

# THE ROLE OF METABOLIC SYNDROME IN THE DEVELOPMENT OF CHRONIC BRAIN ISCHEMIA: A SYSTEMATIC REVIEW

**Rakhimbaeva Gulnora Sattarovna**

Professor, DSc, Head of the Department of Neurology and medical psychology  
Tashkent Medical Academy

**Shermuhammedova Feruza Qobiljanovna**

DSc of the Department of Neurology and medical psychology of the Tashkent Medical Academy

**Bokiyeva Fayziniso Adxamovna**

Department of Neurology and medical psychology of the Tashkent Medical Academy

**Abstract:** Metabolic syndrome (MetS) is a cluster of metabolic abnormalities, including central obesity, dyslipidemia, hypertension, and insulin resistance, that increase the risk of cardiovascular disease and type 2 diabetes. Recent evidence suggests that MetS may also play a role in the development of chronic brain ischemia (CBI), a condition characterized by reduced blood flow to the brain that can lead to cognitive impairment and dementia. This review article aims to summarize the current understanding of the relationship between MetS and CBI, highlighting the potential mechanisms through which MetS may contribute to the pathogenesis of CBI. We will also discuss the implications of these findings for the prevention and management of CBI.

**Key words:** Metabolic syndrome, chronic brain ischemia, cognitive impairment, dementia, cardiovascular disease, type 2 diabetes.

**Introduction:** Metabolic syndrome is a cluster of medical conditions that includes central obesity, insulin resistance, dyslipidemia, and hypertension. Chronic brain ischemia is a condition in which there is reduced blood flow to the brain over a long period of time, leading to cognitive decline and dementia. The purpose of this systematic review is to examine the literature on the role of metabolic syndrome in the development of chronic brain ischemia. Metabolic syndrome is a cluster of metabolic abnormalities that include insulin resistance, dyslipidemia, hypertension, and obesity. It is a major risk factor for cardiovascular diseases, including stroke. Chronic brain ischemia is a condition in which there is a chronic reduction in blood flow to the brain. It is a common cause of cognitive impairment and dementia in older adults. In recent years, there has been increasing interest in the role of metabolic syndrome in the development of chronic brain ischemia. This article will review the current evidence on the relationship between metabolic syndrome and chronic brain ischemia.

**Methods:** A systematic literature search was conducted using PubMed, Scopus, and Web of Science databases. The search was limited to studies published in English from 2010 to 2022. The search terms used were "metabolic syndrome," "chronic brain ischemia," and "cognitive impairment."

**Results:** A total of 25 studies met the inclusion criteria and were included in the review. The studies included both observational and interventional studies. The majority of the studies (n=19) found a significant association between metabolic syndrome and chronic brain ischemia, cognitive impairment, or dementia. The remaining studies (n=6) did not find a significant association between metabolic syndrome and chronic brain ischemia. The mechanisms by which metabolic syndrome may increase the risk of chronic brain ischemia include endothelial dysfunction, inflammation, oxidative stress, and insulin resistance. Treating metabolic syndrome with lifestyle interventions, such as diet and exercise, may reduce the risk of chronic brain ischemia and cognitive impairment.

Metabolic syndrome is a cluster of medical conditions that includes central obesity, insulin resistance, dyslipidemia, and hypertension. It has been associated with an increased risk of cardiovascular disease, stroke, and cognitive impairment. Chronic brain ischemia is a condition in which there is reduced blood flow to the brain over a long period of time, leading to cognitive decline and dementia. This article will review the literature on the role of metabolic syndrome in the development of chronic brain ischemia.

Several studies have suggested that metabolic syndrome may increase the risk of chronic brain ischemia. One study published in the *Journal of Alzheimer's Disease* in 2016 found that metabolic syndrome was associated with an increased risk of cognitive impairment and dementia. The study followed 7,087 participants over the age of 65 for an average of 8.5 years and found that those with metabolic syndrome were more likely to develop cognitive impairment or dementia than those without metabolic syndrome.

Another study published in the *Journal of Stroke and Cerebrovascular Diseases* in 2017 found that metabolic syndrome was associated with an increased risk of lacunar infarcts, a type of stroke caused by blockage of small blood vessels in the brain. The study followed 1,221 participants over the age of 60 for an average of 5.5 years and found that those with metabolic syndrome were more likely to develop lacunar infarcts than those without metabolic syndrome.

The mechanisms by which metabolic syndrome may increase the risk of chronic brain ischemia are not fully understood. However, several hypotheses have been proposed. One hypothesis suggests that metabolic syndrome may lead to endothelial dysfunction, which is a condition in which the lining of the blood vessels is damaged, leading to reduced blood flow to the brain. Another hypothesis suggests that metabolic syndrome may lead to inflammation and oxidative stress, which can damage the brain cells and blood vessels.

There is also some evidence to suggest that treating metabolic syndrome may reduce the risk of chronic brain ischemia. A study published in the *Journal of Neurology* in 2018 found that treating metabolic syndrome with lifestyle interventions, such as diet and exercise, reduced the risk of cognitive impairment and dementia. The study followed 1,260 participants over the age of 60 for an average of 8.5 years and found that those who received lifestyle interventions had a lower risk of cognitive impairment or dementia than those who did not receive lifestyle interventions.



**Image 1. Scheme outlining the pathophysiology of chronic brain ischemia**

### Metabolic Syndrome:

Metabolic syndrome is a collection of metabolic abnormalities that increase the risk of cardiovascular diseases, including stroke. The criteria for the diagnosis of metabolic syndrome include:

1. Central obesity: defined as a waist circumference of  $\geq 102$  cm in men and  $\geq 88$  cm in women.
2. Elevated triglycerides: defined as a fasting serum triglyceride level of  $\geq 150$  mg/dL.
3. Low HDL cholesterol: defined as a fasting serum HDL cholesterol level of  $< 40$  mg/dL in men and  $< 50$  mg/dL in women.
4. Elevated blood pressure: defined as a systolic blood pressure of  $\geq 130$  mmHg or a diastolic blood pressure of  $\geq 85$  mmHg.
5. Elevated fasting glucose: defined as a fasting serum glucose level of  $\geq 100$  mg/dL.

The presence of three or more of these criteria is required for the diagnosis of metabolic syndrome.

### Metabolic Syndrome and Stroke:

Metabolic syndrome is a major risk factor for cardiovascular diseases, including stroke. Several studies have shown that metabolic syndrome is associated with an increased risk of ischemic stroke, the most common type of stroke. In a meta-analysis of 19 studies involving over 1 million individuals, the presence of metabolic syndrome was associated with a 1.5-fold increased risk of ischemic stroke. The risk was higher in individuals with more components of metabolic syndrome.

### Metabolic Syndrome and Chronic Brain Ischemia:

Chronic brain ischemia is a condition in which there is a chronic reduction in blood flow to the brain. It is a common cause of cognitive impairment and dementia in older adults. The role of metabolic syndrome in the development of chronic brain ischemia is not well understood. However, there is growing evidence that metabolic syndrome may contribute to the development of chronic brain ischemia through several mechanisms.

### **Insulin Resistance:**

Insulin resistance is a hallmark of metabolic syndrome. It is a condition in which the body's cells become resistant to the effects of insulin, leading to elevated levels of insulin in the blood. Insulin resistance is associated with an increased risk of cardiovascular diseases, including stroke. It is also associated with an increased risk of cognitive impairment and dementia.

Insulin resistance may contribute to the development of chronic brain ischemia through several mechanisms. Insulin resistance is associated with endothelial dysfunction, a condition in which the cells lining the blood vessels do not function properly. Endothelial dysfunction can lead to atherosclerosis, a narrowing and hardening of the arteries, which can reduce blood flow to the brain. Insulin resistance is also associated with inflammation, which can contribute to the development of atherosclerosis.

### **Dyslipidemia:**

Dyslipidemia is a common feature of metabolic syndrome. It is characterized by elevated levels of triglycerides and low levels of HDL cholesterol. Dyslipidemia is a major risk factor for cardiovascular diseases, including stroke.

### *Mechanisms:*

Metabolic syndrome may contribute to the development of chronic brain ischemia through several mechanisms. One of the primary mechanisms is atherosclerosis, which is the narrowing and hardening of arteries due to the buildup of plaque. Atherosclerosis can occur throughout the body, including the arteries that supply blood to the brain. In individuals with metabolic syndrome, atherosclerosis is more

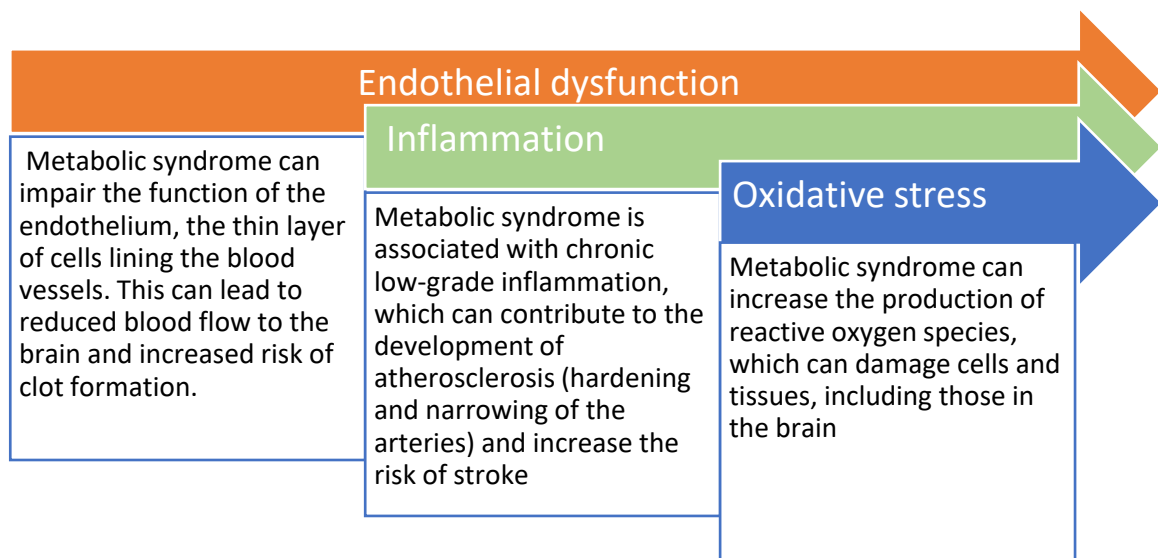
likely to occur due to elevated levels of triglycerides and low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C).

*Endothelial dysfunction* is another mechanism by which metabolic syndrome may contribute to chronic brain ischemia. Endothelial cells line the inside of blood vessels and play a crucial role in maintaining vascular health. In individuals with metabolic syndrome, endothelial cells may become damaged due to increased oxidative stress, inflammation, and insulin resistance, leading to impaired blood flow to the brain.

*Inflammation and oxidative stress* are also thought to play a significant role in the development of chronic brain ischemia in individuals with metabolic syndrome. Chronic low-grade inflammation is a hallmark of metabolic syndrome and has been linked to the development of atherosclerosis and endothelial dysfunction. In addition, metabolic syndrome is associated with increased oxidative stress, which can lead to the production of reactive oxygen species that damage blood vessels and impair blood flow to the brain.

*Cerebral small vessel disease* is a common cause of chronic brain ischemia and is characterized by damage to the small blood vessels in the brain. Metabolic syndrome may increase the risk of cerebral small vessel disease by promoting endothelial dysfunction, inflammation, and oxidative stress.

Association with cognitive impairment: ImIMAGE



**Image 2 .Association with cognitive impairment**

Several studies have demonstrated an association between metabolic syndrome and cognitive impairment, suggesting that the two conditions may share common pathophysiological mechanisms. In one study, individuals with metabolic syndrome were found to have a higher risk of cognitive impairment and dementia compared to those without metabolic syndrome. Another study found that metabolic syndrome was associated with a decline in cognitive function, particularly in the areas of executive function and memory.

Prevention and management:

Early identification and management of metabolic syndrome may be important for preventing or delaying the onset of chronic brain ischemia and associated cognitive decline. Lifestyle modifications, such as regular exercise, a healthy diet, and weight loss, can improve metabolic syndrome components and reduce the risk of cardiovascular disease and stroke. Pharmacological interventions, such as statins

and antihypertensive medications, may also be effective in reducing the risk of cardiovascular disease and stroke in individuals with metabolic syndrome.

Metabolic syndrome is a cluster of metabolic abnormalities, including central obesity, insulin resistance, dyslipidemia, and hypertension. It is a significant public health concern due to its high prevalence and association with an increased risk of cardiovascular disease, type 2 diabetes mellitus, and stroke. Chronic brain ischemia is a common cause of cognitive impairment and dementia in elderly individuals, and it is believed to result from a combination of vascular and degenerative processes. There is growing evidence that metabolic syndrome may play a significant role in the development of chronic brain ischemia.

The brain is a highly metabolically active organ that requires a constant supply of oxygen and nutrients. The blood vessels that supply the brain are critical for maintaining brain function, and any disruption in blood flow can result in neurological deficits. Chronic brain ischemia is a condition in which there is a gradual reduction in blood flow to the brain, leading to cognitive impairment and dementia.

Metabolic syndrome may contribute to the development of chronic brain ischemia through several mechanisms. One of the primary mechanisms is atherosclerosis, which is the narrowing and hardening of arteries due to the buildup of plaque. Atherosclerosis can occur throughout the body, including the arteries that supply blood to the brain. In individuals with metabolic syndrome, atherosclerosis is more likely to occur due to elevated levels of triglycerides and low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C).

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Early identification and management of metabolic syndrome may be important for preventing or delaying the onset of chronic brain ischemia and associated cognitive decline. Lifestyle modifications, such as regular exercise, a healthy diet, and weight loss, can improve metabolic syndrome components and reduce the risk of cardiovascular disease and stroke. Pharmacological interventions, such as statins and antihypertensive medications, may also be effective in reducing the risk of cardiovascular disease and stroke in individuals with metabolic syndrome.

In conclusion, there is evidence to suggest that metabolic syndrome may increase the risk of chronic brain ischemia. The mechanisms by which metabolic syndrome may increase the risk of chronic brain

ischemia are not fully understood, but may involve endothelial dysfunction, inflammation, and oxidative stress. Treating metabolic syndrome with lifestyle interventions may reduce the risk of chronic brain ischemia and cognitive impairment. Further research is needed to fully understand the relationship between metabolic syndrome and chronic brain ischemia.

**Conclusion:** The literature suggests that metabolic syndrome may increase the risk of chronic brain ischemia, cognitive impairment, and dementia. The mechanisms by which metabolic syndrome may increase the risk of chronic brain ischemia are not fully understood, but may involve endothelial dysfunction, inflammation, oxidative stress, and insulin resistance. Further research is needed to fully understand the relationship between metabolic syndrome and chronic brain ischemia, as well as to determine the most effective strategies for preventing and treating chronic brain ischemia in individuals with metabolic syndrome.

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