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Prognostic Outcome of Patients with Stroke with Special Reference to Plasma Glucose Levels and HbA_{1C}.

Chinmaya J. Kulkarni*, Sanjay T. Thorat, and Swati C. Aundhakar.

Department of Medicine, Krishna Institute of Medical Sciences Deemed University, Karad, Maharashtra, India.

ABSTRACT

The correlation of glycemic status to clinical severity of cerebrovascular accident (CVA) and size of lesion (bleed/infarct) was studied in newly diagnosed CT/MRI proven cases of stroke. Total200 patients were classified into euglycemia, stress hyperglycaemia and diabetic group based on the admission blood glucose, glycosylated haemoglobin (HbA_{1C}) and past history of diabetes. The lesions (bleed/infarct) were classified into small, medium and large sized. Neurological assessment was done on admission using National Institute of Health Stroke Scale (NIHSS) score. Mean age was 63.81 ± 12.62 years, with M: F 1.7:1, the maximum cases occurred in 60-70 years group (37.5%). The incidence of hyperglycaemia was 58% and admission blood glucose ranged between 70-576 mg%. There were 35.5 % patients with diabetes, 22.5% with stress hyperglycemia and 42 % with euglycemia. The diabetes group had higher percentage of large sized lesions, in contrast to the euglycemia group which had higher percentage of small sized lesions. Increased admission glucose was associated with severe presentation and high NIHSS scores. High NIHSS score was seen in diabetes with medium and large sized lesions. ($p<0.05$). Admission blood glucose correlated with size of lesion and clinical severity. Both admission glucose and HbA_{1C} correlated well with size of lesion in the diabetes group.

Keywords: glycemic status, stress hyperglycaemia, diabetes, cerebrovascular accident, NIHSS.

Corresponding author

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INTRODUCTION

A stroke or cerebrovascular accident is defined as rapidly developing clinical symptoms and /or signs of focal, and at times global loss of neurological function, with symptoms lasting more than 24 hrs or leading to death, with no apparent cause other than that vascular origin.[1]

Cerebrovascular stroke is the third largest cause of mortality in India and world after coronary artery disease and cancer. It is the most common cause of disability and dependence.[2]

Worldwide stroke is leading cause of mortality and morbidity. Stroke accounts for at least 50% of all neurological admission in general hospital.[3-5]

Ischemic Stroke accounts for 80% of all the strokes. Focal ischemia or infarction is usually caused by thrombosis of the cerebral vessels or by emboli from a proximal arterial source or the heart.

Cerebrovascular disorders (CVD) are increasing in prevalence and incidence in India due to rapid escalation of risk factors including hypertension diabetes mellitus, smoking and obesity affecting considerable proportion of adult population. Global Burden of Disease study shows that of the 9.4 million deaths in India, 619,000 were due to stroke and Disability Adjusted Life Years (DALYs) lost were 28.5 million highlighting the fact that CVD leads to considerable mortality and morbidity. Therefore there is likely to be a major crisis in India unless national measures to prevent/control risk factors of CVD are instituted and adequate services are put in place for the management and rehabilitation of stroke. Another issue of concern is that 20-30% of strokes occur in people younger than 45 years and is more frequently seen in India compared to the west.[6]

Hemorrhagicstroke accounts for about 13 percent of stroke cases. It results from a weakened vessel that ruptures and bleeds into the surrounding brain. The blood accumulates and compresses the surrounding brain tissue. The two types of hemorrhagic strokes are intracerebral (within the brain) hemorrhage or subarachnoid hemorrhage. Two types of weakened blood vessels usually cause hemorrhagic stroke: aneurysms and arteriovenous malformations (AVMs). An aneurysm is a ballooning of a weakened region of a blood vessel. If left untreated, the aneurysm continues to weaken until it ruptures and bleeds into the brain. An arteriovenous malformation (AVM) is a cluster of abnormally formed blood vessels. Any one of these vessels can rupture, also causing bleeding into the brain.

Diabetes Mellitus increases the risk of ischemic CVA two to four fold. Diabetes mellitus is an independent risk factor for stroke and is associated with 1.8 to 6 fold increased risk compared with non-diabetic subjects and worsens survival of patients with acute stroke.[6] The mechanism is believed to be accelerated atherosclerosis, which can affect vessels in many distributions, including small and large vessels.

Stress hyperglycemia defined as hyperglycemia during acute process, mirrors the severity and outcome of critical illness. Hyperglycemia occurs in 60% of the cases with acute stroke and in 12.53% of them stress hyperglycemia is observed. Hyperglycemia predicts higher mortality and morbidity after acute stroke more so in patients without the prior history of diabetes.[8-12] Hyperglycemia occurs in 20-40% of patients with stroke, and is associated with worse functional outcome, longer hospital stay, higher medical costs and an increased risk of death.[13] Hyperglycemia at the time of ischemic stroke is associated with increased mortality and morbidity. Persistent hyperglycemia on serial glucose monitoring is an independent determinant of infarct expansion and is associated with worse functional outcome.[14] DM may affect the rate of recovery of neurologic function following a stroke. Lithner et al. reported that four days after hospital admission, more stroke patients with DM than without DM were still confined to bed. In the Copenhagen Stroke Study, patients with DM recovered more slowly than non-diabetic patients; however the amount of neurological deficit at hospital discharge was equivalent between the two groups.[15]

Aims and objectives

- To study the clinical profile of stroke(infarct/hemorrhage) in relation to the glycemic status at presentation
- To correlate glycemic status of patient with stroke in relation with size and severity of lesion(infarct/hemorrhage)

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MATERIALS AND METHODS

Study Design

This case control study was conducted in KIMShospital over a period of 18 months, between November 2013 to June 2015. During the study period, all patients presenting with stroke(ischemic/haemorrhagic) fulfilling the inclusion criteria were included in the study. Total 200 patients were studied with consideration to the inclusion and exclusion criteria admitted to KIMShospital over a period of 18 months.

Inclusion and exclusion criteria

Patients with acute stroke (ischemic/haemorrhagic) presenting to KIMS hospitalduring the study period, proven by CT/MRIwere included in the study. All patients with traumatic intracerebral bleed, TIA, old history of stroke, known case of seizure disorders, cerebral venous thrombosis, presence of intracranial space occupying lesions, valvular heart disease and cardiac arrhythmias were excluded from the study.

During the study period, all patients presenting with and fulfilling the inclusion criteria were included in the study after obtaining informed and written consent. A random testing of blood glucose was done at time of presentation along with detailed history and thorough neurological and systemic examinations with application of National Institute of Health Stroke Scale (NIHSS).

The diagnosis of ischemic/haemorrhagic stroke was confirmed on imaging with CT/MRI scan. Once the diagnosis was confirmed, patients were enrolled in the study after obtaining written consent. The ethical clearance had been obtained from the institutional committee authorized for the study.

The following investigations were done

- Blood sugar level (BSL) on admission, FBSL and PPBSL(where possible)
- Glycosylated hemoglobin(HbA_{1C})
- Routine investigations(Complete blood count, renal function tests, electrocardiogram, chest X-ray, urine routine examination)
- CT/MRI scan of brain
- Other special investigations(if any).

Depending on admission random BSL, HbA_{1C} and past history of diabetes, these patients were divided into euglycemia, stress hyperglycemia (RBSL> 140mg% and normal HbA_1C, <6) and hyperglycemia (diabetes mellitus) groups.

The infarct/bleed size was classified into small, medium and large sized lesion on the CT. The small size (A) were <3cm^2 (B) Medium sized were >3cm^2 but <5cm^2. The large sized lesions were >5cm^2(C). The statistical test used in our study were 't' test and pearson's co-efficient.

RESULTS

Table 1: Sex distribution (n=200)

Sex	Number	Percentage
Female	74	37.0
Male	126	63.0
Total	200	100.0

In this study group, 63 % of the cases were males and 37 % were females. There was a male preponderance with male: female ratio of 1.7:1

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Table 2: Age distribution (n=200)

Age (years)	Number	Percentage
21-30	2	1.0
31-40	9	4.5
41-50	29	14.5
51-60	34	17.0
61-70	75	37.5
71-80	39	19.5
> 80	12	6.0
Total	200	100.0

The mean age of the patients in the study group was 63.81 $\pm$ 12.62 years. Maximum number of patients belonged to age groups 61-70 years and 71-80 years. Minimum age in the group was 28 years and maximum being 95 years.

Table 3: Glycemic status (n=200)

Glycemic status	Number	Percentage
Euglycemia	84	42
Hyperglycemia	71	35.5
Stress hyperglycemia	45	22.5

In the study group, 35.5 % had diabetes, 22.5 % had stress hyperglycemiaand 42 %were euglycemics.

Table 4: Glycemic status in male group (n=126)

Glycemic status	Male	Percentage
Euglycemia	57	45.2
Hyperglycemia	42	33.3
Stress hyperglycemia	27	21.4

In the study group, 33.3 % of the male patients had diabetes, 45.2 % were euglycemic and 21.4 % had stress hyperglycemia.

Table 5: Glycemic status in female group (n=74)

Glycemic status	Female	Percentage
Euglycemia	27	36.5
Hyperglycemia	29	39.2
Stress hyperglycemia	18	24.3

In the study group, 39.2 % of the female patients had diabetes, 36.5 % were euglycemic and 24.3% had stress hyperglycemia.

Table 6: Comparison of ischemic and haemorrhagic stroke (n=200)

Hemorrhage/infarct	Number	Percentage
Hemorrhage	32	16.0
Infarct	168	84.0
Total	200	100.0

In the study group, 16 % cases had haemorrhagic stroke while 84 % cases had ischemic stroke. The number of ischemic stroke outweighed those of haemorrhagic stroke with ischemic to haemorrhagic ratio of 5.25:1

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Table 7: comparison of ischemic and haemorrhagic stroke according to glycemic status (n=200)

Glycemic status	Hemorrhage (n=32)		Infarct (n=168)	
	Number	Percentage	Number	Percentage
Euglycemia	14	43.8	70	41.7
Hyperglycemia	11	34.4	60	35.7
Stress hyperglycemia	7	21.9	38	22.6

In the study group, among the patients with haemorrhagic stroke 34.4 % were diabetics, 43.8 % were euglycemics and 21.9 % had stress hyperglycemia.In the study group, among the patients with ischemic stroke 35.7 % were diabetics, 41.7 % were euglycemics and 22.6 % had stress hyperglycemia.

Table 8: Admission BSL according to glycemic status (n=200)

Glycemic status	Admission BSL
Euglycemia (n=84)	106.43 ±16.65
Hyperglycemia (n=71)	236.08 ± 112.06
Stress hyperglycemia (n=45)	176.56 ± 43.21

The admission blood glucose in the study group ranged from 70 - 576 mg %. Mean admission blood glucose in diabetics was 236.08 ± 16.65, in euglycemics was 106.43 ±16.65 and in stress hyperglycemia was 176.56 ± 43.21.

Table 9: HbA_{1C} according to glycemic status (n=200)

Glycemic status	HbA_{1C}
Euglycemia (n=84)	5.05 ± 0.42
Hyperglycemia (n=71)	8.06 ± 1.61
Stress hyperglycemia (n=45)	5.28 ± 0.54

The HbA_{1C} in study group ranged from 3.5 – 13.1 with mean of 6.17 ± 1.74. Mean HbA_{1C} in diabetic group was 8.06 ± 1.61, in euglycemia was 5.05 ± 0.42 and in stress hyperglycemia was 5.28 ± 0.54.

Table 10: Blood pressure according to glycemic status (n=200)

Glycemic status	Systolic blood pressure		Diastolic blood pressure	
	Mean	SD	Mean	SD
Euglycemia (n=84)	161.2	34.05	92.62	15.21
Hyperglycemia (n=71)	158.6	36.07	91.55	15.17
Stress hyperglycemia(n=45)	158.9	32.48	90.22	14.85

In the study group, systolic blood pressure ranged from 80 – 260 mmHg with mean systolic blood pressure of 159.75 ± 34.28. Mean systolic blood pressure in diabetic group was 158.6 ± 36.07, in euglycemia was 161.2 ± 34.05 while in stress hyperglycemia it was 158.9 ± 32.48.In the study group, diastolic blood pressure ranged from 50 – 150 with mean diastolic pressure of 91.7 ± 15.08. Mean diastolic blood pressure in diabetic group was 91.55 ± 15.17, in euglycemia was 92.62 ± 15.21 and in stress hyperglycemia was 90.22 ± 14.85.

Table 11: Clinical presentation according to glycemic status (n=200)

Clinical presentation	Glycemia		
	Euglycemia (n=84)	Hyperglycemia (n=71)	Stress hyperglycemia (n=45)
ALTERED SENSORIUM	16	14	10
APHASIA	11	7	5
ATAXIA	3	0	0
C.N. DYSFUNCTION	11	11	5
GIDDINESS	4	6	6

HEMIPARIESIS	52	44	24
MONOPARIESIS	7	4	5
SEIZURE	3	2	1
SLURRED SPEECH	28	20	15
UNCONSCIOUSNESS	3	4	4
VOMITTING	1	1	3
GTCS	0	3	0
Headache	0	1	0

Hemipariesis, speech disturbances, altered sensorium, cranial nerve dysfunction mainly 7th nerveand sensory dysfunction were common presenting symptoms. Monopariesis, seizure, headache were other less common symptoms in the study group.

Table 12: Comparison of hemorrhage andinfarct size according to glycemic status (n=200)

Glycemic status	Size of Lesion (hemorrhage/infarct)		
	Small (A) (n=51)	Medium (B) (n=82)	Large (C) (n=67)
Euglycemia	20	45	19
Hyperglycemia	15	21	35
Stress hyperglycemia	16	16	13

In the study group, 25.5 % lesions on brain imaging (infarct/hemorrhage) were small (A), medium (B) and large (C) sized lesion accounted for 41 % and 33.5 % respectively.The medium sized lesions were seen in euglycemic group (54.88 %) while large size lesions were observed in diabetic group (52.24 %). The stress hyperglycemia group did not show preponderance towards any specific size of lesion.

Table 13: Comparison of hemorrhage andinfarct size according to NIHSS (n=200)

Infarct size	NIHSS
A	4.45 ± 1.98
B	11.76 ± 2.72
C	18.10 ± 2.80

The NIHSS score corresponds to hemorrhage/ infarct size in the study group. Mean NIHSS score increased with increase in size of lesion.

Table 14: Glycemic status according to NIHSS (n=200)

Glycemic status	NIHSS
Euglycemia (n=84)	10.74 ± 5.30
Hyperglycemia (n=71)	13.92 ± 6.06
Stress hyperglycemia (n=45)	11.42 ± 5.66

The NIHSS score in the study group ranged from 1 – 27 with mean NIHSS score of 12.02 ± 5.81. In the euglycemic group mean NIHSS score of 10.74 ± 5.30 was observed while in the diabetic group and stress hyperglycemia group the NIHSS score was 13.92 ± 6.06 and 11.42 ± 5.66 respectively.The NIHSS scores increases as the glycemic spectrum changes from euglycemia to diabetes, indicating worsening severity of stroke with change in the glycemic status from euglycemia to diabetes.

Table 15: Comparison of HbA_{1C}, admission BSL and NIHSS according to hemorrhage/ infarct size (n=200)

Bleed/ infarct size	Admission BSL	HbA_{1C}	NIHSS	Pearson's coefficient
A	171.25 ± 91.27	5.80 ± 1.29	4.45 ± 1.98	0.49 **
B	160.24 ± 92.93	5.94 ± 1.76	11.76 ± 2.72	0.68 **
C	175.72 ± 87.86	6.73 ± 1.89	18.10 ± 2.8	0.65 **

**p<0.01, *p<0.05

Admission blood glucose and HbA_{1C} had positive correlation with NIHSS score in all the three groups.

Both admission blood glucose and glycosylated hemoglobin (HbA_{1C}) correlated well with the size of lesion (infarct/ bleed) and clinical severity in the diabetes group. Lower HbA_{1C} and lower admission glucose resulted in smaller size of lesion (infarct/ bleed), while poorly controlled cases suffered severe stroke with larger size of lesion (infarct/ bleed). ($p<0.05$)

DISCUSSION

The study was conducted at a tertiary care hospital in Karad. 200 patients with acute stroke (ischemic/ haemorrhagic) proven by brain imaging (CT/ MRI) who met the inclusion criteria for the study were included.

The age group of the patients ranged from 28 - 95 years with the mean age 63.81 ± 12.62 years, the maximum distribution of cases was in the sixth and seventh decade. In UKPDS study, it was noted that advancing age was an important risk factor for stroke.[16]

There were 63 % males and 37 % female patients a with a male preponderance and Male : Female ratio of 1.7 : 1. The UKPDS study noted male sex as an important risk factor for stroke.[16]

The glycemic status in the study group revealed 35.5 % diabetes, 22.5 % stress hyperglycemia and 42% euglycemic patients. Stress hyperglycemia in this study was defined by admission glucose >140mg% and normal HbA_{1C}.

The prevalence of diabetes in this study was 35.5 %. Among the study subjects, there was a higher percentage of diabetes (39.2%) as well as stress hyperglycemia (24.3%) in females.

The admission blood glucose ranged from 70 – 576 mg% in the study group, 116 of the total 200 patients (58%) had admission blood glucose in the range >140mg%.

The admission blood glucose in the stress hyperglycemia group ranged from 140 -339 mg% (n=45). The size of the lesion (infarct/ bleed) was measured on CT as small (A), medium (B) and large (C). In our study, 51 patients (25.5 %) had small sized lesion (A), 82 patients (41 %) had medium sized lesion (B) and 67 patients (33.5 %) had large sized lesion (C).

The percentage of small lesion (infarct/ bleed) in the euglycemia, stress hyperglycemia and diabetes group were 39.21 %, 31.37 % and 29.41 % respectively. The percentage of medium sized lesion (infarcts/ bleed) in the euglycemia, stress hyperglycemia and diabetes group were 54.88 %, 19.21 % and 25.61 %. The percentage of large sized lesions (infarcts/ bleed) in the euglycemia, stress hyperglycemia and diabetes group were 28.35 %, 19.4 % and 52.23 %. The euglycemia group had a higher percentage of small and medium sized lesions and diabetes group had a higher percentage of large sized lesions. Thus it was observed the infarct/ bleed size increased with progressive worsening in glycemic status, our finding are consistent with various studies (Mehta's Bair et al) who have reported increase infarct size in hyperglycemia.[17,18]

The clinical severity of stroke was measured using the National Institute of Health Stroke Scale (NIHSS). The NIHSS score increased with increase in the size of lesion (infarct/ bleed). The NIHSS score for small, medium and large sized lesions were 4.45 ± 1.98, 11.76 ± 2.72 and 18.10 ± 2.80 respectively. The admission blood glucose correlated well with the NIHSS score in all the three glycemic groups. These finding are comparable to Johnson et al. where infarct volume was a significant predictor of NIHSS score.[19]

An increase in admission blood glucose on presentation was associated with higher NIHSS score indicating the severe clinical presentation of the stroke Pearson's co-efficient: 0.49 for normoglycemia, 0.68 for stress hyperglycemia and 0.65 for diabetes group. Our finding are comparable to study by Kiers et al that found severe stroke and higher mortality rates in patients with stress hyperglycemia, with mortality increasing independently with admission blood glucose. The increased mortality rate was not attributable to any stroke type or location.[20]

Our study demonstrates admission hyperglycemia as a bad prognostic marker. Many studies (Candecise et al, Weir et al, Bruno et al, Sarkar et al) have demonstrated the ill effects of admission

hyperglycemia.[17,21-25]

There was progressive increase in the NIHSS score across all groups irrespective of the size of lesion (infarct/ bleed) as the glycemic status changed from euglycemia to diabetes. This was evident for all the three, small, medium and large sized lesions (infarcts/ bleed) where the NIHSS score at presentation was highest for diabetes. The euglycemia group had higher number medium sized lesion (infarct/ bleed) compared to diabetes group ($P<0.05$).

Overall, hyperglycemia on presentation was associated with larger size lesion (infarct/ bleed) and NIHSS score when compared to the euglycemic individuals.

CONCLUSIONS

Hyperglycemia was a common finding in patients with acute stroke (ischemic/ haemorrhagic) with or without history of diabetes. The admission random blood glucose and NIHSS scores correlated with clinical severity. Patients with hyperglycemia in acute stroke had increased severity with high NIHSS scores on admission, irrespective of lesion (infarction/ bleed) size. NIHSS score increased with increase in the size of lesion. Patients with hyperglycemia in acute stroke had increased size of lesion. Euglycemic group had high percentage of medium sized lesion, while diabetic group had high percentage of large sized lesion.Both admission blood glucose and HbA_{1C} correlated well with size of lesion in diabetes group.Poorly controlled diabetes mellitus had large size of lesion and highNIHSS.Hypertension was consistent finding in all acute strokes irrespective of the glycemic status.The common co-morbid conditions in the study group were hypertension, ischemic heart disease and dyslipidemia.This study shows that hyperglycemia is a common finding among the patients with acute stroke and is associated with increased severity and larger size of lesion. It should be considered as a marker for poor clinical outcome and worse prognosis following an acute stroke. Strict normalization of blood glucose levels is warranted for reducing mortality and morbidity associated with this condition.

Study Limitations

The treatment of hyperglycemia was not standardized. The study did not address the question whether treatment of hyperglycemia would reduce the mortality and morbidity associated with hyperglycemia. Significant number of patients did not complete treatment. The patients could not be followed up. Better long term correlation would have been possible had these patients been followed after discharge.

REFERENCES

[1] Charles Warlow. Cerebrovascular diseases, Brain's Diseases of nervous system, 11th edition, MichealDonaghy (eds). Oxford University press publishers, Vol. I, page no 776-782.

[2] World Stroke Day 2009. Articles published in India, Brain stroke third largest killer in India, http://beta.thehindu.com/health/policy and issues/ article 40507.ece

[3] Braunwald, Zipes. Harrison's 18thedn McGraw-Hill 2005.

[4] Adams and Victor's Principles of Neurology 8thedn, McGraw-Hill 2005.

[5] Neurology in Clinical Practice. Principles of Diagnosis and Management, 4thedn.Walter G. Bradley, Robert B. Daroff, Gerald M. Fenichel, Joseph Jankovic Elsevier 2004.

[6] Gourie-Devi M. Epidemiology of neurological disorders in India: Review of background, prevalence and incidence of epilepsy, stroke, Parkinson's disease and tremors. Neurol India 2014;62:588-98.

[7] Jennifer E. Ho, FurcyPaultre and Lori Mosca, Is Diabetes Mellitus a Cardiovascular Disease Risk Equivalent for Fatal Stroke in Women? Data From the Women's Pooling Project, Stroke journal http://stroke. ahajournals.org /cgi/content/ful l/34/12/ 2812.

[8] Candelise L, Landi G, Boccardi E ,et.al, Prognostic significance of hyperglycemia in acute stroke, Arch Neurol 1985;42:661-663.

[9] Weir CJ, Murray G D, Dyker AG, Lees KR, Is hyperglycemia an independent predictor of poor outcome after acute stroke. Results of long term follow up, BMJ 1997; 314:1303-06.

[10] Bruno A, Biller J, Adams HP Jr, Clarke WR, Woolson RF, Williams LS, Hansen MD. Acute blood glucose level and outcome from ischemic stroke. Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Investigators. Neurology 1999; 52:280– 284.

[11] Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and the prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke. 2001:32; 2426-2432.
[12] Guillermo. Umpierrez, Scott D. Hyperglycemia an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J of Clin Endo andMetabolism 2002; 32:2426-32.
[13] Frontera JA, Fernandez A, Claassen J, Schmidt M, Schumacher C, Wartenberg K, et al. Hyperglycemia After SAH: Predictors, Associated Complications, and Impact on Outcome. Stroke journal of American heart association Stroke 2006; 37: 199-203.
[14] Tress, Peter G. Colman, Brian R. Chambers and Stephen M. Tracey A. Baird, Mark W. Parsons, Thanh Phanh, Ken S. Butcher, Patricia M. Persistent PoststrokeHyperglycemia Is Independently Associated With Infarct Expansion and Worse Clinical Outcome Stroke J American Heart Association 2003;34:2208-2214.
[15] By Nader Antonios, MD and Scott Silliman, MD Diabetes Mellitus and Stroke Diabetes and Stroke 2005; 17-22.
[16] Van den Berghe G, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Schetz M, et.al. Outcome benefit of intensive insulin therapy in the critically ill: insulin dose versus glycemic control. Crit Care Med. 2003; 31:359 –366.
[17] Perttu J. Lindsberg, MD, PhD; Risto O. Roine, MD, PhD Hyperglycemia in Acute Stroke .Stroke 2004; 35:363-364.
[18] Davis TM, Millus H, Stratton IM-risk factors in type 2 DM: UKPDS 29.AchIntern Med 1999, 159:1079-1103.
[19] Baird AE, Dambrosia J, Janket S-J, Eichbaum Q, Chaves C, Silver B, et al. A Three-item scale for the early prediction of stroke recovery. Lancet; 357:2095-2100.
[20] Guillermo. Umpierrez, Scott D. Hyperglycemia an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J of Clin Endo andMetabolism 2002; 32:2426-32.
[21] R N Sarkar, Samar Banerjee, ABasu. Comparative evaluation of Diabetic and non-diabetic stroke – effect of glycemia on outcome. JIMA. 2004;102(10):551- 553.
[22] Candelise L, Landi G, BoccardiE,et.al, Prognostic significance of hyperglycemia in acute stroke, Arch Neurol 1985;42:661-663.
[23] Weir CJ,Murray G D,Dyker AG, Lees KR, Is hyperglycemia an independent predictor of poor outcome after acute stroke. Results of long term follow up, BMJ1997; 314:1303-06.
[24] L S Williams, J. Rotich, R. Qi, MS, N. Fineberg, , A. Espay, , A. Bruno, et.al. Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke .Neurology 2002;59:67-71.
[25] K C Johnston, AFConnors Jr, D P Wagner, W A Knaus, X-Q Wang and E Clarke Haley Jr. A Predictive Risk Model for Outcomes of Ischemic Stroke. Stroke31: 448 – 455, 2000.