

Neonatal Screening for G-6-PD Deficiency in Both Sexes in the Syrian Coastal Region

Dr. A. Youssef*
Dr. S. Mohammad**

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□ ABSTRACT □

We have screened 830 newborns in the hospitals of the coastal region in Syria for G-6-PD deficiency within the first 48 hrs of life. There are 27% of boys and 18% of girls were deficient, number of girls was more than expected by Hardy-Weinberg law.

The family history for G-6-PD deficiency and the estimation of G-6-PD enzyme in fathers of affected girls suggested that most of the cases are Heterozygous with the normal x chromosome is inactivated by random inactivation (Lyon Hypotheses).

We proved that Screening for G-6-PD deficiency should include both sexes (males and females). It is a simple way that provides us with an important information about G-6-PD deficiency early enough to put the necessary protective plan.

Keywords: G-6-PD, Hardy-Weinberg Law, Lyon Hypotheses.

*Head of Department of Obstetrics & Gynecology, Faculty of Medicine, Tishreen University, Lattakia, Syria

**MD-MRCP-FRCPCH, Ex-Head of Department of Pediatrics, Zahi Azrak Hospital, Lattakia, Syria.

المسح الشامل لتحري نقص خميرة G6PD لدى المولودين حديثاً عند الجنسين في الساحل السوري

الدكتور أحمد حسن يوسف*

الدكتورة سميرة محمد**

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□ ملخص □

لقد أجرينا مسحاً شاملاً لـ 830 مولوداً حديثاً خلال 48 ساعة من الولادة لتحري نقص خميرة غلوكوز . 6 فوسفات، في مشافي المنطقة الساحلية في سورية ووجدنا أن هناك نقصاً في هذه الخميرة لدى 27% من الذكور و18% من الإناث. وعدد الإناث كان أكبر من المتوقع بحسب قانون هارديلي . ولينبرغ. القصة العائلية لنقص خميرة غلوكوز . 6 فوسفات ومعايرة الخميرة عند أبناء الإناث اللواتي لديهن نقص الخميرة تُظهر أن معظم الحالات كانت متخالفة الأمشاج تثبط فيها الصبغي X الطبيعي بالتنشيط العشوائي (نظرية LYON). إن النتائج التي توصلنا إليها تسمح بالقول إنه يجب تطبيق التحري الشامل لكل المولودين حديثاً (ذكور، إناث) حول النقص في هذه الخميرة.

لقد أثبتنا أن المسح الشامل من أجل نقص خميرة غلوكوز . 6 فوسفات يجب أن يشمل كلا الجنسين الذكور والإناث. وهو طريقة بسيطة تقدم لنا معلومات مهمة حول نقص الخميرة من أجل وضع خطة الوقاية اللازمة.

الكلمات المفتاحية: خميرة غلوكوز . 6 فوسفات ، قانون هارديلي . ولينبرغ، نظرية LYON.

* أستاذ في قسم التوليد وأمراض النساء . كلية الطب . جامعة تشرين . اللاذقية . سورية.

** رئيسة قسم الأطفال، المشفى العسكري باللاذقية (سابقاً) ، سورية.

Introduction:

The genetic locus for G-6-PD variants is on the x chromosome, inheritance follows sex linked recessive pattern, the Mediterranean variant is common in Syria with high frequency in coastal region, it carries the risk of kernicterus (1-2) & life-endangering Favism (3) & drug-induced haemolysis which all are preventable if diagnosis made at birth. It was previously believed that only boys are affected, but actually it is our observation that girls are commonly affected and it's compatible with what have been demonstrated in studies elsewhere (4), therefore we planned this neonatal screening for both sexes. We carried out the first neonatal screening in Syria in the coastal region.

Aim of the study:

Early diagnosis (in neonatal life) of G-6-PD deficiency in infants male & female.
Warn the parents of the danger of being enzyme deficient so as to...
Take preventive measures.

Materials & Methods:

All newborn boys and girls born in the coastal region Hospitals between February-May 1998

Table (1): Number of newborn boys and girls born in the coastal region Hospitals

		male	Female
Al-Assad Univ.Hosp.	Lattakia	158	154
Al_Watani Hosp.	Lattakia	293	306
Al_Bassel Hosp.	Tartus		

Heelprik blood specimens were taken on filter paper within 48 hrs of delivery and studied by B.M. Test Kit. This kit is highly specific and sensitive for severe deficiency. It's cheap, used in screening program in Far East on million of babies every year, doesn't need sophisticated technology, can be done in any hospital.

This Method depends on the fluorescence of NADPH under long-wave UV as an indicator of G-6-PD activity.

When NADPH is absent or deficient in G-6-PD deficiency the fluorescence is absent or intermediate according to severity. Figure (1).

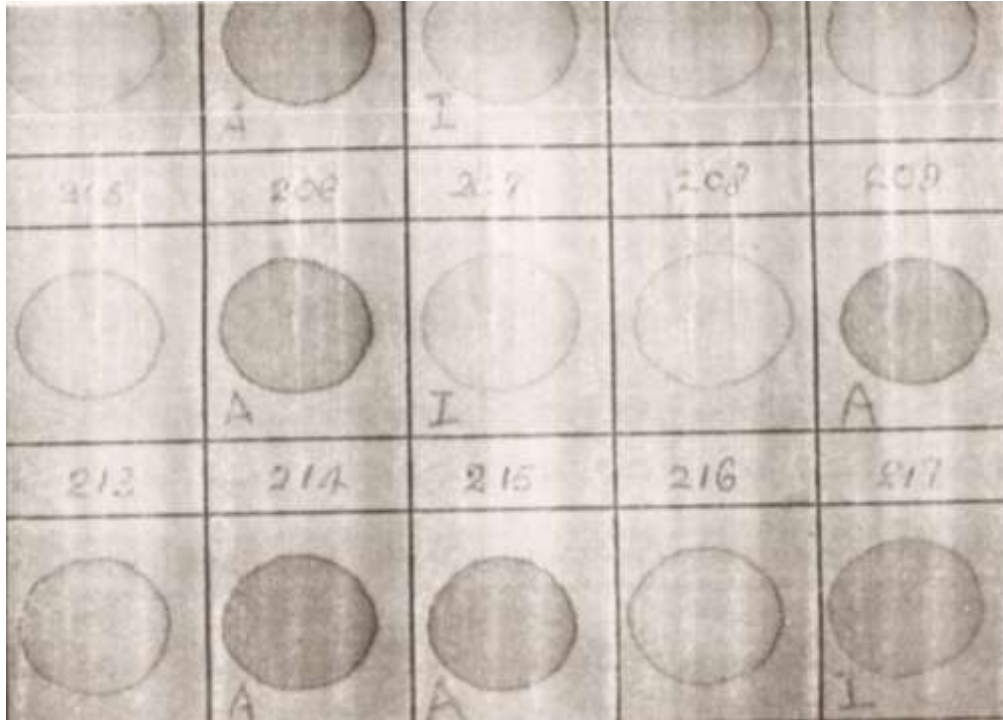


Figure (1): fluorescence of NADPH under long-wave UV
The dark one (fluorescence) is normal G-6-PD .
The light one (no fluorescence) is severely deficient,
there is an intermediate one

NADPH is produced in red cells by the first reaction in pentose phosphate pathway Figure (2), the reaction is between Glucose-6-phosphate and NADP intermediated by G6PD, the NADPH generated keeps Glutathione in reduced form which is essential for protection of red cells from oxidative stress, or oxidative agents, it's absence means red cell death rapidly.

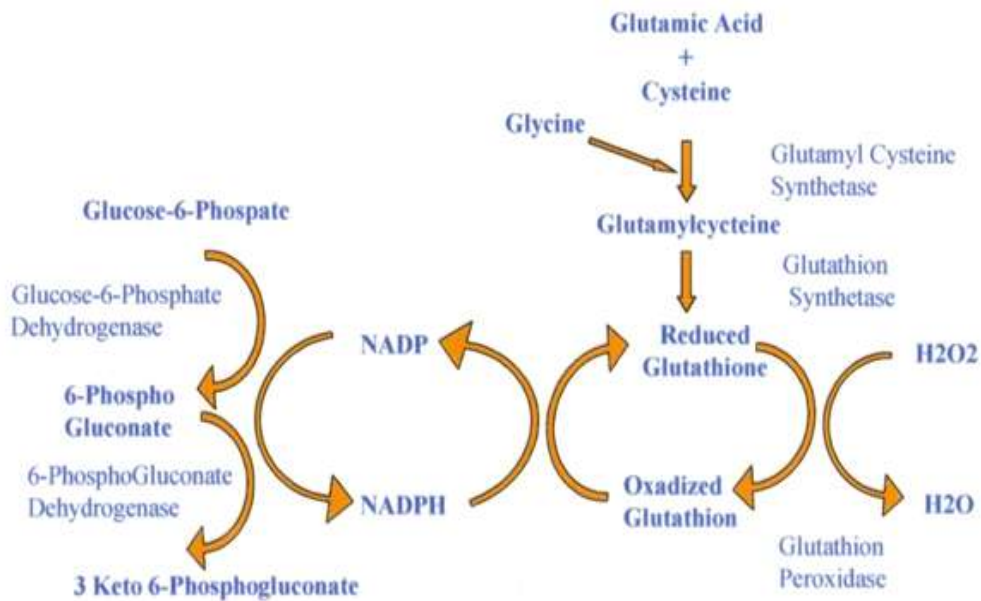


Figure (2): pentose phosphate pathway

Results:

Results from AL-Assad Uni Hospital in (Table 2) & from the ministry of health hospitals: AL- Watani Hospital in Lattakia and AL-Basel Hospital in Tartous in (Table 3)

Table (2): Result of Screening for G-6-PD Deficiency in Al-Assad Univ. Hosp.

Sex	No.	Intermediate def.	Sever def.	% of sever Def.	`No. of Pridedted def.	No. of def. From Mother line	No. of def. From Father line	No. of def. Form Both sides
M	158		56	35%		3	2	
F	154	45	28	18%	18	7	1	1

Table (3): Result of Screening for G-6-PD Deficiency in AL-Bassel Hosp. Tartus and AL-Watani Hosp. Lattakia – Syria

Sex	No.	Intermediate def.	Sever def.	% of sever Def.	`No. of Pridedted def.	No. of def. From Mother line	No. of def. From Father line	No. of def. From Both sides
M	293	10	72	24%		3		
F	306	63	54	18%	15	6	4	1

Discussion:

The aim of our screening program was to diagnose those infants with G-6-PD deficiency early in neonatal life in order to predict those at risk for developing jaundice, to prevent early discharge of these infants, and to warn the parents of the dangers of being enzyme deficient. The screening test we employed was chosen for its simplicity and brevity which lent itself to achieving our goal. Sophisticated technical expertise or equipment is unnecessary and the test can easily be performed in any periphery hospital. Of more concern than the generic classification of females into neonatal, hemizygotes, and homozygotes was the determination of the amount of functioning enzyme. Most likely females hemizygotes with a normal screening test will have sufficient enzyme activity to prevent their suffering from the consequences of G-6-PD deficiency in the neonatal period and vice versa, and therefore a more complicated and time consuming test was deemed unnecessary for our purposes.

One of the most common of all clinically significant enzyme defects is G6PD deficiency. Its incidence in neonates varies in different parts of the world according to ethnic variations our study showed 22.5%. Studies from different parts of the world report different incidence rates. In Spain⁶, France⁷ and Singapore⁸ the incidence rates (1.57, 2.1 and 1.62% respectively) were low, while that of Saudi Arabia⁹, Nigeria¹⁰ and in American Blacks¹¹ (18.4, 40 and 14% respectively) were high. In our country, G6PD deficiency is a common enzyme deficiency in certain regions especially in the Mediterranean region. Its incidence was reported to be 1–5%.¹²

In Our study male sever G.6Pd deficiency was more than female (27%.18%) respectively but severe deficiency female/male ratio was around 3:1, the same result in study from ISTANBUL¹³ was detected a male: female ratio of 3:1, and from Iran.¹⁴

As G-6-PD deficiency is an X linked condition, it is sufficient to establish the maternal origin only to determine the lineage in males. In females, both parental and maternal ancestries should theoretically be determined. However, as some females can be deficient with a normal father we assessed G6PD in fathers who don't have clinical manifestation of G6PD and the results shown in Table1&Table2. In mothers we relied on

clinical history because according to Lyon even heterozygote could be normal if the deficient X chromosome is the inactivated one .

It is of special interest that 15% of G-6-PD deficient infant girls were found to be in of normal father. in this group the incidence of G-6-PD deficiency in females would be expected to be low. Unequal Lyonisation probably accounts for many of these infants. According the Lyon hypothesis, one of the two X chromosomes in each cell is randomly inactivated, and thus the females is a mosaic of 50% maternally derived X chromosomes genes, and 50% parental. There will be thus populations of erythrocytes: one normal for G-6-PD, the other deficient. Non-random lyonisation may lead to a high proportion of G-6-PD deficient cells in any given females -Lyon Hypotheses-. (Figure3)

Based on our findings, we recommend that screening programmes of high risk populations for the prediction of G-6-PD associated neonatal hypebilirobineaemia should include both infant boys and girls, regardless of parental origin.

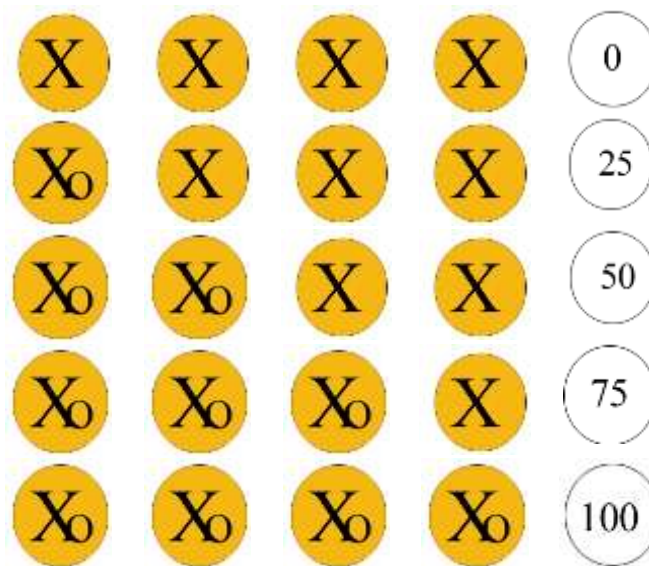


Figure (3): X-Inactivation % of Abnormal Cells

Conclusion:

Screening for G-6-PD deficiency should include both males and females.

Screening is a simple measure that provides valuable information for genetic advises, and gives ample of time for preventive measures of all risks of G6PD deficiency and for parents and child education about the risk and preventive measures.

Neonatal screening for G6PD deficiency is cost-effective in high risk area like ours, and should not be delayed.

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