RESEARCH ARTICLE



Gaps in secondary prevention among stroke survivors in rural Gadchiroli, India: a community-based cross-sectional study [version 1; peer review: 4 approved]

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Abstract

Background: With epidemiological transition, stroke has emerged as a public health priority in rural India. However, population-level information on secondary prevention of stroke from rural areas of India and other low- and middle-income countries remains exceedingly rare.

Methods: In a cross-sectional community-based survey, trained surveyors screened a well-defined population of 74,095 individuals living in 64 villages in Gadchiroli district of India for symptoms of stroke. A trained physician evaluated screen positive patients, diagnosed stroke, measured blood pressure and collected information on prior diagnosis of risk factors and current use of medications using a structured questionnaire.

Results: A total of 265 stroke survivors were identified. Prior diagnosis of hypertension was made in 57.4%, diabetes in 9.8%, hyperlipidaemia in 0.4%, ischaemic heart disease in 1.5%. and atrial fibrillation in 1.1%. Blood pressure was uncontrolled (>140/90) in 46% of stroke survivors. Among men 71.2% used tobacco and 30% used alcohol, while among women 38.2% used tobacco and none used alcohol. Only 40.8% of stroke survivors were receiving antihypertensive medications, while 10.6% were on antiplatelet agents and 4.9% were on statins. In a multivariate analysis, age <50 years (OR 0.2, 95% CI 0.1-0.5), male sex (OR 0.2, 95% CI 0.2-0.8) and lower economic status (no assets vs four assets; OR 0.3, 95% CI 0.1-0.9) were associated with lower odds of receiving medications for secondary prevention of stroke. **Conclusions**: There were significant gaps in secondary prevention of stroke in rural Gadchiroli. Healthcare programmes for secondary prevention of stroke in rural areas will have to ensure that blood pressure is adequately controlled, alcohol and tobacco cessation is promoted and special attention is paid to those who are younger, men and economically weaker.



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Keywords

secondary prevention, stroke, rural, India, community-based, survey



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Introduction

Stroke is the third leading cause of death globally¹. The burden of stroke has now shifted from high income countries (HICs) to low- and middle-income countries (LMICs) like India and 75% of all stroke deaths now occur in these countries². In India close to 700,000 patients died due to stroke in 2016³. Recent studies suggest that stroke has also emerged as a public health problem in rural India where two thirds of India's and about 12% of world's population lives^{4–7}. In a study from central India, stroke was the leading cause of death in a rural community⁴. Prevalence and mortality rates and overall disease burden due to stroke also remain high in rural India^{3,5,6,8}. These data indicate that strategies are urgently needed to reduce the burden of stroke in rural India where healthcare services are often inadequate.

Acute stroke care in the form of thrombolytic therapy and stroke units can improve outcomes after stroke^{9,10} but such care is often not available in rural India¹¹. Therefore, primary and secondary prevention of stroke becomes an important strategy to reduce preventable mortality and disability due to stroke¹². Among primary and secondary prevention, secondary prevention could be relatively easier to achieve from health systems perspective given that patients visit a healthcare facility after acute stroke and the motivation to take medicines for secondary prevention could be higher. However, the status of secondary prevention among stroke survivors in rural India remains largely unknown.

In this study, we assessed the status of secondary prevention among stroke survivors by evaluating prior diagnosis of risk factors, current use of tobacco and alcohol, blood pressure control and use of medications for secondary prevention of stroke in a rural area of Gadchiroli district in central India.

Methods

Ethical statement

The cluster randomized controlled trial under which the study was nested was approved by the institutional ethical committee of SEARCH and the trial is enrolled in the Clinical Trials Registry of India (CTRI/2015/12/006424, 08/12/2015). During the screening survey, verbal consent was obtained from individuals, while written informed consent in the local language was obtained from patients by the physician before collecting information and conducting clinical examination. Consent was obtained for participation in the study and use of data without revealing personal details. Participants were also informed about their freedom to quit at any stage of data collection. Confidentiality of all information obtained was maintained. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Study area

This community-based cross-sectional survey was conducted in Gadchiroli district in central India (Figure 1) which has a total population of 1,072,942 as per the Indian National Census conducted in $2011^{3,13}$. Within this district, 93% of the population lives in rural areas and 38.2% of the population is tribal. The literacy rate of the district is 66.03%. Subsistence farming and farm-labour are the main occupations¹⁴.

Healthcare in the district is provided through the government healthcare system, private practitioners and a few voluntary organizations. There is only one neurologist (YK) and one computerized tomography (CT) scanner in the entire district and facilities to give intravenous tissue plasminogen activator (t-PA) after acute stroke are not available. A large number of informal or unskilled providers also treat various symptoms and are preferred by villagers given their easy availability and accessibility.

Society for Education, Action and Research in Community Health (SEARCH) is a non-governmental organization working in Gadchiroli district since 1986. It has a demographic surveillance system in 86 villages distributed in three clusters of the district: Gadchiroli, Armori and Chamorshi (Figure 1). SEARCH has a population register in these villages which is updated yearly and all births and deaths are recorded.

Sample size

The present study was nested in a cluster randomised controlled trial to assess the effect of a community-based intervention to reduce stroke deaths in rural Gadchiroli and was a part of a baseline assessment of risk factors and secondary prevention of stroke among stroke survivors¹⁵. The trial was conducted in 64 villages selected randomly from 86 villages in the service area of SEARCH in Gadchiroli district. Out of these 64 villages, 32 villages each were randomised to the control and the intervention arm. Individuals were eligible to participate in the study if they were residents of these 64 villages and were prepared to give consent.

Data collection

The details of the data collection method are described previously⁵. Briefly, stroke patients were identified in the community by a three-stage cross-sectional survey. In the first phase, trained community health workers of SEARCH conducted a house-to-house survey from March 2016 to May 2016 using a validated questionnaire to screen the population for symptoms of stroke⁵. The questionnaire inquired about anyone in the family ever having: a) weakness on one side of the body, b) numbness on one side of the body, c) weakness of face, or d) slurring of speech. Stroke was suspected if any one or more of these symptoms were acute in onset and lasted >24 hours. The questionnaire was evaluated locally in an earlier study and had sensitivity of 85% and specificity of 99% for diagnosing stroke5. In the second phase of the study, patients suspected of having stroke were evaluated by a trained physician by making home visits from September 2016 to October 2017. Stroke was defined according to the World Health Organization's clinical definition as a focal (or at times global) neurological impairment of sudden onset, lasting >24 hours (or leading to death), and of presumed vascular origin¹⁶. The physician examined documents available with the

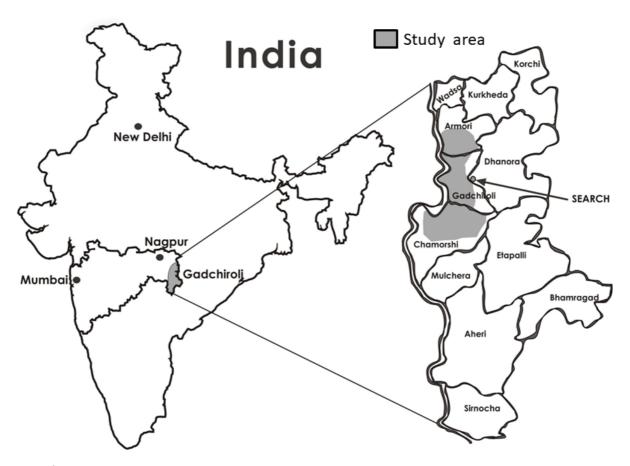


Figure 1. Study area.

patients to collect information on prior medical investigations and diagnoses of risk factors for stroke, inquired about current medication use, measured blood pressure and conducted clinical examination to confirm the diagnosis of stroke. Hypertension was defined as blood pressure >140/90 mm Hg. The information was collected using a structured questionnaire¹⁷.

In the third phase of the study, patients whose diagnosis of stroke was unclear were evaluated by an external neurologist not associated with the trial from August 2017 to October 2017 to confirm the diagnosis of stroke.

Statistical analysis

The information about the population in the 64 villages was obtained from the population register of SEARCH. We analysed group mean differences using the Student's t-test and differences in percentages using the chi-square test. Logistic regression was used to examine the factors associated with use of any medication for secondary prevention of stroke with age, sex, education and economic status as independent variables. Data were analyzed using statistical software Stata version 10 (College Station, TX, USA). We followed STROBE guidelines for observational studies to report our findings.

Results

A total of 265 stroke survivors were identified after screening 74,095 individuals living in 64 villages (Figure 2). Out of these, 102 (38.5%) were women and 163 (61.5%) were men¹⁷. The demographic features of the stroke patients are shown in Table 1. The mean age of the patients was 61.9 years. The majority of the patients were illiterate with a higher number of women being illiterate than men (85.3% vs 33.1%, p<0.001). Regarding occupation, 47.2% were farmers and farm labourers, 35.4% were retired or not working and 14.7% were home makers. Household assets as an indicator of socioeconomic status are as shown in Table 1.

Among risk factors for stroke, hypertension was previously diagnosed in 152 (57.4%) and diabetes in 26 (9.8%). Very few patients were diagnosed with hyperlipidaemia (0.4%), ischaemic heart disease (1.5%) and atrial fibrillation (1.1%) (Table 2).

Among 152 patients with previous diagnosis of hypertension, blood pressure was uncontrolled in 84 (55.3%) patients. Out of 113 stroke patients without prior diagnosis of hypertension, 38 (33.6%) were found to be hypertensive during evaluation.

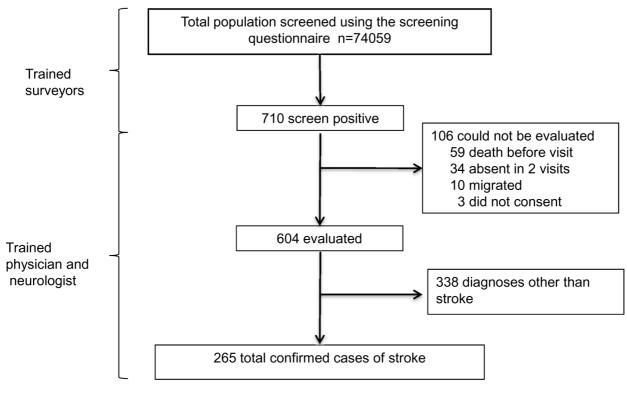


Figure 2. Flow diagram of the study scheme.

Collectively, 190 (71.7%) patients had prior diagnosis of hypertension or hypertension at the rime of evaluation. Blood pressure was uncontrolled (>140/90) in 122 (46%) stroke patients [52 (50.9%) women vs 70 (42.9%) men, p=0.2].

Close to three quarters of men (71.7%) and more than a third of women (38.2%) were using tobacco, mostly smokeless tobacco. About one third (30%) of male stroke survivors were consuming alcohol (Table 2).

Although prior diagnosis of hypertension was made in 152 (57.5%) stroke survivors, only 108 (40.8%) were receiving any antihypertensive medications, with significantly more women (51%) receiving the treatment than men (34.4%, p=0.007) (Table 3). Only 10.6% of patients were receiving antiplatelet agents and even less (4.9%) were receiving a statin. Together, 117 (44.2%) stroke patients were receiving either an antihypertensive, antiplatelet or statin. In multivariate analysis, age <50 years (OR 0.2, 95% CI 0.1-0.5), male sex (OR 0.2, 95% CI 02-0.8) and lower economic status (no assets vs four assets; OR 0.3, 95% CI 0.1-0.9) were associated with lower odds of being on an antihypertensive, an antiplatelet agent or a statin (Table 4).

Discussion

We found a significant gap in secondary prevention of stroke in this rural community despite stroke being a leading cause of death. Close to two thirds of stroke patients were diagnosed with hypertension, about one in twelve patients were diagnosed with diabetes, while few were diagnosed with hyperlipidaemia, heart disease or atrial fibrillation. Less than half of the patients were using antihypertensives and 10% or less patients were on antiplatelet medications and statins. Blood pressure was uncontrolled in close to half of all patients. To our knowledge, this is the first community-based study to evaluate use of medicines for secondary prevention of stroke in a rural community in India. It provides important insights regarding challenges to stroke prevention in a rural region of India where stroke has emerged as a public health priority.

Healthcare for stroke patients remains a challenge in rural India due to difficulties in accessing preventive care for non-communicable diseases. In our study, 57.4% of stroke patients were diagnosed with hypertension. This is an encouraging finding given that the study was conducted in one of the most underdeveloped districts of India. In previous population-based studies on stroke from relatively affluent rural areas of India, close to 90% of stroke patients had hypertension^{18,19} while in studies from rural Bangladesh and South Africa, 67.3% and 71% patients had hypertension, respectively^{20,21}. Diagnosis of diabetes, hyperlipidaemia and ischaemic heart disease was infrequent in our study compared to reports from other community-based studies in rural India, where close to 50% patients had diabetes, 25% patients had hyperlipidaemia and 5-10% patients had atrial fibrillation^{18,19}. However, these studies were conducted in

Table 1. Demographic characteristics of the studypopulation.

	Women (n=102)	Men (n=163)	Total (n=265)
%	38.5	61.5	100
Mean age in years (SD)	61.8 (14.5)	61.9 (13.2)	61.9 (13.7)
Education			
Illiterate	87 (85.3)	54 (33.1)	141 (53.2)
Literate without schooling	1 (0.9)	1 (0.6)	2 (0.8)
Primary	6 (5.9)	61 (37.4)	67 (25.3)
Secondary and higher	8 (7.8)	47 (28.8)	55 (20.6)
Occupation			
Farming and labour	33 (32.4)	92 (56.4)	125 (47.2)
Home maker	39 (38.2)	0 (0.0)	39 (14.7)
Retired or not working due to other reasons	30 (29.4)	64 (39.2)	94 (35.4)
Service/business	0 (0.0)	7 (4.3)	7 (2.7)
Household assets			
Own farm land	88 (86.3)	139 (85.3)	227 (85.7)
Mobile phone	62 (60.8)	115 (70.6)	177 (66.8)
Television	47 (46.1)	87 (53.4)	134 (50.6)
Motorcycle	14 (13.7)	38 (23.3)	52 (19.6)

Table 2. Risk factors diagnosed among patients with stroke.

Risk factors	Women (n=102)	Men (n=163)	Total (n=265)
Prior diagnosis of hypertension	67 (65.7)	85 (52.1)	152 (57.4)
Prior diagnosis of diabetes	8 (7.8)	18 (11)	26 (9.8)
Prior diagnosis of hyperlipidaemia	0 (0.0)	1 (0.6)	1 (0.4)
Prior diagnosis of ischaemic heart disease	2 (2.0)	2 (1.2)	4(1.5)
Prior diagnosis of atrial fibrillation	2 (2.0)	1 (0.6)	3 (1.1)
Current tobacco use	39 (38.2)*	116 (71.2)	155 (58.5)
Current smokeless tobacco use	39 (100)	108 (93.1)	147 (94.8)
Current alcohol use	0 (0)*	49 (30)	49 (18.5)

*p<0.05 for difference between women and men.

Table 3. Medications used for risk factor control among stroke patients.

Medication	Women (n=102)	Men (n=163)	Total (n=265)
Any antihypertensive drug	52 (51)*	56 (34.4)	108 (40.8)
Any antiplatelet medication	9 (8.8)	19 (11.7)	28 (10.6)
Any statin	5 (4.9)	8(4.9)	13 (4.9)
Any antihypertensive/ antiplatelet medications or statin	55 (53.9)*	62 (38)	117 (44.2)

*p<0.05 for difference between women and men.

Table 4. Predictors of use of any medication for secondary prevention of stroke.

	n	Taking medicines for secondary prevention of stroke	OR (95 %CI)
Age			
>50 years	223	110	Reference
≤ 50 years	42	7	0.2(0.1-0.5)
Sex			
Women	102	55	Reference
Men	163	62	0.4 (0.2-0.8)
Education			
Literate	124	51	Reference
Illiterate	141	66	0.8(0.4-1.5)
Number of household assets			
4	47	30	Reference
3	68	29	0.4 (0.2-0.9)
2	67	25	0.4 (0.2-0.9)
1	64	26	0.4 (0.2-0.9)
0	19	7	0.3(0.1,0.9)

academic medical centres and thus the likelihood of diagnosis of these risk factors would be high. The lower rates of diagnosis of risk factors in our study could be due to lack of access to health-care in this district or that the study population is in an earlier phase of epidemiological transition where risk factors such as diabetes and hyperlipidaemia have not yet become common²².

In resource poor settings where acute care for stroke is not easily available, secondary prevention of stroke becomes important to avoid preventable mortality. Longitudinal cohort studies have shown that the risk of cardiovascular events and death remains high for at least 10 years following stroke or transient ischaemic attacks^{23,24}. The annual risk of vascular events was 2-5% in these studies^{23,24} and the 10-year risk of death was $43\%^{24}$. However, secondary prevention of stroke remains inadequate worldwide²². In the Agincourt cohort in rural South Africa, 71% of stroke survivors had hypertension but only 8% were taking antihypertensive treatment²¹. The PURE study assessed the use of medicines for secondary prevention of cardiovascular diseases in multiple countries. In this study, among patients with stroke in rural areas of LMICs, 33.6% were on bloodpressure lowering drugs, 27.3% were on antiplatelet agents and 2.4% were on statins²². Comparatively, in our study, a somewhat higher percentage of stroke patients were on antihypertensive therapy (40.8%) and statins (4.9%) but a lower percentage were on antiplatelet agents (10.6%). However, it needs to be noted that the PURE study was conducted from 2003-2009 while our study was conducted in 2016 so it would be expected that a higher number of patients would be receiving these treatments. The pattern of relatively higher use of blood pressure lowering agents and lesser use of antiplatelet agents and statins that was observed in the PURE study was also found in our study. Given that close to 65% of strokes in rural areas of India are ischaemic¹⁹, use of antiplatelet agents and statins in 10% or less stroke patients indicates a significant gap in the secondary prevention of stroke.

There are several barriers to use of medicines for secondary prevention of stroke in rural areas of LMICs. Availability and affordability of medicines for prevention of stroke are important barriers²⁵. A clinic-based prospective observational study from eastern India found that close to 35% stroke patients discontinued secondary preventive treatment of stroke over a two-year follow up period26. The factors associated with discontinuation of treatment were lower socioeconomic and educational status, lower awareness, haemorrhagic stroke, higher daily cost of treatment and longer distance to the clinic²⁶. In our study too, lower socioeconomic status was associated with lower likelihood of use of medicines for secondary prevention of stroke. In addition, lack of availability of laboratory and imaging services in the district, low awareness among primary care physicians and reliance on informal providers could have contributed to the gap in the secondary prevention of stroke in our study. We are testing a community-based healthcare intervention to address these barriers15.

Among stroke patients, significantly more women were receiving antihypertensive treatment compared to men (51 % vs 34.4%, p<0.05) and the same was true for being on an antihypertensive, antiplatelet treatment or statins (53.9% vs 38%, p<0.05). These findings are in agreement with previous studies on hypertension where more women were taking antihypertensive medications than men^{27–29}. The potential reasons for this difference could be increased contact of women with the healthcare system during pregnancy²⁷ and more concern about health among women leading to a higher motivation to take medicines regularly.

Hypertension is the most important risk factor for stroke³⁰. Despite availability of medicines to control blood pressure, blood pressure control often remains inadequate²⁷. As far as blood

pressure control among stroke survivors is concerned, hardly any population-level information is available from LMICs³¹. In our study blood pressure remained uncontrolled in close to half of the stroke patients. This indicates that in addition to making medications available, there is a need to have adequate follow up to ensure that blood pressure is adequately controlled among stroke survivors who have hypertension.

In order to counter the rising burden of chronic non-communicable diseases, the Government of India has launched the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS)¹⁷, which is one of the largest programmes for prevention and control of chronic diseases in the world. It provides medications free of charge to patients at primary health centres. While this programme actively screens for hypertension, diabetes and cancers it is not currently screening for patients with stroke for secondary preventive treatment. Our findings suggest there is a need to actively seek patients with stroke in rural communities and start such patients on medications to prevent recurrence of cardiovascular diseases and death. As the medications are provided free in this programme, it helps to address the barrier of affordability. Providing preventive treatment at village level under this programme could help improve medication compliance and continuity. Our findings of lower use of stroke prevention medicines among those <50 years, men and those with lower socioeconomic status highlights that such patients would need special attention under the NPCDCS programme in rural areas.

Tobacco and alcohol are important risk factors for stroke³⁰. In our study, close to 70% of men and 40% women stroke patients were using tobacco, mostly smokeless tobacco. Tobacco use was rare among stroke patients in a population-based study in a rural area of Northern India, where only 3% stroke patients were using tobacco¹⁹. On the contrary, in a study from southern India and rural Bangladesh, close to 40% of stroke patients were using tobacco^{18,20}. One in three men with stroke used alcohol in our study. These findings are similar to those from Northern India, where 20% stroke patients were using alcohol¹⁹. Our findings indicate an urgent need to reduce tobacco and alcohol consumption among stroke survivors.

A major strength of our study is the population-based sample of stroke survivors from a well-defined population in a demographic surveillance site. There are also certain limitations. Stroke cases were diagnosed using validated clinical diagnostic criteria as brain imaging was not easily available and affordable in this area. Also, we only recorded healthcare seeking among stroke survivors and not among those who died due to stroke. Some of the screen positive individuals died before evaluation by the physician and it is possible that some of them had stroke and their information was lost. We used self-reported retrospective information regarding treatment received for stroke. However, this information reported by stroke survivors was verbally confirmed by caretakers and consistent with the pattern observed by SEARCH which has been working in this area for more than 30 years. Also, we could measure only blood pressure and blood tests were not conducted given the reluctance of people to give blood for testing. Furthermore, though our study was conducted in a rural area of India, access to healthcare and

socioeconomic status could be variable in various rural regions of India. This will affect use of medicines for secondary prevention for stroke. However, given that secondary prevention of stroke remains suboptimal even in the developed countries²², our findings are likely to be true in other rural regions of India as well.

Conclusions

Secondary prevention of stroke was suboptimal in rural Gadchiroli. The use of medications to prevent stroke was low, close to half of the stroke patients had uncontrolled blood pressure and use of tobacco and alcohol was common. These findings, in the context of high prevalence and mortality due to stroke, highlight an urgent need to improve secondary prevention of stroke in rural India.

Data availability

Underlying data

Figshare: Gaps in secondary prevention among stroke survivors in rural Gadchiroli, India: a community-based cross-sectional study. https://doi.org/10.6084/m9.figshare.13134782.v1¹⁷.

This project contains the following underlying data:

- kalkonde_et_al_data_secondary_prevention.xlsx (Data dictionary with demographic and clinical data)

Extended data

Figshare: Gaps in secondary prevention among stroke survivors in rural Gadchiroli, India: a community-based cross-sectional study. https://doi.org/10.6084/m9.figshare.13134782.v1¹⁷.

This project contains the following underlying data:

- Kalkonde_et_al_physician_questionnaire.pdf (Physician questionnaire)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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Giridhara R. Babu 匝

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This is a very good contribution to the prevention efforts of NCDs in India. The study outlines the significant gaps in secondary prevention of stroke in rural Gadchiroli and offers solutions for future courses of action. It is unfortunate to see the focus only on curative aspects in public discourses and advocacies, often ignoring the prevention aspects. Therefore, this is a valuable contribution to strengthen public health programs in the country if the policymakers take cognisance of the importance of universal coverage of persons with high blood pressure. Similarly, the article underscores the importance of reduction of behavioural risk factors including alcohol and tobacco in rural areas.

Some of the minor review suggestions are provided below are adequately controlled, alcohol and tobacco cessation are promoted and special attention is paid to those who are younger, men, and economically weaker.

SI num Section Comments

Abstract:

- 1. Aim of the study can be mentioned in the abstract.
- 2. The role of surveyor and physicians are not clear. Does the surveyor refer the screened individuals to physicians or it was a house visit? Physician administered the questionnaire or survey staff? What are the risk factors? Please explain.

Introduction:

1. State the aim and objective of the study.

Methods:

- 1. Please provide the details about consent to participation and ethical consent?
- 2. Please define the term stroke survivor in the methods or eligible population.
- 3. Inclusion and exclusion criteria can be mentioned.
- 4. Sample size: The trial was conducted in 64 villages, it will help if the sample size is provided in terms of the number of persons in the area (men/women).
- 5. Data Collection: The interval of 1st phase, 2nd phase, and 3rd phase of the study is more? (1st phase ends in May and the second phase starts from September). History on alarming symptoms was collected in the 1st phase of the survey, where the participants may require immediate referral based on the severity of signs or symptoms. How does this interval justify ethically?
- 6. Data collection: What is the intervention given to the intervention group and how does it differ from the control group?
- 7. Data collection: Please include the section of parameters assessed during the data collection such as risk factors and medication history.
- 8. Data collection: Please mention who has done the data collection and training on data collection.
- 9. Data collection: Please provide information on the tools are used to measure the stroke?
- 10. Data collection: Which medical investigations conducted?
- 11. Data collection: Which instrument is used to collect BP measures digital/manual? Details regarding calibration are needed
- 12. Statistical analysis: Expand abbreviations on first use STROBE expand.
- 13. The method section does not include information on diabetes, hyperlipidemia and IHD diagnosis.

Results:

- 1. Who are the eligible participants? Why is a community based survey conducted if the purpose is to interview stroke survivors?
- 2. Please include which criteria were followed for classifying blood pressure? Please include the citation.
- 3. Age group specified wrongly (>=50years) in the description and please mention statistical significance in terms of p-value.
- 4. Table: Please mention n (%) in table heading for table 1,2,3

Ethical statement:

1. Expand abbreviation for SEARCH

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound? $\ensuremath{\mathsf{Yes}}$

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results? $\ensuremath{\mathsf{Yes}}$

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Non communicable diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 04 December 2020

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Rohina Joshi 匝

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This is a well written and much needed paper about the prevalence of stroke from a rural region of India. The methods and data analysis are well described. The results are presented in detail, and strengths and limitations are described well. I have the following questions/comments:

1. The CHWs conducted the survey in 2016 and the physician assessed the individuals suspected to have strokes in 2017 (1 year later), were incident cases added to the survey?

- 2. Also, the survey may have missed minor strokes/strokes that result in death which would lead to an undercount.
- 3. While the Authors have given some context re public health facilities, it would be useful for the reader to understand the available health care facilities. Does the local PHC pharmacy store essential medicines for hypertension/ DM/ high cholesterol? Is there a 104 service in the villages?
- 4. Please include the age group of the surveyed population (74,095). Did this include population above 30 years or 18 years old adults?
- 5. Minor typo in results rime, instead of time.

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results? $\ensuremath{\mathsf{Yes}}$

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Health Systems

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 03 December 2020

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🖊 🛛 Chetan Vekhande

Division of Neurology, Medicine, University of Alberta, Edmonton, AB, Canada

Mahesh Kate ២

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Secondary Stroke Prevention in Rural and Tribal Region: When Treatment Gaps are as Wide as Valleys.

The authors should be commended for conducting an important study, which quantifies the unmet needs of secondary stroke prevention in rural and tribal regions.

The authors conducted a survey in 64 villages with a total population of 74,095 people to identify people in a three-tiered manner. First, a community health worker went house to house with a validated questionnaire. Patients with suspected stroke were then seen by trained physicians by home visits to diagnose stroke. There was additional confirmation for some borderline cases by an external neurologist if required. A total of 265 stroke survivors were identified with a mean age of 62 years and 62% were male. In patients known to have high blood pressure >50% were uncontrolled. Current tobacco use was noted on 59%. Diabetes, dyslipidemia, and atrial fibrillation were less likely to be diagnosed. Interestingly more women were likely to be on medication compared to men.

A similar study has been conducted in rural Punjab (Northwest region of India) in Ludhiana district in 164 villages with a population of 173, 852¹. A total of 359 first-ever strokes were identified with a mean age of 62 years and 50% were male. The prevalence of hypertension was 89% and current tobacco use at 24%. A small percentage of patients were on medication and had controlled blood pressure. Half (50%) of the stroke patients visited unqualified medical practitioners for acute stroke care.

Though pharmacological management is pivotal for secondary stroke prevention, nonpharmacological measures are important adjuncts as well. Few may argue that they are equally important. In the INTERSTROKE study lack of regular physical activity and diet poor in fruits and vegetables was associated with 58% of population attributable risk of stroke². In Ludhiana rural stroke Registry 17% of patients with first-ever stroke had a sedentary lifestyle and 59% had a high degree of unsaturated fat consumption. In the Gadchiroli population in the current study, 35% were retired and not working. Data about diet is not available.

Both studies (Gadchiroli and Ludhiana) highlight an important 'valley-sized' health care gap in stroke prevention in rural regions. According to the World Bank data (2019), 44% of the world population resides in rural regions this number in India is 60%. In the USA a total of 63% of areas with health care professional shortage were in rural regions (ruralhealthinfo.org). According to the Centre for Disease Dynamics, Economics and Policy (CDDEP) report in 2019 India has a shortage of 600,000 doctors and 2 million nurses. The shortage is magnified in rural and tribal regions.

In addition to the barrier of poor access to health care professionals, the lack of trust in modern systems of health care is evident. This is partly due to costs of treatment and lack of communication between the healthcare providers and patients.

Another important barrier for healthcare delivery and access is disability associated with stroke. We do not have information regarding the modified Rankin scale or some disability assessment measure from the current study. Depending on the premorbid status, stroke severity and associated comorbidities the disability is variable with >50% having some persistent deficits.

Novel policy intervention will be required to bridge these gaps. The authors are conducting a tasksharing trial with mobile outreach clinics and community health workers with the aim to prevent stroke-associated mortality³. In Ludhiana Rural stroke Registry a trial to improve control of hypertension in stroke survivors with task shifting measures with ASHA (Accredited Social Health Activists) and remote physician was conducted recently⁴. A total of 140 patients were randomised to ASHA assisted BP control or standard care available in the region. The authors noted a dramatic 28 mmHg systolic drop in blood pressure in the intervention arm, this was primarily due to the increase uptake in medication. This needs replication in other regions to see clinical effectiveness i.e. a decrease in stroke and mortality. This data will soon be available from the Gadchiroli intervention study.

The healthcare disparity in rural regions poses a formidable challenge. It is important to identify and quantify them which the current study has done. Task sharing may be an effective tool to help us address it, but it remains to be proven in randomised control study.

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Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke, Clinical trials, Neurology, Patient education, secondary stroke prevention

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 01 December 2020

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Rita Krishnamurthi 回

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This is a cross-sectional study of a subset of participants enrolled in a randomized controlled trial. The setting is rural central India. The parent study screened trial participants for stroke risk factors and stroke. The current study aimed to evaluate the status of stroke risk factors in the sample of participants diagnosed with stroke based on a 3-tier system of identification of stroke cases. The premise is that people at high risk of secondary stroke and the associated morbidity and mortality are more easily identifiable and able to be targeted for secondary prevention. The findings showed that just over 57% of the population were diagnosed with hypertension, but only about 41% were receiving any medications. Other risk factors such as diabetes and hyperlipidemia were diagnosed in a very small proportion of the sample. The overall findings suggest significant gaps in secondary prevention, particularly in younger men and those with lower socioeconomic status. These are important findings that, if acted upon, can lead to significant improvements in outcomes.

The authors are to be commended on conducting this research in a highly vulnerable yet challenging community setting, where even the most basic level of healthcare is not easily available to large sections of the community. The mean age of stroke is relatively low (68 years) in this population.

The work is well presented, clearly written, and cites the relevant literature. The study design is appropriate and acknowledges the limitations of the study settings, particularly in terms of stroke diagnosis. The authors provide adequate detail in the paper or via the references to their related work. The analysis is described clearly. The full data is not provided in this manuscript, but references provide links to associated data. I am assuming raw data may be requested.

The Discussion offers sound and reasonable explanations for findings while describing limitations. The one missing element may be suggestions for the use of this data to make an impact on stroke burden.

The authors also mention that this particular population may yet be in the early stages of epidemiological transition and may have a lower prevalence of diabetes and hyperlipidemia than the overall population of India. This may suggest targeted prevention strategies aimed predominantly at hypertension and alcohol use.

I have the following queries:

- From the screening questionnaire, it is unclear if minor strokes were able to be picked up. Were vision problems and any cognitive deficits also screened for?
- From the parent paper (Ref #15) it is seen that participants were screened for stroke risk factors in the community. While screening for hypertension is simple, and stroke diagnoses were established with a questionnaire, it is not clear how the presence of diabetes was confirmed. Were further tests conducted by a physician after urine tests were done?
- How was the dispensation of, and compliance to prescribed medications tested?
- In terms of alcohol and tobacco as risk factors, could the authors clarify whether the type of alcohol used (e.g. homemade or potentially toxic) leading to worse outcomes in men?
 Similarly is there any data on the relative risk of smokeless tobacco versus tobacco smoking for stroke?
- It's mentioned on Page 7 that 65% of strokes are ischemic. This is a lower proportion than would be expected (usually around 75-85%). Could the authors offer any explanation for this in this sample? What would the implications for secondary prevention be for 35% of people with haemorrhagic stroke? For example, would targeting alcohol use be more beneficial in this group.
- The authors point to encouraging government actions to target NCDs that could be a
 possible avenue to target stroke secondary prevention with the dispensation of free
 medications. What mechanisms are in place to allow the delivery of this programme to this
 population?
- Interestingly, it is mentioned that patients are often reluctant to give blood. Is there a role CHW could play in also addressing some of these issues, including low awareness which was also mentioned? For example what specific lifestyle risk factors for hypertension (e.g. high salt intake) could be targeted for prevention?
- Minor typo Page 5 2nd line (rime instead of time)

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? Partly

Are the conclusions drawn adequately supported by the results? $\ensuremath{\mathsf{Yes}}$

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke epidemiology, stroke prevention

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.