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Homocysteine: A Modern Biomarker for Diabetes and Cardiovascular Disease

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Dear Editor,

Homocysteine (Hcy) is a naturally occurring non-essential amino acid that contains the sulfur compound 2-amino-4-mercabtobutanic acid. It can be found in both free and bound structures but not in proteins. In mammals, Hcy plays a significant role in nutritional metabolism.[1] The normal dietary metabolism of Hcy requires adequate amounts of folic acid, vitamin B12, vitamin B6, and vitamin B2 (riboflavin); furthermore, the levels of these vitamins are inversely correlated with the distribution of Hcy levels.[2] In addition, high levels of Hcy destroy the body's arteries if exceeding those of smoking, obesity, or cholesterol itself, and this excess Hcy can be disposed of in two ways: The first is to convert Hcy into methionine by a reaction that depends on the presence of folic acid, vitamin B12, and the enzyme methionine synthase. The second method is to convert it to cysteine through a reaction that depends on the presence of vitamin B6 and the enzyme cystathionine β-synthase (CBS).[3]

Previous studies have indicated that elevated Hcy levels can be a risk factor for developing heart and arterial diseases (e.g., coronary, cerebral, and peripheral) and diabetes as the risk of elevated levels of Hcy is considerably greater than that of other medical conditions such as high blood pressure, high cholesterol levels, and smoking. This high risk is attributed to deficiencies in enzymes (e.g., CBS or methyl tetrahydrofolate reductase [MTHFR]) or cofactors (e.g., folic acid and vitamin B12) in the nutritional metabolism of Hcy.[4,5] As a result, high levels of Hcy can lead to atherosclerosis, causing atherosclerosis. This occurs directly through the accumulation and oxidation of Hcy, thereby generating free radicals that cause scratches and tears in the walls of endothelial cells, accelerate the oxidation of low-density lipoproteins, and promote the process of its absorption by macrophages, leading to the formation of foam cells. Foam cells contribute to the formation of atherosclerotic plaques, which may be accompanied by excessive blood clotting and the formation of clots inside the arteries. This can reduce blood supply to the heart muscle, potentially leading to a heart attack.[6,7]

Furthermore, the most common increase in Hcy may occur due to genetic mutations that cause a deficiency in some enzymes that play an important role in the Hcy metabolism such as genetic abnormalities in the enzyme methionine synthase (genetically), folate, or vitamin B12.[8] The slowdown in the conversion of Hcy to methionine leads to the accumulation of Hcy or genetic defect of the MTHFR enzyme, which requires the synthesis of MTHF. Hereditary hyperhomocysteinemia, a common form of this situation, is caused by a deficiency of the MTHFR enzyme owing to a mutation in the gene that encodes it, namely, C677T. Moreover, a hereditary defect in the enzyme CBS (hereditary) can also contribute to high Hcy levels.[9] Another cause of high levels of Hcy may be a deficiency in vitamin B6, which slows down the conversion of Hcy to cysteine, consequently leading to the accumulation of Hcy in the blood. Thus, it causes several disorders, including abnormal blood clotting, stroke, Alzheimer's disease, delayed growth and development in children, and various cognitive problems.[10]

In conclusion, most micronutrients such as vitamins are involved in some ways in the enzymatic pathway of Hcy metabolism, either as part of a cause or effect. As a result, the imbalance between free radical formation and their control by antioxidants (vitamins) causes

genetic mutations. Consequently, patients may develop diabetes mellitus, cardiovascular disease, and associated complications.

Authors' Contribution

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Competing Interests

There is no conflict of interests.

Ethical Approval

Not applicable.

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