Hemolysis and Mediterranean G6PD mutation (c.563 C>T) and c.1311 C>T polymorphism among Palestinians at Gaza Strip

Mahmoud Sirdah a,b,⁎,1, N. Scott Reading a,1, Sherrie L. Perkins a, Mohammad Shubair c, Lina Aboud d, Josef T. Prchal a,⁎⁎

a Associated Regional and University Pathologists, Inc., ARUP Laboratories and University of Utah, Salt Lake City, UT, USA
b Biology Department, Al Azhar University-Gaza, Palestine
c Department of Laboratory Medical Sciences, Islamic University-Gaza, Palestine
d Al Nasser Pediatric Hospital, Palestinian Ministry of Health, Palestine

⁎⁎ Correspondence to: J. T. Prchal, Hematology, SOM 5C310, University of Utah School of Medicine, Salt Lake City, Utah 84132-2408, USA, Fax: +1 801 585 3432.
⁎⁎⁎ Correspondence to: M. Sirdah, Al Azhar University-Gaza, P O Box 1277, Gaza, Palestine. Fax: +970 282823180.
E-mail addresses: sirdah@alazar.edu.ps, msirdah@hotmail.com (M. Sirdah), josef.prchal@hsc.utah.edu (J.T. Prchal).
1 Equally contributing authors.

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Abstract

Background: The G6PD c.563 C>T deficient mutation is endemic among Mediterranean populations but its clinical significance is not well delineated. We set up to estimate the proportion of G6PD deficient children presenting with hemolytic anemia at Al Nasser Pediatric Hospital at Gaza Strip, Palestine. We then established the prevalence of c.563T Mediterranean mutation and its linkage to c.1311 C>T polymorphism in this population.

Design and Methods: G6PD deficiency was identified in children presenting with hemolytic anemia at Al Nasser Pediatric Hospital by spectrophotometric measurement of G6PD activity. G6PD exon 6 and exon 11 were amplified from genomic DNA and evaluated for c.563T mutation by sequencing and the c.1311T polymorphism by restriction fragment analysis. Seventy X-chromosomes (60 males and 5 females) from G6PD deficient patients and 40 X-chromosomes from a control group known to be not G6PD deficient were tested.

Results: Over 80% of these children presenting with hemolytic anemia were G6PD deficient and 34% of these had the Mediterranean G6PD deficient variant. The allelic frequencies of Mediterranean c.563T and c.1311T polymorphisms among G6PD deficient patients were 0.33 and 0.38 respectively. The c.1311T polymorphism was linked in 95.2% of patients with the Mediterranean mutation, an allele frequency of 0.87, compared to the control non-G6PD deficient group with an allele frequency of 0.18.

Conclusion: We conclude that G6PD deficiency accounts for majority of hemolytic anemia encountered in Gaza children treated at Al Nasser Pediatric Hospital Emergency department. The Mediterranean mutation c.563T, while not accounting for a majority of G6PD deficiency, is common among G6PD deficient Gaza Strip Palestinians and is frequently, but not always, linked to the c.1311T polymorphism. This work provides a foundation for the population screening of Palestinians for G6PD deficiency and for investigations of ancestral origin of the Mediterranean variant in world populations.

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Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is considered one of the most common genetic disorders and is the most common of enzymopathic red blood cell disorders, affecting more than 400 million people worldwide. The disease has been reported in populations from nearly all geographical locations; however it occurs most frequently in areas where Plasmodium falciparum malaria has been endemic. Prevalence estimates are highest in Africa, Asia, the Mediterranean region and the Middle East [1]. The G6PD enzyme has an essential role in maintaining the integrity of erythrocytes, preventing the oxidation of hemoglobin and other cellular proteins by providing reducing power in the form of NADPH via the hexose monophosphate shunt [2]. The G6PD gene maps to the tip of the X chromosome (Xq28), and consists of 13 exons encoding a 515 amino acid protein with a molecular weight of about 59 kDa. Mutations in the G6PD gene may result in diminished functionality and/or stability of the G6PD enzyme, resulting in different levels of enzymatic activity and a wide range of biochemical and clinical presentations; however, the endemic variants are associated only with intermittent, and what is assumed to be rare, hemolytic episodes. Neonatal jaundice and acute hemolytic anemia triggered by exogenous oxidizing agents, such as drugs and fava beans, as well as infections, are principle clinical presentations in most cases. Since it is an X-linked