Gene Mutations and Pregnancy Induced Hypertension: A Meta-Analysis

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Learning Objectives — At the end of this presentation the learner will be able to:
1. Understand MTHFR C677T gene mutations in relation to pregnancy induced hypertension (PIH) in various race-ethnicity groups in the world. 2. Discuss potential epigenetic factors associated with PIH.

Methods
- screened for retrieval (n = 73)
- (n = 14)
- results were inconclusive.

Objectives
- To disseminate current evidence on population genome health and related epigenetic factors, through the meta-analyses of methylenetetrahydrofolate reductase (MTHFR) gene in pregnant women who developed hypertension.
- PIH including preeclampsia, eclampsia are the leading causes of maternal and perinatal mortalities.
- Genetic and environmental factors contribute to its development
- Many studies have reported the association between the MTHFR gene C677T polymorphism and risk of PE, but the results were inconclusive.

Methods
- Cochrane, Embase, PubMed, and Web of Science online databases were searched using relevant key words.

Progression on Selection of Studies

Potential relevant studies identified and screened for retrieval (n = 72)
- 16 meta-analyses
- 57 case control studies

2 studies excluded (not English)
- 2 meta-analyses
- 5 case control studies

Studies excluded for more detail evaluations (n = 54)
- 14 meta-analyses
- 51 case control studies

14 meta-analyses included: 43 case control studies (16 overlapping; 8 without sufficient information)
- Studies with sufficient information fulfilling all inclusion/exclusion criteria in n = 52, 2 studies with 5 and 2 additional race groups, respectively.

Pool Relative Risk of MTHFR 677 Gene Subtypes (57 studies)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>White (24)</th>
<th>Hispanic (4)</th>
<th>South American (4)</th>
<th>South Asia (5)</th>
<th>Middle East (5)</th>
<th>Africa (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/C</td>
<td>357 (11.66)</td>
<td>346 (23.59)</td>
<td>66 (1.90)</td>
<td>31 (1.06)</td>
<td>381 (7.20)</td>
<td>21 (0.90)</td>
</tr>
<tr>
<td>C/T</td>
<td>100 (3.33)</td>
<td>152 (10.02)</td>
<td>2437 (37.71)</td>
<td>62 (1.98)</td>
<td>377 (7.25)</td>
<td>82 (1.98)</td>
</tr>
<tr>
<td>T/T</td>
<td>22 (0.70)</td>
<td>162 (10.76)</td>
<td>2304 (37.42)</td>
<td>40 (1.31)</td>
<td>629 (12.20)</td>
<td>385 (8.90)</td>
</tr>
</tbody>
</table>

MTHFR 677T homozygous (TT) mutation genotype was significantly associated with increased risk of developing PIH (p < 0.001).
- MTHFR 677TT subtype was a significant risk of PIH in White race (RR=1.16, p < 0.05), South American (RR=1.40, p < 0.05), East Asian (RR=1.82, p < 0.001) and in Africa (RR=5.82, p < 0.001).
- Lifestyle factors, body mass index (BMI) before pregnancy (Kg/M²) was an important predictor for the development of PIH.
- Normal weight (BMI < 25) was protective against the development of PIH and preeclampsia (RR=0.75, p < 0.0001); whereas, overweight (BMI ≥ 25-29, RR = 1.52, p < 0.0001) and obesity (BMI > 30, RR = 1.80, p < 0.0001) were associated with increased risk of developing PIH and preeclampsia (376 cases and 2294 controls in 2 studies of Caucasian women).

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