



قال تعالى:

وَلَقَدْ خَلَقْنَا الْإِنْسَانَ مِنْ سُلَالَةٍ مِنْ طِينٍ (12) ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ  
مَكِينٍ (13) ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا  
فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنْشَأْنَاهُ خَلْقًا آخَرَ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ (14)

صدق الله العظيم

سورة المؤمنون الآيات 12-14

# **Dedication**

To the soul of my parents

Who introduced me to the joy of reading from the  
birth enabling such study to take place today

To my daughter

To my brothers and sister

To my friends

I dedicate this work

Dalia Ibrahim

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## Abstract

Preeclampsia is considered to be a multifactorial and multisystemic disorder with a genetic predisposition. Alterations in the renin–angiotensin system are considered to play a significant role in the pathogenesis of the disease.

In order to investigate the possible association of the most common polymorphisms of the renin–angiotensin system genes with preeclampsia we have examined 50 women with preeclampsia, and 50 normotensive pregnant women. DNA samples were genotyped for the M235T polymorphism of the angiotensinogen gene (AGT) using (PCR-RFLP) , plasma renin was determined by enzyme linked immunosorbent assay (ELISA).

Plasma renin was significantly decreased in patients with preeclampsia compared with normotensive pregnant women. The TT genotype of the *M235T* polymorphism was significantly increased in women who developed preeclampsia. In preeclampsia group the frequency of AGT gene, *M235T* missense mutation was 92% (18 were heterozygous and 74 were homozygous), compared with 56% in control group (34 heterozygous, 22 homozygous). In preeclampsia group the frequency of M allele; 26% (n=13) versus 78% (n=39) for the control group, while the frequency of T allele in preeclampsia group; 92% (n=46) versus 56 % (n=28) for the control group. Furthermore, there was a positive risk of developing preeclampsia when having TT genotype, and the results were highly statistically significant (odd ratio=2.597,  $X^2=16.39$ ,  $P=0.00$ ) for TT genotype compared to MM genotype. There was significant positive correlation between plasma renin activity and mean arterial pressure (MAP) ( $r = 0.9$ ,  $P = 0.000$ ). There was no statistical

significance between plasma renin activity and age in preeclampsia group ( $r = 0.044$ ,  $P = 0.759$ ).

In conclusion, plasma renin activity was significantly decreased in patients with preeclampsia. An increased risk for preeclampsia in women carrying the TT genotype of the AGT gene was observed.

## المستخلص

يعتبر تسمم الحمل اضطراب متعدد العوامل مع وجود الاستعداد الوراثي للمرض .  
التغيرات التي تحدث في نظام الرينين أنجيوتنسين تلعب دورا هاما في حدوث المرض .  
من أجل التحقق من وجود ارتباط وراثي محتمل في الطفرات الجينية في نظام الرينين  
قمنا بفحص 50 امرأة مصابة بتسمم الحمل و 50 امرأة سليمة كعينة ضابطة . تم مرمزة الحمض  
النووي لتعدد الأشكال M235T (AGT) من الجين مولد الأنجيوتنسين بواسطة سلسلة تفاعل  
البلمرة وتقييد طول جزء تعدد الأشكال (PCR-RFLP) وقياس تركيز الرينين في بلازما الدم  
بواسطة انزيم مرتبط بالمناعي فحص (ELISA).

أظهرت النتائج انخفاض مستوى رينين البلازما بشكل ملحوظ في المرضى الذين يعانون  
من تسمم الحمل مقارنة بالنساء الحوامل في العينة الضابطة. لوحظ ان هنالك زيادة في النمط  
الجيني TT من تعدد الأشكال M235T بشكل كبير في النساء المصابات بتسمم الحمل. الذين  
لديهم الطفرة M235T في الجين AGT. 92% من المرضى (18 كان متخالف و 74 كانت  
متماثلة اللواقح)، مقارنة مع 56 في المجموعة الضابطة (34 متخالف ، 22 متماثل ) .تواتر  
الأليل M 26% (عدد = 13) مقابل 78% (عدد = 39 ) للمجموعة الضابطة ، في حين أن  
تواتر الأليل T في مجموعة تسمم الحمل ؛ 92% (عدد = 46) مقابل 56% ( عدد = 28)  
للمجموعة الضابطة. علاوة على ذلك، كان هناك خطر إيجابية لحدوث تسمم الحمل عند وجود  
TT الوراثي ، وكانت النتائج ذات دلالة إحصائية عالية (نسبة = 2.597 ،  $X^2 = 16.39$  ،  
(  $P = 0.00$  ) TT الوراثة مقارنة MM الوراثة .كان هناك علاقة إيجابية هامة بين رينين  
البلازما و الضغط الشرياني، ولم تكن هناك أي دلالة إحصائية بين رينين البلازما والعمر في  
مجموعة المرضى  $P = 0.759$  .

من هذه الدراسة نستخلص : انخفاض نشاط رينين البلازما بشكل ملحوظ في المرضى  
الذين يعانون من تسمم الحمل. كذلك زيادة الخطر لحدوث تسمم الحمل عند وجود TT الوراثة.

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### **CHAPTER ONE**

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## **Abbreviation**

| <b>Abbreviation</b> | <b>Meaning</b>                        |
|---------------------|---------------------------------------|
| 2ary                | Secondary                             |
| A <sub>1</sub>      | Absorbance one                        |
| A <sub>2</sub>      | Absorbance two                        |
| AGT                 | Angiotensinogen                       |
| Ang II              | Angiotensin II                        |
| bp                  | Base pair                             |
| C                   | Cytosine                              |
| Con                 | Concentration                         |
| LMP                 | Last menstrual period                 |
| DNA                 | Deoxy ribonucleic acid                |
| DRG                 | Diagnostic reagent                    |
| dsDNA               | Double strands deoxy ribonucleic acid |
| EDTA                | Ethylene diamine tetra acetic acid    |
| ELISA               | Enzyme linked immunosorbant assay     |
| M235                | Methionine variant                    |
| Met                 | Methionine                            |
| mmHg                | Millimeter mercury                    |
| NaCl                | Sodium chloride                       |
| PCR                 | Polymerase chain reaction             |
| PE                  | Preeclampsia                          |

|         |                                      |
|---------|--------------------------------------|
| PIH     | Pregnancy induced hypertension       |
| PRA     | Plasma renin activity                |
| RA      | Renin angiotensin                    |
| RAAS    | Renin angiotensin aldosterone system |
| RAS     | Renin angiotensin system             |
| rpm     | Round per minute                     |
| SBP     | Systolic blood pressure              |
| SDS     | Sodium dodcyle sulphate              |
| STD     | Standard                             |
| T235    | Thronine variant                     |
| T       | Thymine                              |
| TE      | Tris EDTA                            |
| Thr     | Theronine                            |
| Tth111I | Thermus thermopilus 111I             |
| UK      | United kingdom                       |
| UV      | Ultra violet                         |
| WHO     | World health organization            |