Altered physiology in cerebrovascular accidents and its association with diabetes and hypertension in patients presenting to emergency room of a tertiary care hospital in Punjab

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<u>Abstract</u>

Stroke is one of the leading causes of mortality worldwide. There are non-modifiable and modifiable risk factors for stroke. But diabetes mellitus (DM) and hypertension (HTN) are two important modifiable factors which are more strongly linked with incidence of stroke. Recent studies indicate large prevalence of diabetes mellitus and hypertension in our country. Uncontrolled diabetes mellitus and hypertension causes various pathophysiological changes that lead to stroke. Even though available literature supports these findings, not enough data is available to establish diabetes mellitus and hypertension as predisposing or risk factors for stroke incidence in Punjab region. The present study was conducted for a period of six months and included 84 patients. Parameters such as age, sex, known history of diabetes or/ and hypertension, presenting chief complaint/s of limb weakness, slurring of speech, headache, deviation of angle of mouth, vertigo were reviewed and analysed. Results of this study indicate hypertension is a significant risk factor for stroke in 37 (44.0%) patients, followed by both diabetes mellitus and hypertension in 36 (42.8%) patients and diabetes mellitus in 11 (13.1%) patients.

Key Word: CVA, Diabetes Mellitus (DM), Hypertension (HTN).

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Received Date: 01/06/2019 Revised Date: 05/07/2019 Accepted Date: 22/08/2019 DOI: https://doi.org/10.26611/10311211

Access this article online				
Quick Response Code:	Website			
	www.medpulse.in			
	Accessed Date: 24 August 2019			

INTRODUCTION

Stroke constitutes the leading cause of mortality and disability worldwide. According to the India stroke factsheet updated in 2012, the evaluated age-adjusted prevalence rate for stroke ranges between 84 and 262 per one lakhs in rural and between 334 and 424 per one lakhs

in urban areas¹. There arenon-modifiable (age, gender, birth ethnicity, and low weight, hereditary predisposition)and modifiable (hypertension, diabetes mellitus, smoking, dyslipidaemia, postmenopausal physical inactivity and obesity)^{2,3} risk factors for stroke. Among these risk factors, diabetes and hypertension which are rapidly growing in communities and taking a heavy toll on health status of a community, have led to an exponential increase in incidence of stroke. Recent study International Diabetes Federation by evaluates, worldwide approximately 425 million people had DM in 2017 and this number is assumed to rise to 629 million by 2045.⁴ Diabetes prevalence has been rising abruptly in developing countries. Approximately 72.9 million people are effected with DM in India alone⁴. There is no denial that uncontrolled Diabetes can lead to various serious complications like retinopathy, chronic kidney disease, limb amputation, heart disease and stroke⁵.Diabetes

How to cite this rticle: Amit Gulrez, Harinder Singh Sagoo, John Pramod. Altered physiology in cerebrovascular accidents and its association with diabetes and hypertension in patients presenting to emergency room of a tertiary care hospital in Punjab. *MedPulse International Journal of Physiology*. August 2019; 11(2): 61-64. https://www.medpulse.in/Physiology/

causes various pathophysiological changes that lead to stroke, including systematic inflammation, arterial stiffness and endothelial dysfunction^{5,6}. Hypertension is also one of the most prevalent diseases, striking approximately 1.4 billion people worldwide⁷. It is accountable for at least 45% of the mortality from heart diseases and 51% of the mortality from stroke 8 . Hypertension is known to have detrimental effect on the cerebral circulation. It changes the anatomy of blood vessels by producing vascular hypertrophy and remodeling and by promoting atherosclerosis in large cerebral arteries⁹. So, both these factors (diabetes mellitus and hypertension) significantly alter the function and structure of the vascular system. Therefore, there seems to be a linear association between diabetes and hypertension with stroke. Despite the high rates of prevalence of diabetes mellitus, hypertension and stroke in Punjab state, there is very little documentation or studies done to investigate the role of these two risk factors in genesis of stroke. The incriminating factors leading to onset of diabetes or hypertension or both are peculiar to Punjab owing to its genetic pool, dietary and social factors, lifestyle, vices and addictions as well as lack of awareness about stroke. The available literature supports role of these risk factors leading to stroke mostly in western subjects, there are limited studies conducted to find the association between these two risk factors and onset or stroke in Punjab, a population which appears to be more susceptible to stroke owing to above mentioned risk factors. The extent to which diabetes and hypertension, together or in isolation can lead to a cerebrovascular event needs further studies to establish the association between stroke related morbidity, disability or mortality in patients with DM or HTN.

AIM AND OBJECTIVES

1. To study the association between hypertension, diabetes mellitus and cerebrovascular accidents (CVA).

2. To assess the possible alteration in cerebral physiology leading to CVA.

MATERIALS AND METHODS

This retrospective study was conducted for a period of six months by the department of Physiology and Emergency in a tertiary care hospital. The study included patients (n=84) admitted to emergency room with symptoms and signs suggestive or evolving or definitive stroke (CVA) as proven by radiological imaging after admission. The study included only those patients who were either known patients of diabetes or hypertension or both as also those who were diagnosed to be having either of the disease on admission and during the course of their stay in the hospital. Patients data, such as age, sex, known cases of diabetes and hypertension who were admitted with chief complaint of limb weakness, slurring of speech, headache, deviation of angle of mouth, vertigo were reviewed from hospital records for all stroke patients admitted between September and February. The definitive diagnosis of stroke (ischemic and hemorrhagic) was considered based on the clinical presentation and supported by brain imaging (CT scan or MRI) reported by the radiologist. Cases of brain tumours (space occupying lesions), venous thrombosis, cerebral aneurysms, post traumatic paresis or plegia as well as those who did not have either DM or HTN, were excluded from the study.

RESULTS

A total of 84 patients with infarct or hemorrhagic stroke were taken in this study. All these patients were observed to have diabetes mellitus type 2 or hypertension or both. There were 58 males (69.1 %) and 26females (30.9%) involved in this study (Table 1). Stroke incidence was predominant in males (Table 1). Among 84 patients, 52 (61.9%) had ischemic stroke and 32 (38.09 %) had hemorrhagic stroke (Table 2).

		Number	%	
	Male	58	69.1%	
	Female	26	30.9%	
	Total	84		
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Diabetes Mellitus And Hypertension As Risk Factors: 13.1 %patients (8 males and 3 females) with previous history of diabetes mellitus were diagnosed with (11 infarct stroke and 0 hemorrhagic stroke) stroke,44.0% (22 males and 15 females) patients with a history of hypertension were diagnosed with (10 infarct stroke and 27 hemorrhagic stroke) stroke

and 42.8% patients (8 males and 3 females) with a history of both diabetes mellitus and hypertension were diagnosed with (31 infarct stroke and 05 hemorrhagic stroke) stroke (Table 3 and Table 4). In this study, hypertension was observed to be major and a very significal risk factor for stroke in 37 (44.0%) patients, followed by both diabetes mellitus and hypertension in 36 (42.8%) patients and diabetes mellitus in 11 (13.1%) patients.

Table 3: Role of risk factors in stroke								
		Infarct Stroke	e He	Hemorrhagic Stroke		Total		
	Diabetes Mellitus	11 (13.1%)	11 (13.1%)		0			
	Hypertension	10 (11.9%)		27 (32.1%)		37 (44.0%)		
	Diabetes Mellitus and Hypertension both	31 (36.9%)		05 (5.9%)		36 (42.8%)		
	Total	52 (61.9%)		32 (38.1%)		84		
	Table 4: Gender wise distribution of risk factors							
			Male	Female	Total	_		
	Diabetes Mellitus		8	3	11	-		
	Hypertension		22	15	37			
	Diabetes Mellitus and Hypertension both		28	8	36			
	Total		58	26	84	_		

DISCUSSION

It is accepted in the literature that there is strong link between some risk factors(such as hypertension, diabetes mellitus, dyslipidemia, smoking, and age) and the incidence of stroke.¹⁰ Chronic hyperglycemia due to uncontrolled diabetes mellitus increases oxidative stress. leading to microvascular and macrovascular complications like nephropathy, retinopathy, neuropathy cerebrovascular, and cardiovascular events respectively.^{11,12,13} The feasible mechanisms which are responsible for macrovascular complications are formation of large amounts of Reactive Oxygen Species (ROS) such as superoxide anions which reduce the bioavailability of endothelium-derived nitric oxide (NO) by effecting the endothelial wall. There is mobilization of free fatty acids in case of insulin resistance. Due to that, glucose uptake in liver, skeletal muscle and other organs gets inhibited. Moreover, FFA influx mobilization leads to mitochondrial excess production of ROS, also leads to deranged lipid parameters. The poor clearance of LDL by phagocytosis is due to Insulin signaling receptors defect on the macrophages which is responsible for macrophage apoptosis. Necrosis and breakdown plaques rich in lipid which is responsible for formation of atherosclerotic plaques¹⁴.In a case-control study, DM increased the risk of ischemic stroke by 1. 8-6 fold.^{15,16} Hosaini *et al*¹⁷ findings reveal that 29.3% of all stroke patients had hyperglycemia. It has also been found that the presence of diabetes in ischemic stroke patients was 47% higher than that in patients with hemorrhagic stroke. Even in our study there was positive and significant trend between diabetes mellitus and incidence of stroke. According to our findings, 13.1% patients with previous history of diabetes mellitus were diagnosed with ischemic stroke and incidence of ischemic stroke are more than hemorrhagic stroke in diabetic patients. Besides, the noticed excess rates of ischemic stroke incidence

recommend that ischemic stroke patients have a great manifestation to modifiable risk factors whose control through lifestyle improvement can halt a huge percentage of such incidences¹⁸. In the Mumbai stroke registry, men had a higher stroke incidence rate than did women¹⁹ whereas in our study stroke incidence was also predominant in males. It has also been recognized that hypertension is a major risk determinant for stroke (ischemic and hemorrhagic).²⁰ Chronic hypertension contributes to the pathogenesis of stroke via the initiation and acceleration of intracerebral vasculopathy. Due to high intramural pressure there is alteration in the functions of Intracerebral arteries endothelial and smooth muscle which further can increase permeability over blood brain barrier leading to local /multifocal edema. Damaged endothelium interaction with altered blood cell causing the formation of local thrombi and ischaemic lesions. Intracerebral haemorrhage occurs due to degenerative changes in the smooth muscle cells and endothelium. Hypertension induced atherosclerotic changes in the extracranial vessels like aortic arch, heart increases the chances of cerebral lesions due to stenosis of extracranial vessels and dislodgement of embolism²¹.Recently, a prospective study by Sepanlou et al^{22} observed a positive association between hypertension and stroke mortality. The role of hypertension in pathogenesis of stroke has been effectively described²³. Law et al. found that the incidence rate of stroke was dropped by 41% when both systolic and diastolic blood pressure were reduced²⁴. It has been observed in some studies that patients with hypertension had 3 to 4 times higher ischemic stroke risk compared to those without hypertension, and the probability of ischemic stroke increased 1.5 times in patients with borderline hypertension²⁵. This is in agreement with our study which reveals that hypertension was the significant risk factor

for stroke in 44.0% patients, followed by both diabetes mellitus and hypertension in 42.8% patients.

CONCLUSION

This study concludes that out of DM and HTN in diagnosed stroke patients, hypertension is the most important risk parameter for strokeespecially for hemorrhagic stroke as compared to infarct stroke. However, diabetes mellitus and hypertension both are another potent risk factor for CVA. Moreover, diabetes mellitus has also been recognized as significant risk factor but to a much lesser extent as is evident in this study. Therefore, authors recommend that health screening surveys should be conducted frequently by governmental agencies especially in high risk communities like Punjab, to identify the hypertensive and diabetic population so that altered pathophysiological changes can be monitored at early stage as these changes are likely to predispose a person to CVA and in the event of it happening may hasten the progress of the disease resulting in poor outcome. This preventive approach will be helpful to maintain the normal physiology of the cerebral perfusion. Health care professionals and NGO's should also actively engage in spreading awareness in target communities to reduce the burden of disease and reduce the risk of permanent disability or mortality commonly associated with stroke.

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Source of Support: None Declared Conflict of Interest: None Declared