Selective newborn screening of amino acid, fatty acid and organic acid disorders in the Kingdom of Bahrain.

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Consanguinity rates in Arabian Peninsula

NBS Programs In The Region

Retrospective Study in Bahrain

Conclusion
Newborn Screening is **NOT WELL yet recognized** as an essential, preventive public health program in the region.

Some preliminary studies in the region showed the incidences of these disorders are to be higher in the Middle East than anywhere else in the world due to the consanguinity.
Consanguinity
In the Arabian Peninsula, there are high percentages of consanguineous marriages and the tribal nature of marriages
Genetic Disorders

Classification of Genetic Disorders in Arabs according to mode of inheritance (WHO ICD-10, 2010)
Classification of Disorders in Arabs (WHO ICD-10, 2010)
NBS programs in the region

- Slow progress for development and implementation of NBS programs in the region **due to cultural, legal, financial and political issues**

- In most countries in the region there is **only selective screening programs** for metabolic disorders.

- Most of the NBS laboratories in the region do **not have** a complete NBS solution
Retrospective Study in Bahrain

- For the countries where there are no mandatory newborn screening programs, selective screening could be an important diagnostic tool for diagnosis of inborn errors of metabolism.
- Suspected neonates for metabolic disorders from regional hospitals are routinely referred to the Metabolic Biochemical Genetic Unit of Princess Al-Jawhara Centre in Bahrain.
Retrospective Study in Bahrain

- Retrospective data examined for period of **3 years** (2008–2010)
- The incidence of **inborn errors of amino acids, organic acids and fatty acids metabolism** in newborns (aged 3-90 days) suspected with metabolic disorders were investigated.
- A **total of 1645** of infants were referred and investigated for inborn errors of metabolism
- Whole blood spot were obtained by heel prick from children and spotted on Guthrie filter cards
Diagnostic Tests

- Initial and repeat MS/MS blood spot analysis
- Analysis of urinary organic acids using GC-MS
- Analysis of urinary and plasma amino acids using HPLC
- Analysis of plasma and urinary acylcarnitines using LC-MS/MS
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Initial and repeated LC-MS/MS screening</th>
<th>Biochemical confirmation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mable Syrup Urine</td>
<td>High valine, isoleucine and leucine</td>
<td>High plasma and urine valine, isoleucine and leucine</td>
</tr>
<tr>
<td>Argininemia</td>
<td>High Arginine</td>
<td>High plasma arginine</td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>High phenylalanine</td>
<td>High plasma phenylalanine</td>
</tr>
<tr>
<td>Arginosuccinic Aciduria</td>
<td>High arginosuccinic acid</td>
<td>High plasma argininosuccinic acid</td>
</tr>
<tr>
<td>Isovaleric Acidemia</td>
<td>High C4</td>
<td>High urinary isovalerylglycine</td>
</tr>
<tr>
<td>Propionic Acidemia</td>
<td>High C3</td>
<td>High urinary propionic acid</td>
</tr>
<tr>
<td>Methylmalonic Acidemia</td>
<td>High C3</td>
<td>High urinary methylmalonic acid</td>
</tr>
<tr>
<td>Glutaric Aciduria type II</td>
<td>High C4; C5</td>
<td>High isovalerylglycine</td>
</tr>
</tbody>
</table>
### Table 2. Frequency and detection rates of amino acid, fatty acid and organic acid disorders. (51,924 live births, 17 cases, 2008-2010)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>No of Cases (Gender)</th>
<th>Detection rate</th>
<th>Incidence (No./live birth)</th>
<th>Incidence worldwide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mable Syrup Urine Disease</td>
<td>3 (M), 1 (F)</td>
<td>1:548</td>
<td>1:12,981</td>
<td>1: 185,000</td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>1 (M)</td>
<td>1:1645</td>
<td>1:51,924</td>
<td>1:10,000</td>
</tr>
<tr>
<td>Argininemia</td>
<td>1 (M)</td>
<td>1:1645</td>
<td>1:51,924</td>
<td>1:350,000</td>
</tr>
<tr>
<td>Arginosuccinic Aciduria</td>
<td>1 (M)</td>
<td>1:1645</td>
<td>1:51,924</td>
<td>1:70,000</td>
</tr>
<tr>
<td>Isovaleric Acidemia</td>
<td>2 (M)</td>
<td>1:823</td>
<td>1:25,962</td>
<td>1:250,000</td>
</tr>
<tr>
<td>Propionic Acidemia</td>
<td>1 (M), 1 (F)</td>
<td>1:823</td>
<td>1:25,962</td>
<td>1:100,000</td>
</tr>
<tr>
<td>Methylmalonic Acidemia</td>
<td>2 (M), 1 (F)</td>
<td>1:548</td>
<td>1:17,308</td>
<td>1:100,000</td>
</tr>
<tr>
<td>Glutaric Aciduria type II</td>
<td>1 (M), 2 (F)</td>
<td>1:548</td>
<td>1:17,308</td>
<td>1:40,000</td>
</tr>
<tr>
<td>Year</td>
<td>Live Birth</td>
<td>Amino Acid Disorders</td>
<td>Organic Acid Disorders</td>
<td>Fatty acid Disorders</td>
</tr>
<tr>
<td>------</td>
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<td>------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>2008</td>
<td>17,841</td>
<td>2 (1:8,920)</td>
<td>2 (1:8,920)</td>
<td>1 (1:17,841)</td>
</tr>
<tr>
<td>2009</td>
<td>17,022</td>
<td>2 (1:8,511)</td>
<td>2 (1:8,511)</td>
<td>1 (1:17,022)</td>
</tr>
<tr>
<td>2010</td>
<td>17,062</td>
<td>3 (1:5,687)</td>
<td>3 (1:5,678)</td>
<td>1 (1:17,062)</td>
</tr>
</tbody>
</table>

Table 3. Incidence of metabolic disorders according to the type of disorder and birth cohort.
Impact of Consanguinity

1645 infants screened

17 IEMs (12 M, 5 F)

10 (1st cousin marriage)
  7 M 3 F
  5 family history of metabolic disorders
  3 Family history of unexplained death

3 (2nd cousin marriage)
  1 M, 2 F
  2 Family history of metabolic disorders
  1 Family history of unexplained death

This can be attributed to the lack of early detection of such disorders, as well as the lack of parental genetic counseling.
Conclusions

➢ These findings reflect the significant contribution of consanguinity in Bahrain in inherited metabolic disorders.

➢ The data presented in this study are only the beginnings of attempts to estimate the accurate incidence of metabolic diseases in Bahraini population.

➢ These data can be regarded as a guide to how we can provide diagnostic services for metabolic diseases in the future.

➢ This study emphasizes the important role of the specialized laboratories in obtaining such data that to be used for the recommendation of mass screening program in a population at risk.

➢ Such approach should be extended for other metabolic disorders such as mitochondrial disorders in Bahrain.
Acknowledgment

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Thank you for your attention