MPKU Outcomes from Queensland Lifespan Metabolic Medicine Service - An Eight Year Retrospective Review

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WHAT IS THE PROBLEM?

The teratogenic effects of elevated phenylalanine in Maternal Phenylketonuria (MPKU) are well documented1-2. The Australasian Consensus Guidelines for the Management of Maternal Phenylketonuria recommend that PKU pregnancies have best outcomes if planned and when Phe levels are maintained between 70-250umol/L for 3 months prior to conception and for the duration of pregnancy3. To support women in Queensland, our clinic provides education for teenage girls through adulthood and encourages early intervention with dietary advice in planning for pregnancy for healthy foetal development. Due to the frequent occurrence of unplanned pregnancies, our service developed a local procedure for the management of unplanned PKU pregnancies.

AIM

To investigate the percentage of planned and unplanned pregnancies which have occurred within our service and to determine the average time (in weeks of gestation) taken to achieve MPKU Phe levels within the 70-250umol/L recommended range.

WHAT DID WE DO?

We reviewed retrospective clinical notes and databases from January 2014 to September 2021 from all PKU pregnancies within our service. Data for pregnancy planning, weekly Phe results throughout gestation and pregnancy outcomes was collated and analyzed using statistical methods.

<table>
<thead>
<tr>
<th></th>
<th>Planned PKU pregnancy (n=15)</th>
<th>Unplanned PKU pregnancy (n=23)</th>
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</thead>
<tbody>
<tr>
<td>Proportion of total pregnancy (n=38)</td>
<td>39%</td>
<td>61%</td>
</tr>
<tr>
<td>Avg age in years (range)</td>
<td>34 (28-40)</td>
<td>28 (20-39)</td>
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<tr>
<td>Proportion of 1st pregnancy</td>
<td>53%</td>
<td>56%</td>
</tr>
<tr>
<td>Rates of miscarriage</td>
<td>33%</td>
<td>26%</td>
</tr>
<tr>
<td>Avg week of gestation to achieve Phe 70-250umol/L</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Avg Phe at K6 for live births</td>
<td>143</td>
<td>237</td>
</tr>
<tr>
<td>Avg Phe at K13 for live births</td>
<td>215</td>
<td>347</td>
</tr>
</tbody>
</table>

Table 1: Characteristics of Study Population

WHAT DID WE FIND?

A total of 38 known PKU pregnancies were managed by the Queensland Lifespan Metabolic Medicine Service from 2014 until 2021. 39% were planned with the patient undertaking pre-conception dietary advice and weekly to fortnightly Phe monitoring. We observed that the average age of women who had a planned PKU pregnancies was 34 years old, versus an average age of 28 years for unplanned PKU pregnancies. Eleven pregnancies ended due to miscarriage, or termination <K12, with five of these from planned pregnancies. More than half (58%) of the live birth pregnancies achieved Phe levels between 70-250umol/L before or during week 6 of gestation, and 92% had achieved the recommended range at some point within the first trimester, however this was not always sustained as pregnancy progressed. At K13, only 46% of the total MPKU patient population had Phe results within recommended range. Those with unplanned pregnancies reflected a higher proportion (70%) above target and also had a higher average Phe of 347umol/L (range 58-777umol/L) compared to average Phe of 215umol/L (range 78-464umol/L) for planned pregnancies. The average week of gestation it took our women to achieve the recommended MPKU Phe range of 70-250umol/L was week 5 for planned pregnancies, and week 7 for those with unplanned pregnancies. 71% of our MPKU pregnancies resulted in live births. Two pregnancies rarely achieved ideal Phe levels, and both resulted in children born with microcephaly.
WHAT WAS THE OUTCOME?

Finding from our study suggest that unplanned pregnancies are a reality for women with PKU with our data indicating 61% unplanned MPKU. Notification to our service of unplanned pregnancies is occurring soon after the women herself is aware of the pregnancy. Early intervention of our local procedure for management of unplanned pregnancies is enabling these women to achieve an ideal Phe range by week six of gestation with good pregnancy outcomes. The current findings also suggest that maintaining an ideal Phe range during weeks K10-18 may be difficult- particularly for unplanned pregnancies. Further support and resources are needed to assist women though this stage.

DISCUSSION

- Higher average Phe levels between weeks K10-18 could be attributed to common issues such as morning sickness, poor tolerance of PKU formula, inadequate energy intake and weight loss.
- It is unclear why the unplanned MPKU group struggled more so to achieve recommended Phe range between weeks K10-18 compared with planned MPKU pregnancies. This finding warrants further investigation.
- As more than half of pregnancies are unplanned, these results further support the expansion of BH4 to be assessable for all women of child bearing age, rather than waiting until a women with PKU is planning a pregnancy.

References: