forgetfulness in 56.8%, deliberate missing of doses in 12.7%, inability to take the medicine due to side effects in 11.6%, not taking the dose due to increased number of tablets in 10.4%, lack of proper counseling by the physician in 4.6% and cost issues in 3.48%. Again in Nigeria,a study [23], conducted in 2007 showed that the major reasons for non-compliance were miscellaneous factors (60%) related to both patient's attitudes and beliefs (reflecting ignorance), and consultation failure on the part of clinicians. Lack of finances and side effects of medications accounted for 23.8% and 16.2% of non-compliances respectively. But in this respect, our study shows that the top cause behind non-compliance was ignorance or lack of knowledge, followed by normality of BP causing sense of needlessness of the treatment. So the causes of non-compliance are different from those in Pakistan or Nigeria.

A Bangladeshi study conducted in 199014 showed that out of 100 patients studied in Dhaka Medical College Hospital, there were

73(73%) males, 27 (27%) patients had no formal schooling and 53 (53%) had some education. 48 (48%) patients were from middle class and 36 (36%) were poor, 66 (66%) patients were aware that they were hypertensive though only eight (12.9%) were taking anti-hypertensive drugs regularly. 62% of the patients had suffered from stroke within five years of detection of hypertension, and 15 (15%) patients died in the hospital. We also have similar sex distribution of the respondents (all having hypertension as a common factor), we found 65% male, and 35% females among our hypertensive patients.

Most of our cases were from lower socio-economic class and with an average income of 6000- 8000 BDT per month. In the middle class and rich group, there were more controls than cases, whereas in the lower middle class and the poor group, there were more cases than controls. The same thing can be said for the respondents with a monthly income of up-to 4000 BDT. And then again, the number of patients with stroke were much higher in the groups who were illiterate or only had had primary education. Again, it is clearly shown in the charts that in the group with higher education, percentage of patients taking drugs regularly is higher than the other groups, and in respect to social status, in the middle class, and rich group, more patients took antihypertensive drugs regularly whereas the patients from poor and lower socio-economic status more patients took antihypertensive medications irregularly. In our study, it is evident from (Table 3), that occupation, educational level, and social status all are associated with development of stroke, whereas, educational level and social status are associated with habit of taking irregular intake of antihypertensive drugs. Income range of the respondents were associated with neither development of stroke nor the habit of taking irregular intake of antihypertensive medication.

The findings of binary logistic regression analysis are in conformity with the currently available data on stroke. It has been commented that age is the single most important risk factor for stroke [24]. For each successive 10 years after age 55, the stroke rate more than doubles in both men and women [24–26]. Similarly gender has significant association with development of stroke [24]. Though the levels of education, occupation, and socio-economic status are not common risk factors, recent studies show that there is significant association between lower education level and stroke [27]. found that incidence of first-ever stroke was significantly higher among low-educated compared to high-educated men and women [27,28] , has found that lower education level is associated with increased stroke risk in mid-aged women, and is partially mediated by known risk factors, particularly lifestyle and biological factors [28]. In this respect, Our study shows illiteracy is associated with stroke, *p value = 0.016*, and odd's ratio = 20.250.

A very recent Indian study by [29]. On North Indian population showed that the occupations which involve sitting at work were independently associated with the risk of ischemic stroke after adjustment for demographic and risk factor variables (OR 2.2, 95% CI 1.12-3.8) [29]. Not much scientific evidence is available about association between occupational status and stroke. We have found that our small business group has the odd's ratio = 32.423, *p value = 0.006*.

In the setting of stroke, several population-based studies have documented an inverse relationship between socioeconomic status and overall stroke mortality rates [30–33]. It is not known whether this is due to differences in stroke incidence or stroke case fatality rates [34]. A clear socioeconomic gradient in stroke incidence in the Netherlands is observed [35]. There is a strong association among elderly women between socioeconomic status and stroke [36].

The derived odd's ratios from Pearson's chi square model, and odd's ratio from the later done Binary logistic model are not same. The reason for this lies in the differences between two models. The binary logistic model though gave odd's ratio, different from which was found from the original Pearson's model, it helped in identifying some risk factor association among the socio-demographic variables and development of stroke.

We have to mention various limitations of our study here. First, the cases and controls were matched on the basis of age only. Due to scarcity of resources and available volunteers, lack of enthusiasm on the part of the patients due to many causes including social taboos, enough number of patients could not be selected, and stratified random sampling could not be done. It may have given rise to bias seen and unseen. The socio-demographic variables were chosen without any prior knowledge, and the cut-off values were often determined arbitrarily.

Though for better compliance it is advised by many researchers to take necessary steps by the physicians such as, patient education, adoption of easy to follow dosage regimen such as once daily regimen,[37] it is found by another study that even an easy regimen like once-daily schedule may fail to get expected patient compliance [38] and thus may culminate into poor antihypertensive control. But strict adherence to drug regimen is of utmost importance as noncompliance may cause half of antihypertensive drug failures [39].

Key Messages

1. Irregular intake of antihypertensive drugs increases the risk of stroke (significant association is found).

2. In Bangladesh, people of different occupations, educational level, and social status all are associated with development of stroke, whereas, educational level and social status are associated with habit of taking irregular intake of antihypertensive drugs.

3. Significant association with stroke was found with small business group occupation and the illiterate people.

Conclusion

Clearly there is significant association between irregular intake of antihypertensive or discontinuation of antihypertensive drugs in hypertensive adults and the development of stroke. And also the results found in this study demonstrate that there is much deficiency of awareness among the patients about the danger of this harmful practice. In respect of Bangladesh, different occupations, educational

level, and social status all are associated with development of stroke, whereas, educational level and social status are associated with habit of taking irregular intake of antihypertensive drugs. Small business occupational group and illiterates have higher odds of developing stroke. Further study should be done to explain this. The responsibility of non-compliance cannot solely be attributed to the patients [40,41] and the physicians must play an essential role. We recommend raising awareness among both the physicians and the concerned patients.

Acknowledgements

We the authors declare that, we do not have anyone to acknowledge besides us, and we the authors were solely responsible for preparation of this manuscript from conception of the idea to final drafting.

References

1. Bergen DC (1996) The world-wide burden of neurologic disease. Neurology 47(1): 21-5.
2. Feigin VL, Lawes CM, Bennett DA, Anderson CS (2003) Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2(1): 43-53.
3. World Health Organization, Mackay J, Mensah GA (2004). The Atlas of Heart Disease and Stroke [Internet]. World Health Organization. 112
4. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, et al. (2008) Heart disease and stroke statistics–2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 117(4): 25–146.
5. Hossain A, Ahmed N, Rahman M, Islam M, Sadhya G, et al. (2011) Analysis of Socio demographic and Clinical Factors Associated with Hospitalized stroke Patients of Bangladesh. Faridpur Med Coll J 6(1): 19–23.
6. MR Siddiqui, QT Islam, MJ Iqbal, SS Binte-Mosharraf (2013) Sociodemographic status and associated risk factors of the stroke patients in a tertiary care hospital of Bangladesh. Anwer Khan Mod Med Coll J 4(2): 18–22.
7. Allen C, Lueck C, Dennis M (2010) Davidson's principles and practice of medicine. Neurological Disease Edinburgh, New York, Churchill Livingstone/Elsevier.
8. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R, et al. (2002) Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 360(9349): 1903–13.
9. Lawes CM, Bennett DA, Feigin VL, Rodgers A (2004) Blood pressure and stroke: an overview of published reviews. Stroke J Cereb Circ 35(4): 776–85.
10. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, et al. (2000) Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 342(3): 145-53.
11. Turnbull F, Blood Pressure Lowering Treatment Trialists' Collaboration. (2003) Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomized trials. Lancet 362(9395): 1527-35.
12. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, et al. (2006) Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: the American Academy of Neurology affirms the value of this guideline. Stroke J Cereb Circ 37(6): 1583-633.
13. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, et al. (2003) The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA J Am Med Assoc 289(19): 2560-72.
14. Roy PK, Arif SM, Alam MR, Khan FD, Ahmad Q, et al. (1990) Stroke in patients having inadequate or irregular antihypertensive therapy. Bangladesh Med Res Counc Bull 16(2): 52-7.
15. Du X, Cruickshank K, McNamee R, Saraee M, Sourbutts J, Summers A, et al. (1997) Case-control study of stroke and the quality of hypertension control in north west England. BMJ 314(7076): 272-6.
16. Chowdhury NA, Hayee MA, Alam N (1993) Study of complications in hypertensive patients having irregular treatment. Bangladesh Med Res Counc Bull 19(3): 86-93.
17. Cramer JA (1998) Consequences of intermittent treatment for hypertension: the case for medication compliance and persistence. Am J Manag Care 4(11): 1563-8.
18. (1988) The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. WHO MONICA Project Principal Investigators. J Clin Epidemiol 41(2): 105-14.
19. Mayor S (2013) Non-adherence to medication increases stroke risk in patients with high blood pressure. BMJ 347(jul17 2): f4586-f4586.
20. Herttua K, Tabak AG, Martikainen P, Vahtera J, Kivimaki M, et al. (2013) Adherence to antihypertensive therapy prior to the first presentation of stroke in hypertensive adults: population-based study. Eur Heart 34(38): 2933- 9.
21. Munger MA, Van Tassell BW, LaFleur J (2007) Medication Nonadherence: An Unrecognized Cardiovascular Risk Factor. Medscape Gen Med 9(3): 58.
22. Almas A, Hameed A, Ahmed B, Islam M (2006) Compliance to antihypertensive therapy. J Coll Physicians Surg-Pak JCPSP 16(1): 23-6.
23. Amira CO, Okubadejo NU (2007) Factors influencing non-compliance with anti-hypertensive drug therapy in Nigerians. Niger Postgrad Med J. 14(4): 325-9.
24. Ralph L. Sacco, Emelia J. Benjamin, Joseph P. Broderick, Mark Dyken, J. Donald Easton, et al. (1997) Risk Factors. Stroke 28(7): 1507-17.
25. Wolf PA, D'Agostino RB, O'Neal MA, Sytkowski P, Kase CS, et al. (1992) Secular trends in stroke incidence and mortality. The Framingham Study. Stroke 23(11): 1551-5.

26. Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO, et al. (1996) Stroke incidence, prevalence, and survival: secular trends in Rochester, Minnesota, through 1989. Stroke J Cereb Circ. 27(3): 373-80.

27. Löfmark U, Hammarström A (2007) Evidence for age-dependent education-related differences in men and women with first-ever stroke. Results from a community-based incidence study in northern Sweden. Neuroepidemiology 28(3): 35-41.

28. Jackson CA, Jones M, Mishra GD (2014) Educational and homeownership inequalities in stroke incidence: a population-based longitudinal study of mid-aged women. Eur J Public Health 24(2): 231-6.

29. Kumar A, Prasad M, Kathuria P (2014) Sitting occupations are an independent risk factor for Ischemic stroke in North Indian population. Int J Neurosci 124(10): 748-54.

30. Kunst AE, del Rios M, Groenhof F, Mackenbach JP (1998) Socioeconomic Inequalities in Stroke Mortality Among Middle-Aged Men An International Overview. Stroke 29(11): 2285-91.

31. Maheswaran R, Elliott P, Strachan DP (1997) Socioeconomic deprivation, ethnicity, and stroke mortality in Greater London and south east England. J Epidemiol Community Health 51(2): 127-31.

32. Howard G, Russell GB, Anderson R, Evans GW, Morgan T, et al. (1995) Role of Social Class in Excess Black Stroke Mortality. Stroke 26(10): 1759-63.

33. Casper ML, Barnett EB, Armstrong DL, Giles WH, Blanton CJ, et al. (1997) Social class and race disparities in premature stroke mortality among men in North Carolina. Ann Epidemiol 7(2): 146-53.

34. Kapral MK, Wang H, Mamdani M, Tu JV (2002) Effect of Socioeconomic Status on Treatment and Mortality After. Stroke 33(1): 268-75.

35. Smits J, Westert GP, Bos GAM van den (2002) Socioeconomic status of very small areas and stroke incidence in the Netherlands. J Epidemiol Community Health 56(8): 637-40.

36. van Rossum CT, van de Mheen H, Breteler MM, Grobbee DE, Mackenbach JP, et al. (1999) Socioeconomic Differences in Stroke Among Dutch Elderly Women The Rotterdam Study. Stroke 30(2): 357-62.

37. Frishman WH (2007) Importance of medication adherence in cardiovascular disease and the value of once-daily treatment regimens. Cardiol Rev 15(5): 257-63.

38. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M, et al. (2008) Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ 336(7653): 1114-7.

39. Stephenson J (1999) Noncompliance may cause half of antihypertensive drug "failures."JAMA. 282(4): 313-4.

40. Costa FV (1996) Compliance with antihypertensive treatment. Clin Exp Hypertens N Y N 1993.18(3-4): 463-72.

41. Hyman DJ, Pavlik VN (2002) Poor hypertension control: let's stop blaming the patients. Cleve Clin J Med. 69(10): 793-9.