قال تعالى:

وَلَقَدْ خَلَقْنَا الإِنسَانَ مِن سُلَالَةٍ مِّن طِينٍ (12) ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَّكِينٍ (13) ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنشَأْنَاهُ 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* misssense mutation was 92% (18were heterozygous and 74were 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, X2= 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 التى تحدث في نظام الرينين أنجيوتنسين تلعب دورا هاما في حدوث المرض .

من أجل التحقق من وجود ارتباط وراثى محتمل فى الطفرات الجنيه فى نظام الرينين قمنا بفحص 50 امرأة مصابه بتسمم الحمل و 50 امراه سليمه كعينه ضابطه . تم مرمزة الحمض النووي لتعدد الأشكال (AGT) M235T من الجين مولد الأنجيوتنسين بواسطة سلسلة تفاعل البلمرة وتقييد طول جزء تعدد الأشكال (PCR-RFLP) وقياس تركيز الرينين فى بلازما الدم بواسطة انزيم مرتبط المناعي فحص(ELISA).

اظهرت النتائج انخفاض مستوى رينين البلازما بشكل ملحوظ في المرضى الذين يعانون من تسمم الحمل مقارنة بالنساء الحوامل فى العينه الضابطه. لوحظ ان هنالك زيادة فى النمط الجينيTT من تعدد الأشكال*M235T* بشكل كبير في النساء المصابات بتسمم الحمل. الذين لديهم الطفرة*M235T* فى الجين AGT .92% من المرضى (18كان متخالف و 74 كانت متماثلة اللواقح)، مقارنة مع 56 في المجموعة الضابطة(34متخالف ، 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 TTالوراثي ، وكانت النتائج ذات دلالة إحصائية عالية (نسبة =2.597 ، = 16.39 X2 ، (P = 0.00) لTT الوراثي مقارنة MM الوراثي .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 رنيين البلازما بشكل ملحوظ في المرضى الذين يعانون من تسمم الحمل.كذلك زيادة الخطر لحدوث تسمم الحمل عند وجودTT الوراثي.

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Abbreviation

Abbreviation	Meaning
2ary	Secondary
A_1	Absorbance one
A_2	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 immunosourbant assay
M235	Methionie variant
Met	Methionie
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