Influence of Iron Deficiency Anemia on HbA1c: A Review

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Abstract

Hemoglobin A1c (HbA1c) is widely used as a diagnostic tool for diabetes. Many clinical conditions affect erythrocyte turnover which influence HbA1c levels. These levels are lowered by different forms of anemia, but reverse is the case in iron deficiency anemia (IDA). This is suggested by various studies which propose an increase in HbA1c levels in patients with IDA. However, there are studies which negate any influence of IDA over HbA1c levels. In both cases the clinical data is not sufficient to confirm or nullify the role of IDA in increasing HbA1c levels.

Introduction

Hemoglobin A1c (HbA1c), a glycated hemoglobin is formed by an irreversible, slow non-enzymatic catalysis of the β chain of globin in mature hemoglobin (Hb) [1,2]. It is used as a gold standard for monitoring glycemic status for the previous three months (the life span of a red blood cell) in patients with diabetes [3]. HbA1c provides an integrated measure of glycemia which is less susceptible to short-term modulation than blood glucose levels. Also, it helps to keep a track of diabetic therapy within individuals suffering from diabetes. WHO and ADA have approved the use of HbA1c determination for diagnosis of type 2 diabetes [4,5]. The normal range of HbA1c in a healthy person is 4 to 6% [6].

Clinically there are three major factors on which HbA1c levels depend.

A. HbA1c in reticulocytes when released from the bone marrow;

B. Hb glycation rate as red blood cells (RBCs) become older, a function of glucose concentration to which Hb is exposed; and

C. The mean age of RBCs in the circulation [7].

HbA1c levels can be affected by number of factors such as structural hemoglobinopathies, thalassemia syndrome, and alteration in quaternary structure of Hb [8]. Also, HbA1c levels can be changed by different types of anemia [9]. Anemia is the most prevalent form of nutritional deficiency both in developed and developing countries. Globally, 50% of anemic burden is contributed alone by Iron deficiency [10,11]. The clinical profile of many systemic diseases is regulated by the iron [12], which is involved in most important metabolic processes viz. transportation of oxygen, regulation of cell growth and differentiation, deoxyribonucleic acid (DNA) synthesis, and electron transport [13,14].

Iron deficiency anemia (IDA) can increase the red blood cell turnover which can increase glycation of Hb leading to higher HbA1c values as observed in blood loss, hemolysis, hemoglobinopathies, red cell disorders and myelodysplastic disease [15]. There are studies to support the idea that diabetes is influenced by changes in the iron level in a body [16]. Lower levels of serum iron or serum ferritin have been linked with increased glycation of HbA1c [17,18]. It has been reported that there is a bidirectional relationship between iron metabolism and glucose homeostasis, higher iron levels modulate both the action and secretion of insulin [12]. Thus, lower the iron levels, higher is the glycation of HbA1c, leading to its false-high values in diabetic as well as non-diabetic individuals [19].

Brooks et al. [20] reported that a relative absence of iron results in the alteration of quaternary structure of the Hb molecule leading to excessive glycation of the beta globin chain. In another study by Sluiter et al. [21] it was reported that glycation of Hb is an irreversible process thus, with the aging of a cell there is a linear increase of HbA1c in the erythrocyte. El Agouza et al.
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