



ORIGINAL RESEARCH PAPER

Neurology

ROLE OF RANDOM BLOOD GLUCOSE LEVELS IN PROGNOSIS OF ACUTE ISCHEMIC STROKE

KEY WORDS: R.B.S.- random blood sugar

Dr. T. N. Dubey	Proffesor , Department of medicine Gandhi medical College ,Bhopal
Dr.Shubham Dubey*	(M.D.medicine) Senior resident ,department of medicine Gandhi medical college ,Bhopal *Corresponding Author
Dr.Pradeep Tiwari	P.G. resident (3rd year), Department of medicine ,Gandhi medical college, bhopal

ABSTRACT

Introduction – Stroke burden is on a rise in India. Hyperglycemia is related closely to outcome of stroke independent of diabetic status of the patient. High plasma glucose levels are associated with increased mortality and morbidity in stroke.
Material and methods- 100 patients of stroke were evaluated for random blood glucose levels. Infarct size , NIHSS score and complications were compared in normoglycemic group (R.B.S. < 140 mg/dl) and hyperglycemic group (R.B.S. > 140mg/dl).
Results- patients with R.B.S.>140mg/dl were associated with increase in infarct size, NIHSS score,increase in complications like pneumonia, bed sores, urinary tract infections, seizures and death.

Introduction

The definition of stroke ,revised by world health organization is “a neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours” 2

Stroke burden is on rise in India . The reason for rise in stroke burden includes smoking, increased longevity and lifestyle accompanying urbanization. Indians may be genetically predisposed to metabolic syndrome consisting of central obesity, high levels of triglycerides, and low levels of HDL cholesterol and glucose intolerance.6

Hyperglycemia is present in 20-40% with acute ischemic stroke59. The presence of hyperglycemia is associated with increased mortality and morbidity, greater stroke event, and larger infarct volumes.63

Hyperglycemia predicts higher mortality and morbidity after stroke independent of other adverse prognostic factors, more so in patients without prior history of diabetes.60-64

Aims and objectives:

- 1- To study the ischemic stroke patients in relation to glycemic status on admission.
- 2- To correlate the size of infarct in CT scan with relation to glycemic status.
- 3- To follow these patients during hospital stay for clinical recovery using National institute of health stroke scale.[NIHSS]

Material & Methods :- Study was conducted at Hamidia Hospital among 100 patients of stroke over a period of 2 years. 2015-2017 patients were investigated with CT Scan Brain and there RBS at time of admission was taken. Patients NIHSS Score were determined to predict morbidity / mortality and prognosis . Two groups were made of patients with normoglycemia(those with RBS <140 mg/dl) and hyperglycemia(RBS>140 mg/dl) and various parameters were compared in the two groups. Size of infarct was determined by Multi Slice CT Brain scan and Sugar levels were correlated with the size of infarct. Three groups were determined as those with infarct size less than 2cm², 2-5 cm² and greater than 5cm². Occurrence of normoglycemia and hyperglycemia was seen in three infarct size groups.

Results :-

Average age Group of patients who were admitted with stroke was 57.2 years,72% patients being males & 28% being females in study group. Out of all patients,58% patients had normal RBS (<140ms/dl) while 42% patients had RBS (>140 ms/dl).

Out of 72 male patients 50% had normal RBS while 44% had hyperglycemia while out of 28 females 64% had normal RBS while

36% had hyperglycemia.

Mean RBS in normoglycemic group was 117mg/dl while hyperglycemic group was 187 mg/dl.

Size of infarct was determined by Multi Slice CT Brain scan and Sugar levels were correlated with the size of infarct.

Three groups were determined as those with infarct size < 2cm², 2-5 cm² and >5cm².

Out of 48 patients with small size infarcts 40 were normoglycemic while 8 had hyperglycemia.

Out of 40 patients with medium size infarcts 18 had normoglycemia while 22 had hyperglycemia.

Almost all 12 patients who has large infarct were hyperglycemic suggestion that hyperglycemia had direct relation to infarct size.

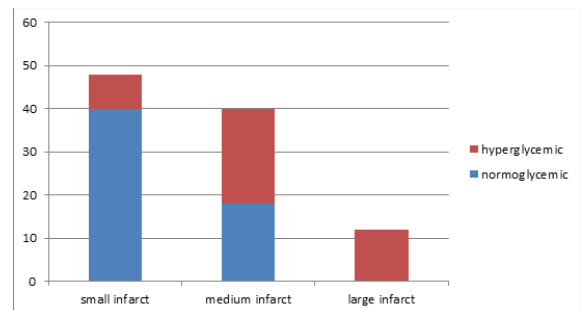


DIAGRAM1-shows distribution of normoglycemic and hyperglycemic patients with variuos infarct sizes.

NIHSS Score were calculated at time of admission

Mean NIHSS Score at time of admission in normoglycemic patients was 5.55 , while in hyperglycemic group was 21.4 [pearson Coefficient r=0.771 (p<0.001)]

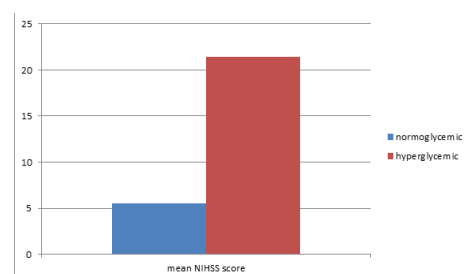


DIAGRAM 2-shows mean NIHSS score in normoglycemic and hyperglycemic patients. This suggested a direct relation between RBS at admission and NIHSS scoring.

Various complications including UTI, pneumonia, seizures, bed sore were studied in the two groups.

Occurrence of urinary tract infection, pneumonia, seizures, bed sore, sepsis and death was more in hyperglycemic group. Acute coronary syndromes were seen equally distributed in two groups with 4 patients each with normoglycemic hyperglycemia being affected.

Death was three times more common in hyperglycemic group with hyperglycemic group with mortality of 6 patients in this group and 2 deaths in normoglycemic group.

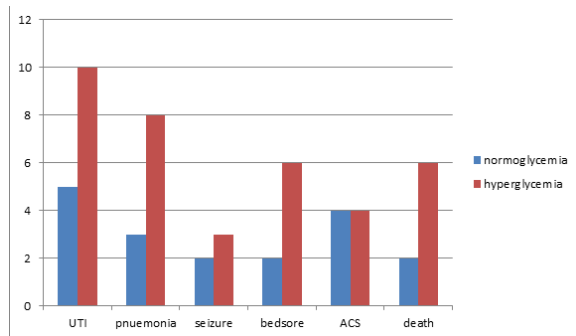


DIAGRAM 3 shows presence of complications in normoglycemic and hyperglycemic groups.

Discussion :- Our study found that hyperglycemia associated with increase in size of infarct. This finding was in accordance with study of (Louise et al.)⁵⁹ who had found that in his study that hyperglycemia was present in 20-40% patients regardless of history of diabetes.

(Tracey et al)⁷³ in his study also had concluded that hyperglycemia was independently related to the infarct size.

NIHSS score was directly related to hyperglycemia in our study. This was supported by previous study of [Gracy et al]³ who had concluded that recovery after stroke was seen commonly in normoglycemic patients. Findings of our study was comparable to Adams et al.⁷⁴ who found in his study that baseline NIHSS score strongly predicted the outcome.

[Johnston et al]⁷⁵ also found in his study that infarct volume was predictor for prognosis of patients and mean NIHSS score for normoglycemic status was lower and that of hyperglycemic group.

Summary and Conclusion -

Hyperglycemia in Stroke (RBS>140mg/dl) was found to have linear relation with infarct size and NIHSS Score and was strong predictor of complication and mortality with patient's having hyperglycemia being at increased risk of complications and death in stroke.

BIBLIOGRAPHY

- Schiller F (April 1970). "Concepts of stroke before and after Virchow". *Med Hist* 14 (2): 115-31.
- World Health Organisation (1978). *Cerebrovascular Disorders* (Offset Publications). Geneva:
- Tapas Kumar BANERJEE MD FRCP (London), *Shyamal Kumar DAS DM (Neurology) National Neurosciences Centre Calcutta, Kolkata, *Bangur Institute of Neurology, Kolkata, India
- Li SC, Schoenberg BS, Wang C, et al. Cerebrovascular disease in the People's Republic of China: epidemiologic and clinical features. *Neurology* 1985; 35: 1708-13.
- Bonita R, Beaglehole R. The enigma of the decline in stroke deaths in the United States - the search for an explanation. *Stroke* 1996;27:370-2.
- Reddy KS, Yousuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*. 1998;97:596-601
- Anand K, Chowdhury D, Singh KB, Pandav CS, Kapoor SK. Estimation of mortality and morbidity due to strokes in India. *Neuroepidemiology* 2001;
- Dalai PM. Burden of stroke: Indian perspective. *International Journal of Stroke*

- 2006;1:164-6.
- Banerjee TK, Mukherjee CS, Sarkhel A. Stroke in the urban population of Calcutta: an epidemiological study. *Neuroepidemiology*. 2001;20:201-7.
- 20: 208-211.25. Wolf PA. Epidemiology of stroke. In: Mohr JP, ChGeeganage, C. M., Bath, P. M. W. (2009). Relationship Between Therapeutic Changes in Blood Pressure and Outcomes in Acute Stroke: A MetaRegression. *Hypertension* 54: 775-781
- Marik, P. E., Varon, J. (2007). Hypertensive Crises: Challenges and Management. *Chest* 131: 1
- Lindenauer, P. K., Mathew, M. C., Ntuli, T. S., Pekow, P. S., Fitzgerald, J., Benjamin, E. M. (2004). Use of antihypertensive agents in the management of patients with acute ischemic stroke. *Neurology*
- (1998). Management soon after a stroke. *DTB* 36: 51-54
- Bell DSH: Stroke in the diabetic patient. *Diabetes Care* 17:213-19, 1994
- McCall AL: The impact of diabetes on the CNS. *Diabetes* 41:557-70, 1992
- Wannamethee SG, Shaper AG, Ebrahim S. HDL cholesterol, total cholesterol, and the risk of stroke in middle-aged British men. *Stroke* 2000; 31:1.882-8
- Iso H, Jacobs DR, Jr., Wentworth D, Neaton JD, Cohen JD. Serum cholesterol levels and six-year mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial. *N Engl J Med* 1989;320:904-10.
- Wolf PH, Abbott RD, Kannel WB (1987). "Atrial fibrillation: a major contributor to stroke in the elderly. The Framingham Study". *Arch. Intern. Med.* 147 (9). 1561-4.
- Gorelick PB (1987). "Alcohol and stroke". *Stroke; a Journal of Cerebral Circulation* 18 (1): 268-71..
- Westover AN, McBride S, Haley RW (April 2007). "Stroke in young adults who abuse amphetamines or cocaine: a population-based study of hospitalized patients". *Archives of General Psychiatry* 64 (4): 495-502.
- Cantu C, Arauz A, Murillo-Bonilla LM, Lopez M, Barinagarrementeria F (2003). "Stroke associated with sympathomimetics contained in over-the-counter cough and cold drugs". *Stroke* 34 (7): 1667-72.
- Andrew G. Bostom, MD, MS; Irwin H. Rosenberg, MD; Halit Silbershatz, PhD; Paul F. Jacques, ScD; Jacob Selhub, PhD; Ralph B. D'Agostino, PhD; Peter W F. Wilson, MD; and Philip A. Wolf, MD
- Philip M W Bath, Stroke Association professor of stroke medicine', Laura J Gray, medical statistician'
- Graeme J. Hankey Potential New Risk Factors for Ischemic Stroke *Stroke*. 2006;37:2181-2188
- "Brain Basics: Preventing Stroke". National Institute of Neurological Disorders and Stroke. Retrieved 2009-10-24
- Shuaib A, Hachinski VC (September 1991). "Mechanisms and management of stroke in the elderly". *CMAJ* 145 (5): 433-43.
- Stam J (April 2005). "Thrombosis of the cerebral veins and sinuses". *The New England Journal of Medicine* 352 (17): 1791-8.
- Guercini F, Acciarresi M, Agnelli G, Pacioni M (April 2008). "Cryptogenic stroke: time to determine aetiology". *Journal of Thrombosis and Haemostasis* 6 (4): 549-54.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C (June 1991). "Classification and natural history of clinically identifiable subtypes of cerebral infarction". *Lancet* 337 (8756): 1521-6..
- Adams HP, Bendixen BH, Kappelle LJ, et al. (January 1993). "Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment"
- Jones TH, Morawetz RB, Crowell RM, et al. Thresholds of focal ischemia in awake monkeys. *J Neurosurg*. 1981; 54:773-782
- Bruno A, Biller J, Adams HP Jr, et al. Acute blood glucose level and outcome from ischemic stroke. *Neurology*. 1999;52:280-284.
- Reith J, Jorgensen HS, Pedersen PM, et al. Body temperature in acute stroke: relation to stroke severity, infarct size, mortality, and outcome. *Lancet*. 1996;347:422-425.
- Hademenos GJ, Massoud TF. Biophysical mechanisms of stroke. *Stroke* 1997;28: 2067-77
- Rothman SM, Olney JW Excitotoxicity and the NMDA receptors. *Trends Neurosci*. 1987; 10:299-302
- Garcia JH, Yoshida Y, Chen H et al. Progression from ischemic injury to infarct following middle cerebral artery occlusion in the rat. *Am J Pathol* 1993; 142:623-635
- Melamed E. Reactive hyperglycaemia in patients with acute stroke. *J Neurol Sci*. 1976; 29: 267-275
- Murros K, Fogelholm R, Kettunen S, Vuorela AL, Valve J. Blood glucose, glycosylated haemoglobin, and outcome of ischemic brain infarction. *J Neurol Sci*. 1992; 111: 59-64.
- Tracey F, Crawford VL, Lawson JT, Buchanan KD, Stout RW Hyperglycaemia and mortality from acute stroke. *Q J Med*, 1993; 86: 439-446.
- van Kooten F, Hoogerbrugge N, Naarding P, Koudstaal PJ. Hyperglycemia in the acute phase of stroke is not caused by stress. *Stroke*. 1993; 24: 1129-1132
- Duckrow RB, Beard DC, Brennan RW. Regional cerebral blood flow decreases during hyperglycemia. *Ann Neurol*. 1985; 17: 267-272.
- Kawai N, Keep RF, Betz AL, Nagao S. Hyperglycemia induces progressive changes in the cerebral microvasculature and blood-brain barrier transport during focal cerebral ischemia. *Acta Neurochir Suppl*. 1998; 71: 219-221.
- Folbergrova J, Memezawa H, Smith ML, Siesjo BK. Focal and perifocal changes in tissue energy state during middle cerebral artery occlusion in normo- and hyperglycemic rats. *J Cereb Blood Flow Metab*. 1992; 12: 25-33.
- Li PA, Shuaib A, Miyashita H, He QP, Siesjo BK, Warner DS. Hyperglycemia enhances extracellular glutamate accumulation in rats subjected to forebrain ischemia. *Stroke*. 2000; 31: 183-192.
- Berger L, Hakim AM. The association of hyperglycemia with cerebral edema in stroke. *Stroke*. 1986; 17: 865-871.
- Mohanty P, Hamouda W, Garg R, Aljada A, Ghanim H, Dandona P. Glucose challenge stimulates reactive oxygen species (ROS) generation by leucocytes. *J Clin Endocrinol Metab*. 2000; 85: 2970-2973.
- Dhindsa S, Tripathy D, Mohanty P, Ghanim H, Syed T. Aljada A. Dandona P Differential effects of glucose and alcohol on reactive oxygen species generation and intranuclear nuclear factor-kappab in mononuclear cells. *Metabolism*. 2004; 53: 330-334
- Chew W, Kucharczyk J, Moseley M, Derugin N, Norman D. Hyperglycemia augments ischemic brain injury: in vivo MR imaging/spectroscopic study with nocardipine in cats with occluded middle cerebral arteries. *AJNR Am J Neuroradiol*. 1991; 12: 603-609.
- Kushner M, Nencini P, Reivich M, Rango M, Jamieson D, Fazekas F, Zimmerman R,

Chawluk J, Alavi A, Alves W. Relation of hyperglycemia early in ischemic brain infarction to cerebral anatomy, metabolism, and clinical outcome. *Ann Neurol*. 1990; 28: 129-135.

50. Wagner KR, Kleinholz M, de Courten-Myers GM, Myers RE. Hyperglycemic versus normoglycemic stroke: topography of brain metabolites, intracellular pH, and infarct size. *J Cereb Blood Flow Metab*. 1992; 12: 213-222.

51. Anderson RE, Tan WK, Martin HS, Meyer FB. Effects of glucose and pao2 modulation on cortical intracellular acidosis, nadh redox state, and infarction in the ischemic penumbra. *Stroke*. 1999; 30: 160-170.

52. Araki N, Greenberg JH, Sladky JT, Uematsu D, Karp A, Reivich M. The effect of hyperglycemia on intracellular calcium in stroke. *J Cereb Blood Flow Metab*. 1992; 12: 469-476.33.

53. Barnes PJ, Karin M. Nuclear factor-kappab: a pivotal transcription factor in chronic inflammatory diseases. *N Engl J Med*. 1997; 336: 1066-1071.

54. Nurmi A, Lindsberg PJ, Koistinaho M, Zhang W, Juettler E, Karjalainen-Lindsberg ML, Weih F, Frank N, Schwaninger M, Koistinaho J. Nuclear factor-kappab contributes to infarction after permanent focal ischemia. *Stroke*. 2004; 35: 987-991.

55. McInnis J, Wang C, Anastasio N, Hultman M, Ye Y, Salvemini D, Johnson KM. The role of superoxide and nuclear factor-kappab signaling in N-methyl-D-aspartate-induced necrosis and apoptosis. *J Pharmacol Exp Ther*. 2002; 301: 478-487.

56. Schneider A, Martin-Villalba A, Weih F, Vogel J, Wirth T, Schwaninger M. NF-kappab is activated and promotes cell death in focal cerebral ischemia. *Nat Med*. 1999; 5: 554-559.

57. Aljada A, Ghanim H, Mohanty P, Syed T, Bandyopadhyay A, Dandona P. Glucose intake induces an increase in activator protein 1 and early growth response 1 binding activities, in the expression of tissue factor and matrix metalloproteinase in mononuclear cells, and in plasma tissue factor and matrix metalloproteinase concentrations. *Am J Clin Nutr*. 2004; 80: 51-57.

58. Gursoy-Ozdemir Y, Qiu J, Matsuoka N, Bolay H, Bermpohl D, Jin H, Wang X, Rosenberg GA, Lo EH, Moskowitz MA. Cortical spreading depression activates and upregulates mmp-9. *J Clin Invest*. 2004; 113: 1447-1455.

59. Louise E. Allport, BMed, FRACP; Ken S. Butcher, MD, PhD, FRCP(C); Tracey A. Baird, MRCP; Lachlan MacGregor, MBBS, MmedSc; Insular Cortical Ischemia Is Independently Associated With Acute Stress Hyperglycemia.

60. Pulsinelli WA, Levy DE, Digsbee B, Scherer P, Plum F. Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes Mellitus. *Am J Med* 1983; 74:540-43

61. Weir CJ, Murray GD, Dyker AG, Lees KR. Is hyperglycemia an independent predictor of poor outcome after acute stroke: Results of a long-term follow-up study. *Brit Med J* 1997; 314:1303-1306.

62. Jorgensen Stroke 25:1977-73, 1994

63. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke*. 2001;32:2426-2432.

64. Alvarez-Sabin J, Molina CA, Ribo M, Arenillas JF, Montaner J, Huertas R, Santamarina E, Rubiera M (2004) Impact of admission hyperglycemia on stroke outcome *Stroke* 35:2493-2498

65. Parsons MW, Barber PA, Desmond PM, Baird TA, Darby DG, Byrnes G, Tress BM, Davis SM (2002) Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging and spectroscopy study. *Ann Neurol* 52:20-28

66. Vanja Basic Kes, Vesna Vargek Solter. *Visnja Supanc, Vida Demarin., Impact of hyperglycemia on ischemic stroke mortality in diabetic and non-diabetic patients Year: 2007 I: 27 II Issue: 5: 352-355*

67. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyincx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: Intensive insulin therapy in the critically ill patients. *N Engl J Med* 2001;345:1359-1367

68. Queale WS, Alexander JS, Brancati FL: Glycemic control and sliding scale insulin use in medical inpatients with diabetes mellitus. *Arch Intern Med* 157:545- 52, 1997.

69. Rodbard HVV, Blonde L, Braithwaite SS, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. *Endocr Pract*. 2007;13:1-68. .

70. American Diabetes Association. Standards of medical care in diabetes--2009. *Diabetes Care*. 2009;32(suppl 1):S13-S61

71. Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL, Higashida RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI, Rosenwasser RH, Scott PA, Wijdicks EF. American Heart Association: American Stroke Association Stroke Council,. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council. . *Stroke*. 2007; 38: 1655-1711

72. Thomassen L, Brainin M, Demarin V, Grond M, Toni D, Venables GS; EFNS Task Force on Acute Neurological Stroke Care. Acute stroke treatment in Europe: a questionnaire based survey on behalf of the EFNS task force on acute neurological stroke care. *Eur J Neurol*. 2003; 10: 199-204

73. Baird TA, Parsons MW, Phan T, Butcher KS, Desmond PM, Tress BM, Colman PG, Davis SM. Persistent poststroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. *Stroke*. 2003; 34: 2208-2214

74. Adams, H. P. Davis, P. H., Leira, E. C., Chang, K. C., Bendixen, B. H., Clarke, W. R., et al. (1999). Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). *Neurology*, 53, 126-131

75. C. Johnston, MD; A. F. Connors, Jr, MD; D. P. Wagner, PhD; W. A. Knaus, MD; X.-Q. Wang, MS; E. Clarke Haley, Jr, MD for the Randomized Trial of Tirilazad Mesylate in Acute Stroke (RANTTAS) Investigators *Stroke*. 2000;31:448-455.