Review Article

Association between Stroke and Diabetes Mellitus with Special Reference to Unani Medicine: A Review

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ABSTRACT

Stroke is the second most frequent cause of death worldwide and the most frequent cause of permanent disability. Stroke by and large results of a more than one predisposing conditions that originated years before the disease. Estimation and assessment of risks factors in population is not only assistive for health care providers but also important to key out persons at elevated risk of stroke and to select proper treatments in clinical studies. Diabetes Mellitus (DM) is an important risk factor in cerebral vascular disease since it causes endothelial proliferation and thickening of the plasmatic membrane in the small blood vessels. Diabetes not only acts as etiological factor but also has a role in prognosis of disease; post stroke hyperglycaemia is often associated with poor prognosis of stroke.

This review paper will address the known knowledge of association between Stoke and Diabetes Mellitus in conventional medicine and will try to establish hypothesis of association between Stoke (*Falij*) and Diabetes (*Ziabetus Shakri*) through Unani Medicine.

Keywords: Stroke, Diabetes, *Falij, Ziabetus Shakri*

Introduction

Stroke is the second most frequent cause of death worldwide and the most frequent cause of permanent disability. Diabetes is a recognized risk factor for stroke.[1] It is believed that the Patients with diabetes are 1.5 to 3time greater risk of stroke as compared with the general population.[2] In fact, Diabetics are at increased risk of both hypertension and stroke. It is not clear if diabetes mellitus confabs an increased risk of stroke that is independent of blood pressure despite the association between DM and stroke, the available data from clinical trials do not support the hypothesis that better blood sugar control decreases stroke risk.[2,3]

Diabetes mellitus is a multifaceted metabolic syndrome with significant effects on the systemic and cerebral vasculature.[4] The incidence and severity of ischaemic stroke are increased by the presence of diabetes, and outcome from stroke is poorer. Diabetes affects stroke in several aspects: in age, in subtype, in mortality, and in speed of recovery. Increased glucose levels on admission independently increase mortality from stroke in non-diabetic when compared to patients in diabetes.[3]

Cerebrovascular Disease and Diabetes Mellitus

Among patients presenting with stroke the prevalence of DM is 3 times that of matched controls. Similarly, patients with diabetes have a 3-4-fold increased risk of stroke. Diabetes

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Mellitus increases the risk of stroke in younger patients (less than 55 yr of age). Additionally, among patients with type 2 diabetes, African Americans and Hispanics have a 2-fold increase in stroke mortality compared to whites.[5,6] Finally, asymptomatic cerebrovascular disease, defined as greater than 50% occlusion in atherosclerotic obstruction in the internal carotid arteries, is 5-foldgreater in diabetic patients as assessed by carotid ultrasonagraphy than age matched non diabetic patients. Stroke mortality and outcomes are also strongly influenced by the presence of diabetes.[7,8] In the Renfrew-Paisley study, a 20 yr follow-up study of men and women aged 45–64 yr of age with stroke; diabetes raised the relative risk of death after stroke by 350%.[9]

The first appearance of cerebrovascular disease in patients with type 2 DM is often a debilitating stroke. Diabetic patients may have a positive history of blindness episodes or there may be transient ischemic attacks history; this positive history is very evocative of cerbrovascular disease and it requires immediate attention and thorough diagnostic investigations. The presence of PAD or CAD in patients with type 2 DM also denotes a high probability of cerebrovascular disease and requires additional evaluation. The screening diagnostic test of choice in evaluation of cerebrovascular disease is the carotid artery ultrasound. Stenosis greater than 50% is considered abnormal and is diagnostic of cerebrovascular disease.[8,10] The Adult Treatment Panel III guidelines identify greater than 50% internal carotid artery stenosis as a coronary heart disease equivalent. Similar to PAD, more severe stenosis suggests a greater risk of a cerebrovascular event, although no studies have been done solely in patients with diabetes. Depending on the degree of stenosis, additional testing to determine the anatomic location and morphology of the stenosis can be useful when planning an interventional therapeutic approach. MRA and CTA give a much more detailed anatomic diagnosis and help in modifying medical and interventional therapies.[10]

Post-Stroke Diabetes

Increased blood glucose level has been seen after acute stroke and is associated with a poor prognosis. Increased blood glucose level observed after an acute stroke is secondary to a stress response and they do not support the theory of hyperglycaemia being damaging to ischaemic nervous tissue. These finding has implication to the treatment of acute stroke with hypoglycaemic agents.[11]

A major of patients suffering from acute stroke have glucose metabolism disorder, and, in most of the cases, this fact has been not recognised. Diabetes abnormally deteriorates the disease prognosis after acute stroke. Therefore, in the post-acute phase, an oral glucose tolerance test is said to be recommended in all stroke patients with or without past history of diabetes. In the post-acute phase, 20.2% had past history positive of diabetes; 16.4% were grouped as

having newly diagnosed diabetes, while 23.1% are found to be having impaired glucose Test and around 0.8% are found to having impaired fasting glucose; and only 19.7% were normoglycemic.[12,13] So, an OGTT screening in the post-acute phase has to be recommended in all stroke patients with no prior previously undiagnosed; DM may be more prevalent than known DM in hospitalised patients with acute stroke. Performing an OGTT at 12 weeks post stroke provides an accurate measurement of the prevalence of DM and IGT in survivors and enables the results to be related to admission values for plasma glucose and HbA1c. This allows their value in predicting the presence of DM in acute stroke patients to be calculated.[12] Admission hyperglycaemia (> 6.1 mmol/l) plus raised HbA1c concentration predicts unrecognised DM in acute stroke patients, with sensitivity of 86% and specificity of 94%.[8] The development of type 2 diabetes is preceded by an extended period of insulin resistance with compensatory hyperinsulinemia and a gradual onset of hyperglycemia. Both hyperglycemia and hyperinsulinemia have been shown to be independently related with increased risk of coronary heart disease (CHD). The role of hyperglycemia and hyperinsulinemia as risk factors for stroke is less well documented. Although some studies have shown hyperglycemia to be independently associated with risk of stroke in non diabetics, The increased risk at higher levels of serum insulin was due in part to the men who developed diabetes in the follow up period.[12,13,14,15]

Key Risk Factors of Stroke

Hypertension Hypertension has long been recognised as the major modifiable risk factor for stroke. The risk of stroke doubles for every 7.5 mmHg increase in diastolic blood pressure and antihypertensive agents have been shown to reduce stroke risk by about 38%. Hypertension is twice as prevalent in diabetic as in non-diabetic individuals and, in patients with diabetes, it is associated with accelerated progression of both microvascular (retinopathy and nephropathy) and macrovascular (atherosclerotic) complications.[1,2,4]

Atrial Fibrillation

AF is the most prevalent cause of cardioembolic stroke; with a relative risk of stroke between 5 and 17.40, the risk of stroke in patients with AF is also associated independently with a number of other risk factors in addition to diabetes.[1,2,4,15]

Lifestyle

Various lifestyle factors in the general population have been associated with increased stroke risk. Modifiable factors attribute relative risks of stroke from cigarette smoking as up to twofold, and from alcohol abuse to four-fold compared with individuals without these habits.[1,2,4,16]

Hyperglycaemia

A fasting plasma glucose level over 5.5 mmol/L is strongly

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associated with ischaemic cerebrovascular events in patients with already existing athero-thrombotic disease.[1,2,4,16,17,18]

Lipid Levels

High titres of LDL-cholesterol are a predictor of stroke in the general population. There is some evidence to suggest that low HDL-cholesterol, which is a key component of the dyslipidaemia typically seen in type 2 diabetes, is also associated with increased risk of ischaemic stroke.[1,2,4,16,17,18]

Un-Modifiable Risk Factors

Age

In those younger than 55 years, diabetes increases the risk of stroke more than 10-fold. The exposure ratio for stroke in the age group 35-54 years was 4.66 in men and 8.18 in women. The risk decreased with increase age.[1,2,4,18]

Sex-specific Differences

Diabetes noticeably increases the risk of stroke in younger subjects as well as women. A large cohort study from the UK including 41,799 subjects with diabetes and 202,733 controls observed the highest risk for stroke attributable to diabetes in younger persons and particularly women. The absolute rate of stroke was 11.91 per 1,000 person-years in individuals with diabetes and 5.55 per 1,000 person-years in the control group.[1,2,4,14,15,19]

Preventing Stroke

Preventing incidence of stroke in diabetic patients is started by identification followed by several interventions of modifiable risk factors, especially hypertension, cigarette smoking, high LDL cholesterol, diabetes mellitus, coronary heart disease, left ventricular hypertrophy, atrial fibrillation, and peripheral vascular disease, etc. Controlling the blood pressure has been proven as an effective prevention of stroke both in diabetic or non diabetic. In the Systolic Hypertension in the geriatric patients trial, the treatment effect (reduced risk of stroke) in the intervention compared to the control group was similar for diabetic and non-diabetic subjects. Complication of treatment also did not appear to vary between diabetic and non-diabetic individuals. Antiplatelet aggregating drugs such as aspirin are effective in decreasing the incidence of stroke, especially among individuals with existing cardiovascular disease or transient ischemic attack. At least one study had shown beneficial effect in both diabetic and non-diabetic individuals. No difference among aspirin and warfarin in the prevention of recurrent ischemic stroke or death or in the rate of major hemorrhage. Consequently, both warfarin and aspirin are reasonable therapeutic alternatives. Smoking cessation will also decrease the risk of stroke. Statins may reduce the incidence of all strokes without any increase in hemorrhagic strokes and this effect is mainly driven by the extent of between-group LDL-C reduction. Carotid IMT (intima-media thickness) progression is also strongly correlated with LDL-C reduction. Anti-hypertensive agents are used in lowering blood pressure for the prevention of vascular event in patients with previous stroke or transient ischemic attack. Vascular prevention is associated positively with the magnitude by which blood pressure is reduced.[2,4,12,15,16,17,20]

The Unani Concept

In Unani literature causes of *Stroke* have been grouped into two principal categories.

One group are causes contributing to obstruction in the pathway of *Roohe Hassas*, keeping a bay its entry into the organs; It leads to blockage in the Vessels, with complete or partial obstructions in the Nerves, Arteries, Veins, Muscles, this blockage may also be present at the site of origin of *Asab*, *Batoone Dimagh* (Ventricles), or in both.[21,22,23,24,25,26]

According to classical texts Definite factors play a role in *Sudda* formation such as Geriatric age, cold and chilled weather, diet in excessive quantity, viscocious and tenacious diets, along with Diabetes Mellitus.[21,22,26]

Other are Causes making the organs non-responsive to *Roohe Hassas* and *Muharrik*. In absence of any *sudda* and with normal entry of *Roohe Hassas* and *Muharrik*, the organs sometimes may not respond to it due to *Fasad* in their *Mizaj* leading to loss of sensation and movement in them. This *Fasa'ad* in *Mizaj* may be due to excessive and abnormal *Hararat, Baroodat, Yaboosat or Ratoobat*, this *Hararat* and *Yaboosat* seldom affects movements and sensation except in extreme conditions. But, if the *Fasa'ad* in *Mijaz* is due to superfluous *Baroodat* and *Ratoobat*, it often causes loss of movement and sensation, *Ziabetes* (Diabetes Mellitus) is consider to be one the cause which changes the *Mizaj* of *Azu* and may lead it non responsive to *RooheHassas*.[21,22,23,24,25,26]

Discussion

Diabetes is a recognized risk factor for stroke, patients with increased level of glucose are found to be more prone to stroke, females and younger diabetics are at a greater risk, while Hyperglycaemia seen after an acute stroke is secondary to a stress response and they do not support the theory of hyperglycaemia being harmful to ischaemic nervous tissue. Preventing incidence of stroke in diabetic patients is started by identification followed by several interventions of modifiable risk factors, especially hypertension, cigarette smoking etc.[1,2,4,14,15,19]

Ancient Unani scholars also had a view about pathology of *stroke* they include obstruction in the pathway of *Roohe Hassas* and non-responsiveness of organs to *Roohe Hassas* and *Muharrik* to be main cause of Stroke. While looking at the pathology and complications of Diabetes Mellitus, it may be said that neuropathy and vascular changes followed

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by diabetes may leads to obstruction of *Roohe Hassas* (due to vascular changes of DM) and non-responsiveness of organs to *Roohe Hassas* and *Muharrik* (due to diabetic related neuropathy). [21,22,23,24,25,26]

Conclusion

Thus, it may be concluded that the ancient Unani scholars were well aware of pathogenesis and relation between Diabetes Mellitus and Stroke, though that may have not discussed it directly, but above inference may be drawn after surveying classical literature regarding causes and etiopathogenesis of Stroke (*Falij*). The knowledge of Unani medicine regarding prevention and treatment of stroke may be used in effective treatment and prevention of stroke in diabetic patients.

Conflicts of Interest: None

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