Glucose-6-Phosphate Dehydrogenase Deficiency

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Glucose-6-phosphate dehydrogenase deficiency is a genetic disorder that occurs almost exclusively in males.

Keywords: genetic conditions

1. Introduction

Glucose-6-phosphate dehydrogenase deficiency mainly affects red blood cells, which carry oxygen from the lungs to tissues throughout the body. In affected individuals, a defect in an enzyme called glucose-6-phosphate dehydrogenase causes red blood cells to break down prematurely. This destruction of red blood cells is called hemolysis.

The most common medical problem associated with glucose-6-phosphate dehydrogenase deficiency is hemolytic anemia, which occurs when red blood cells are destroyed faster than the body can replace them. This type of anemia leads to paleness, yellowing of the skin and whites of the eyes (jaundice), dark urine, fatigue, shortness of breath, and a rapid heart rate. In people with glucose-6-phosphate dehydrogenase deficiency, hemolytic anemia is most often triggered by bacterial or viral infections or by certain drugs (such as some antibiotics and medications used to treat malaria). Hemolytic anemia can also occur after eating fava beans or inhaling pollen from fava plants (a reaction called favism).

Glucose-6-phosphate dehydrogenase deficiency is also a significant cause of mild to severe jaundice in newborns. Many people with this disorder, however, never experience any signs or symptoms and are unaware that they have the condition.

2. Frequency

An estimated 400 million people worldwide have glucose-6-phosphate dehydrogenase deficiency. This condition occurs most frequently in certain parts of Africa, Asia, the Mediterranean, and the Middle East. It affects about 1 in 10 African American males in the United States.

3. Causes

Glucose-6-phosphate dehydrogenase deficiency results from mutations in the *G6PD* gene. This gene provides instructions for making an enzyme called glucose-6-phosphate dehydrogenase. This enzyme is involved in the normal processing of carbohydrates. It also protects red blood cells from the effects of potentially harmful molecules called reactive oxygen species, which are byproducts of normal cellular functions. Chemical reactions involving glucose-6-phosphate dehydrogenase produce compounds that prevent reactive oxygen species from building up to toxic levels within red blood cells.

If mutations in the *G6PD* gene reduce the amount of glucose-6-phosphate dehydrogenase or alter its structure, this enzyme can no longer play its protective role. As a result, reactive oxygen species can accumulate and damage red blood cells. Factors such as infections, certain drugs, or ingesting fava beans can increase the levels of reactive oxygen species, causing red blood cells to be destroyed faster than the body can replace them. A reduction in the number of red blood cells causes the signs and symptoms of hemolytic anemia.

Researchers believe that people who have a *G6PD* mutation may be partially protected against malaria, an infectious disease carried by a certain type of mosquito. A reduction in the amount of functional glucose-6-phosphate dehydrogenase appears to make it more difficult for this parasite to invade red blood cells. Glucose-6-phosphate dehydrogenase deficiency occurs most frequently in areas of the world where malaria is common.

3.1. The gene associated with Glucose-6-phosphate dehydrogenase deficiency

- G6PD

4. Inheritance

Glucose-6-phosphate dehydrogenase is inherited in an X-linked pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. Males have only one X chromosome and females have two copies of the X chromosome. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In females, who have two copies of the X chromosome, one altered copy of the *G6PD* gene in each cell can lead to less severe features of the condition or may cause no signs or symptoms at all. However, many females with one altered copy of this gene have glucose-6-phosphate dehydrogenase deficiency similar to affected males because the X chromosome with the normal copy of the *G6PD* gene is turned off through a process called X-inactivation . Early in embryonic development in females, one of the two X chromosomes is permanently inactivated in somatic cells (cells other than egg and sperm cells). X-inactivation ensures that females, like males, have only one active copy of the X chromosome in each body cell. Usually X-inactivation occurs randomly, such that each X chromosome is active in about half of the body cells. Sometimes X-inactivation is not random, and one X chromosome is active in more than half of cells. When X-inactivation does not occur randomly, it is called skewed X-inactivation.

Research shows that females with glucose-6-phosphate dehydrogenase deficiency caused by mutation of the *G6PD* gene often have skewed X-inactivation, which results in the inactivation of the X chromosome with the normal copy of the *G6PD* gene in most cells of the body. This skewed X-inactivation causes the chromosome with the mutated *G6PD* gene to be expressed in more than half of cells.

5. Other Names for This Condition

- deficiency of glucose-6-phosphate dehydrogenase
- G6PD deficiency
- G6PDD
- glucose 6 phosphate dehydrogenase deficiency

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