

## Metabolic Syndrome and Intracranial Atherosclerosis - A New Link

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Stroke is the most common neurological emergency; the third most common cause of death in developed world. 85% strokes are ischemic, 10% are intracranial hemorrhages (ICH), and 5% are subarachnoid hemorrhages (SAH).<sup>1</sup>

It is the most common reason of disability affects of more than 70,0000 individuals. Metabolic syndrome is associated with an increased risk of cardiovascular events and ischemic stroke.<sup>2</sup> The prevalence of the metabolic syndrome (MetS) is increasing to epidemic proportions not only in the United States and the remainder of the urbanized world but also in developing nations & an increasing trend has been observed in Asian countries.

Urbanization, modern lifestyle, change of food habit cumulatively contributes for this development of metabolic syndrome.

Patient with metabolic syndrome had a 1.6 fold increased risk of stroke has been reported previously in one of the study.<sup>2</sup> Metabolic syndrome is the cluster of vascular risk factors including insulin resistance, elevated blood pressure, hyperlipidemia, and obesity. According to The National Cholesterol Education Program Adult Treatment Panel III (ATP-III), definition of metabolic syndrome requires the presence of 3 or more of the following criteria: abdominal obesity (waist circumference 102 cm in men and 88cm in women) for Asian, IDF criteria is 90 cm in men and 80 cm in women. The ATP III update accepted these same criteria. A high triglyceride level (>150 mg/dl or >1.69 mmol/L), a low HDL cholesterol level (<40 mg/dl or <1.03 mmol/L for men and <50 mg/dl or <1.29 mmol/L for

women), high blood pressure (Systolic >130mm Hg or diastolic >85 mm Hg) and a high fasting plasma glucose concentration (>100 mg/dl).<sup>3</sup>

Metabolic syndrome increases the morbidity and mortality of cardiovascular diseases.

However, few studies have examined the association between the incidence of stroke and metabolic syndrome. One of the prospective observational study conducted in 2010 showed increased incidence of ischemic stroke (65.2%) amongs the patients of metabolic syndrome than the cases of ischemic stroke (55.6%) without metabolic syndrome. Incidence of haemorrhagic stroke was more in the non metabolic syndrome group. So this study concluded that Metabolic syndrome is an independent risk factor for cerebro vascular disease but they are more prone for ischemic stroke.<sup>4</sup>

Many of the studies (Hisayama, NIPPON DATA 80) done previously reported similar kind of results & showed a link between metabolic syndrome & ischemic stroke<sup>5,6</sup>.

MetS is associated with higher risk of stroke and similar or higher risks than elevated fasting blood glucose alone or hypertension alone.<sup>7,8</sup> Further more, there has been little prospective studies on the relationship between MetS and risk of stroke. The study conducted in Japnees found poor correlation of stroke with high waist circumference though high waist circumference is positively associated with the risk of cardiovascular events.<sup>9</sup>

The metabolic syndrome is a risk factor for stroke that seemingly has an underlying metabolic causation. The most accepted & unifying hypothesis to describe the pathophysiology of metabolic syndrome is insulin resistance, which is caused by incompletely understood defect in insulin action.<sup>10</sup> Central obesity is the centerpiece of the metabolic alterations. There is evidence that excess body weight is a predictor of stroke (total, ischemic, and hemorrhagic) in men. Increased waist

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circumference is an important component of the most recent and frequently applied diagnostic criteria for the metabolic syndrome. Accordingly, increased abdominal adiposity contributes to dyslipidemia, hyperglycemia, and hypertension. Recent evidence suggests that increased obesity and insulin resistance state is associated with inflammation. Furthermore, The elevations of inflammatory markers are associated with metabolic risk factors and with accelerated atherosclerotic diseases.<sup>11</sup>

Hypertension remains the most common modifiable risk factor for stroke in the general population which is also the component of metabolic syndrome. In insulin resistant state normal physiological vasodilatory property of insulin is lost but effect of sodium reabsorption in kidneys persist so also its stimulatory effect on sympathetic nervous system. Hypertension accelerates the atherosclerotic process in carotid and vertebral arteries<sup>12</sup> that usually starts in the larger extracerebral arteries, particularly in the carotid bifurcation. This process with time spreads distally to the smaller intracerebral arteries, leading to increased vascular resistance and hypertension during exercise and hence the increased risk of cerebrovascular events. The presence of hypertension as part of the metabolic syndrome was associated with increased risk of acute ischemic as well as hemorrhagic stroke.

Dyslipidemia is a hallmark of the metabolic Syndrome. There is a controversy regarding the association between serum TG levels and stroke. It has been shown that postprandial hypertriglyceridemia is associated with carotid artery atherosclerosis. Nonetheless, in the Copenhagen City Heart Study, a log-linear association between serum TG levels and nonhemorrhagic stroke was found, which was independent of age and sex.<sup>13</sup> In general, in the majority of studies, an inverse association between HDL-C and stroke risk has been documented. In the Northern Manhattan Stroke Study, increased levels of HDL-C were associated with a reduced risk of ischemic stroke in the elderly and among different racial or ethnic groups.<sup>14</sup>

Previous evidence shows that relatively modest lifestyle interventions can have favourable impact on components of the metabolic syndrome, at least in the relatively short term. It is known that good cardiorespiratory fitness and physical activity are related to decreased risk of stroke. Early identification, treatment, and ultimately prevention of the metabolic syndrome present a major challenge for health care professionals and public health policy-makers facing an epidemic of overweight and sedentary lifestyle.

In this issue of VJIM Sondoule AU et-al have published their observations regarding association of Metabolic syndrome with stroke. Results of this study revealed strong and positive association of Metabolic syndrome with acute ischemic stroke but not with acute hemorrhagic stroke. Other components of the syndrome like high blood pressure, low serum HDL and high fasting plasma glucose were also significantly associated with acute stroke. Further they found acute stroke cases with metabolic syndrome were associated with higher morbidity at the end of one month of follow up<sup>15</sup>. Recommendation for screening of patients with acute stroke for metabolic syndrome are needed.

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