

PREDIABETESE AND ISCHEMIC STROKE

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ABSTRACT

Background: Majority of patients presenting to our units with ischaemic strokes have diabetes and hypertension. However there are patients who do not have these classic risk factors. Searching for other risk factors in these patients may help in preventing strokes. Prediabetes as a risk factor for ischaemic stroke in our set up has yet not been taken seriously. This research work has focussed on determining the frequency of prediabetes in ischaemic strokes.

Aim & Objective: To determine the frequency of prediabetes in patients presenting with ischaemic stroke

Material & Methods: A simple proforma having details of the case was filled from each patient who presented to our unit with ischaemic stroke. Record of previous sugar levels and fresh samples taken in fasting state along with HbA1c where needed was kept which was processed later on through SPSS.

Study duration: Prospective study conducted from March 2013 to March 2014

Inclusion/exclusion criteria: Patients with ischemic stroke and atrial fibrillation due to valvular heart disease, prothrombotic diseases, connective tissue disorders and other known causes of ischemic stroke e.g. infective endocarditis, sickle cell anemia, disseminated intravascular coagulation etc were excluded from the study. All other patients whose ages were more than 18 and presented to us with ischemic strokes were included in the study.

Conclusion: Considering the frequency of impaired fasting glucose in patients with ischaemic stroke, it is the need of the hour to assess our patients thoroughly for prediabetes.

Key words: prediabetes, impaired fasting glucose, ischaemic stroke

INTRODUCTION

World wide approximately 470 million people are getting affected by a prediabetic state¹.

Prediabetes is an intermediate metabolic state between normal glucose metabolism and type 2 diabetes, representing a high risk of developing type 2 diabetes in the future^{2,3}. Up to 70% of the patients with prediabetes may develop type 2 diabetes². Prediabetes comprises impaired fasting glucose and/or impaired glucose tolerance and/or impaired glycosylated hemoglobin^{2,3}. The risk of developing type 2 diabetes is approximately 0.7% per year in normoglycemic individuals, whereas patients with impaired fasting glucose or impaired glucose tolerance have a yearly risk of 5-10%². The transition from prediabetes to type 2 diabetes usually takes several years but may also be more rapid².

Patients with prediabetes also have increased risk of cardiovascular diseases, including stroke and recurrent stroke^{4,5,6}. There is a growing recognition

that patients with prediabetes should be treated more aggressively. Both lifestyle modification and antidiabetic drugs lower the risk of developing type 2 diabetes^{7,8}.

Prediabetes and newly diagnosed diabetes can be detected by either fasting plasma glucose levels or an oral glucose tolerance test (OGTT) or glycosylated hemoglobin⁴. Recently, the American Diabetes Association recommended the additional use of glycosylated hemoglobin levels to diagnose diabetes⁹. At present, there is no consensus on using one in preference to the other. In patients with a stroke or TIA, fasting plasma glucose is currently the most commonly measured glycemic parameter to detect prediabetes and/or diabetes¹⁰.

The prevalence of prediabetes in previously non-diabetic patients with a recent ischemic stroke or TIA is on average 37% in the acute phase (within 3 months after the event) and 32% in the postacute phase (≥ 3 months after the event), which is clearly higher than in the overall population^{11,12,13,14,9,10,15,16,17,18,19,20}

Beside other factors the prevalence of diabetes/prediabetes, is influenced by ethnicity²¹, and this factor should therefore be taken into account when considering the prevalence of prediabetes in stroke patients. Time from the event to glucose level assessment also differed between the studies. Some assessed glucose levels in the acute phase (<2 weeks after the event)^{12,13,14,9,15,18,19,20} others in the chronic stroke phase (>3 months after the event)^{11,10,16,17}. Only 3 studies repeated the glucose measurement after 3 months, and

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this revealed that 22-44% of the patients had persistent prediabetes^{15,18,19}.

Majority of patients presenting to our units with ischaemic strokes have diabetes and hypertension. However there are patients who do not have these classic risk factors. Searching for other risk factors in these patients may help in preventing strokes. Prediabetes as a risk factor for ischaemic stroke in our set up has yet not been taken seriously. This research work has focussed on determining the frequency of prediabetes in ischaemic strokes.

MATERIAL & METHODS

A simple proforma having details of the case was filled from each patient who presented to our unit with ischaemic stroke. Record of previous sugar levels and fresh samples taken in fasting state along with HbA1c where available was kept. Inclusion/exclusion criteria applied. The required information was processed through SPSS.

Study duration

Prospective study conducted from March 2013 to March 2014

Inclusion/exclusion criteria

Patients with ischemic stroke and atrial fibrillation due to valvular heart disease, prothrombotic diseases, connective tissue disorders and other known causes of ischemic stroke e.g. infective endocarditis, sickle cell anemia, disseminated intravascular coagulation etc were excluded from the study. All other patients whose ages were more than 18 and presented to us with ischemic strokes were included in the study.

RESULTS

Out of 66 patients with ischaemic stroke, 60 were hypertensives & 6 were normotensives (Table-3). Out of 66 stroke patients, 23 had normoglycemia while 43 were found hyperglycemic (Table-2, bar chart & pie

Table-1; Criteria for diagnosis of prediabetes^{22,23}

Criteria based on;	FASTING PLASMA GLUCOSE	GTT (Two hour glucose tolerance test after ingesting the standardized 75 Gm glucose solution)	HBA1C
levels	110mg/dl to 125 mg/dl(WHO) 100mg/dl to 125mg/dl(ADA)	140 TO 199 mg/dl	5.7 to 6.4 percent

Table-2; Status of patients according to blood glucose levels

N Valid	66
Missing	0

Status of patients according to blood glucose levels

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid DM KNOWN	25	37.9	37.9	37.9
DM new	7	10.6	10.6	48.5
IFG	11	16.7	16.7	65.2
NORMAL	23	34.8	34.8	100.0
Total	66	100.0	100.0	

Table-3; Status of Hypertension in patients with ischemic stroke across different categories of glycemia

Status	Number of patients	%age
HTN (in prediabetics)	9	13.63
HTN(in Known Diabetics)	24	36.36
HTN(in newly Diabetics)	6	9.09
HTN(in normoglycemics)	21	31.81
Non hypertensives	6	9.09
Total	66	100%

Status of patients according to blood glucose level

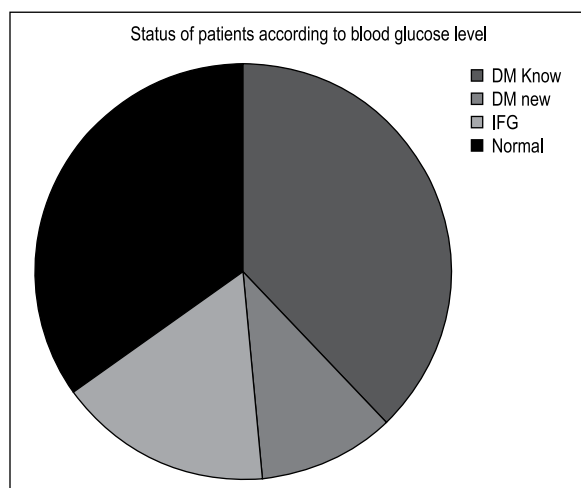
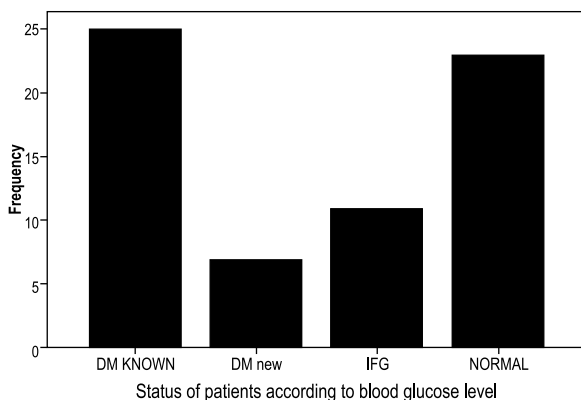


chart). Out of 43 Patients with hyperglycemia 11 had IFG while 32 were found to have frank diabetes (25 known diabetics & 7 newly diagnosed).

DISCUSSION

We studied 66 patients with ischaemic stroke for the frequency of impaired fasting glucose/prediabetes. Eleven (16.67%) patients were found to have prediabetes. All these patients presented to us in the acute phase of stroke. For the diagnosis of prediabetes we applied criteria based on fasting plasma glucose as given in Table-1^{22,23}

The prevalence of prediabetes in previously non diabetic patients with a recent ischemic stroke or TIA is on average 37% (range 29-53%) in the acute phase (within 3 months after the event) and 32% (range 23-46%) in the post acute phase (≥ 3 months after the event), which is clearly higher than in the overall population.^{11,12,13}

Compared to these studies we found IFG/Prediabetes in 16.7 % patients. Multiple factors may be responsible for the difference of our results from the above mentioned studies but few known were related to selection of the patients, criteria for diagnosis of pre-

diabetes and ethnicity. It is a well established fact that the prevalence of diabetes, and also of prediabetes, is influenced by ethnicity²¹, and this factor should therefore be taken into account when considering the prevalence of prediabetes in stroke patients.

Another important factor in diagnosing prediabetes is the time from the event to glucose level assessment which differed between the studies. Some studied glucose levels in the acute phase (<2 weeks after the event)^{12,13,20}, others in the chronic stroke phase (>3 months after the event)^{10,11,16}. Only 3 studies repeated the glucose measurement after 3 months, and this revealed that 22-44% of the patients had persistent prediabetes^{15,18,19}. We took samples for estimation of fasting plasma glucose the next morning after admission of our patient's i.e. in the acute phase.

It is difficult to say that their prediabetic status alone was responsible for their ischemic stroke as 9 patients in this group were hypertensives too. Moreover out of the total 66 patients with strokes 23 (34.84%) were normoglycaemics. Among them 21 were found to have hypertension. Hypertension is a strong risk factor for ischemic stroke and therefore to know the exact influence of glycemic status on the prevalence of stroke the study design must exclude cases of hypertension.

Similarly Out of the total 66 patients with stroke 32 (48.48%) were diabetics & hypertension was found in 30 of them. In our study of stroke patients several categories of glycemic status were found. Normoglycemia was found in 34.8 % while 65.2% had hyperglycemia. Though cases both due to diabetes and prediabetes were observed more than normoglycemia but if prediabetes alone is taken into account then normoglycemia was observed more often than impaired fasting glucose.

Several studies assessed the prevalence of prediabetes based on fasting plasma glucose levels and/or 2-hour postload glucose levels in stroke patient^{11,12,13,14,10,15,16,17,18,19}, 1 study assessed the prevalence based on glycosylated hemoglobin levels²⁰ and only 1 study assessed the prevalence based on all three detection methods⁹. However, inclusion criteria, definition of disturbed glucose metabolism, ethnicity and time between event and glucose measurement differed among these studies, making it difficult to compare them. We did not assess our patients for HbA1c as the facility was not available in the hospital, s lab.

Well designed studies on more patients preferably on normotensive individuals without having other risk factors, and considering only glycemic status of a patient as a risk to stroke may resolve issues regarding frequency of prediabetes in ischemic stroke.

CONCLUSION

Beside other risk factors, patients presenting with ischaemic stroke needs evaluation for prediabetes.

REFERENCES

1. Gerstein HC, Santaguida P, Raina P, Morrison KM, Balion C, Hunt D, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. *Diabetes Res Clin Pract* 2007; 78:305-12
2. Buyschaert M, Bergman M: Definition of prediabetes. *Med Clin North Am* 2011;95:289-297, vii.
3. American Diabetes Association: Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2013;36(suppl 1):S67-S74.
4. Ford ES, Zhao G, Li C: Pre-diabetes and the risk for cardiovascular disease: a systematic review of the evidence. *J Am Coll Cardiol* 2010;55:1310-1317.
5. Lee M, Saver JL, Hong KS, Song S, Chang KH, Ovbiagele B: Effect of pre-diabetes on future risk of stroke: meta-analysis. *BMJ* 2012;344:e3564.
6. Vermeer SE, Sandee W, Algra A, Koudstaal PJ, Kappelle LJ, Dippel DW: Impaired glucose tolerance increases stroke risk in nondiabetic patients with transient ischemic attack or minor ischemic stroke. *Stroke* 2006;37:1413-1417.
7. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393-403.
8. Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT, Khunti K: Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* 2007;334:299.
9. Lindsberg PJ, Tuomi T, Kaste M: Oral glucose tolerance test should be performed after stroke and transient ischemic attack. *Int J Stroke* 2011;6:317-320.
10. Fonville S, Zandbergen AA, Vermeer SE, Dippel DW, Koudstaal PJ, den Hertog HM: Prevalence of prediabetes and newly diagnosed diabetes in patients with a transient ischemic attack or stroke. *Cerebrovasc Dis* 2013;36:283-289.
11. Kernan WN, Viscoli CM, Inzucchi SE, Brass LM, Bravata DM, Shulman GI, McVeety JC: Prevalence of abnormal glucose tolerance following a transient ischemic attack or ischemic stroke. *Arch Intern Med* 2005;165:227-233.
12. Matz K, Keresztes K, Tatschl C, Nowotny M, Dachenhausen A, Brainin M, Tuomilehto J: Disorders of glucose metabolism in acute stroke patients: an underrecognized problem. *Diabetes Care* 2006;29:792-797.
13. Urabe T, Watada H, Okuma Y, Tanaka R, Ueno Y, Miyamoto N, Tanaka Y, Hattori N, Kawamori R: Prevalence of abnormal glucose metabolism and insulin resistance among subtypes of ischemic stroke in Japanese patients. *Stroke* 2009;40:1289-1295.
14. Jia Q, Zheng H, Zhao X, Wang C, Liu G, Wang Y, Liu L, Li H, Zhong L: Abnormal glucose regulation in patients with acute stroke across China: prevalence and baseline patient characteristics. *Stroke* 2012;43:650-657.
15. Jia Q, Zheng H, Liu L, Zhao X, Wang C, Jing J, Liang D, Wang Y, Zhou Y, Dong K, Yang Z, Wang Y: Persistence and predictors of abnormal glucose metabolisms in patients after acute stroke. *Neurol Res* 2010;32:359-365.
16. Lam KS, Ma JT, Woo E, Lam C, Yu YL: High prevalence of undiagnosed diabetes among Chinese patients with ischaemic stroke. *Diabetes Res Clin Pract* 1991;14:133-137.
17. Gray CS, Scott JF, French JM, Alberti KG, O'Connell JE: Prevalence and prediction of unrecognised diabetes mellitus and impaired glucose tolerance following acute stroke. *Age Ageing* 2004;33:71-77.
18. Vancheri F, Curcio M, Burgio A, Salvaggio S, Gruttadauria G, Lunetta MC, Dovico R, Alletto M: Impaired glucose metabolism in patients with acute stroke and no previous diagnosis of diabetes mellitus. *Q J Med* 2005;98:871-878.
19. Dave JA, Engel ME, Freercks R, Peter J, May W, Badri M, Van Niekerk L, Levitt NS: Abnormal glucose metabolism in non-diabetic patients presenting with an acute stroke: prospective study and systematic review. *Q J Med* 2010;103:495-503.
20. Huisa BN, Roy G, Kawano J, Schrader R: Glycosylated hemoglobin for diagnosis of prediabetes in acute ischemic stroke patients. *J Stroke Cerebrovasc Dis* 2013;22:e564-e567.
21. Abdul-Ghani MA, Tripathy D, DeFronzo RA: Contributions of beta-cell dysfunction and insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting glucose. *Diabetes Care* 2006;29:1130-1139.
22. Jellinger, Paul S. "What You Need to Know about Prediabetes." *Power of Prevention*, American College of Endocrinology. Vol. 1, issue 2, May 2009. <http://www.powerofprevention.com/>
23. New Guidelines Urge A1C Test for Diabetes Diagnosis. *HealthDay*. December 29, 2009.