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HYPERGLYCEMIA IN ACUTE SUBARACHNOID HEMORRHAGE

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ABSTRACT

INTRODUCTION: Subarachnoid hemorrhage (SAH) is associated with high inhospital mortality and morbidity. Hyperglycemia occurs frequently in acute medical conditions including SAH and is associated with poor outcome. The aim of the study was to determine the frequency of Hyperglycemia in patients of subarachnoid hemorrhage.

MATERIALS AND METHODS: This was a cross sectional study that was conducted from September 3, 2013 to March 2, 2014 in Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad. All patients who met the inclusion criteria were selected for the study. Subarachnoid hemorrhage was diagnosed on the basis of plain CT scan brain. Random blood sugar levels of all patients of SAH were checked with glucometer on the day of presentation.

RESULTS: A total of 75 patients were included. The mean age of patients was 40.05 years with standard deviation of 15.790 years. Out of 75 patients, 56 (74.67%) patients were male and 19 (25.33%) patients were female. 59 (78.67%) patients with subarachnoid hemorrhage had hyperglycemia while 16 (21.33%) patients had no hyperglycemia.

CONCLUSION: In our study hyperglycemia is frequently found in patients of subarachnoid hemorrhage. Early detection and treatment of hyperglycemia should be a part of initial management so as to minimize the mortality.

INTRODUCTION: Subarachnoid hemorrhage is an acute, critical medical emergency, with incidence of 9 per 100,000 person- years. 85 % of cases of subarachnoid hemorrhage are due to rupture of cerebral aneurysms. Mortality for posterior circulation aneurysms is (10-15% for all aneurysms) higher as compared to anterior circulation aneurysms1.

Clinical features of subarachnoid hemorrhage are severe and generalized, thunderclap headache, vomiting, neck stiffness, loss of consciousness, decerebrate posture, jerking of limbs or deficit of extremities2. Common complications are rebleed, hydrocephalus and reactive vasospasm3. Diagnosis can be made on CT brain, MRA is valuable with 96.7 % sensitivity in detection of intracranial aneurysm.4 Definitive treatment is obliteration of aneurysm via endovascular procedures or surgical clipping1, external ventricular drains prevent secondary hydrocephalus5.

Hyperglycemia occurs frequently in aneurysmal subarachnoid hemorrhage and is associated with delayed cerebral ischemia and poor out come6. Worldwide various studies have identified the frequency and impact of hyperglycemia on the outcome in the patients of subarachnoid hemorrhage but very few local studies are available in even determining the frequency of this commonly prevalent condition in patients of subarachnoid hemorrhage.

The aim of the study was to detect the frequency of hyperglycemia in patients of subarachnoid hemorrhage in our setup to generate the data in local population to emphasize checking the plasma glucose levels as a routine part of investigations in SAH.

MATERIALS AND METHODS:

This was a descriptive case study conducted in the Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad for six months from September 3, 2013 to March 02, 2013 after taking permission from

ethical committee of hospital. A total of 75 patients of subarachnoid hemorrhage were enrolled using non probability consecutive sampling. Sample size was calculated using WHO sample size calculator. An informed written consent was taken from all the patients. All patients of both genders above 13 years of age with subarachnoid hemorrhage (diagnosed on basis of CT scan brain) were enrolled in this study. Diagnostic criteria for SAH was defined on basis of CT scan brain if any one of the following is present on CT Brain: Hyperdensity (blood) in inter hemispheric fissure or sylvian fissure or perimesencephalic cistern with or without ventricular/parenchymal extension. Hyperglycemia was defined as Blood glucose levels >140 mg/dl checked with glucometer on the day of presentation.7 Those patients who had lobar (frontal/parietal/temporal/occipital regions of brain) or central (brainstem/basal ganglia/thalamus) bleed on CT scan brain and Patients having prior history of diabetes mellitus were excluded from the study.

Patients who fulfilled the criteria as per the findings of CT scan brain underwent detailed history and Neurological examination. Random blood sugar levels of all the patients of subarachnoid hemorrhage were checked with glucometer on the day of presentation. The data was entered on a standardized Performa. Data was entered and analyzed using SPSS version 17. Mean and standard deviation was calculated for numerical variables (age). Frequencies and percentages were calculated for categorical variables (gender, hyperglycemia).

RESULTS:

A total of 75 patients were included in this study. The mean age of patients was 34.41±17.12.

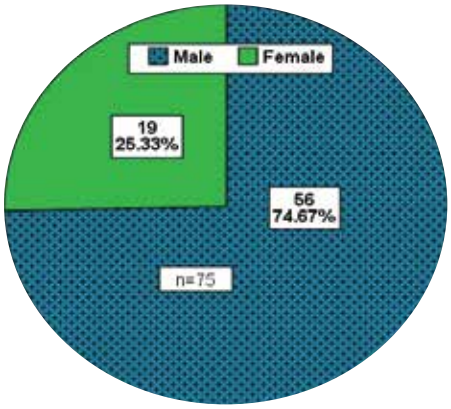
The minimum age of patients was 13 years, maximum age was 75 years, median age of patients was 44 years as shown in table 1:

Table no: 1
Age distribution of patients in years

Total no of patients (n)	Valid	75
	Missing	0
Mean age of patients in years		46.05
Median age of patients in years		44.00
Mode age of patients in years		35
Std. Deviation		15.790
Range age of patients in years		62
Minimum age of patients in years		13
Maximum age of patients in years		75

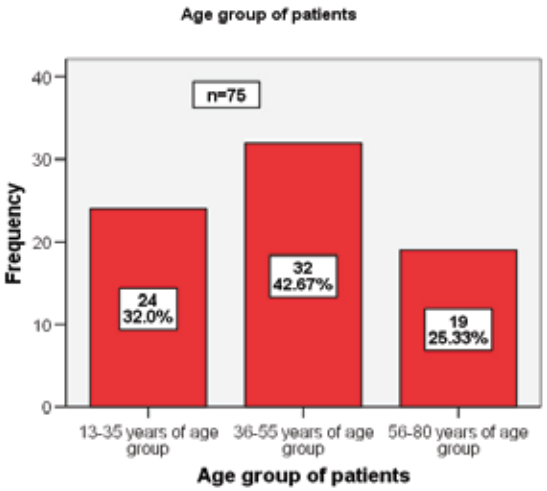
Out of 75 patients, 56 (74.67 %) patients were male and 19 (25.33%) patients were females as shown in Figure 1.

Figure no: 1 Gender of patients



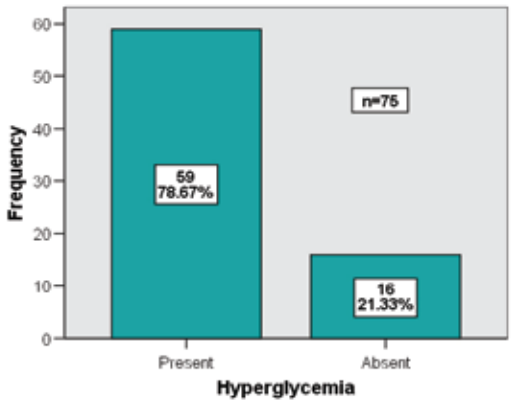
24 patients were in 13-35 years of age group, 32 patients were in 36-55 years of age group and 19 patients were in 56-80 years of age group as shown in figure 2:

Figure no: 2
Distribution of patients in age groups



59 (78.67%) patients with subarachnoid hemorrhage had hyperglycemia while 16 (21.33%) patients did not have hyperglycemia as shown in figure no: 3

Figure no: 3
Hyperglycemia in patients with subarachnoid hemorrhage

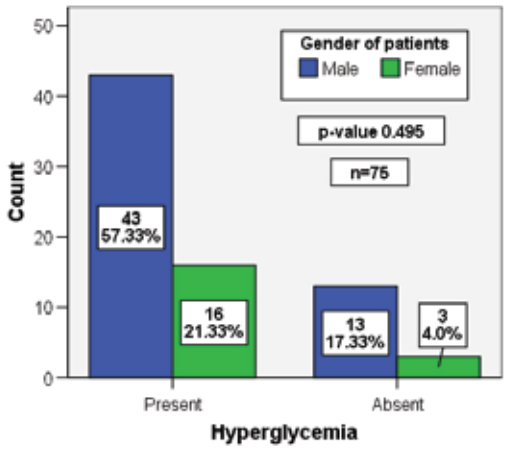


16 patients in 13-35 years of age group had hyperglycemia while 8 patients had no hyperglycemia, 25 patients in 36-55 years of age group had hyperglycemia while 7 patents had no hyperglycemia and 18 patients in 56-80 years of age group had hyperglycemia while 1 patient had no hyperglycemia insignificant p value of 0.083 showing insignificant age predilection as shown in table no: 2

Age group of patients	Hyperglycemia		Total	p-value
	Present	Absent		
13-35 years of age group	16 66.7%	8 33.3%	24 100.0%	**0.083**
36-55 years of age group	25 78.1%	7 21.9%	32 100.0%	
56-80 years of age group	18 94.7%	1 5.3%	19 100.0%	
Total	59 78.7%	16 21.3%	75 100.0%	

43 male patients and 16 female patients had hyperglycemia while 13 male patients and 3 female patients had no hyperglycemia with insignificant p value of 0.495 as shown in figure no: 4

Figure no: 4



DISCUSSION:

Aneurysmal subarachnoid hemorrhage (SAH) is a devastating disease with high morbidity and mortality rates. Although these rates have decreased in the last decades, due to improving institutional care8, still the 30 days case fatality rate is 35-45 percent so subarachnoid hemorrhage is an extremely fatal subtype of stroke.9 Prevention and treatment of neurologic complications such as rebleeding, hydrocephalus, and delayed cerebral ischemia (DCI) are obvious targets to improve prognosis and can be improved with multidisciplinary management approach10. Besides neurologic complications, patients with SAH often have non neurologic medical complications that can influence outcome such as neurocardiogenic injury, neurogenic pulmonary edema, hyperglycemia and electrolyte imbalance11. Hyperglycemia occurs frequently in aneurysmal subarachnoid hemorrhage and is associated with delayed cerebral ischemia and poor out come12. Several mechanisms have been proposed for hyperglycemia, one possible explanation is that following subarachnoid hemorrhage there is activation of hypothalamo-pituitary axis which in turn activates sympathetic nervous system leading to increase release of stress hormones enhancing glucose metabolism. Another possibility is activation of inflammatory response and release of cytokines which contribute to delayed cerebral ischemia3. Inpatient glucose levels above 7.8 mmol/litre (140 mg/dl) are associated with poor out come7. Plasma glucose levels during hospitalization predict the outcome of disease and can be effectively managed with insulin therapy13. Hyperglycemia is common in neurologic insults such as subarachnoid hemorrhage, traumatic brain injury and ischemic stroke, and associated with poor clinical

outcome so intensive insulin therapy (IIT) has been suggested and used in these disorders.14 As treatment options are available for hyperglycemia , it has attracted increasing attention as a target for intervention, although adequate and safe glycemic control is difficult to achieve in patients with SAH. Because hyperglycemia seems to be implicated in the pathway from SAH to poor clinical outcome, insight into these mechanisms may reveal new treatment options.15-16

In our study, the mean age of patients was 46.05 years with standard deviation of 15.790 years. 56 (74.67%) patients were male and 19 (25.33%) patients were female and 78.67% patients of subarachnoid hemorrhage had hyperglycemia. These results of our study were comparable to the results of other studies. In a study conducted by Ghosh S et al17 showed that of the 1090 patients included in the study, 429 (39.36%) were males. The mean age of the females was 4 years less than that of the males. Hyperglycemia at admission was termed as a serum glucose reading of >140 mg/dl on admission and 869 (74.22%) patients were found to have hyperglycemia at admission. Patients with hyperglycemia had 20.48% chance of a good outcome compared to a 64.85% chance of good outcome in patients with no hyperglycemia (P < 0.0001). Patients with hyperglycemia at admission also had a higher risk of death (20.58%).

Kruyt ND et al18 included 17 cohort studies or clinical trials of 4095 patients with aneurysmal subarachnoid hemorrhage admitted within 72 hours that documented admission glucose levels or the rate of hyperglycemia. The mean admission glucose level was 9.3 mmol/L (range, 7.4 to 10.9 mmol/L; 14 studies, 3373 patients) and the median proportion of patients with hyperglycemia was 69% (range, 29 to 100; 16 studies, 3995 patients; cutoff levels of hyperglycemia, 5.7 to 12.0 mmol/L). The pooled OR (8 studies, 2164 patients) for poor outcome associated with hyperglycemia was 3.1 (range 2.3 to 4.3). Cutoff points for defining hyperglycemia varied across studies (6.4 to 11.1 mmol/L), but this had no clear effect on the observed OR for poor outcome.

In another study conducted by Wartenberg KE et al19 found that hyperglycemia (>11.1 mmol/L) was present in 30% of patients at admission. Other frequent medical complications observed were temperature >38.3 degrees C (54%), followed by anemia (36%), hypertension (>160 mm Hg systolic; 27%), hypernatremia >150 mmol/L (22%), pneumonia (20%), hypotension (<90 mm Hg systolic, 18%), pulmonary edema (14%), and hyponatremia <130 mmol/L (14%). Out of these abnormalities, Fever, anemia and hyperglycemia significantly predicted poor clinical outcome after adjustment for age, Hunt-Hess grade, aneurysm size, rebleeding, and cerebral infarction due to vasospasm.

Lanzino G et al20 studied plasma glucose level in 616 patients admitted within 72 hours after SAH. Admission glucose levels showed a statistically significant association with Glasgow Coma Scale scores, volume of blood on computerized tomography (CT) scans, and level of consciousness at admission. Elevated glucose levels at admission correlated with poor outcome. A good recovery, as assessed by the Glasgow Outcome Scale at 3 months, occurred in 70.2% of patients with normal glucose levels (< or = 120 mg/dl) and in 53.7% of patients with hyperglycemia (> 120 mg/dl) (p = 0.002). The death rates for these two groups were 6.7% and 19.9%, respectively (p = 0.001). Increased glucose levels between Days 3 and 7 also predicted a poor outcome; in these sub groups, good recovery was observed in 132 (73.7%) of 179 patients who had normal glucose levels (< or = 120 mg/dl) and 160 (49.7%) of 322 who had elevated glucose levels (> 120 mg/dl) (p < 0.0001). Death occurred in 6.7% and 20.8% of the two groups, respectively (p < 0.0001).

Badjatia N et al21 showed that mean admission blood glucose levels in higher range versus low range (176.6 +/- 40.3 mg/dL vs 162.3 +/- 47.8 mg/dL) and mean inpatient blood glucose values (166.2 +/- 24.7 mg/dL vs. 155.8 +/- 29.7 mg/dL) were significantly higher in patients with vasospasm(a potentially life threatening complication of sub arachnoid hemorrhage). Hyperglycemia was also associated with longer length of stay in the neurointensive care unit (14.5 +/- 7.1 days vs. 11.6 +/- 5.4 days) and poor outcome at discharge (modified Rankin score > or =3: 58.9% vs. 18.8%).

Our study has some limitations that need to be addressed. Determination of association of hyperglycemia with subarachnoid hemorrhage is sparse in literature and this study should be taken as an initial step in determining this association in our local population. Extrapolation of these data should therefore be done in the light of this limitation, although the results have shown that the relationship between hyperglycemia and SAH is robust and consistent.

CONCLUSION:

In our study significant number of patients of subarachnoid hemorrhage had hyperglycemia at hospital admission and this association was found to be consistent. As hyperglycemia in acute subarachnoid hemorrhage is a potential risk factor of delayed cerebral ischemia and warrants poor clinical outcome so

increased plasma glucose levels in previously normoglycemic patients of SAH should not go underrecognised. Further studies are needed to show the effect of hyperglycemia on poor outcome in SAH and for confirmation of potential benefit of adequate glycemic control after subarachnoid hemorrhage.

REFERENCES

1. Sharma S, Chandra PS, Abuzer A, Suri A, Gaikwad S, Mishra NK. Posterior circulation aneurysms: A 10- year institutional analysis. Indian J Neurosurg. 2012;1:119-23.
2. Ropper AH, Samuels MA. Cerebrovascular diseases. In: Davis JK, Sydor AM (editors). Adams and victor's principles of Neurology, 9th ed. Boston, USA: Mc Graw Hill; 2009:746-845.
3. Kruyt ND, Biessels GJ, DeVries JH, Luitse MJA, Vermeulen M, Rinkel GJ. Hyperglycemia in aneurysmal subarchnoid hemorrhage: a potentially modifiable risk factor for poor outcome. J Cereb Blood Flow Metab. 2010;30:1577-87.
4. Shahzad R, Younas F. Detection and catheterization of intracranial aneurysms: Magnetic resonance angiography versus digital subtraction angiography. J Coll Physicians Surg Pak. 2011;21:325- 9.
5. Hayat A, Rodrigues D, Crawford P, Mendelow D. External ventricular drains- can morbidity be reduced. Pak J Neurological Sci. 2009;4:1-3.
6. Latorre JGS, Yichou SH, Nogueira RG, Singhal AB, Carter BS, Ogilvy CS. Effective glycemic control with aggressive hyperglycemia management is associated with improved in aneurysmal subarachnoid hemorrhage. Stroke. 2009;40:1644-52.
7. Schlenk F, Vajkoczy P, Sarrafzadeh A. Inpatient hyperglycemia following aneurysmal subarachnoid hemorrhage and glucose management. Neurocrit Care. 2009;11:56-63.
8. Abdulhasan YB, Abdulraheem N, Simoneau G, Angle MR, Teitelbaum J. Mortality after spontaneous subarachnoid hemorrhage. World Neurosurg. 2018; 112: 799-811
9. Schertz M, Mehdaoui H, Hamlat A, Piotin M, Banydeen R, Mejdoubi. Incidence and Mortality of Spontaneous Subarachnoid Hemorrhage in Martinique. Journal. PLoS ONE. 2016; 11(5): e0155945
10. Brown RJ, Dhar R. Aneurysmal subarachnoid hemorrhage. J Clin Outcomes Manage. 2011;18(5): 223-237.
11. Lantigua H, Ortega-Gutierrez S, Schmidt JM, Lee K, Badjatia N, Agarwal S, Classen J, Connolly ES, Mayer SA. Subarachnoid hemorrhage: who dies and why? Critical Care. 2015; 19:309.
12. Ray B, Ludwig A, Yearout LK, Thompson DM, Bohnstedt BN. Stress-Induced Hyperglycemia After Spontaneous Subarachnoid Hemorrhage and Its Role in Predicting Cerebrospinal Fluid Diversion. World Neurosurg. 2017; 100:208-215.
13. Schmutzhard E, Rabinstein AA. Spontaneous subarchnoid hemorrhage and glucose management. Neurocrit Care. 2011;15:281-6.
14. Godoy DA, Soler C, Videtla W, Fuenzalida LC, Paranhos J, Costilla M, Pinero G, Jibaja M. Hyperglycemia in nondiabetic patients during the acute phase of stroke. Arq Neuro psiquiatr. 2012;70(2):134-139
15. Hughes PD, Becker GJ. Screening for intracranial aneurysms in autosomal dominant polycystic kidney disease. Nephrology (Carlton). 2003;8(4):163-70.
16. Wermer MJ, Koffijberg H, van der Schaaf IC. Effectiveness and costs of screening for aneurysms every 5 years after subarachnoid hemorrhage. Neurology. 2008;70(22):2053-62.
17. Ghosh S, Dey S, Maltenfort M, Vibbert M, Urtecho J, Rincon F. Impact of Hunt-Hess grade on the glycemic status of aneurysmal subarachnoid hemorrhage patients. Neurol India. 2012;60(3):283-7.
18. Kruyt ND, Biessels GJ, de Haan RJ, Vermeulen M, Rinkel GJ, Coert B. Hyperglycemia and clinical outcome in aneurysmal subarachnoid hemorrhage: a meta-analysis. Stroke. 2009;40(6):e424-30.
19. Wartenberg KE, Schmidt JM, Claassen J, Temes RE, Frontera JA, Ostapkovich N. Impact of medical complications on outcome after subarachnoid hemorrhage. Crit Care Med. 2006;34(3):617-23.
20. Lanzino G, Kassell NF, Germanson T, Truskowski L, Alves W. Plasma glucose levels and outcome after aneurysmal subarachnoid hemorrhage. J Neurosurg. 1993;79(6):885-91.

21. Badjatia N1, Topcuoglu MA, Buonanno FS, Smith EE, Nogueira RG, Rordorf GA. Relationship between hyperglycemia and symptomatic vasospasm after subarachnoid hemorrhage. Crit Care Med. 2005;33(7):1603-9.

27. Vincent JL. Relevance of albumin in modern critical care medicine. Best Pract Res ClinAnaesthesiol. 2009;23(2):183-191.

28. SapijaszkoMJ, Brant R, Sandham D, Berthiaume Y. Nonrespiratory predictor of mechanical ventilation dependency in intensive care unit patients. Crit Care Med. 1996;24(4):601-607.

29. Mamary AJ, Kondapaneni S, Vance GB, Gaughan JP, Martin UJ, Criner GJ. Survival in patients receiving prolonged ventilation: factors that influence outcome. Clin Med Insights CircRespirPulm Med. 2011;5:17-26.

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Maher Bano Malik; data collection, data analysis, manuscript writing, manuscript review
Jehangeer Shoro; data collection, data analysis, manuscript writing
Haris Majid Rajput; data collection, data analysis, manuscript writing