Gene mutation and qualitative enzyme assay of G6PD enzyme deficiency in neonatal hyperbilirubinemia

Thesis

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By

Othman Rizk Abdel Meguid Mishref
M.Sc. Pediatrics - Cairo University

Under Supervision of

Prof. Dr. Zahraa Mohamed Ezz El-Deen
Professor of Pediatrics
Faculty of Medicine-Cairo University

Prof. Dr. Shahira Amin Zayed
Professor of clinical Pathology
Faculty of Medicine-Cairo University

Prof. Dr. Nouran Fahmy Hussein
Associate Professor of Pediatrics
Faculty of Medicine-Cairo University

Dr. Tamer Ahmed Abdel Hamid
Lecturer of Pediatrics
Faculty of Medicine-Cairo University

Faculty of Medicine – Cairo University
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التحور الجينى و الكشف الكيفى لنقص إنزيم جلوكوز ٦ فوسفات الهيدروجين فى الأطفال حديثى الولادة الذين يعانون من صفراء بالدم

رسالة

توطئة للحصول على درجة الدكتوراة فى طب الأطفال

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الطبيب/ عثمان رزق عبدالمجيد مشرف

ماجستير طب الأطفال

تحت إشراف

الأستاذة الدكتورة / زهراء محمد عزالدين

أستاذ طب الأطفال

كلية الطب

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أستاذ الباثولوجيا الإكلينيكية و الكيميائية

كلية الطب

جامعة القاهرة

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كلية الطب

جامعة القاهرة

كلية الطب

جامعة القاهرة

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Abstract

Background: Molecular characterization of glucose-6-phosphate dehydrogenase (G6PD) deficiency variants is essential, especially since the biochemical characterization has lost its significance due to the individual variability. As a result, cases can be misdiagnosed. The present study was designed to determine the incidence of G6PD Mediterranean (Med) mutation among Egyptian children with G6PD deficiency as well as its molecular association with the G6PD 1311T silent polymorphism.

Methods: Fifty full term male, Egyptian neonates, presented with neonatal hyperbilirubinemia were subjected to quantitative G6PD enzyme assay. A polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used for detection of G6PD Mediterranean mutation and G6PD 1311 silent polymorphism.

Results: Qualitative assay of G6PD level revealed presence of 21 cases (42%) out of 50 cases with neonatal hyperbilirubinemia had G6PD deficiency. Within the G6PD deficient group, there were 10 cases (47.62%) had mild G6PD deficiency, 4 cases (19.05%) had moderate G6PD deficiency, and 7 cases (33.33%) had severe G6PD deficiency. In this study, all cases with gene mutation were G6PD deficient, where 33.33% (7/21) cases had G6PD Mediterranean mutation (563 C-T), and 28.57% (6/21) cases had G6PD Silent mutation at Position (1311 C-T).

Conclusion: G6PD deficiency seems to be a relatively common cause of neonatal jaundice in Egyptian infants. Detection of this enzymopathy by measuring G6PD level and molecular analysis of gene mutations can give a clue for early diagnosis of G6PD deficiency, monitoring for possible jaundice, and consequent prevention of possible complication as kernicterus in neonatal period, and hemolytic crisis later on.

Key words: G6PD deficiency, Mediterranean mutation, PCR-RFLP, 1311 silent polymorphism.

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List of Abbreviations

AAP	:	American Academy of Pediatrics
ABE	:	Acute bilirubin encephalopathy
B/A ratio	:	Bilirubin/Albumin ratio
CNSHA	:	Chronic Non-spherocytic Hemolytic Anemia
CO	:	Carbon monoxide
DAT	:	Direct agglutinin test
ETCO	:	End tidal carbon monoxide
G6PD	:	Glucose-6-phosphate dehydrogenase
GA	:	Gestational Age
GST	:	Glutathione-s-transferase
Hct	:	Hematocrit
HGB	:	Hemoglobin
IVIg	:	Intravenous immunoglobulin
LED	:	Light Emitting Diodes
OATP2	:	Organic anion transport protein 2
PCR	:	Polymerase chain reaction
PCR-RFLP	:	Polymerase chain reaction- Restriction Fragment Length Polymorphism
snMP	:	Tin-Mesoporphyrin
TCB	:	Transcutaneous bilirubin
TSB	:	Total serum bilirubin
UGT	:	Uridine diphospho glucuronosyl transferase
WHO	:	World Health Organization

Aim of Work

The present study aimed to ascertain the presence of glucose -6-phosphate dehydrogenase (G6PD) enzyme deficiency in male newborns presented with neonatal hyperbilirubinemia, and to detect the presence or absence of G6PD Mediterranean mutation (563 C-T) and 1311 silent polymorphism. As well as, to delineates the magnitude of the problem of G6PD deficiency in Egyptian neonates, and emphasizes the role of early detection of G6PD deficiency by proper screening.