Original Article

Exploring Gender-Specific Stroke Risks in Diabetic Patients: Insights from a Retrospective Analysis of Contributing Factors

Abstract

Background: Diabetics face a higher risk of stroke, and the numbers are rising. In men, gender-specific factors such as lower age and body mass index, and in women, obesity and psychosocial stress contribute to a high risk of stroke. For effective prevention, it is crucial to identify and address these risk factors. **Materials and Methods:** The electronic medical records between January 2017 and December 2021 of previously diagnosed diabetic patients were obtained from a tertiary care hospital in Mangaluru, South India. It was scrutinized from (January 3, 2022, to March 12, 2022) using a validated checklist consisting of 28 items to identify the contributing factors of stroke (CVI = 0.9 and Cronbach's alpha value = 0.83) Descriptive statistics and inferential tests such as the Chi-square, Fisher's exact, and odds ratio (OR) were used. **Results:** Out of 3152, 569 suffered a stroke, while the remaining 2583 did not have a stroke. Out of 569, the majority were males (63.9%). It was found that coronary artery disease (CAD) (OR: 1.43, 95% confidence interval (CI): 0.10–2.07), use of alcohol (OR: 1.58, 95% CI: 1.09–2.29), and smoking (OR: 1.9, 95% CI: 1.29–2.80) were associated with the risk of stroke in men. **Conclusions:** The present study found that CAD and unhealthy habits such as the use of alcohol and smoking have a significant influence on the development of stroke among men and women with diabetes. Effective implementation of programs through early detection, comprehensive management, and prevention requires collaboration among healthcare professionals, researchers, policymakers, and educators.

Keywords: *Coronary artery disease, diabetes mellitus, retrospective studies, stroke*

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Introduction

Developing Nations like India and many other countries are faced with the problems of not only communicable diseases but also non-communicable diseases. Stroke is the leading cause of disability and death among the non-communicable diseases. Diabetes is a major modifiable risk factor for stroke. Diabetes causes microvascular and macrovascular changes, leading to acute and chronic complications, the major one being stroke.[1] Stroke is the lack of oxygen to the brain cells due to obstruction or rupture of an artery to the brain, causing sudden death of the brain cells.[2] Despite significant declines in age-standardized rates, particularly among those over 70 years old, the annual number of strokes and fatalities from stroke climbed significantly from 1990 to 2019. High body mass index was the risk factor for stroke that increased the fastest between 1990 and 2019. The stroke burden is likely to continue rising worldwide if effective primary prevention techniques are not urgently implemented, especially in low-income nations. A systematic analysis concluded that from 1990 to 2019, the absolute incidence of stroke increased by 70%, the prevalence of stroke increased by 85%, and death from stroke increased by 43%.[3] In 2016, there were 13.7 million new incidences of stroke globally; 87% of them were ischemic stroke, and fewer than 5% had an acute ischemic stroke.[4] The incidence of stroke in India ranged from 108 to 172 among 100,000 people per year.[5] Previous studies show factors such as smoking, a sedentary lifestyle, a high-calorie diet, and diabetes mellitus (DM) as independent risk factors for stroke. After an individual is diagnosed with DM, the lifestyle changes they make may lead to a variation in the association between lifestyle factors and stroke among diabetic patients and the general population.[6] DM is a unique noticed factor

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that raises the risk of stroke, and it can be avoided with consistent monitoring, exercise, dietary restriction, and the use of antihyperglycemic drugs.[7] Studies have shown that most stroke was seen in men (72.3%), who were aged over 50 years (75%), and obese (14.6%).[8] Factors such as HTN, smoking, hyperlipidemia, familial history of stroke in type 2 DM (T2DM), and physical inactivity increase the risk of stroke.[9]

Despite variations in other cardiovascular risk factors, women with diabetes have a markedly increased risk of stroke compared to males.[10] After a stroke, the fatality rate among diabetic patients is greater among women.[11] Thus, the researchers are interested in finding out those specific factors that increase the mortality among diabetic women compared to diabetic men affected with stroke. Literature shows that the incidence of stroke is higher in men than women, and men suffer their first stroke earlier than women. However, women have more severe strokes compared to men, and hence, the functional outcome is worse. Women present with unusual symptoms of stroke, such as weakness, fatigue, headache, or lowered consciousness. Male stroke survivors receive good quality care from their spouses. In contrast, female stroke survivors depend on external sources for rehabilitation after stroke, resulting in depression and low QOL following the stroke.[12] A systematic review and meta-analysis reported that among COVID-19 patients, acute CVA was seen in 1.4% (95%), acute ischemic stroke (87.4%) was the most common manifestation, and intracerebral hemorrhage was 11.6%. COVID-19 patients developing cerebrovascular conditions were seen in older adults with HTN, T2DM, and coronary artery disease (CAD).[13] A systematic review and meta-analysis revealed that female-related components that lead to an increased risk of ischemic stroke were disorders related to hypertension in pregnancy. For hemorrhagic stroke, the factors were gestational hypertension and late menopause.[14]

Diabetes increases the risk of stroke by 1.5 times, and mortality due to cardiac conditions or stroke is twice as high compared to those without diabetes.[15] Over the decades, there has been a reduction in the stroke load, but the increase in the rate of diabetes threatens to reverse this. An increased level of glucose in the body leads to a greater risk of stroke.[6] Researchers hope to determine the causes of stroke and the gender-specific risk of stroke among diabetic individuals through this investigation. Understanding gender-based factors is essential to minimize diabetes risk factors as well as poststroke complications. Exploring the gender-specific factors would strengthen early preventive measures such as lifestyle interventions for both male and female diabetics. Hence, the present study was conducted to identify the prevalence of common and gender-specific risk factors for stroke in diabetic patients. The results will help us to identify the contributing factors of stroke among diabetic patients, bridge the gap of knowledge in this area among the South Indian population, and develop simple, cost-effective lifestyle interventions that would prevent stroke in diabetic patients. Hence, a retrospective analysis of risk factors for stroke in both male and female diabetics was undertaken in this study. Therefore, the present study aims to find out those factors that cause differences in the age of occurrence, severity of symptoms, complications, and prognosis of stroke among male and female diabetics to help develop gender-specific interventions for its prevention.

Materials and Methods

Retrospective research design was conducted from January 3, 2022, to March 12, 2022, in a tertiary care hospital located in Karnataka, India, equipped with an electronic medical record (EMR) system. A demographic proforma and a checklist on the causes of stroke were the tools created for this investigation. The five components of the demographic proforma were gender, age, place of residence, food preferences, and BMI. Twenty-eight elements of the checklist identified the factors that contributed to stroke in people with diabetes. The investigator prepared the checklist based on the literature review and consultation with experts. The tools were validated by eight experts in the field and modified based on their opinions and ideas. The tool, along with the problem statement and objectives, was submitted to eight experts in the field of nursing and medicine. Opinions of the experts were obtained, and their suggestions were regarded in modifying the tools. The content validity index (CVI) was determined, and it was discovered that tool 1, the demographic proforma, had a CVI of 1, and tool 2, the checklist for stroke contributing factors, had a CVI value of 0.9. The tool was pretested on a small sample size of 50 records, which shared characteristics with the demographics studied. The tools—the demographic proforma and checklist for contributing factors of stroke—were found to be practical and easy to use. Cronbach's alpha was used to measure the internal consistency reliability, and the result was 0.83, which was deemed reliable.

Before data collection, formal written permission was obtained from the Medical Superintendent and In-charge of the Medical Records Department. The data collection process started on January 3, 2022, until March 12, 2022. EMR of diabetic data that met the inclusion criteria were scrutinized and recorded. The data that met the inclusion criteria were collected and scrutinized using a checklist of the contributing factors of stroke. The data were coded serially according to the time of admission. There were 9310 diabetic data, of which only 3152 met the inclusion criteria. Data from the EMR of 3152 diabetics that met the inclusion criteria were scrutinized based on the checklist for contributing factors of stroke and the baseline demographic proforma. The inclusion criteria included those who have had T2DM for more than 5 years and were admitted to the

hospital between January 2017 and December 2021. The diabetic data with medico-legal cases such as road traffic accidents, assaults, stab injuries, falls, and burns were excluded from the study.

The data were analyzed using IBM SPSS Statistics software (version 20) for Windows. The demographic proforma and contributing factors of stroke were analyzed using descriptive statistics. The association between the factors contributing to stroke among male and female diabetics was analyzed using the Chi-square test/Fisher's exact test. The significant contributing factors were further analyzed using an odds ratio (OR) at 95% confidence interval (CI) to predict the risk of occurrence of stroke among male and female diabetics.

Ethical consideration

The institution's scientific board and institutional ethics committee approved this study plan with the number NUINS/CON/NU/IEC/2020-21/1150 dated 24/05/21. The data collected were coded serially according to their time of admission.

Results

The demographic proforma of the data is reported in Table 1. Table 2 depicts the results of the contributing factors of stroke of the 3152 data categorized into data of diabetics with and without stroke. Table 3 shows that there is an association between CAD (0.05), use of alcohol (0.016), and smoking (0.001) with gender as the p values are < 0.05. Table 4 shows that there is an association between CAD (0.05), use of alcohol (0.016), and smoking (0.001) with gender as the p values are < 0.05. CAD significantly contributes to the development of stroke among male and female diabetics, as the OR (1.43) is higher than the lower limit of 95% CI (0.995). The use of alcohol influences the development of stroke in male and female diabetics as the OR (1.58) is more than the lower limit of 95% CI (1.087), and the p value (0.016) is < 0.05. The study also proved that smoking influences the development of stroke in males and females with diabetes as the OR (1.9) is more than the lower limit of 95% CI (1.286), and the p value (0.034) is < 0.05.

Discussion

In this study, the investigators aimed to investigate gender-specific stroke risks among diabetic patients by conducting a retrospective analysis of contributing factors. The present study found more male diabetic records, which follows a study's result involving 137 (50.6%) males and 134 (49.4%) females.[16] The results cannot be generalized as the present study includes more male diabetics than females. The findings of this study show that most of the data were from patients aged 41–60 years and living in urban areas. The current study showed that the majority were non-vegetarians with normal BMI. Similar studies

Table 1: Demographic variables of the diabetic data (*n*=3152)

Demographic variables		*n* (%)
Gender	Male	2013 (63.90)
	Female	1139 (36.10)
Age in years	<20	180 (5.70)
	21–40	425 (13.50)
	41–60	1447 (45.90)
	>60	1100 (34.90)
Area of living	Urban	1971 (62.50)
	Rural	1181 (37.50)
Dietary habit	Vegetarian	574 (18.20)
	Non-vegetarian	2034 (64.50)
	Mixed	544 (17.30)
Body mass index (kg/m^2)	<18.5	134 (4.30)
	18.5–24.9	981 (31.10)
	25.0–29.9	608 (19.30)
	>30.0	50 (1.60)
	Not recorded	1379 (43.80)

Table 2: Contributing factors of stroke among diabetics with and without stroke (*n*=3152)

Contributing factors	Data of diabetics with stroke (*n*=569) *n* (%)	Data of diabetics without stroke (*n*=2583) *n* (%)
Prior history of heart attack	10 (1.80)	91 (3.50)
Transient ischemic attack	10 (1.80)	22 (0.90)
Chronic kidney disease	183 (32.20)	942 (36.50)
Aneurysm	11 (1.90)	12 (0.50)
Sickle cell anemia	1 (0.20)	11 (0.40)
Obstructive sleep apnea	10 (1.80)	40 (1.50)
COVID-19 infection	42 (7.40)	113 (4.40)
Other comorbid diseases	350 (61.50)	1158 (44.80)
High blood pressure	442 (77.70)	1562 (60.50)
Atrial fibrillation	18 (3.20)	104 (4.00)
Coronary artery disease	192 (33.70)	757 (29.30)
Peripheral vascular disease	53 (9.30)	131 (5.10)
Acute myocardial infarction	22 (3.90)	120 (4.60)
Infective endocarditis	2 (0.40)	35 (1.40)
Structural abnormalities	30 (5.30)	123 (4.80)
Other cardiac disorders	24 (4.20)	84 (3.30)
Family history of stroke	81 (14.20)	53 (2.10)
Family history of diabetes mellitus	96 (16.90)	83 (3.20)
Use of alcohol	176 (30.90)	188 (7.30)
Use of tobacco	85 (14.90)	52 (2.00)
Smoking	147 (25.8) 0	161 (6.20)
Lack of physical exercise	5 (0.90)	41 (1.60)
Hormonal therapy	0 (0)	13 (0.50)
Use of anticoagulants	329 (57.80)	1078 (41.70)
Use of recreational/ over-the-counter drugs	1 (0.20)	5 (0.20)
High red blood cell count	2 (0.40)	8 (0.30)
Hyperlipidemia	303 (53.30)	193 (0.50)

Table 3: Association between contributing factors and gender among diabetics

Contributing Factors	Gender (*n*=569)		Chi-square test/ Fisher's exact test	*p*
	Male	Female		
Chronic kidney disease				
a. Yes	129 (68.90)	54 (29.51)	1.24	0.265**
b. No	254 (65.80)	132 (34.20)		
Other comorbid diseases				
a. Yes	233 (56.57)	117 (62.57)	0.23	0.634***
b. No	150 (68.49)	69 (31.51)		
High blood pressure				
a. Yes	296 (66.97)	146 (33.03)	0.11	0.745***
b. No	87 (68.50)	40 (31.50)		
Coronary artery disease				
a. Yes	119 (61.98)	73 (38.02)	3.74	0.05*
b. No	264 (70.03)	113 (29.97)		***
Family history of stroke				
a. Yes	55 (67.90)	26 (32.10)	0.02	0.903***
b. No	328 (67.21)	160 (32.79)		
Family history of diabetes mellitus				
a. Yes	59 (61.46)	37 (38.54)	1.798	0.180***
b. No	324 (68.50)	149 (31.50)		
Use of alcohol				
a. Yes	106 (60.23)	70 (39.77)	5.81	0.016*
b. No	277 (70.48)	116 (29.52)		***
Use of tobacco				
a. Yes	60 (70.59)	25 (29.41)	0.49	0.485***
b. No	323 (66.74)	161 (33.26)		
Smoking				
a. Yes	83 (56.46)	64 (43.54)	10.60	0.001*
b. No	300 (71.09)	122 (28.91)		***
Use of anticoagulants				
a. Yes	218 (66.26)	111 (33.74)	0.39	0.532***
b. No	165 (68.75)	75 (31.25)		
Hyperlipidemia				
a. Yes	196 (64.69)	107 (35.31)	2.03	0.154***
b. No	187 (70.30)	79 (29.70)		

*p<0.05, two-tailed. **Fisher's exact test. ***Chi-square test

have reported that those in the age group of more than 60 years are at more risk of developing stroke (74.2%); stroke was seen in patients from the urban area of living (69%), vegetarian people exhibited 60% lower chances of ischemic stroke and 65% for hemorrhagic stroke, and BMI was normal in 56.6%. However, an increased risk of ischemic stroke by 5% was observed for BMI > 20.[17-20] Diabetes and gender have a substantial interaction. However, data for dietary preference and BMI cannot be used to generalize the findings as there was no data on dietary preference and BMI in the current study.

Among the contributing factors of HTN, the use of anticoagulants, hyperlipidemia, alcoholism, CKD, smoking, familial history of stroke, and physical inactivity were elicited in the current study, which is consistent with a study report, where HTN is one of the most common causes of stroke (66.9%). Alcohol consumption was observed in 27.5%, smoking in 55%, and dyslipidemia in 50% of the samples.[21] Similar studies reported CKD (2.1%), familial history of stroke (12.3%), and physical inactivity (11.2%) as the factors contributing to stroke.[6] CKD was seen in most of the collected data, while in another study, it was reported only in 2.1%. CKD is a separate risk factor for stroke, and it can affect stroke risk in a variety of ways. The researcher feels that as all the data collected were those of diabetics, CKD is a risk factor for stroke and a chronic complication of diabetes. A study found an approximately 60%–80%

Table 4: Gender-specific risk of stroke among diabetics using odds ratio and 95% CI*

Contributing factors	Gender		Odds Ratio	95% CI for odds ratio
	Male *n* (%)	Female *n* (%)		
Coronary artery disease				
a. Yes	119 (61.98)	73 (38.02)	1.43	0.995–2.065
b. No	264 (70.03)	113 (29.97)		
Use of alcohol				
a. Yes	106 (60.23)	70 (39.77)	1.58	1.087–2.287
b. No	277 (70.48)	116 (29.52)		
Smoking				
a. Yes	83 (56.46)	64 (43.54)	1.9	1.286–2.795
b. No	300 (71.09)	122 (28.9)		

*CI: Confidence Interval

increase in risk of ischemic stroke after the use of hormonal contraceptives.[22,23] However, in the present study, none of the diabetic patients had a history of hormonal therapy.

Vascular risk variables in Chinese stroke patients exhibit distinct age and gender distribution patterns, underscoring the necessity of patient-specific secondary preventive interventions.[24] Younger strokes are more common in men and are strongly correlated in both sexes with comorbid conditions and bad social practices.[25]

Other comorbid diseases were seen in the majority of the data in the present study and in a similar study, more than 2 comorbidities were seen as cancer (3.4%), COPD (0.9%), nephropathy (4.3%), and prior history of stroke (4.3%).[26] Comparatively, COPD in the presence of other conditions can increase the risk of stroke.[27] These comorbid conditions can lead to an increased risk of stroke in an individual compared to one without these comorbid conditions.

HTN was seen in most of the present study data, and a similar study reported HTN in 66.9%.[21] HTN is one of the most common causes of stroke in an individual as it leads to narrowing, leaking, and bursting of the blood vessels. CAD accounted for a significant portion; in a similar study, CAD accounted for 32.5%.[10] In CAD, plaques form resulting in stroke by obstructing blood flow to the brain.

A familial history of stroke was reported in the data. A similar study reported that 12.3% had a familial history of stroke among first-degree relatives.[28] Researchers acknowledge the significance of genetic vulnerability in predisposing individuals to stroke by including familial history of stroke in the data. More focused preventive and therapeutic approaches may be developed as a result of a better understanding of the genetic foundations of stroke risk. In this study, we retrospectively analyzed contributing factors to look at gender-specific stroke risks among diabetic patients.

A considerable portion of the data in this study indicated that they had consumed alcohol and were smokers. A similar study reported that only 27.5% of the samples consumed alcohol, and 55% of the samples were smokers.[21] People may try to relax, decompress, or improve their social interactions to deal with stress or lessen unpleasant emotions such as sadness, nervousness, or boredom. Moreover, peer pressure, cultural norms, social pressure, family history, and media and advertising exposure can all have a big impact on individual attitudes and behaviors, which can lead to drinking and smoking.

In ischemic stroke patients, males were more likely to have hypertension, DM, and the habit of smoking and drinking; however, there were no appreciable differences in the mortality rate between the sexes.[28]

Physical inactivity was reported as the least cause in the current study, compared with 11.2% in a similar study. The low percentage of physical activity is due to the limited availability of data regarding physical activity. However, we know that physical inactivity can lead to obesity and result in other factors contributing to the risk of stroke. Physical inactivity shows a significant association with an increased risk of total and ischemic stroke in women with diabetes, whereas physical inactivity, smoking, and overweight/obesity show no significant association in men with diabetes.[22] Males are more likely to experience a myocardial infarction (MI), although women die from strokes more frequently than males.[14] Male and female patients experience different rates of stroke; though age is a significant linked factor, CAD, HTN, diabetes, atrial fibrillation, use of oral contraceptives, and other risk factors are also substantial.[29]

A majority had a prior history of using anticoagulants; correspondingly, a prospective cohort study reported that subjects with oral anticoagulants had a risk of recurrent ischemic stroke.[15] Anticoagulants are frequently used to prevent blood clots, although their efficacy varies, and people may occasionally still have strokes while taking anticoagulant medication. This may be due to several factors, such as insufficient dosage, non-adherence to medication, and underlying medical disorders that raise the risk of stroke. A significant portion of the data had hyperlipidemia, while only 50% had dyslipidemia in another study among diabetic patients with stroke.[21] Hyperlipidemia may also increase the risk of other cardiovascular conditions, such as CAD, which can obliquely increase the chance of stroke.

From the present study and the studies mentioned earlier, it is observed that a history of prior stroke is a risk for recurrent stroke, irrespective of the presence of diabetes. A person with other comorbid conditions such as CKD, COPD, and asthma is noticed to contribute to stroke. Apart from this, conditions such as hypertension and CAD are also contributive. It is also found that a familial history of stroke and diabetes is essential due to genetic factors.

Lifestyle habits such as the use of alcohol, smoking, and living a sedentary life are also causative factors. Patients undergoing hormonal therapy and using anticoagulants are at higher risk of getting a stroke than those not under such treatments. A significant association was seen between gender and contributing factors such as CAD, consumption of alcohol, and smoking. Similar studies have suggested that pre-existing CAD increases the risk of stroke ($p = 0.002$) and smoking ($p = 0.006$).[30,31] However, a study reported that the consumption of alcohol has no association with an increased risk of stroke in diabetic patients ($p = 0.237$).[32] However, we cannot ignore the harmful effect alcohol has on the liver and the pancreas. Compared to women, men are more likely to be smokers, have DM, suffer MI, and they also have a higher risk of ischemic stroke.[33] Stroke rates are higher in men than in women, and relevant confounders include DM, HTN, systolic blood pressure, and the type of stroke.[34] Among adult patients, the most prevalent modifiable risk factors for stroke are DM, smoking, alcoholism, and HTN.[35]

This study found that CAD, alcohol consumption, and smoking have a significant influence on the development of stroke among men and women with diabetes. Similar studies have reported that females with CAD and stroke are at risk of being diagnosed with DM; males with CAD are at higher risk of having DM compared to those without CAD.[36] In a study, it was observed that there is a significant risk of acute ischemic stroke with pre-existing CAD.[37] Between stroke patients with and without DM, a study reported that in diabetic patients, alcohol consumption and smoking pose a risk of stroke.[21] For Malaysians with T2DM who have had a stroke in the past, ischemic heart disease is the leading risk factor for stroke recurrence in both sexes. The study reported that ischemic heart diseases were found to be related to stroke in men (OR: 1.728; 95% CI: 1.071–2.818) and women (OR: 5.859; 95% CI: 2.269–13.752) with diabetics. Duration of hypertension and diabetes has been found to be associated with recurrence in both genders ($p < 0.05$). Another factor resulting in recurrence in men was smoking.[38]

It is possible that the physiological responses of men and women to risk factors, including smoking, alcoholism, and CAD, can differ. Genetic predispositions, variances in body composition, and hormonal variables can all influence how these risk factors affect a person's risk of stroke and cardiovascular disease differently. Distinct patterns of smoking and alcohol intake have been linked to an elevated risk of cardiovascular diseases and stroke in both men and women. Diverse levels of alcohol intake and smoking prevalence among genders may be dictated by societal and cultural standards, resulting in differing degrees of exposure to these risk factors. Disparities in treatment compliance, quality of care, and access to healthcare among genders may be responsible for discrepancies in stroke risk factor management and results. The study had data gaps in some EMR, it took a long time to review the EMR in the official medical records department, and some scanned data had illegible markings.

Conclusion

This study revealed that there is an increased risk of stroke in diabetic patients and identified the gender-specific risk of stroke. Interventions can be planned out to prevent stroke in high-risk patients. Through this study, the researchers have understood that there is an increased risk of stroke among diabetics with CAD and habits such as consumption of alcohol and smoking. Various contributing factors for stroke differ from person to person, and this risk is higher in certain conditions and hence has to be identified at an earlier phase. Even though gender-specific risk is of predominant significance, studies with regard to this subject are limited.

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Conflicts of interest

Nothing to declare.

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