

A Study Of Prevalence And Prediction Of Unrecognised Diabetes Mellitus And Impaired Glucose Tolerance Following Acute Stroke In A Hospital

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Abstract :Introduction: Stroke is a common medical emergency and is the most common cause of physical disability. Diabetes mellitus is known to increase the risk of ischemic stroke by 2-4 folds. The prevalence of recognized diabetes mellitus in acute stroke patients is between 8-20% and 6-42% of patients may have undiagnosed diabetes mellitus before presentation with stroke. **Aim:** To study the prevalence and prediction of unrecognized diabetes mellitus and impaired glucose tolerance following acute stroke and to measure the accuracy of hyperglycemia and elevated glycosylated hemoglobin concentration in predicting the presence of unrecognized diabetes mellitus at 3 weeks post stroke. **Materials and Methods:** This a prospective observational study conducted on acute stroke patients who were not known diabetics admitted in medical and neurology wards of IGGGH &PGI ,puducherry between Feb 2015 and Jan 2016.A detailed history was taken from all the patients followed by thorough physical examination and stroke was confirmed by CAT scan. Random, fasting, post prandial blood sugar and glycosylated hemoglobin levels were done. Treatment for stroke along with appropriate treatment for glycemic control was initiated. At 3weeks post stroke follow up in OPD oral GTT was done and HbA1c levels were estimated. **Results:** 33.3% of patients were diagnosed to have prediabetes and 23.3% were diagnosed as diabetics based on OGTT. 2h post load glucose on OGTT at admission and elevated HbA1C were found to be good predictors of diabetes and prediabetes after acute stroke. **Conclusion:** A thorough investigation of acute stroke patients by estimating fasting ,2h post load glucose on OGTT and HbA1C levels could help in detecting a significant number of previously unrecognized diabetes and prediabetes.

Key words; Acute stroke, Diabetes mellitus,

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I. Introduction

Stroke is the third most common cause of death in developed world after cancer and ischemic heart disease¹. The incidence of stroke is rising steeply in developing countries because of adoption of unhealthy life styles¹. Diabetes mellitus apart from increasing the risk of stroke ^{2,3} also confers a poor prognosis in terms of increased mortality, stroke recurrence^{4,5} and impaired neurological recovery^{6,7}. Cerebral blood flow disturbances, impaired cerebrovascular reactivity and damage to large and small extra and intra cranial cerebral vessels have been found in humans and animals with diabetes. Combination of some or all of these factors may underlie high incidence and worst outcome of stroke in patients with diabetes. Post stroke hyperglycemia is a frequent finding in patients presenting with acute stroke, occurring in up to 60% of patients overall and in approximately 12-53% of acute stroke patients without prior diagnosis of diabetes. Hyperglycemia detected during acute illness may also be the first clinical evidence of underlying undiagnosed type 2 DM⁸. The issue of hyperglycemia in patients with acute stroke continues to generate a lot of debate. The major difficulty in clinical studies lies in interpreting the admission glucose concentration. This value may be influenced by a number of factors including the stress of an acute medical illness^{9,10}, the interval between onset of the stroke and blood sampling and any underlying illness especially a latent diabetic state¹¹. Since there is a paucity of local data regarding undiagnosed diabetes in stroke patients, the current study was conducted to determine the frequency of newly diagnosed diabetes in acute ischaemic stroke patients.

II. Aims and objectives

To study the prevalence and prediction of unrecognized diabetes mellitus and impaired glucose tolerance following acute stroke and to measure the accuracy of hyperglycemia and elevated glycosylated hemoglobin concentration in predicting the presence of unrecognized diabetes mellitus at 3 weeks post stroke.

III. Material and Methods

Study design: This is a prospective observational study.

Inclusion criteria: All cerebro vascular disease patients admitted within 72 hours of onset of stroke without prior history of DM.

Exclusion criteria: 1. Stroke patients with known diabetes mellitus.

2. Any other cause that presents with clinical features similar to stroke such as subdural hematoma, epilepsy, subarachnoid hemorrhage.

3. Any prior neurological disability from previous stroke or other diseases. Careful history was obtained from the participants and attendants regarding the complaints and co morbid illnesses. And a thorough physical examination was conducted and then confirmation of stroke was done by taking a CAT scan. Stroke was classified into ischaemic or hemorrhagic. Random blood sugar levels were done by glucometer immediately after admission. Fasting; Post prandial blood sugar levels, glycosylated hemoglobin and 2hour post load glucose levels following OGTT were done on the next day. Treatment for stroke was initiated along with appropriate glycemic control.

Patients were asked to come for follow up three weeks after discharge and oral GTT was done again. Patients were given 75 Gms of oral glucose mixed in 100 ml of water to be taken within 3 minutes. Simultaneously HbA1c level was also estimated.

Diagnosis of diabetes mellitus: the new revised criteria as per the ADA for diagnosis of diabetes are 1. Symptoms of diabetes plus RPG concentration more than 200 mg/dl

2. FPG more than 126 mg/dl (no caloric intake for at least 8 hours)

3. HbA1C more than 200mg/dl on oral GTT (not recommended for routine clinical use)

Glucose tolerance is classified into three categories according to ADA 2011 guidelines.

1. Normal glucose homeostasis
2. Impaired glucose homeostasis (IFG/IGT)
3. Diabetes mellitus

Fasting plasma glucose <100 mg/dl, a 2hr post prandial plasma glucose <140 mg/dl and HbA1c < 5.6 are considered to be normal glucose homeostasis. Fasting plasma glucose between 101-125 mg/dl, 2hr post prandial plasma glucose between 140-199 mg/dl and a HbA1c levels between 5.7 and 6.4% are termed to have impaired glucose homeostasis or pre diabetes. A fasting plasma glucose>140 mg/dl, 2hr post prandial glucose > 200 mg/dl and HbA1c ≥6.5 are classified as diabetes mellitus. Using this data prevalence and prediction of newly diagnosed diabetes mellitus and impaired glucose homeostasis were calculated with the help of statistical methods.

IV. Observations & Results

Table 1. Age distribution and mean age based on age groups

Age Group	Frequency	Percentage	Mean Age	SD
<40	1	1.7	38.0	0.00
41-60	55	91.7	49.61	5.79
>60	4	6.7	62.75	2.21
Total	60	100	50.30	6.66

Out of 60 patients a maximum of 55 were in the age group of 41-60, 4 were above 60 years of age and only one was below 40 years.

Table 2. Gender distribution

Gender	Frequency	Percentage
Male	39	65.0
Female	21	35.0
Total	60	100

Among the participants males (65%) outnumbered the females (35%).

Table 3. Distribution of type of stroke

Stroke	Frequency	Percentage
Ischemic	52	86.7
Hemorrhagic	8	13.3
Total	60	100

Stroke was predominantly of ischemic type (86.7%), while hemorrhagic type was seen in only 13.3 %

Table 4. Distribution of Random blood sugar

RBS	Frequency	Percentage
<200	20	33.3
>200	40	66.7
Total	60	100

Random blood sugar was <200 in 33.3% of study participants and >200 in 66.7%

Table 5. Comparison of mean fasting blood sugar levels among normal, IGT and diabetic groups at admission and 3 weeks post stroke.

FBS	Admission			3 weeks		
	N	Mean	SD	N	Mean	SD
Normal	23	89.65	4.90	25	83.00	7.11
IGT	20	115.55	5.56	21	110.57	6.00
DM	17	182.23	27.51	14	160.78	20.32
Total	60	124.80	41.45	60	110.80	32.31

The mean FBS immediate post stroke was high when compared to mean FBS 3 weeks post stroke in normals, IGT and diabetic groups. This could be due to immediate stress induced PSH.

Table 6. Comparison of post prandial blood sugar levels among normal, IGT and diabetic groups at admission and 3 weeks post stroke.

PPBS group	Admission			3 weeks		
	N	Mean	SD	N	Mean	SD
Normal	23	128.17	5.91	26	120.61	9.23
IFG/IGT	20	170.55	14.92	20	160.15	12.018
DM	17	279.05	49.93	14	217.78	17.12
Total	60	185.05	68.11	60	156.46	40.13

The mean PP immediate post stroke was high when compared to mean FBS 3 weeks post stroke in normals, IGT and diabetic groups. This could be due to immediate stress induced PSH.

Table 7. Comparison of mean HbA1c levels among normal, IGT and diabetic groups at admission and 3 weeks post stroke.

HbA1C group	Admission			3 weeks		
	N	Mean	SD	N	Mean	SD
≤5.6	24	4.95	0.31	24	4.89	0.32
5.7-6.4	22	6.00	0.16	22	5.96	0.19
≥ 6.5	14	7.30	0.53	14	7.13	0.50
≥ total	60	5.89	0.97	60	5.80	0.93

Table 8. Comparison of mean HbA1C at admission and 3 weeks post stroke.

Parameter	N	Mean	SD	t	P value
HbA1C on admission	60	5.89	0.97	3.24	0.002
HbA1C after 3 weeks	60	5.80	0.93		

V. Results

In the present study the prevalence of dysglycemics was 61.33% of which 33.33% were pre diabetics and 28.33% were diabetics($p=0.000$).During the follow up study after 3 weeks of discharge OGTT was done.2hours post load glucose levels were showing the prevalence of dysglycemia as 56.66% of which pre diabetics were 33.33% and diabetics were 23.3%. The difference between these levels can be explained by the stress induced hyperglycemia immediately after acute stroke.

Based on HbA1c level the prevalence of pre diabetes was 36.67% and diabetes was 23.33% immediately after stroke. The prevalence rates didn't change even after 3 weeks of follow up ($p=0.002$). This could be because the HbA1c levels will represent the glycemic control for a duration of 90-120 days. The presence of hyperglycemia and elevated HbA1c are good predictors of diabetes after acute stroke.

VI. Discussion

The data collected from 60 patients in the study was discussed and compared with results of other similar studies. (Dave JA et al ¹², Vancheri F et al ¹³ and Gray CS et al ¹⁴)

Age distribution

The mean age in the present study was 50.3 ± 6.6 years and the range was 38 -66 years. In Dave JA et al study the mean age in normoglycemics was 59 and in dysglycemics was 62 .In Vancheri F et al study the mean age was 69.5 years in IGT 70.5 years and in diabetics it was 72.Gray CS et al reported that the mean age in his study was 75 and the range was 42-93.

Gender distribution

In our study males (58%) were more than females (42%).This well corresponds with the observation of all the other three studies.

Type of stroke

In the present study ischemic stroke (86.7%) outnumbered hemorrhagic stroke (13.3%). The percentage of ischemic stroke was 73.75% and 82% and percentage of hemorrhagic stroke was 7.92% and 18% in Matz K et al¹⁵ and Gray CS et al respectively.

Mean admission fasting blood glucose levels.

In our study Mean admission fasting blood glucose level was 124.8mg/dl. The mean FPG in normoglycemics was 89.65 mg/dl in pre diabetic group it was 115.55mg/dl and in diabetic group it was 183.23 mg/dl. The mean FPG for dysglycemic population was 146.64 mg/dl. Dave JA et al reported that the mean FPG was 91.8mg/dl, 104.4mg/dl for normoglycemics and dysglycemics respectively. In Vancheri F et al study the mean FPG was 100.8 ± 12.6 mg/dl, 108 ± 16.2 mg/dl and 115.2 ± 23.4 mg/dl in normoglycemics, prediabetics and diabetics respectively. In the present study normoglycemics were 38.34%, 33.33% patients were prediabetics and 28.33% were diabetics. In Dave JA et al study 39% were normoglycemics, 61% were dysglycemics. Among the dysglycemics 4% were diabetics and 37% proved to be pre diabetic. In Vancheri F et al study 15.6% subjects belonged to normoglycemic group, 38.5% belonged to prediabetic group and 45.9% were diabetics.

Mean admission 2h plasma glucose (post loading)

In our study mean 2h PG was 185.0mg/dl. In normoglycemic, prediabetic, diabetic and dysglycemic populations the mean 2hPG was 128.17, 175.55, 279.05 and 220.4mg dl respectively. In Dave JA et al study the mean 2h PG in normoglycemics and dysglycemics was 163.8mg /dl and 196.2 mg/dl respectively. According to Vancheri F et al study 154.8 ± 39.6 mg/dl, 187.2 ± 25.2 mg/dl and 223.2 ± 36 mg/dl were the mean 2h PG levels in normoglycemic, prediabetic and diabetic groups respectively.

Mean 3 week FPG

In the present study the mean FPG was 110.8mg/dl. In normoglycemics it was 83 mg/dl in prediabetics was 110.57 mg/dl, in diabetics was 160.78m/dl and in dysglycemic group it was 130.65mg/dl. Among the 17 diabetics found on admission 14 remained as diabetics, 2 became prediabetic and 1 became normoglycemic. The mean FPG level decreased in all the categories. Dave JA et al reported that the mean FPG 3 months post stroke for normoglycemic group was 90 mg/dl and for dysglycemic group was 108m/dl. Among 17 patients who were diagnosed as diabetics on admission and came for follow up, 5 remained as diabetics, 6 became prediabetics and 6 became normoglycemics. Among the 27 normoglycemics one became diabetic 6 turned out to be prediabetics and the remaining 20 continued to be normoglycemics. The mean FPG levels decreased in all the three categories.

In Vancheri F et al study the men FPG during follow up after 3 months for normoglycemic group was 99±9 mg/dl, for prediabetics it was 109.8 ±12.6 mg/dl and for diabetics it was 120.6±16.2 mg/dl. Among the 44 diagnosed as diabetics at admission after 3 months 28 remained as diabetics, 9 reverted back to prediabetic stage and 7 became normoglycemics. Among the 37 prediabetics at admission 7 became diabetics, 16 remained as prediabetics and 14 reverted to normoglycemic stage.

In Gray CS et al study he noted that the mean FPG during follow up after 12 weeks was 90.9 mg/dl, 93.6 and 114.42 mg/l for normoglycemic, prediabetic and diabetic groups respectively.

Mean 3 week 2h PG

In the present study the mean 2h PG after 3 weeks was 156.46 mg/dl. The mean 2hPG values were 120.61, 160.15, 217.78 and 130.65 mg/dl among normoglycemic, prediabetic, diabetic and dysglycemic populations respectively. Among the 17 diabetics found on admission 4 remained as diabetics, 2 became prediabetic and one became normoglycemic.

Among the 20 prediabetics 18 remained as prediabetics 2 became normoglycemics and the mean 2h PG levels in all the categories were decreased. Dave JA et al reported that the mean 2hPG during follow up after 3 months for normoglycemic group was 102.6 and for dysglycemic group was 151.2mg/dl. In Vancheri F et al study the mean 2hPG at 3 months follow up was 122.4±10.8, 172.8±19.8 and 252±37.8 mg/dl in normoglycemic, prediabetic and diabetic groups respectively. In Gray CS et al study the mean 2h PG at 12 weeks follow up was 112.32, 166.5 and 248.22 mg/dl in normoglycemics, prediabetics and diabetics respectively.

Mean admission HbA1C

In the present study the mean HbA1C at admission was 5.89%. Among normoglycemics it was 4.95%, 6.0% in prediabetics and 7.3% in diabetics. Dave JA et al reported that mean HbA1c immediate post stroke for normoglycemic group was 5.6% and for dysglycemic group was 5.8%.

Vancheri F et al reported that the mean HbA1C at the time of acute phase of stroke for normoglycemics was 5.8±1.1 and for prediabetics was 6.0±1.7. Gray CS et al noted that HbA1C was 5.72%, 5.69% and 6.56% for normoglycemics, prediabetics and diabetics respectively in acute phase.

Mean 3 week HbA1C

In the present study mean HbA1c after 3 weeks was 5.8%. Among the normoglycemics the mean HbA1C was 4.89%, in prediabetics it was 5.96% and in diabetics 7.13%. Gray CS et al noted that the mean HbA1C at follow up after 3 weeks was 5.65% for normoglycemics, 5.6% for prediabetics and 6.23% for diabetics.

Final outcome:

In this prospective observational study to evaluate glucose homeostasis in those patients who were without prior diagnosis of diabetes and presented with acute stroke using FPG, OGTT and HbA1C at admission and again after 3 weeks of discharge, 33.3% were found to be prediabetics and 28.4% were found to be diabetics, together called as dysglycemics accounting for 61.7% of the study subjects ($p < 0.001$) immediate post stroke. However 3 weeks after discharge 33.3% were prediabetics and 23.3% were diabetics put together 56.6% ($p < 0.0001$). The difference between the prevalence of dysglycemia at admission and post 3 weeks is assumed to be due to stress response during acute stroke. The outcome of the study is in concordance with other studies.

Dave JA et al noted that prevalence of dysglycemia at admission was 61% and 3 months after discharge was 21%. Vancheri F et al noted the prevalence of dysglycemia at admission was 84.3% and at 3 months after discharge 74% were dysglycemics. Gray CS et al noted that the prevalence of unrecognized diabetes was 15% and IGT was 27% after 12 weeks.

VII. Conclusion

Unrecognized DM is more common in acute stroke patients than that was thought earlier. This study emphasizes the need to actively investigate for DM and impaired glucose tolerance in the recovery period. The early identification of DM and IGT enables intensive and thorough management of stroke which in turn helps in reducing the risk of recurrence thereby improving long term prognosis.

VIII. Abbreviations

ADA	American diabetes association
DM	Diabetes mellitus
FPG	Fasting plasma glucose
HbA1C	Glycosylated hemoglobin
2h PG	2 hour post load glucose
IGT	impaired glucose tolerance
OGTT	Oral glucose tolerance test
PSH	Post stroke hyperglycemia

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