J. Product. & Dev., 27(2): 201 - 217 (2022)

FOREHEAD BOX PROTEIN P3 POLYMORPHISM AS A RISK FACTOR OF PREECLAMPSIA: SEVERITY ASSOCIATION

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ABSTRACT:

Pre-eclampsia is a major cause of maternal and fetal mortality and morbidity. The incidence of pre-eclampsia is 2-10%, depending on the population studied and definitions of pre-eclampsia. Significantly more infants were delivered before the onset of labour and by caesarean section in the group with pre-eclampsia. This study aimed to investigate the association of studied groups with albuminuria, BMI, blood pressure, gestational age, baby wt, age, placental wt, mode of delivery, abortion, fox p3 polymorphism and genotype. Total 75 (25 normotensive women as a control group, 25 women with mild preeclampsia, 25 women with severe preeclampsia) women were enrolled in this study. The anthropometric measurements and clinical characteristics of different study groups as age(18-40), BMI(21-35), diastolic blood pressure(70-150), systolic blood pressure(100-200),abortion(0,1,2),placental wt(300-480),baby wt (2200-3800), albumin (0,1,2,3),mode of delivery (Normal & cs), genotype (GG,TT,TG), gestational age (35-41), and result was analyzed. Placenta samples were collected from the patients attended the Obstetrics and Gynaecology clinic, and informed consents will be obtained from all of them. Age and BMI were taken for each participant.

The most important characteristic of Tregs is their expression of the transcription factor FOXP3. Participants with heterozygous (TG) and homozygous (TT) genotypes had higher BMI compared to those with wild-type (GG, TT, TG) genotypes. Therefore, The women with GG and TG genotypes were severe PE than TT ones and all these associations were statistically significant ($P<0.05$). Participants with heterozygous (TG) and homozygous (TT) genotypes had higher BMI compared to those with wild-type (GG) genotypes. Women with a history of abortion who

conceived again with the same partner had nearly half the risk of preeclampsia. In Conclusion, Increasing BMI is associated with increased risks of adverse obstetric outcomes.

***Conclusively,** the protective effect of a prior abortion operated only among women who conceived again with the same partner. An immune-based etiologic mechanism is proposed, whereby prolonged exposure to fetal antigens from a previous pregnancy protects against preeclampsia in a subsequent pregnancy with the same father.*

Key words : FOXP3 ,pregnancy outcome, Polymorphism, proteinuria, severe preeclampsia, Blood pressure, Polymorphism, pre-eclampsia, Preeclampsia, abortion, body mass index, Pregnancy

INTRODUCTION

Preeclampsia (PE) is a severe complication of pregnancy with a worldwide incidence of 2-10%. It is also, one of the leading causes of maternal and perinatal morbidity and mortality. PE has been associated with insufficient trophoblast invasion of maternal spiralarteries, impaired placental perfusion, and widespread endothelial cell dysfunction (Wang and Cao *et al*., 2010; Cao *et al.*, 2010).

Preeclampsia, a human-pregnancy-specific disease defined as the occurrence of hypertension and significant proteinuria in a previously healthy woman on or after the 20th week of gestation (Kvehaugen *et al.*, 2017).

Normal pregnancy requires a relative maternal immune tolerance of the fetus. We know that women are at increased risk of preeclampsia in their first pregnancy, and with new partners.4De-creased exposure to semen from the father of the child, preconception also has resulted in an increased risk of pre-eclampsia.4Taken together, these observations have led to the hypothesis that preeclampsia may in part be immune mediated. This article focuses on the possibility of an immune component in the development of preeclampsia, and specifically, the role of regulatory T-cells (Tregs) and the Forehead Box P3 (FOXP3) gene. The FOXP3 gene is located at Xp11.23. It has been demon-strated in mouse models that inactivation of FOXP3 results in a lack of Tregsand notable organ-specific autoimmu-nity (Dekker *et al.*, 2002 and Sakaguch *et al.*, 2010)

It is the most common medical complication of pregnancy whose incidence has continued to increase worldwide, and it is associated with significant maternal morbidity and mortality, accounting for about 50,000 deaths worldwide annually (Duley *et al*., 2009). Risk factors for preeclampsia include nulliparity, multifetal gestations, previous history of preeclampsia, obesity, diabetes mellitus, vascular and connective tissue disorders like systemic lupus erythematosus and antiphospholipid antibodies, age >35 years at

first pregnancy, smoking, and African American race. Among primiparous women, there is a disparity among ethnic groups as the risk in African American women is twice that of Caucasian women, and the risk is also very high in women of Indian and Pakistani origin (Eiland *et al*, 2012). Preeclampsia may be mild or severe depending on the degree of blood pressure elevation, degree of proteinuria, extent of edema and the presence of signs and symptoms, including epigastric pain, severe headache and blurred vision. However, severe preeclampsia can result in bleeding disorders and death (Sibai, 2003). Preeclampsia shares many pathophysiologic features with atherosclerosis. Endothetial dysfunction, insulin resistance, and inflammation are recognized features of preeclampsia *(*Roberts *et al.*, 2010).

Several previous studies have found an association between Foxp3 gene polymorphisms and autoimmune diseases, such as systemic lupus erythematosus (Fontenot *et al.*, 2003*)*, autoimmune thyroid diseases (Santner-Nanan *et al*, 2009*)*, type I diabetes *(*Toldi *et al.*, 2008), and allergic rhinitis (Quinn *et al.*, 2011). The decreased expression of Foxp3 in preeclampsia demonstrates that the reduction of Trigs numbers may result in the imbalance of immunologic tolerance between the mother and fetus, thereby participating in the pathogenesis of preeclampsia. However, the association between Foxp3 polymorphisms and preeclampsia has not been reported so far. Preecalmpsia was defined as sustained pregnancy-induced hypertension with proteinuria. Hypertension was defined as sustained blood pressure (BP) readings of 140/90 mm Hg or higher, with readings taking place 6 hrs or more apart; or a sustained 15- mm Hg rise in diastolic BP from the first- trimester values; or a 30-mmHg rise in systolic BP also from the first trimester values.

The ISSHP defines proteinuria as a protein concentration of 30 mg/dL or greater (or 1+ on a urine dipstick) in 2 or more random urine specimens collected at least 4 hrs apart. Overweight (body mass index [BMI] more than 25 kg/ m^2) and obesity (BMI more than 30 kg/m^2) have become a major health problem in western countries. T-regulatory cells (T_{reg}) are important in balancing immune responses and maintaining peripheral tolerance. Current evidence suggests that asthma is characterized by a relative deficiency in T_{reg}, allowing T helper 2 cells to expand. TT genotype is associated with a reduced risk for pre-eclampsia, hypertensive SGA and abnormal uterine artery Doppler. These findings suggest that the TT genotype may protect against these pregnancy disorders (Andraweera *et al*., 2011).

Therefore, the purpose of this study was to examine the role of increased TT genotype is associated with a reduced risk for pre-eclampsia. We also aimed to investigate the association between Foxp3 polymorphisms and preeclampsia in Egyptian women with severe and mild preeclampsia and from women with normal pregnancy.

MATERIALS AND METHODS

Study population:

The study included 75 women attended the Obstetrics and Gynaecology department, Maternity Hospital - Ain Shams University, and informed consents will be obtained from all of them. The patients were divided into 3 groups: Normal pregnant women (n=25), Mild pregnant women (25)and severe pregnant women (25) aged 18-40 years. The patients were divided into 3 groups: normotensive women (n=25) that will be taken as a control group, women with mild preeclampsia (n=25) & severe preeclampsia (n=25). The diagnosis of preeclampsia will be made using criteria of the International Society of the Study of Hypertension in Pregnancy (ISSHP), and grouped as having mild preeclampsia , severe preeclampsia and control group . As well as a control group (n=25) healthy volunteers, with age and sex matched with patient groups. An thropometric measurements, such as weight, height, BMI, systolic and diastolic blood pressure was assessed.

Genotyping:

DNA extraction and purification from less than 10 mg Placenta tissue carried out using (QIAamp DNA Investigator Kit, QIAGEN, USA). Genotyping of FOXP3 rs3761548 was performed with TaqMan allelic discrimination on real-time polymerase chain reaction system (Applied Biosystems). Approximately 1% of samples were run in duplicate and no discrepancies in results were observed.

PCR amplifications were performed in 2ml reaction volumes using Amplifier Kit (TaqMan Investigator, USA) according to the manufacturer's protocol. Information on PCR conditions for the selected SNPs. DNA samples were subjected to 35 cycles of PCR in an (TaqMan® , Thermoscientific, USA) under the following conditions: 95°C for 2 min; 93°C for 20 s, 72°C for 45 s, repeated for 35 cycles; 65°C for 40 s, and 72°C for 5 min, 4°C ∞ for store.

SNPs were identified using real-time polymerase chain reaction and melting curve analysis of Kit (TaqMan, Thermoscientific, USA) according to the manufacturer's protocol. The cycle conditions were as follows: activation of the polymerase at 95℃ for 2 min, denaturation of the template DNA at 95℃ for 5 sec; 60℃ for 10 sec; 72℃ for 15 sec, repeated for 40 cycles; then step of 95℃ for 15 sec; 55℃ for 15 sec; 95℃ for 5 sec.

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 17 software (SpssInc, Chicago, ILL Company). Categorical data were presented as number and percentages, using Chi square test (X^2), or Fisher's exact test (FET) to analyze them. Odds ratios (OR) and the corresponding 95% CI were

computed when applicable. Quantitative data were tested for normality using Shapiro-Wilks test, assuming normality at P>0.05. ANOVA was used to analyze normally distributed variables among 3 independent groups. While non-parametric variables were analyzed using Kruskal Wallis test (KW). Significant ANOVA and KW tests were followed by post hoc multiple comparisons using Bonferroni tests to detect the significant pairs. The accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant). Genotype distributions in the studied groups were in Hardy-Weinberg equilibrium for gene polymorphisms (data not shown). Hardy-Weinberg equilibrium was calculated according to OEGE - Online Encyclopedia for Genetic Epidemiology studies ***(***Rodriguez *et al*., 2009). A *p*-value of less than 0·05 was considered to indicate statistical significance.

RESULTS AND DISCUSSION

Human Foxp3 gene located at chromosome Xp11 containing 11exons and 10 introns 23. Foxp3is not only a sign of CD4 CD25Treg cells activation, but also correlated with cells' functions (development and maintenance of cells) in human. FOXP3 expression now serves as the most specific marker of Tregs and it has been used to determine the proportion of Tregs in humans with a variety of disease states **(Guerin *et al*., 2009)**.Genotyping of rs3761548 was performed with TaqMan allelic discrimination on real-time polymerase chain reaction system (Applied Biosystems).Many researches have been reported the association between FOXP3 variants and several disorders such as autoimmune thyroid diseases (AITDs) **(Ban *et al*, 2007)** type I diabetes, rheumatoid arthritis **(André *et al*., 2009)** and pre-eclampsia **(Jahan e*t al*., 2013)**.Pre-eclampsia is a multifactorial disorder in which many genes and many risk factors may play role. It is also possible that FOXP3 gene polymorphisms are involved in pre-eclampsia predisposition through an interaction with other genes.

The present results indicated that Foxp3 TT genotype was significantly associated with reduced PE risk compared with GG genotype. Combination of GT/GG was also significantly associated with increased PE risk. Our data provided more evidence to support the potential role of Foxp3 polymorphisms in PE susceptibility. Case-control study including 50 women with preeclampsia(mild & severe) and 25 healthy normotensive controls was conducted.

Results from ANOVA for the data included in the Table1 indicated statistically significant differences in baseline characteristics between the 3 groups of pregnant women (Normal, mild PE and severe PE) investigated in age ≥ 40 years (P= 0.55), or casual BP values at the time of the first visit to

the hospital (*P*<0.001 for both SBP and DBP). gestational age at delivery (*P*<0.001), placental weight (p<0.001), Baby weight (*P*=0.001) and BMI (P=0.003).

Diastolic Blood Pressure (DBP >80 mmHg) was 74.0±5.0 for normal gp , 92.4±4.3 for mild PE and 114.0±10.0 for severe PE . Systolic Blood pressure (SBP >120 mmHg) was 112.0±8.6 for normal gp , 143.6±4.8 for Mild PE and 173.6±16.0 for severe PE (Table 1). Otherwise, The statistically differences in baseline characteristics between genotypes investigated in casual BP values at the time of the first visit to the hospital (SBP(P=0.48) , DBP(P=0.42)), gestational age at delivery (*P*<0.002), placental weight (p<0.046), Baby weight (*P*=0.018) and BMI (P=0.44). Also, DBP was 105.9 ±15.01 for GG, 101.7±12.36 for GT and 100±10.95 for TT and SBP was (162.2±20.4, for GG , 145.4±19.3 for GT and 154.5±16.3 for TT).

Women who have the obesity were more exposed to severe PE (72%), comparing to mild PE 16% and normal ones 32%.

Table 1: Characteristics of study participants according to rs3761548 genotypes.

Variable	Severe PE (n=25)	Mild PE (n=25)	Normal (n=25)	P	GG	TG	TT	P
Age (ys)	26.7± 6.57	25.2± 0.67	25.3± 4.59	0.55 (NS)	—	——	——	——
BMI (kg/m^2)	30.6± 3.02	27.5± 2.73	27.7± .38	0.003 (S)	29.4± 3.09	29.4± 3.16	28.0± 3.72	0.44 (NS)
DBP (mmHg)	114.0± 10.0	92.4± 4.3	74.0± 5.0	<0.001 (HS)	105.9± 15.01	101.7± 12.36	100± 10.95	0.42 (NS)
SBP (mmHg)	173.6± 16.0	143.6± 4.8	112.0 ±8.6	<0.001 (HS)	162.2± 20.4	145.4± 19.3	154.5± 16.3	0.48 (NS)
Gestational age (w)	Median = 38	Median =40	Median= 40	<0.001 (HS)	Median = 38	Median =39	Median =40	0.002 (S)
Placental weight (gm)	Median =300	Median =413	Median= 450	<0.001 (HS)	Median =312.5	Median =400	Median= 420	0.046 (S)
Baby weight (gm)	Median =2750	Median =3000	Median= 3000	=0.001 (HS)	Median =2750	Median =2900	Median= 3000	0.018 (S)

The TT genotype of the maternal Foxp3 polymorphism was associated with a reduced risk for pre-eclampsia.The maternal factors that were significantly associated with studied groups and genotypes included: BMI, presence of Albumine, presence of Abortion, Mode of delivery and the rate

of cesarean delivery which was significantly higher in the group with severe preeclampsia (72%); this mode of delivery was usually for fetal indications (Table 2). Table 2 clarified the statistically significant association was (P=0.001) between obesity and severe PE, (P<0.001) between albuminuria and severe PE, (P<0.05) between mode of delivery and PE, (P<0.05) between mode of delivery and genotype frequency. In opposite, There were no statistically significant association between obesity and preeclampsia (P>0.05), obesity and genotype frequency (P>0.05), abortion and genotype frequency (P>0.05), albumin in urine and genotype frequency (P>0.05). Regarding the allelic distribution of the Foxp3 polymorphism, total of 26 participants (Normal 16%, Mild PE 32%, Severe PE 56%) had the GG genotype, also 22(Normal 20%, Mild PE 40%, Severe PE 28%) had the GT genotype and 27(Normal 64%, Mild PE 28%, Severe PE 16%) had the TT genotype (**Table 3**).

The present study demonstrated that BMI of women with severe PE (mean = 30.6) were significantly (P<0.05) higher than those of women with mild PE and normal women (P>0.05) **(Table 1).** Diastolic blood pressure (DBP) mean values of women with severe and mild PE (114 and 92.4 respectively) were significantly (P<0.05) higher than those of normal women (74), also there was a significant difference between severe and mild PE. The same results were found regarding SBP among severe, mild and normal groups 173.6, 143.6 and 112 respectively**. (***P*<0.001**).** There is significant difference between systolic (SBP) and diastolic blood pressure (DBP) in sever PE and mild PE. These results agreed with **(Hermida *et al*., 2000)** who mentioned the differences in blood pressure between healthy and severe pregnancies can be observed as early as in the first trimester of pregnancy.**(Table 1).**

GG genotype was only associated with an increased risk for SGA and a reduction in customized birthweight centileACE A11860G genotype is associated with small for gestational age babies (SGA) **(Zhou *et al*., 2013) (Table 1).**Gestational age at birth and neonatal and placental weight were significantly lower in women with preeclampsia as compared to controls.**Chedraui *et al, (2*015)** found that the frequency of the TT mutant genotype of the C677T polymorphism was higher in the placenta of pregnancies **(Chedraui *et al*., 2015)** (Table 1).

There was a significant association (P=0.001) between obesity and severe PE, 72% of severe PE women were obese compared to 16% and 32% of those with mild PE and normal ones respectively**.** Our obese patients have genotype (59.1%), TG genotype and TT genotype (27.3%), nevertheless genotype TT has lower percentage preeclampsia **(Table 2).** Albumin at (Nil) value was in normal group (96%). on other hand, Mild & severe were 0% in the PE groups. Overt albuminuria (> 300 mg/24 h) severe

Table 2: Genotype &the studied groups regarding Albumin, BMI, Abortion and mode of delivery**.**

Itmes	**GG, %**	**TG, %**	**TT, %**	**Normal, % (n=25)**	**Mild PE % (n=25)**	**Severe PE, % (n=25)**
BMI(Normal) % within Foxp3	9.1	0	18.2	24	12	4
BMI(Overweight) %within Foxp3	31.8	64.7	54.5	44	72	24
BMI(Obese) %within Foxp3	59.1	35.3	27.3	32	16	72
Albumin (Nil)	----	----	----	96	0	0
Albumin (+)	31.8	52.9	54.5	0	80	8
Albumin (++)	31.8	29.4	18.2	4	20	36
Albumin (+++)	36.4	17.6	27.3	0	0	56
Abortion(Nil)	77.3	76.5%	72.7	76	76	80
Abortion(1)	18.2	11.8	27.3	20	16	20
Abortion(2)	4.5	11.8	.0	4	8	0
Mode of delivery (NVD)	9.1	58.8	45.5	64	40	28
Mode of delivery (C.S)	90.9	41.2	54.5	36	60	72

Table 3: Comparing the studied groups regarding Foxp3 gene polymorphism.

Variable	**Severe PE (n=25)**		**Mild PE (n=25)**		**Normal (n=25)**		**OR (95%CI)**	**P**
	No.	**%**	**No.**	**%**	**No.**	**%**	**0.55 (NS)**	
GG	14	56.0	8	32	4	16.0	0.003 (S)	<0.001 (HS)
TG	7	28.0	10	40	5	20.0	<0.001 (HS)	0.033 (S)
TT	4	16.0	7	28	16	64.0	Ref	**----**
G	35	70.0	26	52	13	26.0	<0.001 (HS)	<0.001 (HS)
T	15	30.0	24	48	37	74.0		<0.001 (HS)

Overt albuminuria (> 300 mg/24 h) was found in one plus (+) 8% and in 2 plus 36% and in 3 plus 56% **(Table 2).**

The previous result revealed that the increasing of albumin is associated with severity of PE. The albumin excretion in urine correlates significantly to the albumin during pregnancy. **(Risberg *et al*., 2004) (Table2).** We observed in my result the pregnant women have zero abortion we found severe PE(76%), Mild PE(76%),normal(80%) and the pregnant women have +1 abortion we found severe PE(20%),mild PE(16%),normal (20%) in other hand pregnant women have +2 abortion we found severe PE (4%) ,mild PE(8%), normal (0%). This shows increasing number of abortion decreasing severe PE shows that there was no statistically significant association (P>0.05) between obesity and preeclampsia. we assessed that Women without a history of abortion served as the reference group in logistic regression analyses. Women with a history of abortion who conceived again with the same partner had nearly half the risk of preeclampsia. In contrast, women with an abortion history who conceived with a new partner had the same risk of preeclampsia as women without a history of abortion **(Table 2) (Saftlas *et al*., 2003)**.

The effect of severe pre-eclampsia on the outcome of infants of very low birth weight was studied in a prospective case control study of 75 of infants of comparable gestation. Significantly more infants were delivered before the onset of labour and by caesarean section in the group with pre-eclampsia .The gestational age (38 w) and baby weight(2750 gm) of women with severe PE were significantly lower than normal women.(40.0 w and 3000 gm) (P<0.05) in **(Table 1).** These babies tended to be smaller and had a higher incidence of hyaline membrane disease, patent duct usarteriosus, pulmonary air leak, and hypotension. They also required more intensive treatment with oxygen and mechanical ventilation.

The significant difference in birth weight was still apparent at 2 years of age **(Szymonowicz and Yu, 1987) .** Mode of delivery and PE severe (72%) and Mild PE (60%) women had C.S compared to (36%) of normal ones.Moreover, the induction was not connected with higher rates of Cesarean section or an adverse neonatal outcome **(Kompmans *et al*., 2009).** Furthermore, women with mild preeclampsia and unfavorable cervix profited more from the induction than other women **(tajik *et al*., 2012).** This agrees with the study from **(Alanis *et al*., 2008).**in which preterm neonates had also no adverse outcome after induction of labor. Although vaginal delivery in preeclampsia is deemed to be safe, most of the studies showed higher rates of Cesarean section in the preeclamptic

group than in the control group in **Table 2.** My results in **Table 2** shows the frequency of genotype among severe PE and normal groups. It was found that women with GG and TG genotypes were more severe PE than TT ones. And T allele were lower preeclampsia than G allele. There is an increase in regulatory T (Treg) cells, which has an important role. We hypothesised that percentages of Treg cells are decreased in preeclamptic patients. We conclude that a deficiency of regulatory T cells may play a role in the pathophysiology of preeclampsia **(Jelmer *et al.*, 2009).** TT genotype is associated with a reduced risk for pre-eclampsia, hypertensive SGA and abnormal uterine artery Doppler. These findings suggest that the TT genotype may protect against these pregnancy disorders **(Andraweera *et al.*, 2011)**.

Association of the single-nucleotide polymorphism (SNP) with BMI was assessed using linear regression models. Participants with heterozygous (TG) and homozygous (TT) genotypes had higher BMI compared to those with wild-type (GG) genotypes. the lowest for placental position of TG versus the TT genotype was posterior location (P = 0.0464). The allele G caused more female embryos than T Allele**(Heydarzadeh *et al.*, 2019)** as shown in **Table 2**. .

The risk factors for spontaneous abortion in fetal genotypes comparing with their mothers and healthy controls **(Yalcintepe *et al.*, 2014).**In the cases of unexplained RSA, TT genotype tended to increase according to the number of previous spontaneous abortions in the Japanese population **(Kobashi*et al.*, 2005).** polymorphism might be a risk factor of lead-related high blood pressure **(Lee *et al.*,2016).***GG was associated with the development of albuminuria in diabetic patients and with the reduction in GFR* **(Ibraheem *et al.*, 2019)** as shown in **(Table** 3). This study clarified that during pregnancy there is an increase in regulatory T (Treg) cells, which has an important role in regulating tolerance to the immunologically distinct fetus. We hypothesised that percentages of Treg cells are decreased in preeclamptic patients (table 9,10,11). T-regulatory cells (T_{reg}) are important in balancing immune responses and maintaining peripheral tolerance.

Current evidence suggests that asthma is characterized by a relative deficiency in T_{reg}, allowing T helper 2 cells to expand. In this study, we aimed to evaluate circulating T_{reg}, defined by the protein FOXP3 **(Provoost *et al.*, 2009).**CT genotype showed increased risk of breast cancer compared with TT carriers**.** CT genotype may increase an individual's susceptibility to breast cancer by breaking the balance between T reg-mediated immune tolerance and *FOXP3* -controlled tumor-suppressive effect **(Zheng *et al.*, 2013**).

The present data were in agreement with **(Gholami *et al* , 2016)**, the higher frequency of the C allele in the controls has a protective function. However, in the genotype level there was no significant association. The key finding of the present study was that a common variant (GG) of **rs3761548** in the regulatory region of the Foxp3 gene was associated with the development of severity in preeclampsia pregnant women, in addition, the G allele has a protective factor in patients with micro albuminuria and macro albuminuria**.**

A series of recent publications suggest that Tregs may be involved in the pathogenesisof preeclampsia. Sasaki et al assessed Tregs in placentas of women withpreeclampsia. They used Immunohisto-chemical staining of placental tissue to detect the expression of Foxp3 in placental Tregs by using antibodies against FOXP3. They published that the average percentage of cells expressing FOXP3 was less in women with preeclampsia than healthy controls. They also compared the percentage of Tregs in the peripheral blood between women with preeclampsia and both pregnant and nonpregnant healthy controls. They found a significant decrease in the number of Tregs in women with preeclampsia **(Sasaki *et al*,, 2007).**

Conclusion:

The genetic polymorphism in FOXP3 gene(rs3761548) may contribute to the pathogenesis of preeclampsia's -regulatory cells (T_{reg}) are important in balancing immune responses and maintaining peripheral tolerance and are defined by the protein FOXP3.Otherwise, CT genotype increased risk of PE compared with TT carriers.

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التعدد المظهرى للبروتين P3 كعامل خطوره في تسمم الحمل

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تسمم الحمل سبب رئيسي لوفيات واعتلال الأمهات والجنين. تتراوح نسبة حدوث مقدمات الارتعاج من 2 إلى 10٪ ، اعتمادًا على السكان المدروسين وتعريفات تسمم الحمل. تم تسليم عدد أكبر بشكل ملحوظ من الرضع قبل بدء المخاض وبالعملية القيصرية في المجموعة المصابة بمقدمات الارتعاج. هدفت هذه الدراسة إلى التحقق من ارتباط المجموعات المدروسة بالبيلة الزلالية ، مؤشر كتلة الجسم ، ضغط الدم ، عمر الحمل ، وزن الطفل ، العمر ، وزن المشيمة ، طريقة الولادة ، الإجهاض ، تعدد أشكال الثعلب p3 والنمط الجيني.

تم تسجيل إجمالي 75 (25 امرأة معتدلة الضغط كمجموعة ضابطة ، و 25 امرأة مصابات بمقدمات الارتعاج الخفيفة ، و 25 امرأة مصابات بمقدمات الارتعاج الشديدة) في هذه الدراسة. .FOXP3 كان لدى المشاركين ذوي الأنماط الجينية متغايرة الزيجوت (TG) والمتجانسة (TT) مؤشر كتلة جسم أعلى مقارنةً بالأنماط الجينية من النوع البري GG) ، TT، .(TGلذلك ، كانت النساء المصابات بالأنماط الجينية GG و TG PE شديدة من تلك التي TT وكانت كل هذه الارتباطات ذات دلالة إحصائية$P <0.05$) . ترتبط زيادة مؤشر كتلة الجسم بزيادة مخاطر نتائج الولادة الضائرة. وبالتالي ، فإن التأثير الوقائي للإجهاض السابق لا يعمل إلا بين النساء اللواتي حملن مرة أخرى مع نفس الشريك. تم اقتراح آلية مسببة قائمة على المناعة ، حيث يحمي التعرض المطول لمولدات المضادات الجنينية من حمل سابق من تسمم الحمل في حمل لاحق مع نفس الأب.

ان معدل تسمم الحمل الطبيعي يكون أقل في الوزن الطبيعي وقيمة أكبر في الوزن الزائد ولكن من ناحية أخرى يظهرمعدل تسمم الحمل الشديد نسبة أعلى في السمنة وأقل قيمة في الوزن الطبيعي والوزن الزائد ، نلاحظ أن النسبة العالية من الحالات الشديدة كانت سمنة ولكن خفيفة وطبيعية كانت زيادة الوزن. ان النساء ذوات مؤشر

كتلة الجسم المنخفض وعدد أقل يعانين من زيادة الوزن أو السمنة.كما ان النساء اللواتي لديهن تاريخ من الإجهاض وحملن مرة أخرى مع نفس الشريك كان لديهن ما يقرب من نصف خطر الإصابة بتسمم الحمل. على النقيض من ذلك ، فإن النساء اللواتي لديهن تاريخ إجهاض وحملن مع شريك جديد لديهن نفس مخاطر الإصابة بتسمم الحمل مثل النساء اللواتي ليس لديهن تاريخ من الإجهاض.

التوصية:

أن زيادةالألبومين ترتبط مع شدة تسمم الحمل. كما وجد أن إفرازالألبومين في البول يرتبط ارتباطًا وثيقًا بالألبومين أثناء الحمل. على الرغم من أن الولادة المهبلية في حالة تسمم الحمل تعتبر آمنة ، إلا أن معظم الدراسات أظهرت معدلات أعلى في الولاده القيصريه في المجموعة المسببة للالتهاب أكثر من المجموعة الضابطة.