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

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Dr. S. Mohammad**

(Received 30 / 5 / 2010. Accepted 21 / 4 / 2011)

∇ 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-Weinverg 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 in activation (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-Weinverg Law, Lyon Hypotheses.

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المسح الشامل لتحري نقص خميرة G6PD لدى المولودين حديثاً

عند الجنسين في الساحل السوري

الدكتور أحمد حسن يوسف
الدكتورة سميرة محمد

(تاريخ الإبداع 30 / 5 / 2010. قبّل للنشر في 21 / 4 / 2011)

ملخص

لقد أجرينا مسحاً شاملًا لـ 830 مولوداً حديثاً خلال 48 ساعة من الولادة لتحري نقص خميرة غلوكوز. 6 فوسفات، في مساحي المنطقة الساحلية في سوريا ووجدنا أن هناك نسبة في هذه الخميرة لدى 27% من الذكور و18% من الإناث. وعدد الإناث كان أكبر من المتوقع بسبب قانون هاردي - وينبرغ. القصة العائلية لنقص خميرة غلوكوز. 6 فوسفات ومعايرة الخميرة عند أبناء الإناث اللواتي لديهن نقص الخميرة (LYON) تُظهر أن معظم الحالات كانت متلازمة الأشجار تثبيث فيما يسمى X الطبيعي بالثاني العشائي (نظرية)

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 سريعة تقدم لنا معلومات مهمة حول نقص الخميرة من أجل وضع خطة الوقاية اللازمة.

الكلمات المفتاحية: خميرة غلوكوز. 6 فوسفات، قانون هاردي - وينبرغ، نظرية LYON.

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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>
<thead>
<tr>
<th></th>
<th>male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Assad Univ.Hosp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lattakia</td>
<td>158</td>
<td>154</td>
</tr>
<tr>
<td>Al_Watani Hosp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lattakia</td>
<td>293</td>
<td>306</td>
</tr>
<tr>
<td>Al_Bassel Hosp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tartus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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-ware 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).
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.
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>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Intermediate def.</th>
<th>Sever def.</th>
<th>% of sever Def.</th>
<th>No. of Predicted def.</th>
<th>No. of def. From Mother line</th>
<th>No. of def. From Father line</th>
<th>No. of def. From Both sides</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>158</td>
<td>56</td>
<td>35%</td>
<td></td>
<td></td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>F</td>
<td>154</td>
<td>45</td>
<td>28</td>
<td>18%</td>
<td>18</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Intermediate def.</th>
<th>Sever def.</th>
<th>% of sever Def.</th>
<th>No. of Predicted def.</th>
<th>No. of def. From Mother line</th>
<th>No. of def. From Father line</th>
<th>No. of def. From Both sides</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>293</td>
<td>10</td>
<td>72</td>
<td>24%</td>
<td></td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>306</td>
<td>63</td>
<td>54</td>
<td>18%</td>
<td>15</td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

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 Arabi9, 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 severe 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 Iran14.

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 haepliobineaemia should include both infant boys and girls, regardless of parental origin.

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.
References:


