



FREQUENCY OF UNDIAGNOSED DIABETES MELLITUS IN PATIENTS WITH ISCHEMIC STROKE

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Abstract

Introduction: Diabetes mellitus is a significant risk factor for ischemic stroke, but many patients have an unrecognized diabetes prior to stroke.

Objective: To determine the frequency of undiagnosed diabetes mellitus in patients with ischemic stroke.

Methods: This descriptive cross-sectional study was done in the Hameed Latif Hospital Lahore from March, 2025 to August, 2025. Patients aged 18 years and older who had been diagnosed with ischemic stroke (IS) by computed tomography (CT) or magnetic resonance image (MRI) were recruited by non-probability consecutive sampling, for a total of 150 patients. Those with known diabetes were not included. Fasting plasma glucose and glycated hemoglobin (HbA1c) were measured and diabetes was defined as FPG ≥ 126 mg/dL or HbA1c $\geq 6.5\%$. Descriptive statistics were used.

Results: The mean age was 59.4 ± 11.8 years, and 91 patients (60.7%) were male. Undiagnosed diabetes was identified in 31 patients (20.7%; 95% CI 15.0 to 27.8). It was more frequent in patients aged 60 years or above (64.5% vs 51.3%) and often coexisted with hypertension (74.2%), dyslipidemia (54.8%), smoking (38.7%), and obesity (32.3%). The mean fasting glucose and HbA1c in this group were 148.6 ± 24.8 mg/dL and $7.1 \pm 0.6\%$, respectively.

Conclusions: About 20% of ischemic stroke patients did not have a previous diagnosis of diabetes. It is recommended to do routine glucose and HbA1c testing at admission to allow early treatment and secondary prevention.

Keywords: undiagnosed diabetes mellitus; ischemic stroke; frequency; HbA1c; fasting plasma glucose; cardiovascular risk factors.

Introduction

Ischemic stroke is a disorder of the brain caused by the interruption of cerebral blood flow, typically from an occlusion of an artery, and is an important cause of death and disability. It is indicative of the interplay of vascular, metabolic, hematological and behavioral factors. Evaluation of acute stroke may identify previously undocumented major risk factors, suggesting that a patient's known history may be incomplete (1). Chronic hyperglycemia is especially significant in the context of diabetes mellitus, as it is a risk factor for endothelial dysfunction, atherosclerosis, inflammation, platelet activation and vascular remodeling, which in turn predispose to cerebrovascular events (2).

There is a relationship between diabetes mellitus and ischemic stroke. Hyperglycemia, insulin resistance, dyslipidemia, oxidative stress, inflammation and atherosclerosis are mechanisms by which type 2 diabetes increases cerebrovascular risk. Diabetic patients may also have hypertension, obesity, smoking exposure or lipid abnormalities, which are other risk factors for stroke (3). The relationship is significant because of the interplay of metabolic and vascular mechanisms that may affect the pathogenesis and the effect of ischemic stroke in people with diabetes (4). If diabetes has not been diagnosed before, these abnormalities can go untreated and cause vascular injury to occur before it is known. If left untreated, diabetes can go undiagnosed for years as hyperglycemia may occur slowly and may not have any symptoms. Some people, therefore, have a glucose test first because they experience a vascular event. Unrecognized risk factors should be identified during the workup of ischemic stroke because the discovery of these factors may affect secondary prevention and follow-up (5). The setting also offers a chance to assess markers of disease progression that are of a biological nature. Neutrophil-to-lymphocyte ratio has been found to be related to stroke progression and functional outcome, which shows the role of systemic inflammatory responses in ischemic brain injuries (6).

There are many factors that may increase the risk of stroke, and metabolic abnormalities can occur in conjunction with vascular or thrombotic contributors. Studies of the JAK2V617F mutation have found that an acquired prothrombotic abnormality occurs more commonly in patients with ischemic stroke than in matched controls, suggesting that biological abnormalities can be detected during stroke investigation, albeit in a silent manner (7). Cardiac disorders are also relevant, especially atrial fibrillation that may result in cardioembolic cerebral ischemia. Changes in clinical patterns have been observed in studies of ischemic stroke in women with AF, highlighting the importance of assessing cardiac and metabolic risk factors together when evaluating stroke (8). Vascular risk can be further modified by lifestyle behavior in patients with diabetes. Smoking is a known modifiable exposure and studies of persons with type 2 diabetes have shown that changes in smoking status correlate with cardiovascular disease incidence and mortality (9). There is also observational evidence of the use of pioglitazone in patients with diabetes and previous ischemic stroke to assess its association with the risk of dementia (10). These results highlight the importance of recognizing diabetes in the evaluation of stroke and the chance to start managing risk factors, educating patients, and providing follow-up care in addition to stroke treatment.

Evidence of the importance of detecting diabetes is supported by evidence of undiagnosed disease. For cardiovascular cohorts, undiagnosed type 2 diabetes was found to be associated with an excess risk of cardiovascular conditions, such as ischemic stroke, in both women and men, with a higher excess risk

among women (11). Cardiovascular evaluation is also important throughout the stroke care process as cardiac complications are common following stroke (12). Therefore, the lack of a previous diagnosis of diabetes should not be seen as the lack of metabolic risk, especially in patients with ischemic stroke and other cardiovascular risk factors. Population evidence in recent years has suggested that there are missed opportunities for identifying modifiable risk factors in healthcare. A record linkage study in England found that the incidence of stroke remained stable but that undiagnosed diabetes and hypertension became more common among younger adults during the COVID-19 period, especially ethnic-minority groups (13). In addition, cardiovascular conditions that may accompany AF should be recognized, as the prevalence of AF might be underdiagnosed if only cases that have been documented in acute-care settings are counted (14). The results indicate that it is important to consider previously unknown risk factors in the evaluation of patients presenting with ischemic stroke in a systematic manner.

Metabolic risk can be on a continuum from insulin resistance to prediabetes to diabetes to cerebrovascular disease. Insulin resistance has been linked to stroke incidence in hypertension, and the triglyceride-glucose index is a surrogate measure of insulin resistance, which may have cerebrovascular implications prior to the diagnosis of diabetes (15). Mechanisms of stroke also differ by age. Multicenter evidence comparing the causes of ischemic stroke in young and non-young adults shows that there is heterogeneity in the causes of ischemic stroke, suggesting that metabolic assessment should be used in addition to the evaluation of etiologies, and not as a substitute. (16) Therefore, patients who had ischemic stroke without a known history of diabetes could be a significant population to consider for biochemical assessment. Multidisciplinary and individualized analyses of strokes of unknown origin highlight the need for detailed analysis on a case-by-case basis, especially when standard explanations fall short (17). Measurement of glucose and application of diagnostic criteria can help to uncover a patient's metabolic risk that was not previously known and can help with counseling, confirmatory testing, treatment and monitoring. The frequency of undiagnosed diabetes among ischemic stroke patients is therefore important in clinical practice since it quantifies an unrecognized risk burden and may support the implementation of screening and secondary-prevention strategies in routine clinical practice and stroke care services.

Objective: To determine the frequency of undiagnosed diabetes mellitus in patients presenting with ischemic stroke.

Materials And Methods

Study Design: A descriptive cross-sectional study was conducted.

Study Setting: The study was conducted at Hameed Latif Hospital, Lahore.

Study Duration: The study was conducted over six months, from March, 2025 to August, 2025.

Sample Size: A sample of 150 patients presenting with ischemic stroke was included.

Sample Technique: Non-probability consecutive sampling technique

Inclusion criteria: Patients aged 18 years or older who presented with clinically suspected acute ischemic stroke and had ischemic stroke confirmed by computed tomography or magnetic resonance imaging were included. Undiagnosed diabetes was assessed in patients without a previous diagnosis of DM. Informed consent patients were included.

Exclusion criteria: Patients with known diabetes mellitus, hemorrhagic stroke, transient ischaemic attack (TIA) with no radiological evidence of infarction, pregnancy, severe hepatic or renal disease with a significant effect on glucose metabolism, or where clinical information was unreliable.

Methods

After admission to Hameed Latif Hospital, Lahore, patients were subjected to a structured clinical evaluation if they were eligible. Demographic data (age, sex), medical history and vascular risk factors (hypertension, smoking, dyslipidaemia, obesity, family history of diabetes) were collected. Information about clinical signs of neurological disease and stroke was recorded. Brain computed tomography or magnetic resonance imaging was used to confirm the diagnosis of ischemic stroke and to exclude intracranial hemorrhage. Blood samples from veins were drawn to measure the level of fasting plasma glucose and glycated hemoglobin (HbA1c). When laboratory results were compatible with accepted diagnostic criteria for diabetes mellitus, but the patient had not previously been diagnosed with the disease, they were considered as having undiagnosed diabetes mellitus. Fasting plasma glucose ≥ 126 mg/dl or HbA1c $\geq 6.5\%$ was regarded as suggestive of DM and confirmatory testing was done if clinically warranted. Descriptive statistics were used to determine the frequency of undiagnosed diabetes. Categorical variables were described as frequencies and percentages and continuous variables were described as mean $\pm$ standard deviation.

Results

A total of 150 patients with radiologically confirmed ischemic stroke were included in the analysis. The mean age of the study population was 59.4 ± 11.8 years (range 34–82 years), and 91 patients (60.7%) were male and 59 (39.3%) were female. There were 31 patients with previously undiagnosed diabetes mellitus (20.7%, 95% CI 15.0 to 27.8), the remaining 119 (79.3%) did not meet the diagnostic criteria. About 20% of ischemic stroke patients, then, were undiagnosed with diabetes prior to stroke. The frequency and distribution of age group, sex and stroke territory in each group are presented in Figure 1.

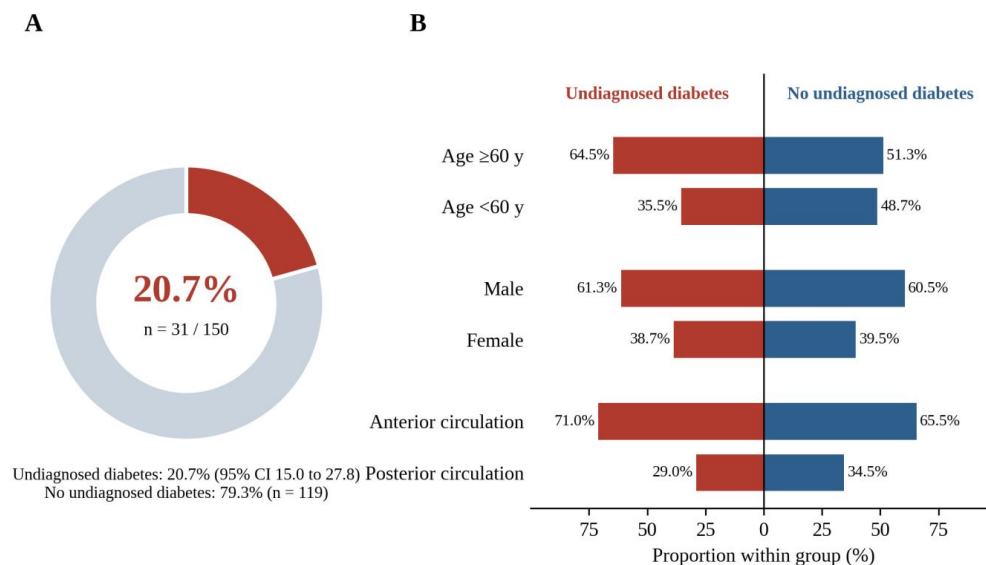


Figure 1. Undiagnosed diabetes mellitus and distribution of undiagnosed diabetes mellitus by age group, sex and stroke territory among patients with ischemic stroke (N = 150). (A) Percentage of patients who have not been diagnosed with diabetes (Wilson method 95% CI). (B) Butterfly chart of the percentage distribution of each characteristic in the undiagnosed diabetes group (left) and the group without undiagnosed diabetes (right).

Older patients had a higher incidence of undiagnosed diabetes. Of the 31 patients with newly detected diabetes, 20 (64.5%) were aged 60 years or above and 11 (35.5%) were younger, compared with 61 (51.3%) and 58 (48.7%), respectively, among patients without undiagnosed diabetes. There was no significant difference between the two groups in terms of sex distribution; there were 19 (61.3%) males with undiagnosed diabetes and 72 (60.5%) males in the other group. The most prevalent vascular risk factor overall was hypertension (86 patients, 57.3%), followed by dyslipidaemia (41.3%), smoking (34.0%) and obesity (23.3%). Both groups' demographic and risk factor profile is summarized in Table 1.

Table 1. Demographic Characteristics and Vascular Risk Factors According to Undiagnosed Diabetes Status

Characteristic	Undiagnosed diabetes (n = 31)	No undiagnosed diabetes (n = 119)	Total (N = 150)
Age group			
Age ≥60 years	20 (64.5%)	61 (51.3%)	81 (54.0%)
Age <60 years	11 (35.5%)	58 (48.7%)	69 (46.0%)
Sex			
Male	19 (61.3%)	72 (60.5%)	91 (60.7%)
Female	12 (38.7%)	47 (39.5%)	59 (39.3%)
Vascular risk factors			
Hypertension	23 (74.2%)	63 (52.9%)	86 (57.3%)
Dyslipidemia	17 (54.8%)	45 (37.8%)	62 (41.3%)
Smoking	12 (38.7%)	39 (32.8%)	51 (34.0%)
Obesity	10 (32.3%)	25 (21.0%)	35 (23.3%)

Note. Values are presented as n (%). Percentages are calculated within each column. Risk factors were not mutually exclusive.

Established vascular risk factors were consistently more prevalent among patients with undiagnosed diabetes. Hypertension was present in 23 patients (74.2%) in this group compared with 63 (52.9%) in the group without diabetes, and dyslipidemia was observed in 17 (54.8%) compared with 45 (37.8%). Obesity (32.3% vs 21.0%) and smoking (38.7% vs 32.8%) showed smaller differences in the same direction. These findings indicate that previously unrecognized diabetes frequently occurred alongside

other major cardiovascular risk factors. The size of the difference for each risk factor and the combined risk profile of the two groups are illustrated in Figure 2.

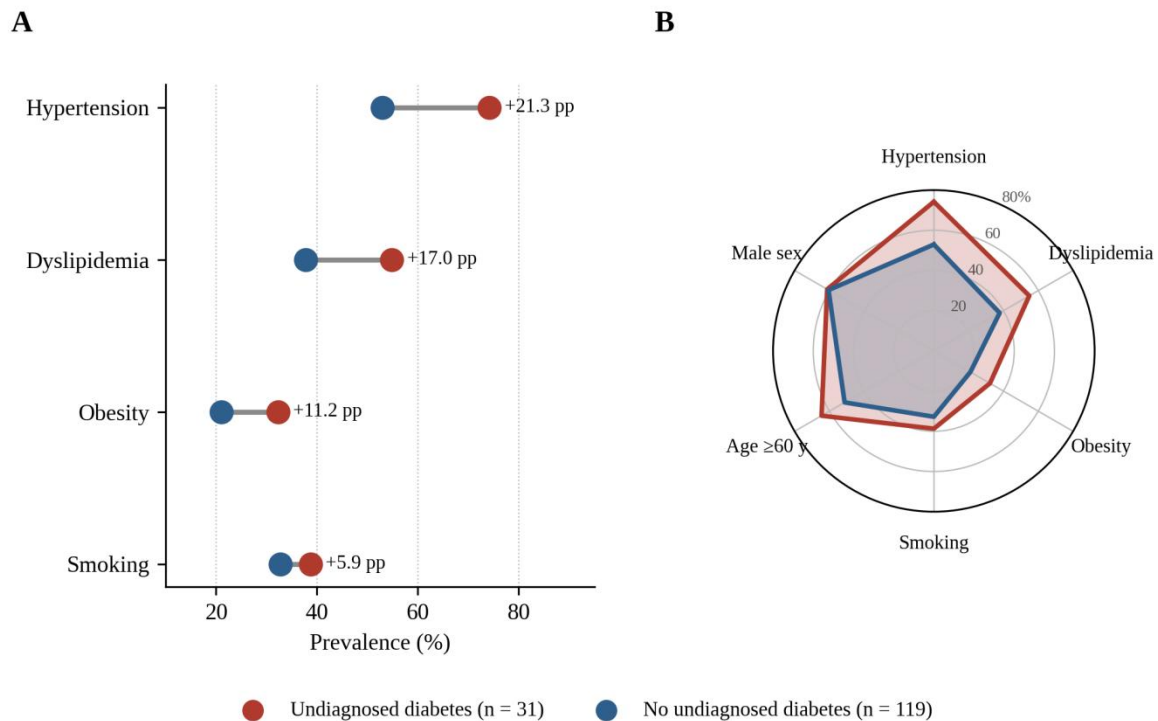


Figure 2. Comparison of vascular risk factors between patients

Table 2 shows the clinical and laboratory features of both groups. Patients with undiagnosed diabetes were slightly older (62.1 ± 10.7 vs 58.7 ± 11.9 years) and had markedly higher mean fasting plasma glucose (148.6 ± 24.8 vs 101.3 ± 13.6 mg/dL) and HbA1c ($7.1 \pm 0.6\%$ vs $5.5 \pm 0.4\%$) than the remaining patients. Anterior circulation stroke was more common in both groups, 22 patients with undiagnosed diabetes (71.0%) and 78 without diabetes (65.5%), and posterior circulation stroke was more common in 9 (29.0%) and 41 (34.5%) patients with and without diabetes, respectively. In summary, the results suggest that there is a significant proportion of undiagnosed diabetes in patients with ischemic stroke.

Table 2. Clinical and Laboratory Characteristics of Patients According to Undiagnosed Diabetes Status

Variable	Undiagnosed diabetes (n = 31)	No undiagnosed diabetes (n = 119)	Total (N = 150)
Continuous variables, mean $\pm$ SD			
Age (years)	62.1 ± 10.7	58.7 ± 11.9	59.4 ± 11.8
Fasting plasma glucose (mg/dL)	148.6 ± 24.8	101.3 ± 13.6	—
HbA1c (%)	7.1 ± 0.6	5.5 ± 0.4	—

Variable	Undiagnosed diabetes (n = 31)	No undiagnosed diabetes (n = 119)	Total (N = 150)
Stroke territory, n (%)			
Anterior circulation	22 (71.0%)	78 (65.5%)	100 (66.7%)
Posterior circulation	9 (29.0%)	41 (34.5%)	50 (33.3%)

Note. Continuous variables are presented as mean $\pm$ standard deviation and categorical variables as n (%). HbA1c = glycated hemoglobin. Laboratory values for the total sample are not shown because the diagnostic grouping was based on these measures.

Discussion

This study revealed that 31 out of 150 ischemic stroke patients were diagnosed with diabetes, which accounts for 20.7% of the population. This suggests that there are a significant number of stroke patients that may have a metabolic disease without being diagnosed. Rêgo et al. highlighted the fact that acute ischemic stroke may uncover significant undocumented vascular risk factors (1). The observed frequency is clinically significant since diabetes is a significant risk factor for cerebrovascular disease. Liu et al. identified interacting risk factors for acute ischemic stroke in type 2 diabetes patients: metabolic and vascular abnormalities (2). Thus, newly diagnosed diabetes might be a significant element of undiagnosed vascular risk. Diabetes contributes to stroke risk by endothelial dysfunction, insulin resistance, oxidative stress, inflammation, dyslipidemia and accelerated atherosclerosis. Maida et al. outlined the interconnected molecular and vascular mechanisms that link diabetes and ischemic stroke (3). The present discovery can be used to assess glucose metabolism in the evaluation of ischemic stroke.

Lack of a previous diagnosis of diabetes does not mean that glucose metabolism is normal. Hyperglycemia can be asymptomatic until a vascular problem occurs. Maida et al. emphasized the relationship between diabetes, vascular injury, inflammation and cerebrovascular complications (4). Patients may be identified for confirmation, counseling, treatment and monitoring through routine glycemic assessment. Clustering of vascular risk factors was observed: hypertension was present in 74.2% of patients with undiagnosed diabetes, and dyslipidemia was present in 54.8% of patients with undiagnosed diabetes. Chang et al. highlighted the importance of medical management after ischemic stroke (5). Treatment outcomes were not evaluated but if coexisting risks are identified, this may help to facilitate a broader secondary prevention. By definition, patients with undiagnosed diabetes had higher fasting glucose and HbA1c levels and acute stroke can have inflammatory responses. Xu et al. found that the neutrophil to lymphocyte ratio was related to stroke progression and functional outcome (6). This gives some biological context to the joint consideration of metabolic and inflammatory abnormalities.

Ischemic stroke must not be the only cause of diabetes. Kristiansen et al. found that acquired prothrombotic conditions were associated with ischemic stroke, and that a high prevalence of JAK2V617F mutation was observed in patients with ischemic stroke (7). Investigation of other stroke mechanisms should therefore be complemented by metabolic assessment. Cardiac causes are still relevant for evaluation of ischemic stroke. Teppo et al. studied women with AF and ischemic stroke and showed important clinical considerations (8). Therefore, the diagnosis of undiagnosed diabetes should

be part of a comprehensive evaluation, which should include a consideration of cardioembolic and other causes. 38.7% of patients with undiagnosed diabetes reported smoking, which suggests that there is another modifiable risk factor. Jeong et al. found associations between smoking behavior changes and cardiovascular disease incidence and mortality in patients with type 2 diabetes (9). This helps to enable smoking cessation and lifestyle counseling following the diagnosis of diabetes.

Post-stroke diabetes diagnosis may affect more than just glucose control. A number of studies have shown that the use of pioglitazone is associated with a decreased risk of dementia in patients with diabetes and prior ischemic stroke (10). This study is not able to assess treatment effects, but the detection of diabetes will allow for lifelong metabolic management. However, even though a sample was not collected to establish sex-specific predictors, men accounted for 61.3% of patients with undiagnosed diabetes. In a study of cardiovascular risk associated with prediabetes and undiagnosed diabetes, Yoshida et al. found sex differences (11). Further research is needed to determine if similar patterns exist in stroke patients in larger studies. Cardiovascular complications may also occur with stroke; thus, integrated assessment is necessary. There is evidence that stroke-heart syndrome is a problem after acute stroke and can affect outcomes (12). Thus, the diagnosis of diabetes should be made in conjunction with a proper cardiovascular assessment and not as a single laboratory value.

The vascular risk profile of stroke patients may evolve over time. Kamtchum-Tatuene et al. investigated changes in stroke incidence and the prevalence of modifiable risk factors, and showed that there were changing trends in important risk factors (13). The results of this study indicate that the local monitoring of metabolic risk in modern stroke patients is warranted. Other vascular diseases may be underdiagnosed. Noubiap et al. showed that reported prevalence of AF could underestimate the true burden of the condition if ascertainment is incomplete (14). The same problem can arise in the case of diabetes, if screening is not done on a regular basis, which supports systematic biochemical assessment of stroke patients.

The results can also be interpreted in the context of metabolic dysfunction. Huang et al. identified a relationship between T2 with stroke incidence in patients with hypertension (15). This indicates that insulin resistance could be a factor in the development of cerebrovascular risk before the clinical onset of diabetes. 20 out of 31 patients had undiagnosed diabetes, which was more common in those aged 60 years or more. Ohya et al. showed that the difference in ischemic stroke between young and non-young adults exists (16). Therefore, age should be taken into account when interpreting metabolic profiles and possible stroke mechanisms. Lastly, Golubnitschaja et al. pointed out that ischemic stroke of unknown origin (ischemic stroke) should be assessed individually and in a multidisciplinary fashion (17). The current results confirm this strategy, as they indicate that metabolic assessment can reveal an unknown risk factor. The cross-sectional and single-center design and small sample size, however, limit the generalizability, suggesting the need for larger prospective studies.

Conclusion

In this descriptive cross-sectional study of 150 patients of ischemic stroke at Hameed Latif Hospital, Lahore, 31 patients (20.7% CI 15.0-27.8) were found to be previously undiagnosed diabetes mellitus patients. About 20% of all stroke patients had therefore an unrecognized metabolic risk factor prior to the stroke. Undiagnosed diabetes was more prevalent in the older age group (60 years or more) and was often accompanied by hypertension, dyslipidaemia, obesity and smoking. The sex distribution and

stroke territory were generally comparable among groups. These findings point to a significant unrecognized burden of diabetes in ischemic stroke. All stroke patients should be screened for diabetes on admission with routine measurement of both fasting plasma glucose and HbA1c, for confirmatory testing, treatment and secondary prevention to be started promptly. Further larger multicenter studies are recommended to confirm these results.

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