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Subclinical hypothyroidism, dyslipidaemia, diabetes and vitamin D status in Nepalese patients with ischemic and haemorrhagic stroke

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ABSTRACT

Introduction: Subclinical hypothyroidism (SCH), dyslipidaemia, diabetes and vitamin D are known to be associated with adverse cardiovascular events, including stroke. We aimed to explore the differences in SCH, dyslipidaemia, diabetes and vitamin D among stroke types.

Materials and methods: A cross–sectional study was conducted from January 2015 to December 2017 at Neuro and Allied Clinic, Bhairahawa, Nepal. Seventy–five stroke patients diagnosed by a Neurologist were evaluated for conventional risk factors, levels of thyroid function test, lipid profile, random blood sugar, HbA1C and vitamin D. Descriptive statistics were obtained and differences in SCH, dyslipidaemia, diabetes and vitamin D between stroke types were determined Mann–Whitney U test.

Results: The median(IQR) age was 57(20) years and 69.9% (n=58) were male. Sixty three out of 75 stroke patients were ischemic. The difference in the median (IQR) of laboratory findings between ischemic and haemorrhagic stroke was 4(3) µlU/ml and 3(4.5) µlU/ml for TSH, 1(1) pg/ml and 1(1) pg/ml for T3, 7(3) µg/dl and 7.5(3) µg/dl for T4, 169(32) mg/dL and 165(30) mg/dL for total cholesterol, 104(28) mg/dL and 107.5(28.5) mg/dL for LDL, 138(55) mg/dL and 137.5(57) mg/dL for TG, 38(1) mg/dL and 37(1) mg/dL for HDL, 120(30) mg/dL and 123.5(31) mg/dL for RBS, 26(7) ng/mL and 29(9.75) ng/mL for vitamin D. However, there was no statistically significant difference in all the parameters across the types of stroke.

Conclusion: Our study suggests that there is no significant differences in SCH, dyslipidaemia, diabetes and vitamin D among stroke types.

Keywords: Subclinical hypothyroidism, Dyslipidaemia, Diabetes, Vitamin D, Stroke

INTRODUCTION

Stroke is a leading cause of death and long–term disability globally. According to WHO, 15 million people suffer from stroke worldwide each year, one–third of them die while another one–third are permanently disabled.[1] In Nepal, it is estimated that 50,000 people per year are affected with stroke, with 15,000 annual deaths.[2] The common risk factors for stroke are age, smoking, hypertension, diabetes, dyslipidaemia, subclinical hypothyroidism (SCH) and atrial fibrillation.[3,4]. Previous stroke significantly increases risk of further episodes. Certain racial, ethnic and socioeconomic groups are also at greater risk of stroke.[5] The effects of stroke depend on which part of the brain is injured and how severely it is affected. A very severe stroke can cause sudden death.[1]. Mainly, stroke is classified as ischemic or haemorrhagic types, with ischemic stroke accounting for approximately 85% of the total number.[6] Pathophysiological condition like thrombosis, haemorrhage, and embolism may cause interruption of the blood supply to the brain, which cuts off the supply of oxygen and nutrients, causing damage to the brain tissue and leads to highly destructive condition that is stroke. Among the several risk factors of stroke, SCH, which is defined as a serum thyroid stimulating hormone (TSH) level more than 4.2 µlU/ml, with a normal free triiodothyronine (FT3) and free thyroxine (FT4) concentration has been associated with hypercholesterolemia, atherosclerosis, and an increased carotid intima–media thickness. It has been reported that younger patients with SCH have an increased risk of stroke events and fatal stroke compared to euthyroidism.[7] Similarly, dyslipidaemia which is a major risk factor for coronary heart disease (CHD), has an unclear role in the pathogenesis of ischemic stroke. However, elevated levels of Low density lipoprotein–C (LDL–C) and low levels of high density lipoprotein–C (HDL–C) can increase the risk of ischemic stroke though the role of increased triglyceride (TG) levels is not yet clear. It has also been suggested that elevated levels of LDL–C might also increase the risk of haemorrhagic stroke.[8] Likewise diabetes is a well–established risk factor for stroke. It can cause pathologic changes in blood vessels at various locations and can lead to stroke if cerebral vessels are directly affected. Additionally, mortality is higher and post stroke outcomes are poorer in patients with stroke having uncontrolled glucose levels.[9] Lower vitamin D status is also associated with an increased risk of ischemic stroke.[10] Vitamin D (25–hydroxyvitamin D is most commonly known for its effects on bone metabolism and calcium homeostasis.[11]

Diagnosis of stroke depends on clinical examination and is further supported by various neuroimaging techniques. Blood biomarkers can be used in clinical setting in order to diagnose stroke, differentiate stroke types, or even predict primary or reoccurring stroke.[6] Rapid diagnosis and timely treatment improves the outcome in patients with ischemic stroke, but a rapid and sensitive blood test for ischemic stroke does not exist.[12] Data investigating thyroid function, lipid profile, blood glucose, haemoglobin A1C (HbA1C) and vitamin D in different stroke types from Nepal are rare in literature, if not at all. Therefore, present study was conducted to explore the differences in SCH, dyslipidaemia, diabetes and vitamin D among stroke types.

MATERIALS AND METHODS

A cross–sectional study was conducted between January 2015 to December 2017 on patients diagnosed with stroke at Neuro and Allied Clinic, Bhairahawa, Nepal. Both new and old cases of stroke were included. Data on sociodemographic (age, sex), and laboratory parameters (thyroid function test, Lipid profile, random blood sugar [RBS], HbA1C, serum vitamin D were collected using standard proforma. Thyroid function test (TFT) included T3 (normal: 0.560 – 1.880pg/ml), T4 (normal: 4.584 – 11.888µg/dl) and TSH (normal: 0.4–4.2 µlU/ml). TSH level above the normal range with levels of T3 and T4 in normal range

was indicative of SCH. Similarly, the blood levels of total cholesterol (TC), HDL, LDL and TG were determined to observe their lipid profile. Elevated blood level of TC or LDL or TG or low level of HDL was indicative of dyslipidaemia. RBS ›200 mg/dL or HbA1C above 6.5% was indicative of diabetes. Furthermore, serum vitamin D was classified as deficient (‹10 ng/mL); insufficient (10–29 ng/mL); sufficient (30–100 ng/mL) and potential intoxication (›100 ng/mL). TFT and vitamin D levels were measured using enzyme–linked immunosorbent assay or ELISA method whereas HbA1C was measured using Tubidometry and Nephailometry. All other laboratory parameters were determined through semi–automated chemistry analyser. Descriptive statistics were obtained, and the differences in SCH, dyslipidaemia, diabetes and vitamin D among stroke types were determined using χ^2–test.

The ethics approval for this study was taken from the institutional review committee of Shree Medical and Technical College, Bharatpur, Nepal and permission was taken from the clinic authority prior to data extraction.

RESULTS

The median (IQR) age was 57(20) years. Majority of the patients (58, 69.9%) were male. Sixty three out of 75 stroke patients were ischemic (Fig 1).

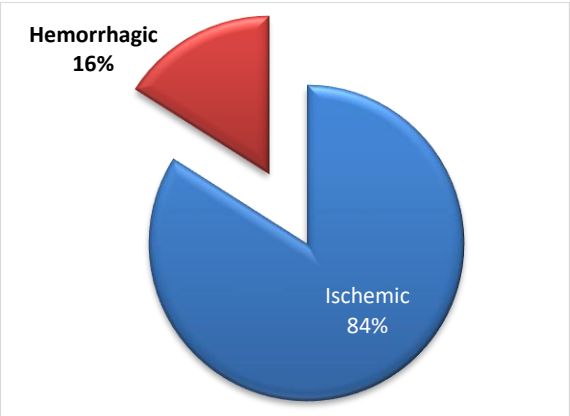

Fig. 1: Distribution of stroke types

The blood levels of the determinants of SCH, dyslipidaemia, diabetes and vitamin D are shown in Table 1. The median(IQR) TSH was 3.8(2.9) µlU/ml but ranged from 0.01 to as high as 27.5 µlU/ml. The mean±SD TC was 168.6±30.9 mg/dL and the median(IQR) LDL, TG and HDL were 104.0(27.7) mg/dL, 138.0(50.0) mg/dL and 37.2(1.1) mg/dL. The highest level of TC, LDL and TG were 250, 179 and 281 mg/dL respectively whereas the lowest level of HDL was 23.0 mg/dL. The RBS ranged from 6.1 to 227.0 mg/dL with median(IQR) level of 120.0(29.0) mg/dL whereas the HbA1C ranged from 6.1 to 9.9% with media(IQR) level of 6.1(0.3)%. Vitamin D level varied from 8.2 to 109.0 ng/mL with median(IQR) level of 27.0(7.0) mg/mL

Table1: Blood levels of the determinants of subclinical hypothyroidism, dyslipidaemia, diabetes and vitamin D.

Determinants	Blood level	Range
[a]TSH(µlU/ml)	3.8(2.9)	0.01–27.5
[a]T3 (pg/ml)	1.3(0.5)	0.6–9.0
[a]T4 (µg/dl)	7.3(2.6)	1.3–19.6
[b]TC (mg/dl)	168.6±30.9	91.0–250.0
[a]LDL (mg/dl)	104.0(27.7)	27.0–179.0
[a]TG (mg/dl)	138.0(50.0)	37.1–281.0
[a]HDL (mg/dl)	37.2(1.1)	23.0–148.0
[a]RBS (mg/dl)	120.0(29.0)	61.0–227.0
[a]HbA1C (%)	6.1(0.3)	4.7–9.9
[a]Vit D (ng/mL)	27.0(7.0)	8.2–109.0

[a]median(IQR); [b]mean±SD
Abbreviations: TSH, Thyroid Stimulating Hormone; T3, triiodothyronine; T4; Thyroxine; TC, Total Cholesterol; LDL, Low Density Lipoprotein; TG, Triglycerides; HDL, High Density Lipoprotein; RBS, Random Blood Sugar; Hb, Haemoglobin; Vit D, Vitamin D

SCH, insufficient vitamin D, diabetes and dyslipidaemia were prevalent slightly higher in ischemic stroke as compared to haemorrhagic stroke but this difference was not statistically significant. About 29% (18/63) of those with

ischemic stroke had SCH as compared to 25.0% (3/12) of those with haemorrhagic type. Vitamin D deficiency was observed in 1/63 participants with ischemic stroke whereas 71.4% of those with such stroke had insufficient vitamin D level in blood as opposed to 50% (6/12) of those with haemorrhagic stroke.

Table 2: Difference in clinical parameters between stroke types (n=75)

Characteristic		Stroke type		P– value
		Ischemic n(%)	Haemorrhagic n(%)	
[a]Age		57(18)	56.5(28)	0.811
[b]Sex	Female	17(27.0)	4(33.3)	0.729
[b]SCH		18(28.6)	3(25.0)	1.000
[b]Vitamin D	Deficient	1(1.6)	0	0.358
	Insufficient	45(71.4)	6(50.0)	
	Sufficient	16(25.4)	6(50.0)	
	Potential intoxication	1(1.6)	0	
[b]Diabetes		1(1.6)	0	1.000
[b]Dyslipidemia		43(68.3)	7(58.3)	0.519

[a]Mann–Whitney U test, [b]Chi–square test

DISCUSSION

Stroke is one of the common neurological problems in Nepal.[3] The median (IQR) age in our study was 57(20) years, similar finding (58.5 years) has been previously reported.[13] A large study showed that the mean age of stroke significantly decreased from 71.2 years in 1993/1994 to 69.2 years in 2005 while the proportion of all strokes under age 55 years has increased from 12.9% in 1993/1994 to 18.6% in 2005.[14] This signify that the prevalence of stroke in young population is in an increasing trend in Asian countries. This might be due to several factors such as lack of awareness regarding cause of stroke, urbanization, modernization, passive life style, increasing trends of smoking and tobacco consumption, hypertension, diabetes, dyslipidaemia, as well as changes in lifestyle and diet.[15] Our findings suggested that ischemic stroke was more common than haemorrhagic. Previous study in Kathmandu also reported similar result.[13] Global stroke epidemiology is changing rapidly. Although age–standardized rates of stroke mortality have decreased worldwide in the past two decades, the absolute numbers of people who have a stroke every year, and live with the consequences of stroke or die from their stroke, are increasing. Regular updates on the current level of stroke burden are important for advancing our knowledge on stroke epidemiology and facilitate organization and planning of evidence–based stroke care.[16] Patients with ischemic stroke had slightly higher prevalence of SCH, insufficient vitamin D, diabetes and dyslipidaemia as compared to haemorrhagic stroke but this difference was not statistically significant. SCH is known to increase the risk of cardiovascular events[17] but the risk of stroke is not yet clear.[7] In addition to this finding, our study also showed that those with ischemic stroke had slightly higher proportion of dyslipidaemia. Dyslipidaemia is a major risk factor for coronary heart disease but its role in the pathogenesis of ischemic stroke is less clear. There are also conflicting findings regarding the association of dyslipidaemia with ischemic stroke from epidemiological studies. Overall, elevated LDL and low HDL levels appear to increase the risk of ischemic stroke.[18]

Our study had some limitations. While we determined the differences in several parameters, we did not have identical groups of stroke types in terms of age and sex that might have influenced the findings. Also the prevalence of haemorrhagic stroke was relatively lower than ischemic stroke, hence the statistical power to differentiate may be limited due to the smaller number of patients with haemorrhagic stroke.

CONCLUSION

Our study suggests that there is no significant differences in SCH, dyslipidaemia, diabetes and vitamin D among stroke types. Further study in larger group and multiple settings might be necessary.

COMPETING INTEREST

The authors declare that there are no competing interests regarding the publication of this paper.

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