

Comparison of Unfavorable Outcome with and without Persistent Hyperglycemia in Patients Presenting with Acute Ischemic Stroke

SAFDAR HUSSAIN ARAIN¹, ABDUL GHAFOOR MAGSI², FAHIM AHMED SOOMRO³, MUHAMMAD MUNWAR ALI⁴, ALI HYDER MUGHERI⁵, ABRAR SHAIKH⁶

¹Associate Professor & Head of Neurosurgery Department, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat

²Assistant Professor of Neurology, Chandka Medical College/Shahheed Mohtarma Benazir Bhutto Medical University, Larkana

³Assistant Professor of Neurology, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat

⁴Assistant Professor of Neurosurgery, Chandka Medical College/Shahheed Mohtarma Benazir Bhutto Medical University, Larkana

⁵Associate Professor of Gastroenterology, Chandka Medical College/Shahheed Mohtarma Benazir Bhutto Medical University, Larkana

⁶Professor & Dean Research & Postgraduate Studies, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat Pakistan

Correspondence to Dr. Abdul Ghafoor Magsi, Email: drmagsi@hotmail.com Cell: 0333-3668623

ABSTRACT

Aim: To compare the unfavorable outcome with and without persistent hyperglycemia in patients presenting with acute ischemic stroke.

Study Design: Prospective observational study

Place and duration of study: Department of Neurology, Chandka Medical College/Shahheed Mohtarma Benazir Bhutto Medical University, Larkana from 1st January 2021 to 30th September 2021.

Methodology: Seventy ischemic stroke patients within the age group of 50-70 years were enrolled. There radiological imaging, clinical characteristics as well as sugar blood analysis was continuously monitored. The patients were divided into Group I and Group II (both having 35 patients each). Group I were those ischemic stroke patients with persistent hyperglycemia while Group II were those ischemic stroke patients who had no hyperglycemia. A comparison of primary and secondary outcomes of both groups was made and entered in a well structured questionnaire.

Results: There was no significant variance among males and females of both groups. the mean rank of group I of ischemia and duration of hospitalization was much higher than group II. A significantly higher number of patients (74.2%) in group I with uncontrolled hyperglycemia lost their lives. The mechanical ventilation (82.8% vs 31.4%), vasopressin (85.7%vs 34.2%) and hemorrhagic transformation (31.4%vs 8.5%) was significantly higher in group I than group II respectively.

Conclusion: There is a significant risk of unfavorable outcome in ischemic stroke patient with persistent hyperglycemia including a higher risk of mortality and mechanical ventilation requirement.

Key words: Hyperglycemia, Ischemic Stroke, Diabetes, Complications

INTRODUCTION

Stroke is one of the most important causes of mortality and disabilities all over the globe. Diabetes is one of the known factor of stroke occurrence.^{1,2} Diabetes is a growing chronic and highly prevalent disease which according to predicted results, will affect 642 million people in year 2040.³ High frequency of patients who suffered from stroke have hyperglycemia without a patient of diabetes.⁴ Diabetic patients who suffered from stroke had more chances of neurological disability as compared to non-diabetic patient.

Data of large multicenter study showed that, 26% of the stroke patient had the past history of diabetes. Similarly, studies also proved that, approximately 20–33% patients with stroke may have diabetes mellitus.⁵⁻⁷ Various studies have demonstrated relation between increased mortality rate and comorbid diabetes.^{8,9} Few researchers suggested that patients with stress or acute hyperglycemia are more prone to stroke whereas others researchers argued that chronic dysglycemia in stroke patients causes major modifications in pathological processes.^{9,10}

HbA1c testing prove to be a beneficial measure to predict past 120 days' glucose in blood, thus minimizing the misdiagnosis potential that leads to stress hyperglycemia.¹⁰ This test has several advantages over fasting glucose measure. Studies have also showed that it can also predict the incidence chances of stroke.¹¹ There is dire need for the estimation and understanding of high risk stroke population, prognosis and its related complication. Present study was design to determine the stroke prevalence in patients with and without hyperglycemic history. This study will provide comparative analysis of stroke between hyperglycemic groups.

MATERIALS AND METHODS

The prospective observational study was conducted at Department of Neurology, Chandka Medical College/Shahheed Mohtarma Benazir Bhutto Medical University, Larkana from 1st January 2021 to 30th September 2021 after approval from IRB and 70 patients were enrolled. A written informed consent was taken from each patient before initializing of the study. The inclusion criteria was based on patients suffering from diabetes mellitus as well as presented with ischemic-stroke. Patients having multiple comorbidities were excluded from the study. The total patients were divided into two groups. Group 1 had those patients having uncontrolled levels of hyperglycemia while

Received on 10-10-2021

Accepted on 24-03-2022

Group II had patients with controlled sugar levels (<150 mg/dl). Each group had 35 patients adjusted for their age. Ischemic strokes were identified through clinical symptoms as well as radiological imaging (CT scans), magnetic resonance imaging as well as carotid duplex. ECG was performed. The sugar levels of each patients was randomly measured after 2 hours of fasting while complete fasting blood sugar was taken with 10 hours post intake of food. HbA1C levels were also tested. All the biochemical testing required a withdrawal of 5cc blood from each patient which was further converted into serum through centrifugation at 3000rpm. The samples were stored at -20°C until analysis. The ischemic stroke patients were continuously monitored under strict observation and their sugar levels were repeatedly tested either in hourly pattern for those on insulin-infusion or every 4 hourly in normal RBS patients. The ischemia stroke was determined by the 15-item neurological assessment score. It provided a complete severity assessment at admission and discharge. It included consciousness level, eye-movement, visual field integrity, strength in arms and legs, facial movement, coordination, speech, sensations, language as well as neglect. The scoring ranged from 0-42 and categorized as none at 0, mild at 1-4, moderate at 5-15, moderate-severe at 16-20 and severe at 21-42. All patients were given a standard management protocol which was followed for the hemodynamics, respiratory-parameters, duration of hospital, mortality 30-day follow-up, hemorrhagic-transformation, requirement of ventilator or vasopressin for arterial BP maintenance by 70-100 mmHg. The data was recorded on a well-structured questionnaire and analyzed through Pearson Chi square for independence and univariate regression analysis tools. Skewed data was expressed as median, interquartile-range (25th-75th percentile) by using SPSS version 25.0. (p value<0.05 significant).

RESULTS

There was no significant variance among males and females of both groups, however in uncontrolled glycemic patients the ration of females was higher than males while it was vice versa in normal random blood sugar (RBS) group. The mean BMI was within normal range in both groups while the mean rank of ischemia in accordance with the ischemic stroke score was much higher in group I than group II. The RBS was also significantly higher in group I (Table 1).

The primary and secondary outcome comparison among groups showed an obvious change among both groups, where the mean rank of group I of ischemia was much higher than group II. Similarly there was a high presentation of mean rank of hospital stay in group I. A significantly higher number of patients (74.2%) in group I with uncontrolled hyperglycemia lost their lives while 28.5% of controlled

hyperglycemia ischemic stroke patients also died. The overall percentage of patients requiring mechanical ventilation, vasopressin and hemorrhagic transformation was significantly higher in group I than group II (Table 2).

The univariate analysis available showed that the RBS value of twenty four hours at a cut off of greater than 145mg/dl presented a significant and a good variation power for a thirty day mortality with area under curve (AUC) as 0.81 which was classified correctly through 80.1% accuracy carrying a risk mortality ratio (odds ratio) of 1.031 (Table 3).

Table 1: Comparison of baseline characteristics within groups I and II

Variable	Group I	Group II	P value
Gender			
Male	16 (45.7%)	18 (51.4%)	0.655
Female	19 (54.3%)	17 (48.6%)	
Age (years)	66.7±3.2	57.1±6.6	< 0.001
BMI (kg/m ²)	23.6±1.5	23.7±1.4	0.421
RBS on admission (mg/dl)	238.7±32.9	122.1±8.0	< 0.001
RBS after 24 h (mg/dl)	251.0±53.1	128.0±837	< 0.001
Ischemia on admission			
Median	33/9	2.7	< 0.001
IQR	27.0–39	2.1–9.1	
Mean rank	54.59	26.41	

Table 3: Univariate analysis of random blood sugar

24-h RBS	Cutoff	Sensitivity %	Specificity %	AUC	95% CI	Accuracy %	Odds ratio	95% CI	P value
> 145		79.06	83.79	0.81	0.71- 0.879	80.1	1.031	1.0121 to 1.0331	< 0.001

DISCUSSION

After stroke, clinical presentation greatly differs and depends on many contributing factors and underlying health conditions.¹² Analysis and exact evaluation of expected outcome is crucial for patient management and treatment plan and to give appropriate prognostic information to the relative and patients itself.¹³ Diabetes is the root cause of many diseases due to sharing common predisposing genes and maintaining overall hemostasis of the body. It is also one of the most prevalent causes of stroke as reported in many studies.

Numerous studies have demonstrated that, stress hyperglycemia is main predictor of stroke.¹⁴⁻¹⁶ Danish study has showed association of plasma glucose level with high rate of hospital mortality.¹⁷ Regardless of the large data, it is still indefinite to connect hyperglycemia to stroke severity or to associate it with brain damage. A study conducted on 811 acute ischemic stroke patients and highlighted that high glucose level was strongly found in patients especially with 72 hours' fatality.¹⁸ It is also noteworthy that rate of glucose level deviation from normal could also worsen the situation and further exacerbate the situation by causing damaging effect to brain¹⁹.

Glucose control through lifestyle modification, maintaining healthy weight, avoiding saturated fat intake, dietary habits changes, certain medications such as glucose lowering agents, increasing physical activity, augmenting fiber intake and prevention of other associated risk factors including blood pressure and dyslipidemia could prove effective towards stroke prevention.

CONCLUSION

There is a significant risk of unfavorable outcome in ischemic stroke patient with persistent hyperglycemia including a higher risk of mortality and mechanical ventilation requirement in comparison to those ischemic stroke patients with normal glycemic values.

Conflict of interest: Nil

REFERENCES

- O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet* 2010; 376:112-23.

Table 2: comparison of primary and secondary outcomes in group I and II

Variable	Group I	Group II	P value
Ischemia on discharge			
Median	2.1	1.1	0.04*
IQR	1.1–2.1	1.1–1.1	
Mean rank	27.34	17.38	
Duration in hospital (days)			
Median	15.1	10.1	< 0.001
IQR	11.6–21.1	7.2–13.1	
Mean rank	49.93	31.10	
Mortality			
No	9 (25.7%)	25 (71.5%)	< 0.001
Yes	26 (74.3%)	10 (28.5%)	
Mechanical-ventilation			
No	6 (17.2%)	24 (68.5%)	< 0.001
Yes	29 (82.8%)	11 (31.4%)	
Vasopressor requirement			
No	5 (14.2%)	23 (65.7%)	< 0.001
Yes	30 (85.8%)	12 (34.3%)	
Haemorrhagic transformation			
No	24 (68.6%)	32 (91.4%)	0.001
Yes	11 (31.4%)	3 (8.6%)	

- Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet Glob Health* 2013;1(5): e259-81.
- International Diabetes Federation. *IDF Diabetes Atlas*, 7th edn Brussels: International Diabetes Federation, 2015.
- Melamed E. Reactive hyperglycaemia in patients with acute stroke. *J Neurol Sci* 1976;29:267-75.
- O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet* 2016; 388: 761-75.
- Gray CS, Scott JF, French JM, Alberti KGMM, O'Connell JE. Prevalence and prediction of unrecognised diabetes mellitus and impaired glucose tolerance following acute stroke. *Age Ageing* 2004; 33: 71-7.
- Zahra F, Kidwai SS, Siddiqi SA, et al. Frequency of newly diagnosed diabetes mellitus in acute ischaemic stroke patients. *J Coll Physicians Surg Pak* 2012; 22: 226-9.
- Eriksson M, Carlberg B, Eliasson M. The disparity in long-term survival after a first stroke in patients with and without diabetes persists: the Northern Sweden MONICA study. *Cerebrovasc Dis* 2012; 34: 153-60.
- Lei C, Wu B, Liu M, et al. Association between hemoglobin A_{1c} levels and clinical outcome in ischemic stroke patients with or without diabetes. *J Clin Neurosci* 2015; 22: 498–503.
- Hjalmarsson C, Manhem K, Bokemark L, et al. The role of prestroke glycemic control on severity and outcome of acute ischemic stroke. *Stroke Res Treat* 2015; 2014: 1–6.
- d'Emden MC, Shaw JE, Colman PG, et al. The role of HbA_{1c} in the diagnosis of diabetes mellitus in Australia. *Med J Aust* 2012; 197: 220–21.
- Flint AC, Smith WS. Predicting long-term outcomes for ischemic stroke based on admission variables (www.strokerounds.org). *Stroke Rounds* 2004;2:1–6.
- Olai L, Omne-Ponte M, Borgquist K, et al. Prognosis assessment in stroke patients at discharge from hospital. *Age Ageing* 2007;36:184–9.
- Khairollah A, Nicholas B, Geoffrey G. Hyperglycaemia and mortality. *J R Soc Med* 2007;100:503-7.
- Jorgensen H, Nakayama H, Raaschou HO, et al. Stroke in patients with diabetes. The Copenhagen Stroke Study. *Stroke* 1994;25:1977-84.
- Baird TA, Parsons MW, Phan T, et al. Persistent poststroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. *Stroke* 2003;34:2208-14.
- Capes SE, Hunt D, Malmberg K, et al. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke* 2001;32:2426–32.
- Nardi K, Milia P, Eusebi P, Paciaroni M, Caso V, Agnelli G. Predictive value of admission blood glucose level on short-term mortality in acute cerebral ischemia. *J Diabetes Complications* 2012; 26:70-76.
- Gaillard T, Miller E. Guidelines for stroke survivors with diabetes mellitus. *Stroke* 2018; 49:e215–7.