Comparative Evaluation of Diabetic and Non-Diabetic Stroke and the Study of Effect of Glycemic Levels on the Outcome of Stroke

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Abstract: Introduction: Diabetes poses a major health problem globally and is one of the top five leading causes of death in most developed countries. A substantial body of evidence suggests that it could reach epidemic proportions particularly in developing and newly industrialized countries⁴. Diabetes mellitus is a risk factor for both an excess incidence of and mortality from Stroke⁵. The first edition of Diabetes in America documented the strong association of diabetes with risk of stroke, especially strokes due to vascular disease and infarction. ⁶<u>Aim</u>: To study and compare the clinical profile of stroke with respect to age, sex, stroke type, stroke severity, prevalence of risk factors, and outcome in diabetics and non-diabetics. To study and correlate the effect of admission glucose levels on the outcome of diabetic and non-diabetic strokes. Methods: After obtaining approval from the IEC and valid informed consent, the participants were recruited into the study. The present study is a prospective case control observational study. This study was conducted on 100 patients with stroke(out of which 50 patients were diabetic or found to have diabetes, and 50 were non-diabetic stroke patients) admitted to King George hospital, Visakhapatnam. Results: The mean age in Diabetic stroke patients was 56.8±9.74 and in Non-Diabetic stroke patients was 60.5±30.1). History of cranial nerve involvement was in 26% of diabetics and 28% of non-diabetics. Visual disturbance was present in 10% of diabetic patients. Speech disorder was present in 24% of diabetics and 26% of non-diabetics. Altered sensorium was present in 44% of diabetics and 38% of non-diabetic patients. Among diabetic stroke patients 86% were known diabetics where as 14% were newly detected diabetics. 52% of diabetic stroke patients and 44% of non-diabetic stroke patients had no history of addictions in the past. History of tobacco chewing was 10% in diabetics and 6% in non-diabetics. Alcoholism was 18% in diabetics and 28% in non-diabetics. Smoking was in 20% diabetics and 22% in nondiabetics. 50% of diabetic stroke patients and 66% of non-diabetic stroke patients had normal ECG. 18% of diabetics and 20% of non-diabetics had LVH. 66% of diabetics had 56% of non-diabetics had infarction on CT BRAIN. 34% of diabetics and 44% of non-diabetics had hemorrhage on CT BRAIN. Diabetic stroke patients had longer duration of hospital stay 8.52 ± 4.35 days compared with non-diabetics 6.62 ± 3.77 days. 64% had fair recovery in diabetic group as compared to 80% in non-diabetic group.24% had poor recovery in diabetic and 10% had poor recovery in non-diabetic group. Death was seen in 12% of diabetic and 10% non-diabetic patients. <u>Conclusion</u>: Commonest modifiable risk factors in stroke are hypertension, smoking, dyslipidemia, alcohol consumption, and diabetes mellitus. Early diagnosis, treatment including lifestyle modification and prevention of diabetes may reduce the development of stroke and its complications and it presents a major challenge for health care professionals facing an epidemic of both diabetes and stroke.Keywords:Diabetes, Stroke, Awareness, clinical research, health-care providers.

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I. Introduction

World Health Organization defines the clinical syndrome of "stroke" as 'rapidly developing clinical signs of focal (or global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin.¹

It is important to recognize that it is not a single disease but a syndrome resulting from numerous different pathophysiological processes which result in similar end organ damage². The majority (about80%) of stroke is ischemic; the remainder result from primary hemorrhage either intracerebral or into the subarachnoid space. Ischemic stroke is often thought as a single entity but, in fact it may be the result of quite different disease processes^{2,3}.

Diabetes poses a major health problem globally and is one of the top five leading causes of death in most developed countries. A substantial body of evidence suggests that it could reach epidemic proportions particularly in developing and newly industrialized countries⁴. Diabetes mellitus is a risk factor for both an excess incidence of and mortality from Stroke⁵. The first edition of Diabetes in America documented the strong association of diabetes with risk of stroke, especially strokes due to vascular disease and infarction⁶.

Bell⁷ has reviewed the literature describing the relationship between diabetes and stroke. Most ischemic strokes in diabetic patients are due to occlusion of small Para median penetrating arteries. The occlusions cause small infarcts within the white matter of the brain.

In the Multiple Risk Factor Intervention Trial (MRFIT) in 1973-75, 12-year mortality was determined for 5,163 men age 35-57 years who reported taking medication for diabetes and 324,815 men without a history of diabetes⁸.

The risk of mortality from stroke was increased 2.8-fold (95% confidence interval (CI) 2.0-3.7) among those with diabetes, even after adjusting for age, race, income, and cardiovascular risk factors. The risk of stroke mortality was greatest for non-hemorrhagic stroke (relative risk 3.8) than for subarachnoid (1.1) or intracranial hemorrhage $(1.5)^9$.

In the community of Rancho Bernardo, CA, 3,778 men and women who were age 50-79 years in 1972-74 were evaluated during the next 12 years for fatal and nonfatal stroke. The risk of stroke was significantly higher among diabetic men and women compared with those without diabetes¹⁰.

The improved clinical diagnosis of stroke by computerized tomography and magnetic resonance imaging has probably increased the measured incidence of stroke in the population, especially among older individuals who receive more frequent and intensive medical care. Further, there is probably a very high prevalence of "silent" cerebral infarction that can be documented by these new noninvasive techniques. The incidence and prevalence of stroke among diabetic patients may, therefore, be higher now than was suggested in the past. The incidence of stroke also increases with increasing age. Thus, many stroke patients may have undetected diabetes at the time of the stroke; subsequent examination in the hospital or following treatment for stroke may identify the previously undetected diabetes. The reported prevalence of diabetes among stroke patients as compared with those without a stroke may therefore be inflated by differences in ascertainment.

Diabetes potentiates stroke by favoring thrombosis by increasing concentration in blood of prothrombotic factors like fibrinogen and von willebrand factor. It also increases platelet adhesiveness. Fibrinolytic capacity is decreased through increased concentrations of plasminogen activator inhibitor type 1.

Diabetes also favor's atherogenesis because of various lipid abnormalities like hypertriglyceridemia, low HDL cholesterol and high triglyceride-enriched HDL. Glycosylation of lipoproteins and oxidation of lipoproteins leads to atheroma formation.

The relative risk of stroke in diabetics approximately doubled compared to with that in patients without diabetes. Clinical profile of stroke is different in diabetics compared in non-diabetics in many aspects. Keirs et al found that diabetics have more severe initial stroke. Intracerebral hemorrhages are less frequent in diabetic patients whereas lacunar infarcts are more frequent in diabetics.

There are many factors which alter the outcome of stroke. Hyperglycemia predicts higher mortality and morbidity after acute stroke independently of other adverse prognostic factors, such as older age, type and severity of stroke and non–reversibility of the neurological deficit. The effect of hyperglycemia on mortality is large^{11,12,13,14,15,16}.

McCall has noted that a higher blood glucose level at hospital admission predicts a poorer prognosis after a stroke, irrespective of whether the patient is diabetic or not. Also, the degree of disability after the stroke may be worse among individuals with elevated blood glucose at the time of the stroke. Animal models showed that hyperglycemia alone worsens the ischemic brain damage from a stroke¹⁷.

Hyperglycemia is common among patients with acute stroke, occurring in upto 60% of patients overall and approximately 12-53% of acute stroke patients without prior diagnosis of diabetes^{18,19,20}.

The adverse effect of hyperglycemia is possibly due to anaerobic metabolism of glucose, worsening of intracellular and extracellular acidosis^{14,16,19,21}.

Wier et al. also showed that raised plasma glucose concentration after acute stroke predicts a poor prognosis after correcting for age, stroke severity, and stroke subtype. Raised plasma glucose concentration is therefore unlikely to be solely a stress response and should arguably be treated actively^{12,19}.

The present study was undertaken in a prospective manner to comparatively evaluate stroke in diabetic and non-diabetic patients and to study the effect of glycemic levels on the outcome of stroke.

II. Aims And Objectives

To study and compare the clinical profile of stroke with respect to age, sex, stroke type, stroke severity, prevalence of risk factors, and outcome in diabetics and non-diabetics. To study and correlate the effect of admission glucose levels on the outcome of diabetic and non-diabetic strokes.

III. Materials And Methods

Study design: After obtaining approval from the IEC and valid informed consent, the participants were recruited into the study. The present study is a prospective case control observational study. This study was conducted on 100 patients with stroke(out of which 50 patients were diabetic or found to have diabetes, and 50 were non-diabetic stroke patients) admitted to King George hospital, Visakhapatnam during the period from November 2016 to September 2018

Patients who were admitted with history of acute stroke and confirmed by thorough physical examination and CT BRAIN to have stroke, and were satisfying the inclusion and exclusion criteria were studied.

Inclusion criteria

- 1. All stroke patients with diabetes (cases).
- 2. Diabetes was confirmed on the basis of past history of diabetes , history of taking oral hypoglycemic drugs or insulin, previous medical records suggestive of diabetes or previous reports of blood sugar or HbA1C confirming the diagnosis of diabetes according to WHO criteria.
- 3. Non-diabetics admitted with high blood sugar levels underwent repeat blood sugar (48 hours after admission) and HbA1C estimation. Those satisfying WHO criteria were labeled as newly detected diabetics and included as cases otherwise were labeled as stress hyperglycemics and included as controls.

Exclusion Criteria

- 1. Patients receiving diabetogenic drugs.
- 2. Patients having severe stroke who died before it could be established whether they had diabetes or not.
- 3. Patients with severe stroke who died before it could be established whether they had stroke or not.

After admission detailed history regarding temporal profile of stroke and risk factors like hypertension, diabetes mellitus, smoking, alcohol intake, previous strokes were taken.

Detailed neurological examination was done and stroke score based on MRC scale was obtained during admission. Three stroke severity categories were developed.

Mild	=4
Moderate	3 – 2
Severe	1 – 0

Stroke score based on MRC (Medical Research Council)scale

Grade 0 : No contraction

Grade 1: Flicker of contraction

Grade 2: Active movement with gravity eliminated

Grade3: Active movement against gravity

Grade 4: Active movement against gravity and moderate resistance

Grade 5: Active movement against gravity and full resistance(normal power). Prognosis of these patients was assessed on the basis of improvement or deterioration based on MRC scale.

Simple hierarchal scale was used to assess upper and lower limb qualitative function on admission and after 6 weeks. Patients were graded according to best unassisted functional outcome achieved as below-

Upper limb :

- 1. Normal
- 2. Fasten button
- 3. Hold cup
- 4. No use

Lower limb :

- 1. Normal
- 2. Climb stairs
- 3. Walk on flat surface
- 4. Stand
- 5. No use

Neurological outcome after 6 weeks was graded as follows-Good: Patients who can return to normal or previous activites, mild hemiparesis, mild dysphasia(MRC=4)

Fair: Patients who are independent in activities of daily living but are unable to return to previous activities, moderate paresis, moderate dysphasia (MRC 3-2)

Poor : Patients who are dependent on others for daily living activities, severe paresis to plegia, aphasia (MRC 1-0).

This assessment was done immediately after admission and it was repeated after 6 weeks in survivors. Patients were categorized as dead or survived with or without improvement. The following investigations were done in all the cases –

- 1. Complete hemogram
- 2. RBS on admission
- 3. FBS (48 hours after admission)
- 4. HbA1C
- 5. Blood Urea/ Serum Creatinine
- 6. ECG
- 7. Lipid profile (including total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol).
- 8. CT Scan Brain

TABLE – 2: Age Distribution Years			
Age (Years)	Diabetic	Non diabetic	
35-44	10	18	
45-54	36	22	
55-64	34	20	
65-74	14	24	
75-84	6	16	

IV. Results

TABLE – 3: Mean Age

	Diabetic	Non diabetic
Age (mean)		
(Years)	56.8	60.5

The mean age in Diabetic stroke patients was 56.8 ± 9.74 and in Non-Diabetic stroke patients was 60.5 ± 30.1 . Maximum patients were in the age group from 45-54(36%) in Diabetic stroke and 65-74(24%) in Non-Diabetic group. Difference in mean age in study was not statistically significant.

TABLE – 4 Sex Distribution		
Sex	Diabetic	Non diabetic
Male	37(73)	

Out of 50 Diabetic stroke patients 37 were males and 13 were females where as in Non-Diabetics 35 were males and 15 were females. Percentage of male population in both the groups were higher.

13(27

PRESENTING COMPLAINTS

Female

TABLE – 5: Weakness			
Weakness	Diabetic	Non diabetic	
Hemiparesis (HP)	45(90)	45(90)	
Brachial monoparesis(BMP)	5(10)	5(10)	

TABLE – 6: Conscious Level

Consciousness	Diabetic	Non diabetic		
Alert(A)	28 (56)	31(62)		
Response to pain stimulus(P)	8(16)	7(14)		
Unconscious(U)	6(12)	5(10)		
Responds to verbal commands(V)	8(16)	7(14)		

TABLE –7: Speech Disorder

Speech disorder	Diabetic	Non diabetic
Absent	38(76)	37(74)
Broca's Aphasia (BA)	10(20)	10(20)
Global Aphasia(GA)	2(4)	3(6)

TABLE – 8: Cranial Nerve Involvement

Cranial nerve involvement	Diabetic	Non diabetic
Involved	13(26)	14(28)
Not involved	37(74)	36(72)

TABLE -9: Visual Disturbance

Visual disturbance	Diabetic	Non diabetic
Present	5(10)	0
Absent	45(90)	50(100)

 $X^2 = 1.4 \text{ P} > 0.05 \text{ NS}$

35(70)

15(30)

TABLE – 10 : Other Complications			
Other complications	Diabetic	Non diabetic	
Present	5(10)	4(8)	
Absent	45(90)	46(92)	
$X^2 = 0.0 P > 0.05$	NS		

Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both the groups had hemiparesis/hemiplegia and 10% had monoparesis/monoplegia). History of cranial nerve involvement was in 26% of diabetics and 28% of non diabetics. Visual disturbance was present in 10% of diabetic patients. Speech disorder was present in 24% of diabetics and 26% of non-diabetics. Altered sensorium was present in 44% of diabetics and 38% of non-diabetic patients. Other complications like headache and unsteadiness of gait, convulsions was present in 10% of diabetics and 8% of non-diabetics.

TABLE – 11:	Past History
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Past History	Diabetic	Non diabetic	P* Value, sig
Hypertension(HTN)	35(70)	17(34)	P<0.05 S
Ischemic heart disease(IHD)	13(26)	4(8)	P>0.05 NS
Previous Stroke	18(36)	6(12)	P>0.05 NS
Newly Diagnosed Diabetic(NDD)	7(14)	0	P>0.05 NS

Among diabetic stroke patients 86% were known diabetics where as 14% were newly detected diabetics.

70% of diabetic stroke patients had past history of hypertension compared to 34% in non-diabetic group which was statistically significant.

Previous history of IHD was present in 26% of diabetics and 8% of non-diabetic stroke patients.

Previous history of stroke was present in 36% of diabetics and 12% of non-diabetic stroke patients.

Personal history	Diabetic	Non diabetic
Tobacco Chewing(TC)	5(10)	3(6)
No Addictions(NHA)	26(52)	23(46)
Alcohol(AL)	9(18)	14(28)
Smoking(SM)	10(20)	11(22)

52% of diabetic stroke patients and 44% of non-diabetic stroke patients had no history of addictions in the past. History of tobacco chewing was 10% in diabetics and 6% in non-diabetics. Alcoholism was 18% in diabetics and 28% in non-diabetics. Smoking was in 20% diabetics and 22% in non-diabetics. Smoking and alcohol consumption was more frequent in the non-diabetic group

TABLE – 13: Blood Pressure							
	Diabetic		Non diabetic				
Parameter	Mean	SD	Mean	SD	Mean difference	t value	P* value, sig
Systolic BP	143	22.6	160	13.2	17	4.59	P<0.001 S
Diastolic BP	86.5	12.9	95.0	7.35	8.5	4.04	P<0.001 S

TABLE -	13:	Blood	Pressure
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The mean systolic blood pressure on admission was 143 ± 22.6 in diabetic group and 160 ± 13.2 in non-diabetic group. The difference was statistically significant.

The mean diastolic blood pressure on admission was 86.5 ± 12.9 in diabetic group and 95 ± 7.4 in non-diabetic group. The difference was statistically significant.

	Diabetic		Non diabetic				
	Mean	SD	Mean	SD	Mean difference	t value	P* value, sig
Admission RBS (mg)	212	75.30	128.42	42.48	84	6.83	P<0.0001 HS

The mean blood sugar on admission in diabetic group was 212 ± 75.30 compared with 128.42 ± 42.48 in non-diabetic group.

The difference was statistically significant.

	Diabetic		Non diabetic				
Lipid Profile	Mean	SD	Mean	SD	Mean Difference	t value	P* value, sig
HDL (mg)	33.06	8.31	41.7	10.6	8.6	4.51	P<0.05 S
LDL (mg)	107.8	37.76	121.96	37.95	14.16	1.87	P>0.05 NS
Triglyceride (mg)	182.88	91.05	140.5	36.84	42.38	3.05	P<0.05 S
TCL (mg)	176.2	47.43	187.58	42.02	11.38	1.26	P>0.05 NS

TABLE – 15: LIPID PROFILE

HDL (mg)

The mean HDL cholesterol was 33.06 ± 8.31 in the diabetic group and 41.7 ± 10.6 in the non-diabetic group. The mean LDL cholesterol was 107.8 ± 37.76 in the diabetic and 121.96 ± 37.95 in the non-diabetic group. The mean triglycerides was 182.88 ± 91.05 in the diabetic and 140.5 ± 36.84 in the non-diabetic group. TCL was 176.2 ± 47.43 in the diabetic and 187.58 ± 42.02 in the non-diabetic group.

Mean triglycerides was higher in the diabetic group and mean HDL was lower in diabetic group as compared to the non-diabetic group. Both the values were statistically significant.

TABLE – 16: ECG						
ECG	Diabetic	Non diabetic				
Infarct (INF)	6(12)	3(6)				
Ischemia(ISC)	10(20)	4(8)				
Left Ventricular Hypertrophy(LVH)	9(18)	10(20)				
Normal (N)	25(50)	33(66)				

50% of diabetic stroke patients and 66% of non-diabetic stroke patients had normal ECG. 18% of diabetics and 20% of non-diabetics had LVH.

20% of diabetics and 8% of non-diabetics had ischemia.10% of diabetics and

6% of non-diabetics had infarction on ECG.

CT Brain	Diabetic	Non diabetic	P* Value, sig					
Infarct (INF)	33(66)	28(56)	P<0.05 S					
Hemmorhage(HEM)	17(34)	22(44)	P<0.05 S					

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66% of diabetics had 56% of non-diabetics had infarction on CT BRAIN. 34% of diabetics and 44% of non-diabetics had hemorrhage on CT BRAIN.

Hemorrhagic strokes were more frequent in the non-diabetics and ischemic strokes in the diabetic stroke groups. The difference was statistically significant.

		Diabetic	Non diabeti	ic			
Parameter	Mean	SD	Mean	SD	Mean differe nce	t value	P* value, sig
Duration of hospital stay	8.52	4.35	6.62	3.77	1.9	2.9	P<0.05 S

TABLE - 18 : DURATION OF HOSPITAL STAY

Diabetic stroke patients had longer duration of hospital stay 8.52 ± 4.35 days compared with non-diabetics 6.62 ± 3.77 days. The difference was statistically significant

TABLE - 19 : ASSOCIATION	BETWEEN OUTCOME AND RBS
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Diabetics		RBS			
Outcome	Range	Mean	SD	P* Value, sig	Significant pairs**
FR (n=32)	90-380	183.62	73.51		
PR (n=12)	205-296	251	29.24	P<0.001 HS	1&2, 1&3
D (n=6)	215-378	313.5	67.36		

* Oneway ANOVA

** Studentised Newman Keul's test

Non Diabetics		R	BS		
Outcome	Range	Mean	SD	P* Value, sig	Significant pairs**
FR (n=40)	80-226	118	31.81		
PR (n=5)	82-190	148.4	49.01	P<0.001 HS	1&2, 1&3
D (n=5)	106-230	195.8	50.73		

* Oneway ANOVA

** Studentised Newman Keul's test

Outcome	Diabetic	Non diabetic
FR	32(64)	40(80)
PR	12(24)	5(10)
D	$X^2 = 4.4 \text{ P} > 0.05 \text{ NS}$ 6(12)	5(10)

	Diabetic		Non diabetic	
Outcome	Mean	SD	Mean	SD
FR	183.62	73.51	118	31.81
PR	251	29.24	148.4	49.01
D	313.5	67.36	195.8	50.73

64% had fair recovery in diabetic group as compared to 80% in non-diabetic group.24% had poor recovery in diabetic and 10% had poor recovery in non-diabetic group. Death was seen in 12% of diabetic and 10% non-diabetic patients. Overall outcome was better in the non-diabetic stroke patients.

In the diabetic group; patients with a fair recovery had a mean RBS of 183.62 ± 73.51 , patients with poor recovery had a mean RBS of 251 ± 29.24 , patients who died had a mean RBS of 313.5 ± 67.36 .

In the non-diabetic group; patients with a fair recovery had a mean RBS of 118 ± 31.81 , patients with poor recovery had a mean RBS of 148.4 ± 49.01 , patients who died had a mean RBS of 195.8 ± 50.73 .

Overall in both the groups patients with a higher admission RBS value had a poor outcome. The difference was statistically significant in both the groups.

V. Discussion

Stroke is a common clinical problem, current treatment for patients with established stroke is relatively ineffective. Approximately 50% of patients are left with permanent disability. Effective risk factor intervention offers a real hope of reducing stroke morbidity and mortality. Certain risk factors have been consistently identified as significant predictor of stroke outcome, while some are less consistent.

The present study involved 100 patients who satisfied the inclusion and exclusion criteria out of which, 50 were diabetic stroke patients and 50 non-diabetic stroke patients. Out of the 50 diabetic stroke patients 43 were known diabetics and 7 were detected to have type 2 diabetes during hospital stay.

AGE INCIDENCE:

In the present study, the mean age in Diabetic stroke patients was 56.8 ± 9.74 . and in Non-Diabetic stroke patients was 60.5 ± 30.1 . Maximum patients were in the age group from 45-54(36%) in Diabetic stroke and 65-74(24%) in Non-Diabetic group.

Study	Age in years		
Study	Diabetics	Non -Diabetics	
Zafar A ¹²⁵ et al (2007)	59.5 (±11.82)	60.4 (±14.80)	
Megherbi SE^{126} et al(2003)	70.7±10.2	71.7±13.1	
Kamel A^{127} et al(2006)	58.8 ± 10.1	61.6±12.5	
Sarkar RN ¹²⁸ et al	51.2	67	
Present study	56.8±9.74	60.5 ± 30.1	

In the Copenhagen Stroke Study (Jorgensen H^{129} et al 1994) the diabetic stroke patient was 3.2 years younger than the nondiabetic stroke patient (P < .001).

The observation in the present study, that Stroke occurs at a younger age in diabetics than in non-diabetics was similar to the other studies.

		Diabetics		Non-diabetics	
Study	Male	Female	Male	Female	
Zafar A^{125} et al (2007)	56%	44%	68%	32%	
Ramel A ^{rar} et al(2006) Present Study	52% 73%	48% 27%	60% 70%	40% 30%	

The observation in the present study, that men were at greater risk for stroke in both the diabetic and nondiabetic group was similar to the above studies.

Our observation was contrary to that by Seppo Lehto¹³⁰ et al 1996, who found women at greater risk for stroke than men.

PRESENTING COMPLAINTS :

Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both the groups had hemiparesis/hemiplegia and 10% had monoparesis/monoplegia). History of cranial nerve involvement was in 26% of diabetics and 28% of non diabetics .Visual disturbance was present in 10% of diabetic patients. Speech disorder was present in 24% of diabetics and 26% of non diabetics.

Altered sensorium was present in 44% of diabetics and 38% of non-diabetic patients. Other complications like headache, unsteadiness of gait and convulsions was present in 10% of diabetics and 8% of non diabetics.

RISK FACTORS FOR STROKE :

a. Previous history of hypertension:

Study	Diabetics	Non-diabetics
Sarkar RN ¹²⁸ et al	70.9%	47.6%
Zafar A ¹²⁵ et al (2007)	92%	86%
Kamel A^{127} et al(2006)	60%	48%
Megherbi SE^{126} et al(2003)	59.1%	45.5%
Present Study	70%	34%

The observation in the present study, that previous history of hypertension was more common in the diabetics than in the non-diabetics was similar to the above studies. Similar results were also found by Kiessla BM¹³¹ et al 2005 and in the Copenhagen Stroke Study (**Jorgensen H etal 1994**).

b. Previous history of ischemic heart disease

Study	Diabetic	Non-diabetic
Zafar A ¹²⁵ et al (2007)	32%	28%
Kamel A ¹²⁷ et al(2006)	36%	28%
Present Study	27%	8%

The observation in the present study, that previous history of ischemic heart disease was more common in the diabetics than in the non-diabetics was similar to the above studies.

c. Previous stroke :

Study	Diabetic	Non- Diabetic
Zafar A ¹²⁵ et al (2007)	18%	18%
Sarkar RN ¹²⁸ et al	15.8%	5.7%
Present Study	36%	12%

In the present study, previous history of CVA was more common in the diabetic group which was similar to the study by Sarkar RN^{128} et al and is contrary to the study by Zafar A^{125} et al (2007) which found similar incidence in both the groups.

PERSONAL HISTORY :

Study	Diabetics		Non-Diabetics	
	Smoking	Alcoholism	Smoking	Alcoholism
Megherbi SE ¹²⁶ et al(2003)	34.9%	25.6%	37.6%	31.7%
Present Study	20%	18%	22%	28%

The observation in the present study, that current or previous smoking was distributed equally between the 2 groups, but alcohol consumption was low in the diabetic group was similar to the above study.

Blood Pressure on admission:

Study	Diabetics	abetics		Non-Diabetics	
	SBP	DBP	SBP	DBP	
Kamel A ¹²⁷ et al(2006)	156.8±23.3	94.4±11.6	143.2±14.0	86.8±8.0	
Present Study	143 ± 22.6	86.5±12.9	160±13.2	95.0±7.4	

The observation in the present study, that mean systolic and diastolic blood pressure on admission was higher in the non-diabetic than the diabetic group, was contrary to the above study.

Diabetics were under treatment for hypertension than non-diabetic, which could be the explanation for low blood pressure on admission in diabetics than non-diabetics.

GLYCEMIC STATUS ON ADMISSION :

Study	Diabetic		Non-DIABETIC
Kamel A ¹²⁷ et al(2006)		259.8±63.9	173.6±33.4
Present Study		212±75.30	128.±42.5

The observation in the present study, that admission RBS was higher in the diabetic group than in the nondiabetic group was similar to the above study.

ECG:

50% of diabetic stroke patients and 66% of non-diabetic stroke patients had normal ECG. 18% of diabetics and 20% of non-diabetics had LVH. 20% of diabetics and 8% of non-diabetics had infarction.

STROKE TYPE :

In the present study, 66% of diabetics had 56% of non-diabetics had infarction on CT BRAIN. 34% of diabetics and 44% of non-diabetics had hemorrhage on CT BRAIN. Hemorrhagic strokes were more frequent in the non-diabetics and ischemic strokes in the diabetic stroke groups.

In the study by Sarkar RN^{128} et al ischemic stroke were higher in diabetic group (66%) as compared to non-diabetic group (56%). Haemorrhagic stroke was higher in non-diabetic group (44%) than in diabetic group (34%).

In the Copenhagen Stroke Study (Jorgensen H^{129} et al 1994) intracerebral hemorrhages were six times less frequent in diabetic patients.

DURATION OF HOSPITAL STAY

Duration of hospital stay was longer in diabetic than in the non-diabetic group. The mean duration of hospital stay was 8.52 ± 4.35 days in diabetic and 6.62 ± 3.77 days in the non-diabetic group.

Control of blood sugar and treatment of other complications in diabetic subjects like hypertension, ischemic heart disease, diabetic nephropathy took longer time and was the cause of longer stay in the hospital.

LIPID PROFILE :

In the present study, diabetic patients had higher mean triglycerides (182.88 ± 91.05 Vs 140.5 ± 36.84) and lower HDL (33.1 ± 8.31 Vs 41.7 ± 10.6) as compared to non-diabetic group.

Kamel A^{127} et al(2006) found higher triglycerides in the diabetic group (211.6±80.2 Vs 166.5±35.8) as compared to the non-diabetic group.

Seppo Lehto¹³⁰ et al. 1996 also observed hypertriglyceridemia and low HDL in diabetic stroke patients.

STROKE OUTCOME:

Diabetic Vs Non-diabetic stroke

In the present study, stroke patients with diabetes had a poor outcome compared to stroke patients without diabetes. Similar observations were made by Megherbi SE^{126} et al(2003), KamelA¹²⁷ et al(2006) and in the Copenhagen Stroke Study (**Jorgensen H¹²⁹ et al 1994**).

Hyperglycemia on admission and outcome

In the present study, patients with high admission blood sugar had a poorer outcome as compared to those with lower blood sugar values in both the diabetic and non-diabetic study groups. Similar observations were made by $McCall^{17}$ et al. and Fuentes B^{132} et al.

In the Copenhagen Stroke Study (Jorgensen H^{129} et al 1994) increased glucose levels on admission independently increase mortality from stroke in non diabetic but not in diabetic patients.

The influence of diabetes mellitus as an independent predictor of the incidence of ischemic stroke is well recognized and relates to a variety of causes. Recent analyses of both prospective and case control studies have confirmed the importance of acute hyperglycemia as a predictor of outcome after stroke.

Hyperglycemia worsens outcome and increases rate of mortality from stroke.

Two mechanisms have been postulated to explain the negative influence of hyperglycemia on outcome following stroke: (1) poorer reperfusion due to vascular injury and a loss of vascular tone through oxidation of nitric oxide dependent mechanisms; and (2) increased acidosis, perhaps from lactic acid/acid sensing channels, leading to further tissue injury.

VI. Conclusion

Commonest modifiable risk factors in stroke are hypertension, smoking, dyslipidemia, alcohol consumption, and diabetes mellitus. Commonest non modifiable risk factors are increasing age, male sex and family history of stroke.

Diabetes is an independent risk factor for stroke.

Stroke in diabetes differs from that of stroke in non-diabetics with respect to age, sex, stroke type, stroke severity, prevalence of risk factors, and outcome.

Early diagnosis, treatment including lifestyle modification and prevention of diabetes may reduce the development of stroke and its complications and it presents a major challenge for health care professionals facing an epidemic of both diabetes and stroke.

Hyperglycemia at stroke onset is associated with higher risk of poor outcome independent of the other variables. Treatment or prevention of modifiable risk factors can reduce the mortality and morbidity of stroke.

VII. Summary

- Ø The mean age in Diabetic stroke patients was 56.8±9.74 and in Non-Diabetic stroke patients was 60.5±30.1. Maximum patients were in the age group from 45-54(36%) in Diabetic stroke and 65-74(24%) in Non-Diabetic group.
- Ø Out of 50 Diabetic stroke patients 37 were males and 13 were females where as in Non-Diabetics 35 were males and 15 were females. Percentage of male population in both the groups were higher.
- \emptyset Stroke patients in both study groups presented with history of motor weakness as their most common presenting complaint (90% in both the groups had hemiparesis/hemiplegia and 10% had monoparesis/ monoplegia).
- Ø 70% of diabetic stroke patients had past history of hypertension compared to 34% in non diabetic group which was statistically significant.
- Ø Previous history of IHD was present in 26% of diabetics and 8% of non-diabetic stroke patients.
- □ Previous history of stroke was present in 36% of diabetics and 12% of non-diabetic stroke patients.
- Ø The mean systolic blood pressure on admission was 143± 22.6 in diabetic group and 160±13.2 in nondiabetic group. The mean diastolic blood pressure on admission was 86.5± 12.9 in diabetic group and 95±7.4 in non-diabetic group.
- Ø The mean blood sugar on admission was significantly higher in diabetic group (212 ± 75.30) compared with in non-diabetic group (128 ± 42.5) .
- □ The mean HDL cholesterol was lower in the diabetic group (33.06 ± 8.31) compared to that in the non-diabetic group (41.7 ± 10.6) .

The mean triglycerides was significantly higher in the diabetic (182.88 \pm 91.05) than in the non-diabetic group(140.5 \pm 36.84).

- Ø Diabetic patients had greater percentage of ischemic stroke(66%) as compared to non-diabetic patients(56%). Hemorrhages were less in diabetic stroke patients(34%) as compared to non-diabetics(44%).
- Ø Diabetic stroke patients had longer duration of hospital stay 8.52 ± 4.35 days compared with non-diabetics 6.62 ± 3.77 days.

References

- Goldstein M, Barnett HJM, Orgogozo JM, Sartorius N.Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on stroke and other cerebrovascular disorders. Stroke1989;20:1407-31
- [2]. Wade S. Smith, Claiborne Johnston, J Donald Easton, Denis L. Kasper.Harrison's Principle of internal medicine,19thEdn Vol.2, McGraw Hill Medical Publishing Division; 2017.
- [3]. Maurice Victor, Allan Ropper H. Adams and Victors principles of neurology. 11thEdn. McGraw Hill Publishing Division, 2016:821-917.
- King H, Aubert RE, Herman WH: Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998; 21:1414-1131.
- [5]. Turin T.C.; Okamura T.; ; Diabetes and lifetime risk of stroke and subtypes in an urban middle-aged population; Journal of Diabetes and its Complications (2017) 31:5 (831-835). May 2017
- [6]. Kuller LH, Dorman JS, Wolf PA: Cerebrovascular disease and diabetes. Chapter XVIII in Diabetes in America, Harris MI, Hamman RF, eds. NIH publ. no. 85-1468, 1985.
- [7]. Bell DS: Stroke in the diabetic patient. Diabetes Care 1994; 17:213-19.
- [8]. Stamler J, Vaccaro O, Neaton JD, for the MRFIT Research
- [9]. Group: Diabetes, other risk factors, and 12- yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993;16:43
- [10]. Neaton JD, Wentworth DN, Cutler J, Stamler J, Kuller L, for the MRFIT Research Group: Risk factors for death from different types of stroke. Ann Epidemiol 1993; 3:493-99.
- [11]. Liao C.-C.; Shih C.-C.; Impact of diabetes on stroke risk and outcomes: Two nationwide retrospective cohort studies; Medicine (United States) (2015) 94:52;e2282.2015.
- [12]. Candelise L, Landi G, Boccardi E, Orazio EN. Prognostic significance of hyperglycemia in acute stroke. Arch Neurol 1985; 42:661-3.
- [13]. Weir CJ, Murray GD, DykerAG, Lees KR. Is hyperglycemia an independent predictor of poor outcome after acute stroke. Results of a long term follow up study. Br Medical J 1997; 314:1303-6.
- [14]. Hirata T.; Okamura T.Association between glycemic control and incident stroke Overview from an epidemiologic study; Circulation Journal (2018) 82:6 (1499-1500).
- [15]. Ina K.; Hayashi T.; Lower HDL cholesterol is associated with the risk of stroke in diabetic individuals with poor glycemic control, Diabetes Research and Clinical Practice (2014) 106(S17). 2014
- [16]. Parsons MW, Barber PA, Desmond PM, Baird TA, et al. Acute hyperglycemia adversely affects stroke outcome. Ann Neurol 2002; 52:20
- [17]. Kushner M, Nencini P, Reivich M, Rango M, Jamieson, et al. Relation of hyperglycemia early in ischemic brain infarction to cerebral anatomy metabolism and clinical outcome. Ann Neurol 1990; 29:129-134.
- [18]. Ergul A.; Hafez S ;Impact of Comorbidities on Acute Injury and Recovery in Preclinical Stroke Research: Focus on Hypertension and Diabetes; Translational Stroke Research (2016) 7:4 (248-260).
- [19]. Singh A.; Brooks D.D Pre-stroke glycemia in patients with diabetes; Diabetes and Metabolic Syndrome: Clinical Research and Reviews (2017) (S891-S893).
- [20]. Cyprich J.; Boehme A.K ;Pre-morbid glycemic control in patients with type II diabetes does not modify short-term outcome in acute ischemic stroke Stroke (2016) 47 SUPPL. 1.
- [21]. Gallego Muñoz C. Diabetic patient with poor glycemic control and acute stroke; Pharmaceutical Care Espana (2016) 18:3 (130-134)
- [22]. Camara-Lemarroy C.R; Glucose and stroke: What about glycemic variability? Journal of the Neurological Sciences Feb(2017) 373 (242-243)
- [23]. Stephen MacMahon. Introduction: The global burden of stroke. J Chalmers. Science Press, London. 2002; 1-6.
- [24]. Doyle PJ. Measuring health outcomes in stroke survivors. Arch Phys Med Rehabil 2002; 83 (Suppl.2):S39-43.
- [25]. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet .1997; 349:1269-76.
- [26]. MurrayCJL, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997; 349:1498-504.
- [27]. Kim O.; Ovbiagele B Race-Ethnic Disparities in Cardiometabolic Risk Profiles among Stroke Survivors with Undiagnosed Diabetes and Prediabetes in the United States; Journal of Stroke and Cerebrovascular Diseases (2017) 26:12 (2727-2733)
- [28]. Dalal PM, Dalal KP, Vyas AC. Strokes in the young population in west-central India some observations on changing trends in morbidity and mortality. Neuroepidemiology 1989; 8:160-4.
- [29]. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance in India. Diabetes Atlas. Gan D Ed. International Diabetes Federation, 2006: pp 15-103.
- [30]. King H, Aubert RE, Herman WH: Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998; 21:1414-1131.
- [31]. Fall CH. Non- industrialized countries and affluence. Br Med Bull 2001; 60:33-50.
- [32]. Bjork S, Kapur A, King H. Global policy: aspects of diabetes in India. Health Policy 2003; 66:61-72.
- [33]. Zimmet P, Taylor R, Ram P, King H, Sloman G, Raper R, et al. Prevalence of diabetes and impaired glucose tolerance in the biracial Melanesian and Indian population of Fiji. A rural urban comparison. Am J Epidemiol 1983; 118: 673-688.
- [34]. Louis R. Caplan, "stroke A clinical approach" 4thedn.,ButterworthHeipemann, 2009: 24-26,72-73,101, 518-523,531-538 pp.
- [35]. Lacey B.; Lewington S; Age-specific association between blood pressure and vascular and non-vascular chronic diseases; a prospective cohort study The Lancet Global Health (2018) 6:6 (e641-e649).;
- [36]. Guo J.; Guan T. Lifestyle Factors and Gender-Specific Risk of Stroke in Adults with Diabetes Mellitus: A Case-Control Study; Journal of Stroke and Cerebrovascular Diseases (2018) 27:7 (1852-1860)
- [37]. Shinton R, Beevers G. "Metaanalysis of relation between cigarette smoking and stroke". Br Med J 1989 ;298: 789-794

- [38]. Bogousslavsky J, Mille GV, Rigli F. "The Laussane stroke registry: Analysis of 1000 consecutive patients with first stroke". Stroke 1988; 19:1083-1092.
- [39]. Jorgensen HS, Nakayama H, Raaschou HO, Gam J. "Silent infarction in acute stroke patientsprevalences, localization, risk factors and clinical significance. The Copenhagen Stroke Study". Stroke 1994; 25:97-104.
- [40]. Alloubani A.; Hypertension and diabetes mellitus as a predictive risk factors for stroke; Diabetes and Metabolic Syndrome: Clinical Research and Reviews (2018) 12:4 (577-584).
- [41]. Zhang Y.; Jiang X ;Risk of stroke and coronary heart disease among various levels of blood pressure in diabetic and nondiabetic Chinese patients; Journal of Hypertension (2018) 36:1 (93-100).
- [42]. Tang X.N.; The Role of Diabetes, Obesity, and Metabolic Syndrome in Stroke; Neurology (2017) 37:3 (267-273).
- [43]. Iso H, Jacobs DR, Went Worth D, Neaton J. "Serum cholesterol levels and six year mortality from stroke in 3,50,977 men screened for multiple risk factor intervention trial" N-Engl J Med 1989; 320: 904-910.
- [44]. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation.2003;107:363-369
- [45]. Muir KW, Weir CJ, Alwan W, Squire IB, Lees KR.C-reactive protein and outcome after ischemic stroke. Stroke. 1999;30:981-985
- [46]. Napoli MD, Papa F, Bocola V. C-reactive protein in ischemic stroke, an independent prognostic factor. Stroke. 2001;32:917-924.
- [47]. Elkind MS, Tai W, Coates K, Paik MC, Sacco RL. High sensitivity C-reactive protein, lipoprotein-associated phospholipase A2 and outcome after ischemic stroke. Arch Intern Med.2006; 166:2073-2080.
- [48]. Venkat P.; Chopp M; Blood-brain barrier disruption, vascular impairment, and ischemia/ reperfusion damage in diabetic stroke; Journal of the American Heart Association (2017) 6:6 Article Number: e005819
- [49]. Adams HP, Norris JW. Ischemic cerebrovascular disease, CNS Series 2003:1-46.
- [50]. Giles WH, Croft JB, Greenlund KJ, Ford ES, Kittner SJ. Total Homocysteine concentration and the Likelihood of Nonfatal stroke. Stroke 1998; 29: 2473-2477.
- [51]. Broderick JP, Swanson JW. Migraine- related strokes: Clinical profile and prognosis in 20 patients. Arch Neurol 1987; 44: 868-871.
- [52]. Uemura J.; Glycemic variability should be associated with the ischemic volume expansion and neurological deterioration in acute stroke; Stroke (2014) 45 SUPPL. 1.
- [53]. Mitchell A, Kirckpatrick P. Hyperglycemia after acute stroke may occur as result of neuroendocrine response. Br Medical J 1997; 315:810-1.
- [54]. Heros R. Stroke early pathophysiology and treatment. Stroke 1994; 25:1877-1881.
- [55]. Pearson K.;Glycemic load is associated with increased odds of cognitive impairment in the reasons for geographic and racial differences in stroke (REGARDS) cohort; Circulation (2016) 133 SUPPL. 1
- [56]. 53-Kroemer G, Pepit P, Zanzami N, Vayssiere JL, Mignotte B. The biochemistry of programmed cell death. FASE BJ 1995; 1277-1287.
- [57]. Jauch-Chara K.; OltmannsK.M.Glycemic control after brain injury: Boon and bane for the brain ;Neuroscience (2014); 65:101-148
- [58]. Gracia JH, Liu K, Yoshiday . Brain microvessels factors altering their potency after the occlusion of a middle cerebral artery (Wistar rat). Am J Pathol 1994; 145:728-40.
- [59]. KaczmarekJ ;Glycemic control or dual endothelin receptor antagonism reverses diabetes-mediated dysfunctional cerebral neovascularization and remodeling pattern; Stroke (2014) 45 SUPPL. 1.
- [60]. Del Zoppo G J, Schmidt-Schonbein G W, Mori E, Copeland BR, Chang CM.Polymorphonuclear leukocytes occlude capillaries following middle cerebral artery occlusion and reperfusion. Stroke 1991; 22:1276-1283.
- [61]. Pulsinelli WA. The ischemic penumbra in stroke. Sci Med 1995; 1:16-25.
- [62]. Hakim AM. Ischemic penumbra, the therapeutic window. Neurology 1998; 51(Suppl 3):S44-S46.
- [63]. Adams DH, Shaw S. Leukocyte-endothelial interactions and regulation of leukocyte migration. Lancet 1994; 343:831-836.
- [64]. Schor K, Braun M. Platelets as a source of vasoactive mediators. Stroke 1999; 21:IV32-IV35.
- [65]. Garcia JH, Yoshiday Y, Chen H, Li Y, Zhang ZG, Lian J, et al. Progression from ischemic injury to infarct following middle cerebral artery occlusion in the rat. Am J Pathol 1993; 142:623-635.
- [66]. Choi DW. Ischemia- induced neural apoptosis. CurrOpinNeurobiol 1996; 6:667-672.
- [67]. Uemura J.; Glycemic variability should be associated with the ischemic volume expansion and neurological deterioration in acute stroke; Stroke (2014) 45 SUPPL. 1
- [68]. Garcia JH, Ho Khang-Loon, Pantoni L. Pathology in Barnett, Henry JM, Mohr JP, Stein BM, Yastu FM (eds). Stroke Pathophysiology, Diagnosis and Management. 3rdEd, Philadelphia, PA: Churchill Livingstone; 1998.
- [69]. Hart RG, Easton JH. Hemorrhagic infarcts. Stroke 1986; 17:586-89.
- [70]. Garcia JH. Morphology of global cerebral ischemia: A review. Crit Care Med 1988; 16:979.
- [71]. Wiggins WS, Moody DM, Toole JF, Laster W, Ball MR. Clinical and computed tomography study of hypertensive intracerebral hemorrhage. Arch Neurol 1978; 5:832.
- [72]. Ghanachandra Singh K.; A study on the clinical profile of stroke in relation to glycaemic status of patients; Journal, Indian Academy of Clinical Medicine (2014) 15:3-4 (177-181).
- [73]. Allen CMC. Clinical diagnosis of the acute stroke syndrome. Q J Med, 1983; 52:515-523.
- [74]. Fisher CM. The arterial lesions underlying lacunes. ActaNeuropathol(Berl)1969;12:1.
- [75]. Furlan AJ, Whisnant JP, The decreasing incidence of primary intracerebral hemorrhage. A population study. Ann of Neurol, 1984; 5:367.
- [76]. Kendall BE, Radue E. Computed tomography in spontaneous intracerebral hematoma. Br J Radiol, 1978; 51:563.
- [77]. Wolf PA.Prognosis for stroke syndrome. American academy of Neurology. Symposium on CVD.1984.
- [78]. Branstater ME, Prognostication in stroke rehabilitation in Chino N
- [79]. Melvin (es).Functional evaluation of stroke patients. Tokyo, Springer Verlag 1996; 93-102.
- [80]. Abu-Zeid HA, Choi NW, Hsu PH, Maini KK. Prognostic factors in the survival of 1,484 stroke cases observed for 30-48 months, diagnostic types and descriptive variables. Arch Neurol 1978; 35:121-5.
- [81]. Warlow CP, Dennis MS, et al. In Stroke: a practical guide to management. London, Blackwell Science 1996:360-84.
- [82]. Bansal BC, Agarwal AK, Rewari BB. Hypertension in acute stroke:current recommendations, in Manoria PC (ed) Postgraduate medicine(Neurology), APL, Bhopal, 1998; XII (PartII): 69-76.
- [83]. Cariberg B, Asplund K. Hagg E. The prognostic value of admission blood pressure in patients with acute stroke. Stroke 1993; 24; 1372-5.
- [84]. Robinson T, Waddington A, Ward-Close S. High 24 hour acute stroke systemic blood pressure predicts poor 30 day outcome. Cerebrovasc Dis 1996;Suppl 2:6.

- [85]. Passero S, Burgalassi L. Blood pressure and short term outcome in primary intracerebral hemorrhage. Cerebrovascular disease 1996:Suppl 2:110.
- [86]. Melamed E. Reactive hyperglycemia in patients with acute stroke. J NeurolSci 1986; 29: 267-75.
- [87]. Jorgensen HS: Nakayama H, Reith J, Olsen TS. Acute stroke with atrial fibrillation the Copenhagen study. Stroke 1996; 27:1765-1769.
- [88]. Broderick JP, Philips SJ, Whisnant JP, et al. Incidence rates of stroke in the eighties: The end of the decline in stroke. Stroke 1989; 20:577-82.
- [89]. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke: the Framingham study. Stroke 1982; 13:290-95.
- [90]. Ralph L. Sacco. Pathogenesis, classification, and Epidemiology of Cerebrovascular disease. Merritt's Neurology. 10th Edition; Lipincott Williams and Wilkins, 2000; 35:228.
- [91]. Maurice victor, Allan H. Ropper. Cerebrovascular diseases. Adam's and Victor's principles of Neurology. 9th Edition: Mac Graw Hill, 2009; 857.
- [92]. Hacke-w, Schwab-S, Horn-M, SprangerMDe, Georgia-M,van-Kummer-R. Malignant Middle cerebral artery territory infarction: clinical course and prognostic signs. Archives of Neurology: 1996; April 53(4): 309-315.
- [93]. Salgado AV, Ferro JM, Gouveia-Oliveira A. Long term prognosis of first ever lacunar strokes. A hospital based study. Stroke 1996; 27:661-666.
- [94]. Akbar DH, Mushtaq M. Clinical profile of stroke: The experience at King Abdulaziz University Hospital SQU Journal for scientific research: medical sciences 2001; I: 35-38.
- [95]. Hier DB, Edelstein G. Deriving clinical prediction rules from stroke outcome research. Stroke 1991; 22:1431-6.
- [96]. Charles Warlow. Stroke, transient ischemic attacks and intracranial venous thrombosis. MichealDonaphy. Brain's diseases of the Nervous system: 12th edition: Oxford University press, 2009; 845.
- [97]. Brott T. Adams HP, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurement of acute cerebral infarction: A clinical examination scale. Stroke 1989; 20:864-70.
- [98]. Mahoney FI, Barthel DW. Functional evaluation; The Barthel Index. Maryland State Medical J 1965; 14: 61-5.
- [99]. Kenneth W.Lindsay. Ian Bone. Neurology and Neurosurgery illustrated. Fifth Edition: Churchill Livingstone, 2010; 210,243-252.
- [100]. Jennett B. Development of Glasgow Coma and Outcome Scales: Nepal Journal of Neuroscience 2005; 2:24-28.
- [101]. Johnston KC, Connors AF Jr, Wagner DP, knaus WA, Broad JB, Bonita R, et al. A predictive risk model for outcomes of ischemicstroke.Stroke.2000 Feb;31(2):448-55.
- [102]. Steering Committee of the Physician's Health Study Research Group. Final report on the aspirin component of the ongoing physician's health study. N Engl J Med 1989; 321:129-35.
- [103]. Shepherd J, Cobbe SM, Ford I, Isles CJ, Lorimer AR, Macfarlane PW, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. N Engl J Med 1995 Nov 16; 333(20): 1301-7.
- [104]. Plehn JF, Davis BR, Sacks FM, Rouleau JL, Pfeffer MA, Bernstein V, et al. Reduction of stroke incidence after myocardial infarction with pravastatin: The Cholesterol and Recurrent Events (CARE) study. The Care Investigators. Circulation 1999 Jan 19; 99(2): 216-23.
- [105]. Antiplatelet Trialists' Collaboration: Collaborative overview of randomized trials of antiplatelet therapy: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ 1994 Jan 8; 308(6921): 81-106.
- [106]. Dyken ML, Barnett HJM, Easton JD, Fields WS, Fuster V, et al. Low dose aspirin and stroke. "It ain't necessarily so "Stroke 1992; 23:1395-9.
- [107]. Solomon DH, Hart RG. Antithrombotic therapies for stroke prevention. CurrOpinNeurol 1994;7:48-53.
- [108]. THE DUTCH TIA STUDY GROUP: A comparison of two doses of aspirin (30mg vs 283mg a day) in patients after a transient ischemic attack or minor ischemic stroke. Stroke 1993; 94:138-9.
- [109]. THE SALT COLLABORATIVE: Swedish Aspirin low dose trial (SALT) of 75mg. Aspirin as secondary Prophylaxis after cardiovascular ischemic events. Lancet 1991; 338:1348-9.
- [110]. UK-TIA Study Group. United Kingdom Transient Ischemic Attack (UK-TIA) Trial: final results. J NeurolNeurosurg Psychiatry 1991; 54:1044-54.
- [111]. The Canadian Cooperative Study Group. A randomized trial of aspirin and sulfinpyrazone in the earlier stroke. N Eng J Med 1978; 299:53-9.
- [112]. Hass WK, Easton JD, Adams HP Jr, Pryse-Phillips W, Molony BA, Anderson S, et al. Ticlopidine Aspirin Stroke Study Group. A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high risk patients. N Engl J Med 1989; 321: 501-7.
- [113]. CAPRIE Steering Committee: A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). Lancet 1996 Nov 16; 348(9038): 1329-39.
- [114]. Diener HC, Cunha L, Forbes C, Silvenius J, Smets P, Lowenthal A. European Stroke Prevention Study. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J NeurolSci 1996 Nov; 143(1-2): 1-13.
- [115]. Tijssen JG: Low-dose and high-dose acetylsalicylic acid, with and without dipyridamole: a review of clinical trial results. Neurology 1998 Sep; 51(Suppl 3): S15-6.
- [116]. The Scandinavian Simvastatin Survival Study: Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease. Lancet 1994 Nov 19;344(8934): 1383-9.
- [117]. Scott JF, Robinson GM, O'Connell JE, Alberti KGMM, Gray CS, Prevalence of admission hyperglycemia across clinical subtypes of acute stroke. Lancet.1999; 353:376-377.
- [118]. 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.
- [119]. Kernan WN, Inzucchi SE, Viscoli CM, Brass LM, Bravata DM, Horwitz RI. Insulin resistance and risk for stroke. Neurology. 2002; 59:809-815.
- [120]. Kawai N, Keep RF, Betz AL.Hyperglycemia and the vascular effects of cerebral ischemia. Stroke. 1997; 28:149-154.
- [121]. Steinberg HO, Tarshoy M, Monestel R, Hook G, Cronin J, Johnson A, etal.Elevated circulating free fatty acid levels impair endothelium dependent vasodilation. J Clin Invest. 1997; 100:1230-1239.
- [122]. Song E-C, Chu K, Jeong S-W, Jung K-H, Kim S-H, Kim M, et al. Hyperglycemia exacerbates brain edema and perihematomal cell death after intracerebral hemorrhage. Stroke.2003; 34:2215-2220.
- [123]. Lindsberg PJ, Kaste M. Thrombolysis for ischemic stroke. CurrOpinNeuro 2003;16:73-80.

- [124]. Lindsberg PJ, Soinne L, Ronie RO, Salonen O, Tatlisumak T, Kallela m, et al.Community-based thrombolytic therapy of acute ischemic stroke in Helsinki. Stroke. 2003; 34:1443-1449.
- [125]. Alvarez-Sabin J,Molina CA, Montaner J, Arenillas JF, Huetas R, Ribo M et al. Effects of admission hyperglycemia on stroke outcome in reperfused tissue plasminogen activator-treated patients. Stroke.2003; 34:1235-1241.
- [126]. Zafar A, Shahid SK, Siddiqui M, Khan FS. Pattern of stroke in type 2 diabetic subjects versus non diabetic subjects. J Ayub Med Coll 2007;19(4):64-67.
- [127]. Megherbi SE, Milan C, Minier D, Couvreur G, Osseby GV, Tilling K et al.Association between diabetes and stroke subtype on survival and functional outcome 3 months after stroke .2003;34:688.
- [128]. Kamel A, Azim HA, Aziz SA, GhaffarA.Cerebral infarction in diabetes mellitus: A comparative study of diabetic and non-diabetic ischemic stroke.Egypt J. Neurol. Psychiat. Neurosurg., 2006, 43(1): 167-177.
- [129]. Sarkar RN, Banerjee S, Basu A. Comparative evaluation of diabetic and non-diabetic stroke: Effect of glycemia on outcome.J Indian Med Assoc 2004 Oct;102(10):551-3.
- [130]. Jorgensen H, Nakayma H, Raaschou HO. Stroke in patients with diabetes. The Copenhagen Stroke Study. Stroke 1994; 25:1977–84.
- [131]. LehtoS,Rönnemaa T, Pyörälä K. Predictors of stroke in middle-aged patients with non-insulin-dependent diabetes. *Stroke*.
 [132] M. Kleinere L, Kleinere D, Wei D, et al. Endemiedent of indemiedent in activity diabetes the anatomic stroke in a stroke.
- [132]. Kiessla BM, Khoury J, Kleindorfer D, Woo D, et al. Epidemiology of ischemic stroke in patientswith diabetes: the greater Cincinnati/Northern Kentucky Stroke Study. Diabetes Care 2005;28:355–9.
- [133]. Fuentes B, Castillo J, Jose BS, Leira R, Serena J, et al. The prognostic value of capillary glucose levels in acute stroke. 2009; 40:562-568.
- [134]. Nyika D. Kruyt, Geert Jan Biessels, J. Hans DeVries & Yvo B. Roos et al. Hyperglycemia in acute ischemic stroke: pathophysiology and clinical management. *Nature Reviews Neurology* 6, 145-155 (March 2010).
- [135]. N.K. Mishra, N. Ahmed, MD, A. Davalos, et al. Thrombolysis outcomes in acute ischemic stroke patients with prior stroke and diabetes mellitus. Neurology November 22, 2011 vol. 77 no. 21 1866-1872.
- [136]. Yuan Fang, Shihong Zhang, Bo Wu1 and Ming Liu et al. Hyperglycemia in acute lacunar stroke: A Chinese hospital-based study. Diabetes & Vascular Disease Research10(3) 216–221 .2012.
- [137]. JeyarajDuraiPandian and PaulinSudhan, v et al. stroke epidemiology and stroke care services in indiav.15(3); 2013 Sep PMC3859004.
- [138]. <u>SeemaAbhijeetKaveeshwark</u>¹ and <u>Jon Cornwall</u> etal. The current state of diabetes mellitus in India. Australas Med J. 2014; 7(1): 45–48.

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