Possible association of 3′ UTR +357 A>G, IVS11-nt 93 T>C, c.1311 C>T polymorphism with G6PD deficiency

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**ABSTRACT**

**Background:** Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common X-linked inherited enzymopathic disorder affecting more than 500 million people worldwide. It has so far been linked to 217 distinct genetic variants in the exons and exon-intron boundaries of the G6PD gene, giving rise to a wide range of biochemical heterogeneity and clinical manifestations.

**Objectives:** Reports from different settings suggested the association of intronic and other mutations outside the reading frame of the G6PD gene with reduced enzyme activity and presenting clinical symptoms. The present study aimed to investigate any association of other variations apart of the exonic or exonic intronic boundaries in the development of G6PD deficiency.

**Methods:** Sixty-seven unrelated Palestinian children admitted to the pediatric hospital with hemolytic crises due to G6PD deficiency were studied.

**Results:** In our Palestinian cohort of 67 (59 males (M) and 8 females (F)) G6PD-deficient children, previously hospitalized for acute hemolytic anemia due to favism, molecular sequencing of the G6PD gene revealed four cases (3M and 1F) that did not have any of the variants known to cause G6PD deficiency, but the 3′ UTR c.*+357A>G (rs1050757) polymorphism in association with IVS11-nt 93 T>C; c.1311 C>T; polymorphism.

**Conclusion:** We now provide an additional evidence from Palestinian G6PD-deficient subjects for a possible role of 3′ UTR c.*+357 A>G, IVS11-nt 93 T>C; c.1311 C>T; polymorphism for G6PD deficiency, suggesting that not only a single variation in the exonic or exonic intronic boundaries, but also a haplotype of G6PD should considered as a cause for G6PD deficiency.

**KEYWORDS**

Glucose-6-phosphate dehydrogenase (G6PD) deficiency; Gaza Palestine; 3′ UTR +357 A>G; IVS11-nt 93 T>C; c.1311 C>T; polymorphism

**Introduction**

Affecting more than 500 million people worldwide, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common X-linked (cytogenetic location: Xq28) inherited enzymopathic disorder which has been reported in peoples from nearly all geographical locations; however predominates where *Plasmodium falciparum* malaria is or had been endemic. The G6PD plays a crucial part in sustaining the integrity of red blood cells (RBC) by preventing the oxidation of hemoglobin and other cellular proteins through the reducing power of NADPH generated by G6PD in the hexose monophosphate shunt (pentose phosphate pathway). G6PD deficiency is associated with 217 distinct genetic variants in the exons and exon-intron boundaries of the G6PD gene [1,2]. These genetic variants result in diminished stability and or activity giving rise to a wide range of biochemical heterogeneity and clinical manifestations. This disorder is classified into five categories based on enzyme activity and clinical presentations [3]. Class I variants encompass the severely deficient cases with chronic non-spherocytic hemolytic anemia, while class V variants cause increased G6PD activity. The principle clinical presentation of G6PD deficiency is an acute hemolytic anemia (AHA) triggered by an exogenous drug or ingestion of fava beans that may require transfusion in children.

Recent studies from different populations have addressed probable and potential associations between some intronic and non-coding region polymorphisms and the biochemical and clinical presentation of G6PD-deficient subjects [4–10]. In the present study we aim to explore the association of 3′ UTR c.*+357 A>G (rs1050757), c.1365-13T>C, and/or c.1311C>T polymorphisms for G6PD deficiency, suggesting that not only a single variation in the exonic or exonic intronic boundaries, but also a haplotype of G6PD should considered as a cause for G6PD deficiency.