Frequency of recurrent strokes at different systolic blood pressure levels among patients with previous ischemic stroke

Section A-Research paper

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ABSTRACT
Introduction: Recurrent stroke after previous stroke may be prevented by effective controlling of blood pressure and may reduce the morbidity and mortality. However, optimal range of blood pressure (BP) at which risk of recurrence is minimal is not known. This study was conducted in order to determine frequency of recurrent stroke among patients at various blood pressures.
Objective: To determine categories of BP in patients with stroke and frequency of recurrent stroke among those patients.
Methods: Study Design: Descriptive case series
Setting: Department of Medicine, Lahore General Hospital, Lahore
Duration: Six months after approval of synopsis: from 06-06-2020 to 29-12-2020
Systolic blood pressure readings of all 275 patients included in study were recorded and were categorized upon SBP level: very low–normal (<120 mmHg), low-normal (120-130 mmHg), high-normal (130-140 mmHg), high (140-150 mmHg), and very high (>150 mmHg). Patients were followed for a period of 6months for occurrence of recurrent stroke.
Results: Fifty-seven (20.7%) patients had very low normal BP, 58 (21.1%) patients had low normal BP, 75 (27.3%) patients had high normal BP, 55 (20%) patients had high BP and 30 (10.9%) patients had very high BP. Recurrent stroke was seen among 55(20%) patients.
Conclusions: Majority of patients had high normal blood pressure. Recurrent stroke was present in almost one fifth of patients with previous stroke. The frequency of recurrent stroke was highest among patients with systolic blood pressure > 150 mm of Hg.
Keywords: ischemic stroke; recurrent stroke; hypertension

INTRODUCTION

Stroke referred to a debilitating illness that is caused by deficient blood supply to the brain. It is defined as an abrupt onset of characteristic neurological deficit that is attributable to a focal vascular cause lasting for more than twenty four hours.[1,2]

Stroke is a leading cause of disease and death throughout the world. [3] The age adjusted annual death rate from stroke is 116 per 100,000 populations in USA and some 200 per 100,000 in UK, some 12% of all deaths. It is higher in black African populations than in

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Caucasian. [4] Approximately 80% of strokes are due to ischemic cerebral infarction and 20% to brain hemorrhage.[5]

Stroke is a medical emergency and can cause permanent neurological damage, complications and death. It is not a diagnosis but a clinical syndrome with numerous causes. Clinical symptoms of ischemic stroke depend on the anatomical location of the thrombus. Stroke usually presents with an acute loss of brain functions. These functions usually involve the realm of motor, sensory, language, vision, visuo-spatial perception or consciousness. Clinical examination along with neuroimaging leads to a proper diagnosis of stroke due to cerebral infarction.[6]

Defining stroke type helps in determining the most effective therapy and is clearly related to prognosis. Computed tomography or magnetic resonance imaging should be performed to confirm the type of stroke. [7] A stroke is occasionally treated with thrombolysis, but usually with supportive care like speech therapy, physiotherapy and occupational therapy and secondary prevention with antiplatelet drugs, blood pressure control, statins, and in selected patients with carotid endarterectomy and anticoagulation. [8,9]

Epidemiologic studies of the risk factors for stroke are important for determining the origin and its prevention. In the past several decades many studies have successfully identified a number of risk factors. Risk factors or risk marker for cerebral infarction are classified according to their potential for modification (non modifiable, modifiable, or potentially modifiable) and strength of evidence (well documented or less well documented). Non modifiable risk factors include age, sex, low birth weight, race/ethnicity, and genetic factors. Well documented and modifiable risk factors include hypertension, diabetes, atrial fibrillation, exposure to cigarette smoke and certain other cardiac conditions, dyslipidemia, carotid artery stenosis, post menopausal hormone therapy, poor diet, physical inactivity, and obesity. Less well documented or potentially modifiable risk factors include metabolic syndrome, alcohol abuse, oral contraceptive use, hypercoagubility, inflammation and infection. [10-13]

After an incidence of stroke, the risk of developing another event of stroke i.e. "recurrent stroke" is high i.e. frequency of developing stroke within 48 hours is 4 – 5 % and at 90 day is 10.5%.[14] Recurrent stroke are more likely to be more disabling or fatal than first-event strokes. The high frequency of recurrences underscores the importance of secondary prevention. [15]

Stroke is a disease with well-defined modifiable risk factors. Several interventions are effective in both the primary and secondary prevention of stroke and may reduce the incidence of stroke by as much as 50–80%. [16] Hypertension is the most important modifiable risk factor for stroke. [17] Effective control of hypertension has the potential to reduce the risk of primary stroke by nearly 40%, but unfortunately half of all hypertensive patients receive no treatment and of those who do, not more than half are adequately controlled. [18]

A large body of evidence exists based on case series, population studies, and clinical trials demonstrating that control of hypertension reduces risk of initial stroke. It has also been demonstrated that treatment of isolated systolic hypertension in the elderly will reduce risk of stroke. Control of BP for reduction of risk of stroke recurrence has not been demonstrated consistently.[19] Although lowering BP in hypertension appears to be beneficial in reducing stroke risk, the optimal level of reduction has also not been well studied. Perfusion of the brain is normally maintained within a wide range of SBP and DBP. Lowering BP, especially in older individuals who may well have vascular narrowing and less resilient vessels, may reduce perfusion of the brain, resulting in syncope or even stroke. It is well accepted that chronic hypertension impairs cerebrovascular autoregulation and, together with the pathological narrowing of cerebral vessels in individuals with chronic hypertension, provides a plausible basis for inquiring whether maintenance of BP below an optimal level may be detrimental. It has been postulated that a J-shaped relationship may exist between BP and stroke risk, with control below an "optimal" level resulting in increased stroke frequency and cardiac ischemia. [20]

Although, guidelines suggest maintaining a normal blood pressure (BP) as a systolic BP (SBP) of less than 120 mm Hg and a diastolic BP (DBP) of less than 80mmHg in persons with a prior stroke, [21] recent evidence suggesting no benefit in achieving more aggressive SBP targets in high risk patients with diabetes, [22] and perhaps even harm, there is mounting interest in exploring the adequate

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level of SBP for the prevention of recurrent strokes.[23]

In a study by Ovbiagele B, et al, [24] observational analysis of a multicenter trial involving 20330 patients with recent ischemic strokes were recruited. Patients were categorized based on their systolic blood pressure levels: very low–normal (<120 mm Hg), low-normal (120-130 mm Hg), high-normal (130-140 mm Hg), high (140-150 mm Hg), and very high (>150 mm Hg). The primary outcome was first recurrence of stroke. The patients were followed up for 1 week, 1 month, 3 month and 6 months. The recurrent stroke rates were 8.0% for the very low–normal SBP level group, 7.2% for the low-normal SBP group, 6.8% for the high-normal SBP group, 8.7% for the high SBP group, and 14.1% for the very high SBP group. This has been known that hypertension can increase the risk of stroke and blood pressure of the patients with previous stroke should be optimized. But, the ideal level of the blood pressure at which stroke can be prevented is not yet known. In study by Ovbiagele B, et al, [24] it was noticed that at higher level of blood pressure, the incidence of stroke was high. So, I wanted to conduct this study to determine the frequency of recurrent stroke at different systolic blood pressure levels among patients with previous stroke. This will help us in determining a blood pressure level with minimum frequency of recurrent stroke. By determining that level, we will know a BP level at which lowest frequency of recurrent stroke will be noticed. In future, the patients with higher frequency of recurrent stroke in any category of BP will be labeled as high risk and prompt management to control the BP will be started in order to maintain an optimal BP.

MATERIAL AND METHODS
STUDY DESIGN
Descriptive case series
SETTING
Department of Medicine, Lahore General Hospital, Lahore
SAMPLE SIZE
The calculated sample size was 275 cases with 3 % margin of error, 95 % confidence level taking expected percentage of recurrent stroke i.e. 6.8 % at for the high-normal SBP group (130-140 mm Hg).
DURATION WITH DATES
Six months after approval of synopsis

SAMPLING TECHNIQUE
Non probability purposive sampling

SAMPLE SELECTION
INCLUSION CRITERIA
• Gender: both male and female
• Age: 20-45 years
• All the patients with history of ischemic stroke (as per operational definition).
EXCLUSION CRITERIA
• Patients having history of brain surgery.
• Critically ill patients on ventilatory support
• Patients presenting with other associated diseases like diabetes mellitutus (Fastign sugar level > 100 mg/dL) or myocardial infarction (diagnosed on ECG and raised Troponin I level)
• Patients with Chronic renal failure
• Patients showing fluctuation of > 10 mm of Hg during follow up period.

DATA COLLECTION PROCEDURE
Two hundred and seventy five cases fulfilling inclusion criteria were registered through Outpatient department of Medicine, Lahore General Hospital, Lahore. Demographic history [including age (in years) and sex (male or female) was taken. Informed consent was taken through patients. Systolic blood pressure reading of all the patients at time of presentation was recorded by using a standard and validated Omron sphygmomanometer (Omron Healthcare Inc) with an appropriately sized cuff applied to the upper nondominant arm at heart level. SBP was categorized as: very low–normal (<120 mm Hg), low-normal (120-130 mm Hg), high-normal (130-140 mm Hg), high (140-150 mm Hg), and very high (>150 mm Hg). The patients were followed up for a period of 6 months for the presence of recurrent stroke (as per operational definition). Data was collected by a 4th year resident on a specially designed proforma (attached).

DATA ANALYSIS PROCEDURE
All the collected data were entered into SPSS version 10 and analyzed. The qualitative data like demographics (sex; male or female), presence of recurrent stroke (yes or no) were analyzed in the category of blood pressure [very low normal, low-normal, high-normal,

high, and very high] and was presented as frequency distribution.

Quantitative data like age (in years) and systolic blood pressure were presented as means and standard deviations.

RESULTS

The total number of patients included in the study was 275 (including both males and females).

Distribution of patients by Age:
The mean age of the patients included in the study 40.76 + 4.60 years [range 24-45]. There were 3 (1.1%) patients of age range of 20 – 25 years, 11 (4%) patients of age range of 26 – 30 years, 27 (9.8 %) patient of age range of 31 – 35 years, 99 (36%) patients of age range of 36 – 40 years and 135 (49.1%) patient of age range of 41 – 45 years of age. (Table 1)

Distribution of patients by Sex:
Patients were also distributed according to sex. There were 171 (62.2 %) male patients in the study, while 104 (37.8%) patients were female. Male to female ration was 1.71:1. (Figure 7)

Distribution of patients by different systolic blood pressure levels:
There were 57 (20.7%) patients who had very low normal blood pressure, 58 (21.1%) patients had low normal blood pressure, 75 (27.3%) patients had high normal blood pressure, 55 (20%) patients had high blood pressure and 30 (10.9%) patients had very high blood pressure. (Table 2)

Distribution of patients by presence of recurrent stroke:
Recurrent stroke was seen among 55 (20%) patients, while 220 (80%) patients did not have recurrent stroke. (Figure 8)

Stratification of different systolic blood pressure levels with presence of recurrent stroke
Among 57 patients with very low normal blood pressure, recurrent stroke was seen among 7 (12.3%) patients, while 50 (87.7%) patients did not suffer from recurrent stroke. Among 58 patients with low normal blood pressure, recurrent stroke was seen among 9 (15.5%) patients, while 49 (84.5%) patients did not suffer from recurrent stroke. Among 75 patients with high normal blood pressure, recurrent stroke was present among 14 (18.7%) patients, while 61 (81.3%) patients did not suffer from recurrent stroke. Among 55 patients with high blood pressure, 12 (21.8%) patients suffered from recurrent stroke while 43 (78.2%) patients did not suffer from recurrent stroke. Among 30 patients with very high blood pressure, 13 (43.3%) patients suffered from recurrent stroke and 17 (56.7%) patients did not suffer from recurrent stroke. Chi-square test was applied to determine if there is any significant difference between these groups. P-value was 0.10, hence statistically not significant. (Table 3)

Age	No. of patients	Percentage
20 – 25	3	1.1
26 – 30	11	4
31 – 35	27	9.8
36 – 40	99	36
41 – 45	135	49.1
Mean + SD	40.76 + 4.60	
Range	24 – 45	

Key:
SD   Standard deviation

Table 1: Distribution of patients by age (n=275)
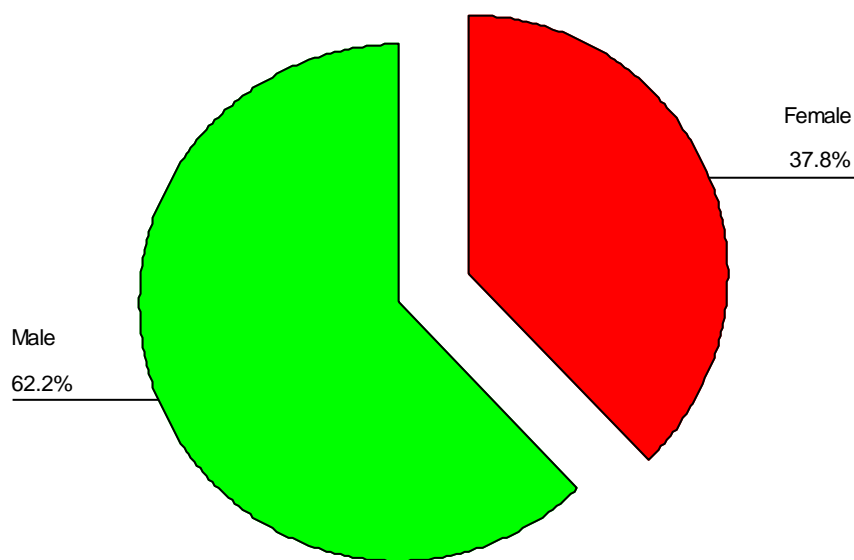
Figure 7: Distribution of patients by sex (n=275)

Systolic blood pressures	No.	%
Very low normal (<120 mm of Hg) (n = 57)	57	20.7
Low normal (120 – 130 mm of Hg) (n = 58)	58	21.1
High Normal (130 – 140 mm of Hg) (n = 75)	75	27.3
High (140 – 150 mm of Hg) (n = 55)	55	20
Very high (> 150 mm of Hg) (n = 30)	30	10.9

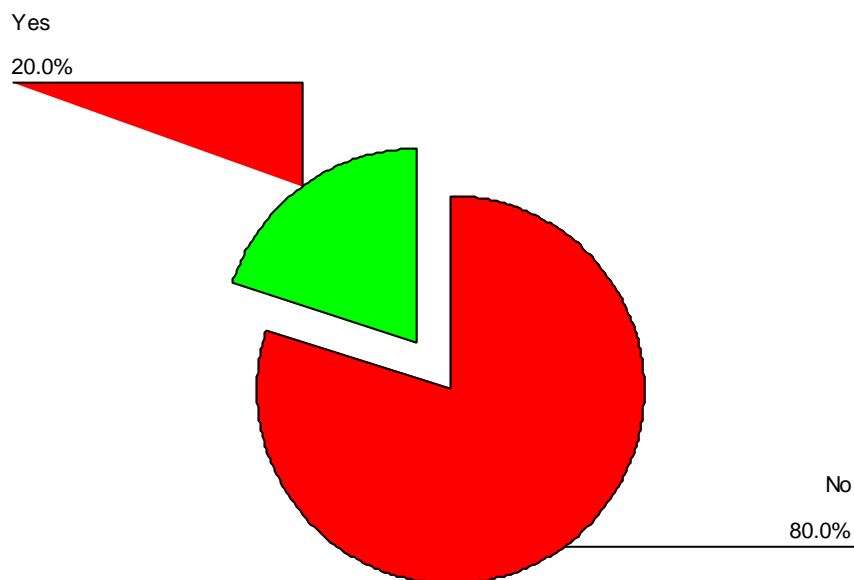**Table 2:** Distribution of patients by systolic blood pressure levels   (n=275)

Yes

20.0%

No

80.0%

Figure 8: Distribution of patients by presence of Recurrent stroke (n=275)

Systolic blood pressures	Recurrent Stroke	
	Yes	No
	No. (%)	No. (%)
Very low normal (<120 mm of Hg) (n = 57)	7 (12.3)	50 (87.7)
Low normal (120 – 130 mm of Hg) (n = 58)	9 (15.5)	49 (84.5)
High Normal (130 – 140 mm of Hg) (n = 75)	14 (18.7)	61 (81.3)
High (140 – 150 mm of Hg) (n = 55)	12 (21.8)	43 (78.2)
Very high (> 150 mm of Hg) (n = 30)	13 (43.3)	17 (56.7)
p-value	0.10	

Key:
SD   Standard deviation
Table 3: Stratification of different systolic blood pressure levels with presence of recurrent stroke (n=275)

DISCUSSION

This study was conducted in an outpatient department of teaching hospital to detect the frequency of patients with recurrent stroke after a cerebral infarction at different levels of the blood pressure. The results of this study showed that majority of the patients (43.3%) with recurrent stroke had blood pressure at very high level (more than > 150 mm of Hg). In literature, there are only a few studies that have worked on this topic. Up to my knowledge, this is the second study in across the globe that has discussed the frequency of recurrent stroke at different levels of blood pressure.

The mean age of the patients in our study was 40.7 + 4.60 years. A higher mean age of the patients was observed in a study by Song T, et al, [24] i.e. 60.87±12.46 years. The mean age of the patients in study by Ovbiegele et al, [25] was 65.03 + 9.03 years. The majority of the patients in our study were male i.e. 62.2%. This male dominance was also observed in study by Song T, et al. [114] In their study, the male patients approximately 67% population of the study. In study by Ovbiegele et al, the male population consisted of the 64% patients. This also verifies the observation that male are effected more with cerebrovascular events as noted in previous studies. The frequency of stroke recurrence in our study was 20%. In another study by Hillen T, et al, [26] the recurrent stroke was seen among 19% patients with history of previous stroke. Hier et al [115] involving 1273 patients with an ischemic stroke, the frequency of recurrence was 13%. And the recurrences were associated with hypertension.

We observed that majority of the patients in our study had high normal blood pressure i.e. 27.3% patients had high normal blood pressure. The patients with very high blood pressure were least of all (10.9%). Otherwise, no significant difference of systolic blood pressures was observed among different groups of systolic blood pressure. We observed that 43.3% patients with recurrent stroke had a very high blood pressure (> 150 mm of Hg). However, the frequency of patients with recurrent stroke was lowest for the patients with blood pressure in the range of < 120 mm of Hg. A similar observation has also been made by Ovbiegele et al, who documented that stroke recurrence was most frequent among the patients (14.% patients in their study had recurrent stroke) at very high levels i.e. > 150 mm of Hg. And the recurrent stroke rates were lowest (6.8%) for the patients at high normal systolic blood pressure (130 – 150 mm of Hg). So, this can be observed that the frequency of recurrence was high at systolic blood pressure more than 150 mm of Hg. However, this difference of different values was statistically non-significant ($p > 0.05$).

This study was an effort to determine the optimal blood pressure levels which should be maintained by the physicians in follow up of the patients with previous history of stroke to prevent from recurrence. This study had certain limitations. This was a single center study with limited population size. This study represented a population of tertiary care unit. These frequencies of recurrence or subgroups of blood pressures may be different at other setups. So, more trials are required to be conducted at different clinical setups.

CONCLUSION

This study concludes that majority of patients with previous stroke had high normal blood pressure. Approximately one fifth population of patients with previous stroke may have recurrent stroke. The frequency of recurrence was highest among patients with systolic blood pressure > 150 mm of Hg and lowest for patients with systolic blood pressure lower than 120 mm of Hg. However, the difference of recurrence in various subgroups of systolic blood pressure was not significant statistically. It is suggested that physicians should try to maintain a systolic blood pressure at lower than 140 mm of Hg among previous stroke patients.

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ANNEXURE
PROFORMA
Frequency of Recurrent stroke at different systolic blood pressure levels among patients with previous stroke

Case No. _____ Date _____Hospital registration No._____
Name_____ Age _____ Sex_____
Address:_____
DIAGNOSIS_____

Systolic Blood pressure levels:
- very low–normal (<120 mm Hg)
- low-normal (120-130 mm Hg)
- high-normal (130-140 mm Hg)
- high (140-150 mm Hg)
- and very high (>150 mm Hg)

Recurrent stroke:
           YES   **NO**