Prevalence of stroke and stroke risk factors in a South-Western community of Nepal

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ABSTRACT

Background: Stroke related studies in Nepal are primarily hospital-based and mainly from the capital city. We aimed to estimate the prevalence of stroke and stroke risk factors in the South-Western community of Nepal.

Methods: A cross-sectional study was conducted from May to August 2018 among 549 randomly selected Nepalese participants from diverse ethnicity, aged ≥15 years, in a region with the availability of neurological support facilities. Data were collected using a stroke questionnaire designed for the purpose. Stroke was identified by enumerators using the Balance-Eyes-Face-Arms-Speech-Time (BEFAST) scale, and a senior neurologist confirmed it. We assessed the presence of major risk factors associated with stroke.

Results: The crude and age-standardised prevalence of stroke were 2368 and 2967 per 100,000 respectively. Of all the surveyed participants, 61% (n=335) reported consumption of full-fat dairy products >3 days per week, 87.6% (n=481) reported a high intake of salt (>5g/day), 83.6% (n=459) with a low intake of fruits and vegetables (<400g/day), 45.2% (n=248) with perceived stress related to work or home, 51.6% (n=283) with financial stress (283, 51.6%), 86.7% (n=457) with low high-density lipoprotein (HDL), 96.2% (n=507) with high blood urea nitrogen, 47.1% (n=356) were either overweight or obese 20.4% (n=112) with hypertension and 6.2% (n=34) with diabetes.

Conclusion: The prevalence of stroke in the community of the South-Western part of Nepal is relatively higher than that estimated in South-Asia and global context. Our findings suggest an urgent community intervention, particularly with healthy lifestyles changes for future stroke prevention in the high-risk group.

Keywords: epidemiology, risk factors, Nepal, prevalence, stroke, community

WHAT IS ALREADY KNOWN ON THIS SUBJECT?

The global prevalence of stroke is rising. Stroke prevalence and risk factors in Nepal are soley hospital-based and mainly based on its capital city. There are no community level stroke studies to reflects upon the actual burden of stroke and potential risk factors in the population.

WHAT THIS STUDY ADDS?

The stroke prevalence in the study site was lower than the hospital prevalence but higher to that in the South-Asian and global context. A considerable population without stroke bear potential risk factors of stroke and demands an urgent community intervention for future stroke prevention.

INTRODUCTION

The global burden of stroke in 2016 suggests that stroke is associated with approximately one million deaths and 22 million disability-adjusted life-years (DALYs) in South Asia, of which nearly 15,000 deaths 330,000 DALYs occurred in Nepal.[1] Stroke incurs a substantial economic burden to the national healthcare system[2] and is often unaffordable to low-income families, particularly for those bearing all the treatment costs.

Several risk factors, including non-modifiable (age, race) but often modifiable, are associated with a higher risk of stroke.[3] INTERSTROKE study reported hypertension, physical activity, apolipoprotein ApoB/ApoA1 ratio, diet, waist-hip ratio, psychosocial factors, current smoking, cardiac causes, alcohol consumption and diabetes mellitus as ten potentially modifiable risk factors of stroke.[4] These modifiable risk factors were associated with nearly 90% of the population attributable stroke risk in each major region of the world, among diverse ethnic groups, in both sexes and all ages.

With the growing evidence on the global burden of stroke and its associated risk factors, it is, therefore, essential for a country to have reliable data on stroke for its effective management. A systematic review of epidemiologic studies from 1980 to 2010 reported that the stroke prevalence in South Asia ranged from 45 to 471 per 100,000;[5] however, reliable community-based data on stroke prevalence from Nepal is lacking. A recent study from a hospital-based setting in the capital city Kathmandu found that 64 per 1000 patients had the first-ever stroke.[6] Stroke studies so far in Nepal are solely hospital-based, and the majority of them are limited to the capital city.[7] Together with that, findings reported from clinical settings do not truly reflect the potential risk factors of stroke in the communities as they are presented with severe cases only. Therefore, we aimed to determine the prevalence of stroke and its risk factors at the community level of the South-Western part of Nepal.

METHODS

Study design and population

A community-based cross-sectional study was conducted from May to August 2018 among those living at their current place of residence for at least six months and was aged ≥15 years at the time of the survey. We excluded all those who were non-permanent resident, were living in a military base or group quarters, hospitalised patients, prisons, and nursing homes.

Study site

This study was conducted in the Rupandehi district, South-Western part of Nepal (Fig 1). This district was purposively selected based on the availability of neurological support facilities (stroke clinic, neurologist experienced in stroke, stroke officers, stroke nurses, and computer tomography scan), diversified ethnic population, and neurological-based laboratory facility.

Sample size and sampling

A sample size of 600 was estimated based on the prevalence of cerebrovascular accident from a hospital-based study in non-specialist hospital (2%) in 2009-2010,[8] design effect of 1.5, 95% confidence interval, 5% error margin and domain size of 12 (area: urban and rural; gender: male and female; age: 15-44 years, 45-74 years and >74 years) and response rate of 90%. In Nepal, each district is comprised of two smaller units-urban areas (municipality/sub-metropolitan city/metropolitan city) and rural areas (villages and rural municipalities) based on economy, population and infrastructure development.

We carried out a multistage stratified-clustered random sampling. Eligible participant from each home was selected through a simple random sampling method. The required sample size for each ward or cluster was based on the population proportion of the latest national census and its predictive census of 2018.[9] Of the estimated 600 participants, only 549 (91.5%)

responded and took part in the study. The details of the sampling procedure are provided in Fig 2.

Survey tool and data collection

The survey tool was developed by reviewing stoke specific literature suitable for our study (supplemental tool 1).[4 10 11 12] The survey collected information on sociodemography, stroke, physical activity, diet, alcohol intake, tobacco use, psychological factors, general health, biochemical parameters, anthropometry, clinical parameters and disease condition. For more details on the definition of the key parameters of the tool and survey tool, refer to the supplemental definition 1. Pictorial diagrams were used to acquire information on tobacco products, and to estimate the serving size of fruits and vegetables. The enumerators were trained on the aspects of data collection and received additional training on stroke identification from a stroke team lead by a neurologist.

Stroke identification

Stroke was identified using the Balance-Eyes-Face-Arms-Speech-Time (BEFAST) scale.[13] The presence of more than one BEFAST symptoms after the stroke onset was defined as stroke. Stroke cases identified by the enumerators were considered for neuroimaging. A senior neurologist, through the home visit and neuroimaging data along with follow-up in the neurological clinic, ruled out evidence of stroke mimics and verified stroke cases. Cases without neuroimaging were confirmed based on neurological deficits explained with a cerebral arterial territory involvement (middle cerebral artery stroke), or involvement of a specific cerebral location (thalamic stroke). These cases were labelled as an unknown type of stroke. Enumerators were health care professionals with previous work experience in a neurological facility. The senior neurologist provided training on stroke identification to the enumerators.

Statistical analysis

The data (supplemental dataset 1) were analysed using IBM-SPSS 25.0 (IBM Corporation, Armonk, NY, USA). The normality test was performed for numeric variables using the Kolmogorov-Smirnov test (P>0.05), and descriptive statistics were determined for all variables. Crude age-specific prevalence of stroke per 100,000 and age-standardised prevalence was calculated by direct standardisation method. The 95% confidence interval for the prevalence was determined using population proportion while the Clopper-Pearson method using exact binomial distribution was used to calculate the 95% confidence interval for the risk factors.

Ethics

Ethical approval was obtained from the National Institute of Neuro and Allied Sciences-Institutional Review Committee (IRC #09/018), Kathmandu, Nepal. An initial verbal consent followed by written consent for interview and blood samples was collected from the participants. For those who were unable to provide consent for themselves due to medical reasons, a proxy consent from family/relatives or caregivers were sought.

RESULTS

Out of a total of 549 participants, the median(IQR) age of the participants was 40 (19) years, and 52.1% were female. The majority of the participants were married (n=470, 85.6%), a quarter of them had no formal education (136, 24.8%), and the majority of them were currently unemployed (306, 55.8%).

Table 1 depicts the sociodemographic characteristics of the study population (those with and without stroke). There was no statistically significant difference amongst the two groups (those

with and without stroke) on sociodemographic characteristics except for age (p<0.001). The median (q1, q3) age in those without stroke was 39 (30, 48) years, while those with stroke was 60 (52.5, 70) years (refer to supplemental table 1 for age composition of the stroke and non-stroke groups). The majority of the participants were from urban areas (93.1% without stroke, and 92.3% with stroke).

Table 1. Sociodemographic characteristics of the study population

Characteristics		**Study population (n=549)**		
		Without stroke (n=536) n (%)	**With Stroke (n=13) n (%)**	**P-value**
Age in median (q1, q3) years		39 (30, 48)	60 (52.5, 70)	<0.001*
Area of residence	Urban	499 (93.1)	12 (92.3)	0.611
	Rural	37 (6.9)	1 (7.7)	
Sex	Male	256 (47.8)	7 (53.8)	0.878
	Female	280 (52.2)	6 (46.2)	
Marital Status	Not married	77 (14.4)	2 (15.4)	1.000
	Married	459 (85.6)	11 (84.6)	
Level of education	No formal schooling	131 (24.4)	5 (38.5)	0.117
	Up to high school	318 (59.4)	4 (30.8)	
	College degree or above	87 (16.3)	4 (30.8)	
Current work status	Employed	83 (15.5)	2 (15.4)	0.505
	Self-employed	155 (29.0)	2 (15.4)	
	Unemployed	298 (55.5)	9 (69.2)	

Note: All p-values were derived from Chi-square test except for age Mann-Whitney U test was used;
*significant.

Table 2 shows the age-standardised prevalence of stroke in the sampling population ≥15 years using the WHO standardised population. It shows that the crude prevalence was 2368 per 100,000, while the age-standardised prevalence was 2967 per 100,000.

Table 2. Age-standardised stroke prevalence using WHO standardised population

Age group	WHO standard age (percent)	Study population	Number of stroke cases	Age-specific prevalence per 10^5	Age-standardised prevalence per 10^5
15-19	8.47	45	0	0	0
20-24	8.22	44	1	2273	256
25-29	7.93	40	0	0	0
30-34	7.61	67	0	0	0
35-39	7.15	75	0	0	0
40-44	6.59	98	0	0	0
45-49	6.04	46	1	2174	180
50-54	5.37	35	2	5714	343
55-59	4.55	20	2	10000	624
60-64	3.72	32	1	3125	160
65-69	2.96	13	2	15385	624
70-74	2.21	14	2	14286	433
75-79	1.52	12	2	16667	347
80-84	0.91	4	0	0	0
85+	0.63	4	0	0	0
Crude prevalence per 100,000 (95% CI) = 2368 (1096; 3640)					
Age-standardised prevalence per 100,000 (95% CI) = 2967 (1548; 4386)					

We did not identify any new case of stroke during the study period in the sampling population. Of the 13 confirmed stroke cases, one had a subsequent stroke within 28 days of the first stroke (Table 3). The stroke duration ranged from 1 to 5 years, with a mean ± standard deviation of 2.3±1.3 years. The majority of stroke cases were managed in hospital (11, 84.6%), had an ischemic stroke (9, 69.2%), and diagnosed using computer tomography and magnetic resonance imaging (9, 69.2%). About two-thirds (n=8, 61.5%) of individuals with stroke were physically independent before stroke while the remaining were dependent. The assessment of medication information showed that the majority of the stroke patients received antihypertensive medications (8, 61.5%). Four out of 13 patients received anticoagulants, antidiabetics and lipid-lowering agents while two received antiplatelet agents.

Table 3. Information on stroke (n=13)

Stroke details		**n (%)**
Presence of stroke		13 (2.4)
Subsequent stroke within 28 days of the first stroke		1 (7.7)
Mean ± SD duration after the onset of stroke in years (n=12)		2.3 ± 1.3
How was the patient managed in the community?	In hospital	11 (84.6)
	Insufficient data	1 (7.7)
	Other medical consultation	1 (7.7)
What subtype of stroke was diagnosed?	Ischemic stroke	9 (69.2)
	Intracerebral haemorrhage	1 (7.7)
	Unspecified type	3 (23.1)
How was the diagnosis of stroke subtype verified?	Clinical diagnosis alone	4 (30.8)
	By diagnostic technique*	9 (69.2)
What was the physical ability of the patient pre-stroke?	Independent	8 (61.5)
	Dependent	5 (38.5)
What medications had the patient received for treatment and management of stroke?	Anticoagulants (n=7)	4 (57.1)
	Antiplatelets (n=9)	2 (22.2)
	Lipid-lowering medications (n=9)	4 (44.4)
	Antihypertensive (n=10)	8 (80.0)

*_Diagnostic technique_: Includes computer tomography and magnetic resonance imaging; SD: standard deviation

Table 4 illustrates the proportions of stroke risk factors in participants who had a stroke versus no stroke. The baseline characteristics, including the age of the two groups, were different. Our findings suggest that risk factors associated with stroke and without stroke are common in Nepalese community. We found no difference in full-fat dairy consumption (stroke: 8, 61.5% vs non-stroke: 327, 61.0%) among the two groups unlike lower intake of salt (stroke: 10, 76.9% vs non-stroke: 471, 87.9%) and higher intake of fruits and vegetables (stroke: 12, 92.3% vs non-stroke: 447, 83.4%) in the stroke group compared to non-stroke. More than one-third of those without stroke perceived stress at work or home (212, 39.6%) and had at least one life event (96, 36.8%). Clinical depression was observed in 23.1% (n=3) of those with stroke (3, 23.1%) while in 2.0% (n=16) of those without stroke. The majority of participants without stroke reported themselves as having good health (487, 91.2%). The biochemical evaluation indicated that out of 527 participants with biochemical measurement, 86.8% of those without stroke had low HDL, and 92.3% had high blood urea nitrogen. Similarly, the majority of them with stroke also had low HDL (84.6%), while all of them (n=13) had high blood urea nitrogen. About half of the participants (251, 47.3%) without a stroke and over one-third (5, 38.5%) with stroke were overweight. More than two-thirds of those with stroke (9, 69.2%) had hypertension, unlike 19.2% (n=103) who did not have a stroke.

222 **Table 4. Prevalence of potential risk factors of stroke in those with or without stroke (n=549)**

Potential risk factors			**Study population**			
			Without stroke		**With Stroke**	
			n (%)	**95% CI**	**n(%)**	**95% CI**
Physical activity (n=547)	Insufficient		72 (13.5)	10.7; 16.6	4 (33.3)	9.9; 65.1
Dietary intake	Unprocessed red meat >3 d/wk		205 (38.2)	84.1; 42.5	2 (15.4)	1.9; 45.4
	Full-fat dairy products >3 d/wk		327 (61.0)	56.7; 65.2	8 (61.5)	31.6; 86.1
	High salt		471 (87.9)	84.8; 90.5	10 (76.9)	46.2; 95.0
	Low fruits and vegetables		447 (83.4)	80; 86.4	12 (92.3)	64.0; 99.8
Alcohol (n=545)	Consumption		126 (23.7)	20.1; 27.5	0	0; 24.7
Tobacco use	Cigarette smoking		78 (14.6)	11.7; 17.8	2 (15.4)	1.9; 45.4
	Smokeless tobacco		97 (18.1)	14.9; 21.6	1 (7.7)	0.2; 36.0
Psychological factors	Perceived stress at work or home	Some of the time	212 (39.6)	35.4; 43.8	2 (15.4)	1.9; 45.4
		Several periods	31 (5.8)	4.0; 8.1	3 (23.1)	5.0; 53.8
	Financial stress	Minimal	136 (25.4)	21.7; 29.3	1 (7.7)	0.2; 36.0
		Moderate to severe	143 (26.7)	23.0; 30.6	3 (23.1)	5.0; 53.8
	Clinical depression‡		16 (3.0)	1.7; 4.8	3 (23.1)	5.0; 53.8
	Occurrence ≥1 life event (n=274)		96 (36.8)	30.9; 42.9	13 (100)	75.3; 100
Health status (n=547)	Good		487 (91.2)	88.5; 93.5	6 (46.2)	19.2; 74.9
Biochemical measurements (n=527)	Elevated C-reactive protein		40 (7.8)	5.6; 10.4	2 (15.4)	1.9; 45.4

	Hyperglycaemia	18 (3.5)	2.1; 5.5	3 (23.1)	5.0; 53.8
	High cholesterol	7 (1.4)	0.5; 2.8	0	0; 24.7
	Low HDL	446 (86.8)	83.5; 89.6	11 (84.6)	54.6; 98.1
	High serum creatinine	4 (0.8)	0.2; 2.0	1 (7.7)	0.2; 36.0
	High Blood Urea Nitrogen	494 (96.1)	94.1; 97.6	13 (100)	75.3; 100
Anthropometric measurement (n=544)	Overweight and above	251 (47.3)	43.0; 51.6	5 (38.5)	13.9; 68.4
Disease condition	Hypertension	103 (19.2)	16; 22.8	9 (69.2)	38.6; 90.9
	Diabetes	31 (5.8)	4.0; 8.1	3 (23.1)	5.0; 53.8
	Thyroid disorder	31 (5.8)	4.0; 8.1	0	0; 24.7

Abbreviations: *CI:* confidence interval; *d*: day; *HDL*: high-density lipoprotein; *wk*: week;

Note: *95% CI:* Refers to the percentage; *Insufficient physical activity*: Low or no physical activity; *Tobacco use*: Current or past users; *Health status*: Self-assessment of health status; *Hyperglycaemia*: Non-fasting Blood Glucose Level>200mg/dl; *High cholesterol*: ≥240mg/dl; *Low HDL*: ≤40mg/dl (Male) and ≤50 mg/dl (Female); *High serum creatinine*: >1.2mg/dl (Male) and >1.1mg/dl (Female); *High Blood Urea Nitrogen*: >20mg/dl; *Overweight and above*: BMI ≥25 kg/m^2; *Clinical depression*: Feeling sad, blue or depressed for two weeks or more in a row in the past 12 months along with ≥5 positive responses on questions on losing interest, feeling tired or low on energy, gaining or losing weight, trouble falling asleep, difficulty concentrating, thinking of death and feeling of worthless; *Hypertension*: Systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg, or currently taking any anti-hypertensive medication: *Diabetes and thyroid disorder*: Identified based on the use of antidiabetic and anti-thyroid medications

DISCUSSION

Our study found that the crude and age-standardised prevalence of stroke ≥15 years in the South-Western Community of Nepal was 2368 and 2967 per 100,000 population respectively. Stroke risk factors were common in the study population irrespective of whether or not they had a stroke, and the majorities were modifiable. The common risk factors were poor dietary intake, high prevalence of psychological factors, poor biochemical measurement, high BMI and presence of co-morbidities.

So far, we are not aware of any community or population level study from Nepal that has reported on the prevalence of stroke. Our finding suggests that the prevalence of stroke in the South-Western community of Nepal is higher compared to the South Asian estimates (crude prevalence: 45 to 471 per 100,000 and age-adjusted prevalence: 47-545 per 100,000)[5] and the global estimates (crude prevalence: 1083.10 per 100,000 and age-adjusted prevalence: 1180.40 per 100,000).[14] We found that most of the stroke cases were ischaemic, while a quarter was unspecified. Although ischaemic stroke is the most common stroke type worldwide,[4] most hospital-based studies in Nepal have reported a higher incidence of haemorrhagic stroke.[6] The case-fatality rate of haemorrhagic stroke is generally higher relative to that of ischemic stroke.[6] [15] As our study was community-based, it included stroke survivors only, that partly explains the higher prevalence of ischaemic stroke. In the present study, stroke cases were mostly managed in the hospital but there were also cases with insufficient data or other medical consultations. These suggest that not all the cases of stroke in this setting reach the hospital. It also reflects that only hospital-based prevalence are likely to underestimate the true burden of stroke. Hence, a combination of case-fatality from hospital and stroke cases from the community might provide a better estimate of stroke burden.

The findings of our study on stroke risk factors are consistent with previous studies that have reported several non-modifiable and modifiable risk factors associated with stroke.[3 4] Although

age was one of the major non-modifiable risk factors of stroke in our study, and has been widely reported in the published literature,[3] another hospital-based Nepalese study[16] reported an increase in the prevalence of stroke in adults below 45 years, particularly associated with lifestyles factors and presence of co-morbidities. Similar risk factors have been observed in a national survey on non-communicable disease risk factors in Nepal,[17] and a study in the capital city Kathmandu on cardiovascular risk factors.[18]

The dietary intake of the participants from our study showed consumption of red meat, full-dairy products, high salt intake, low intake of fruits, and vegetables were common among the study participants. These have been reported to be associated with increased risk of stroke.[19-22] The findings from our study on salt, fruits and vegetable intake are similar to the result from a study in a peri-urban community of Nepal.[18]

The behavioural risk factors of stroke observed in our study were smoking, consumption of smokeless tobacco and alcohol consumption. The majority of the participants in our study had never smoked or used smokeless tobacco. History of cigarette smoking has been commonly reported on stroke patients from hospitals in Nepal.[7] Previous community-based studies on cardiovascular[18] and non-communicable diseases[17] in Nepal have reported more current smokers than the current or past smokers in our study. Nevertheless, even a low consumption of cigarettes (approximately one per day) carries a risk of developing stroke as high as 50% of that of high consumption.[23] With regards to acohol consumption, in the present study we reported that all those who had stroke did not consume alcohol currently, while one-fourth of those without stroke were currently consuming alcohol in varying quantities. A review of hospital-based stroke studies from Nepal had reported variability on alcohol consumption habit among stroke patients.[7] This reflects that those with stroke might be consuming alcohol in the past but were aware of the negative consequence of alcohol consumption to their current health.

The important psychological risk factors of stroke reported in our study were depression and stress. Though we reported an overall low prevalence of clinical depression among the study population, it was prevalent in more than one-fifth of those with stroke. This could be a result of stroke rather than a direct cause of the stroke, but due to the cross-sectional design of our study and with small sample size, the causality could not be established.

In the present study, the biochemical evaluation showed elevated CRP in some andelevated BUN in majority of the participants. CRP is a marker of systemic inflammation[24] and studies in Nepal have shown high CRP in patients with stroke, particularly ischemic stroke.[25 26] Increased BUN is an indicator of poor renal function,[27] which in turn could be associated with stroke,[28] though renal impairment is common in hospitalised Nepalese patients with haemorrhagic stroke.[29]

One-fifth of the overall participants and over two-thirds of those with stroke had hypertension. The overall prevalence of hypertension in our study was 20.4%, which was 5.3% lower than the finding from a national survey in Nepal.[17] This might be because those aged ≤45 years were lower in our population compared to that survey. It should also be considered that those treated for stroke might have risk factors such as hypertension, diabetes and hyperlipidaemia modified in hospital.

There are many limitations to our study. This study was conducted in the South-Western part of Nepal and thus may not represent the general population of the country. We only included participants aged 15 years and above, so our study methodologically excluded stroke cases in children. The possibility of recall bias among participants in self-reported questions should be taken into account. Our study does not represent the fatal stroke cases in the hospital. We also did not have validated stroke-negatives, and as a result of that few stroke cases might have been missed. Diabetes was self-reported, and not all the cases were diagnosed. One of our limitations is the small sample size of stroke from a statistical perspective. Many of the age-specific cells

are empty and therefore, the precision/stability of estimates could have been impacted due to small sample size. Therefore, special attention has to be taken into account while interpreting our findings. Despite these limitations, this study is probably the first attempt in Nepal to undertake a survey of stroke prevalence and determinants of its risk factors at a community level. The actual stroke cases and those that were stroke mimics such as Bell's palsy were verified by a senior neurologist with a home visit and a follow-up visit in a neurological clinic, consequently assuring high validity of the prevalence.

In conclusion, our study suggests that the prevalence of stroke in the community of the South-Western part of Nepal is relatively higher than other South-Asian countries and a global estimate. Community awareness on stroke and its risk factors is highly recommended for future prevention of stroke, and lifestyle changes could be beneficial in this context.

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AUTHOR CONTRIBUTIONS

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SUPPORTING INFORMATION

Supplemental tool 1. Stroke Instrument v.1.0

Supplemental definition 1. Definition of key parameters of the survey instrument v.1.0

Supplemental dataset 1. Dataset of stroke and stroke risk factors

Supplemental table 1. Age composition of the stroke and non-stroke groups