

# DISCONTINUED ANTI-HYPERTENSIVE MEDICATION: A CASE CONTROL STUDY ON THE STROKE PATIENTS

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## Abstract

*Though it is long known that irregular intake of antihypertensive may cause harm, but still there is much lack of awareness among the patients in this matter. This case controlled study was done in Dhaka Medical College Hospital, Dhaka, to determine the relationship between discontinuation of antihypertensive drugs and the risk of stroke among hypertensive patients. Number of cases was 72. Control group was selected via random sampling of stroke free treated hypertensive group, similar in age to stroke cases. Sampling technique was random systematic sampling. The relationship was determined employing statistical methods including Chi-square ( $\chi^2$ ) test using computer programs, and significant association between discontinuation of antihypertensive and development of stroke in hypertensive adult patients was found  $\chi^2(1, N= 103) = 32.637, p < 0.001$ . Odd's ratio is 15.83.*

**Key words:** Antihypertensive drugs, stroke patients.

*J Dhaka Med Coll. 2013; 22(2) : 173-178.*

## Introduction

Stroke and stroke related complications have become so common now-a-days that the word "Stroke" is no longer only a medical term, rather it has gained access to the layman's dictionary. Stroke has been commented to be the most common neurological disease<sup>1</sup>. The burden of the disease is increasing both in our country and globally<sup>2,3</sup>. In Bangladesh, there is no adequate data on incidence and mortality from stroke<sup>4</sup>. 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<sup>5</sup>. According to yearbook of Department of Medicine at Dhaka Medical College & Hospital (2012), 14.83% of total admission was due to stroke. Among them 59.39% were ischemic stroke, 38.69% were hemorrhagic stroke & 1.92% were undefined CVD<sup>6</sup>. In a recent Bangladeshi study<sup>7</sup> shows that 53% of patients had ischaemic stroke, 40% intracerebral

haemorrhage and only 2% subarachnoid haemorrhage. 72% of the patients were male and 28% were female. The World health Organization has defined stroke as, "Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with non-apparent cause other than vascular origin"<sup>8</sup>. Stroke has certain recognized stroke risk factors<sup>9</sup> among which some are fixed like age, gender, heredity, previous vascular event and high fibrinogen level and some are modifiable like high blood pressure, heart disease (atrial fibrillation, heart failure, endocarditis), diabetes mellitus, hyperlipidemia, smoking, excess alcohol consumption, polycythemia, OCP, social deprivation, etc. Blood pressure is among 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

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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<sup>10</sup>. Meta-analyses of randomized controlled trials have shown that BP lowering is associated with a 30% to 40% reduction in risk of stroke<sup>11-13</sup>. Risk reduction is greater with larger reductions in BP without clear evidence of a drug class-specific treatment effect<sup>13</sup>. 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<sup>14</sup> and are detailed in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7)<sup>15</sup>. However, unfortunately, patients do not understand the importance of maintaining regular intake of stroke. A Bangladeshi study<sup>16</sup> described this condition quite elegantly, where it was shown 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 5 years of detection of hypertension, and 15% patients died in the hospital. A British study<sup>17</sup> in 1997 demonstrated that Risk of stroke was clearly related to quality of control of blood pressure with treatment. 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<sup>18</sup>, 100 cases of hypertensive complications due to irregular drug-therapy were studied in medicine units of Dhaka Medical College Hospital, Dhaka, for the period of one year from February 7, 1989 to February 6, 1990. Among those, stroke had headed the list (48%) manifesting in various ways e.g. cerebral haemorrhage with focal neurological signs e.g. hemiplegia, hemiparesis, aphasia etc. Hypertension associated with varying degrees of cardiac ischaemias and heart failure was seen in 14% and 10% cases respectively. Highest incidence of

complications was seen in 1-5 years after detection of hypertension with mean age of 55 +/- 18.70 years. The purpose of this case control study is to establish the association between noncompliance of antihypertensive drugs and stroke.

### Methods

It was a case-control study. Study population was selected as follows. The cases were selected as hypertensive patients who sustained a fatal or non-fatal ischaemic or haemorrhagic stroke. Number of cases was 72. Control group was selected via random sampling of stroke free treated hypertensive group, health cooperation enrollers; similar in age to stroke cases. Sampling technique was random systematic sampling. Place of study was Dhaka Medical College Hospital, Dhaka. Duration of the study was from January 3, 2013 to June 6, 2013. Method of data collection was done with questionnaire and interviews along with case record forms. For data analysis, Chi square test was employed.

### Results

To look from the angle of discontinuation of drugs, a total of 103 subjects were studied (Table I - Case or control by Frequency of discontinuation of drug Cross tabulation), 72 cases were taken along with 31 controls were selected matching with the case group. Out of 72 cases, 57 (79.2%) discontinued antihypertensive drugs frequently, whereas only 15 (20.8%) discontinued antihypertensive drugs rarely. In contrast with that out of 31 controls, 6 (19.4%) discontinued antihypertensive drugs frequently and 25 (80.6%) discontinued antihypertensive drugs rarely. So the case group constituted 90.5% of the group discontinuing antihypertensive drugs frequently, whereas controls consisted 9.5%. So 63 patients out of 103 took antihypertensive drugs irregularly which is 61.2% of the total patients, and only 40 out of 103 (38.8%) took antihypertensive drugs regularly.

**Table-I**  
Case or control by Frequency of discontinuation of drug Cross tabulation

		Frequency of discontinuation of drug		Total
		Antihypertensive drug discontinued frequently	Antihypertensive drug discontinued rarely	
Case or control	Case	Count	57	72
		% within Case or control	79.2%	100.0%
		% within Frequency of discontinuation of drug	90.5%	69.9%
Control	Control	Count	6	31
		% within Case or control	19.4%	100.0%
		% within Frequency of discontinuation of drug	9.5%	30.1%
Total	Total	Count	63	103
		% within Case or control	61.2%	100.0%
		% within Frequency of discontinuation of drug	100.0%	100.0%

A Chi square test (Table 2 – Chi Square test for discontinuation of drugs) was performed and from these results there is highly significant association between discontinuation of antihypertensive and development of stroke in hypertensive adult patients,  $\chi^2(1, N= 103) = 32.637, p < 0.001$ . Odd's ratio is 15.83.

**Table-II**  
Chi Square test for discontinuation of drugs

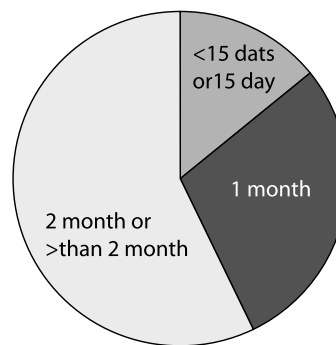
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	32.637 <sup>a</sup>	1	.000		
Continuity Correction <sup>b</sup>	30.167	1	.000		
Likelihood Ratio	33.456	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	32.320	1	.000		
N of Valid Cases	103				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 12.04.

b. Computed only for a 2x2 table

Among these patients, (Fig. 1. Duration of absence of treatment before development of stroke) 51.6% of patients developed stroke within 15 days of discontinuation of drugs, and 16.1% within 1 month, 18.8% within 2 month or >than 2 month of the same. 13.5% of patients' data were missing.

Among the causes of discontinuation of drugs (Table 3 - Frequency of reason for discontinue Frequencies) were ignorance or lack of awareness (29.2%), economical (25.2%), asymptomatic (21.6%), difficulty in collecting medicine (15.4%), others (8.6%).



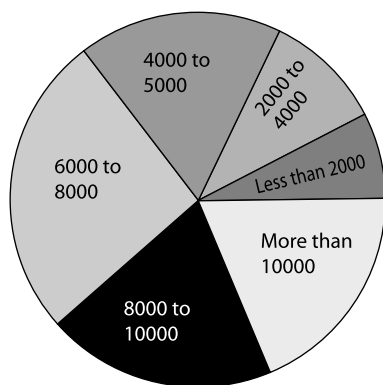
**Fig.-1.** Duration of absence of treatment before development of stroke

**Table-III**  
Frequency of reason for discontinue Frequencies

Reasons for discontinue drugs <sup>a</sup>		Responses		Percent of Cases
		N	Percent	
Reasons for discontinue drugs <sup>a</sup>	Lack of awareness	18	25.6%	29.2%
	Economical	12	19.0%	25.2%
	Asymptomatic	15	23.8%	21.6%
	Difficulty in collecting medicine	7	11.1%	15.4%
	Others	11	17.5%	8.6%
Total		63	100.0%	100.0%

a. Group

The incomes of the respondents are shown in the following figures, Fig. 2. Income of the respondents in pie chart:



**Fig.-2:** Income of the respondents in pie chart

**Discussion**

A total of 103 subjects were studied (Table I - Case or control by Frequency of discontinuation of drug Cross tabulation), 72 cases were taken along with 31 controls were selected matching with the case group. Out of 72 cases, 57 (79.2%) discontinued antihypertensive drugs frequently, whereas only 15 (20.8%) discontinued antihypertensive drugs rarely. In contrast with that out of 31 controls, 6 (19.4%) discontinued antihypertensive drugs frequently and 25 (80.6%) discontinued antihypertensive drugs rarely. So the case group constituted 90.5% of the group discontinuing antihypertensive drugs frequently, whereas controls consisted 9.5%. So 63 patients out of 103 took antihypertensive drugs irregularly which is 61.2% of the total patients, and only 40 out of 103 (38.8%) took antihypertensive drugs regularly.

A Chi square test (Table-II) was performed and from these results there is highly significant association between discontinuation of antihypertensive and development of stroke in hypertensive adult patients,  $\chi^2(1, N=103) = 32.637, p < .001$ . Odd's ratio is 15.83. Hence, it is clearly evident from our study, that discontinuation of antihypertensive increases the risk of stroke greatly, which is similar to the opinion of Mayor (2013)<sup>19</sup>, Du et al. (1997)<sup>17</sup>, etc. According to a population based study by Herttua et al. (2013)<sup>20</sup>. The latter study conducted on the basis of the data collected from the period spanning 1<sup>st</sup> January 1995 to 31<sup>st</sup> December 2007 from the Finnish National Register. Of the 73,527 hypertensive patients aged 30 years or older and without pre-existing stroke or cardiovascular disease, 2,144 died from stroke and 24,560 were hospitalized due to stroke during the follow-up. At the 2- and 10-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. The corresponding odds ratio (OR) for stroke hospitalization was 2.74 (95% CI: 2.35–3.20) at Year 2 and 1.71 (95% CI: 1.49–1.96) at Year 10. In the stroke-event year, the ORs were higher, 5.68 (95% CI: 5.05–6.39) for stroke death and 1.87 (95% CI: 1.72–2.03) for hospitalization. Among those using agents acting on the renin-angiotensin system

combined with diuretics or-blockers, these ORs were 7.49 (95% CI: 5.62–9.98) and 3.91(95% CI: 3.23–4.75), respectively. The associations between non-adherence and stroke followed a dose –response pattern — the poorer the adherence, the greater the risk of death and hospitalization due to stroke. 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 Munger et al. (2007)<sup>21</sup>.

A Bangladeshi study conducted in 1990<sup>16</sup> showed of the 100 patients studied in Dhaka Medical College Hospital, Dhaka, 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 8 (12.9%) were taking anti-hypertensive drugs regularly. 62% of the patients had suffered from stroke within 5 years of detection of hypertension, and 15 (15%) patients died in the hospital.

In our study, the main causes of discontinuation of antihypertensive medication were lack of awareness (28.6%), financial constraint (19.0%), asymptomatic (23.8%), difficulty in collecting medicine (11.1%) & others (17.5%). A Malaysian study found that non-compliance of antihypertensive medication was significant association low-level of knowledge, low educational level, practices of traditional medicine, dissatisfaction with services by the health staffs, obesity, difficulties in transportation to the clinics and unawareness about their disease<sup>22</sup>. In another study in Congo, five themes emerged as possible explanations for non-compliance: Side effects discouraged patients from taking medication; patients took medication only when they experienced perceived symptoms of hypertension; poor knowledge of the disease and the medication used; lack of support by family members; and difficulty in obtaining antihypertensive medication<sup>23</sup>. Hence, causes of non-compliance found in our study are consistent with other studies.

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<sup>24</sup>, it is found by another study that even an easy regimen like once-daily schedule may fail to get expected patient compliance<sup>25</sup> and thus may culminate into poor antihypertensive control.

### Conclusion

There is significant association between discontinuation of antihypertensive medication and the stroke. Much awareness should be raised among both the patients and the physicians. Further study should be conducted to gather further evidence concerning this.

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