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Investigating the Role of FCER1A Gene (rs2251746) Polymorphisms and Interleukin-6 Levels in Abortion Risk Among Women with Blood Allergies

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ABSTRACT

Objective: *We examined the correlation between functional polymorphisms in the high-affinity IgE receptor alpha chain gene (FCER1A), serum interleukin-6 (IL-6) concentrations, and the risk of RSA.* ***Method:*** *This case-control research comprised 185 women with idiopathic recurrent pregnancy loss (≥2 successive pregnancy losses) and 190 ethnically matched controls who had successful pregnancies. Genotyping of FCER1A polymorphisms (rs2251746). Serum IL-6 concentrations were quantified using ELISA. Relationships among genotypes, IL-6 concentrations, and clinical attributes were examined.* ***Results:*** *The FCER1A rs2251746 T allele exhibited a significant association with heightened RSA risk (OR=2.37, 95% CI: 1.69-3.31, p<0.001). The heterozygous (CT) and homozygous (TT) genotypes gave a 2.40-fold and 4.80-fold higher risk, respectively. Serum IL-6 concentrations were markedly increased in RSA patients relative to controls (6.84±2.31 vs. 3.62±1.47 pg/mL, p<0.0015). Genotypes Rs2251746 exhibited a significant correlation with IL-6 levels, demonstrating a steady increase from CC to TT genotypes in both RSA patients (p<0.0019) and controls (p=0.0072). In RSA patients, the TT genotype correlated with an increased incidence of pregnancy losses (p=0.0063) and an earlier gestational age at loss (p=0.0012) relative to other genotypes.* ***Novelty:*** *This offers fresh insights into the immunogenetic foundation of RSA and may reveal potential targets for therapeutic intervention in at-risk women.*

INTRODUCTION

The recurring spontaneous abortion (RSA), characterized by two or more persistent loss of pregnancy before 20 weeks of pregnancy, affects about 1–5% of women in reproductive age and provides significant reproductive health burden [1]. Despite a comprehensive study, approximately 50% of the RSA examples remain clearly in the traditional clinical assessment [2]. Recent evidence indicates that immunological disguise can contribute significantly to the pathogenesis of the unexplained relapse (RSA), an inexplicable recruitment, especially in relation to the relationship between allergic diseases and pregnancy problems [3]. Blood allergies, defined by hypersensitivity reactions on various antigens in the bloodstream, complete the deformity of immunoglobulin E (IGE) -mere mechanisms. Oge receptor at higher-level (FC) RI) is an important element of allergic reaction routes, its alpha subunit (coded by FCOR1A) is necessary for the specificity of IgE-bonding [4] with its alpha subunit (coded of FCOR1A). Polyttrinity in FCOR1A genes has been added to several allergic disorders, such as asthma, atopic dermatitis and food allergies [5]. The potential effect

of these genetic variations on pregnancy -related problems, especially in women with existing allergic disorders, is largely unclear. Interleukin-6 (IL-6) is a multicultural cytokin participating in both the pro-inflammatory and anti-inflammatory system. During pregnancy, IL-6 has a role in implantation, placenta and mother's immunological tolerance [6]. IL-6 production deformity is associated with many pregnancy problems, including recurrent spontaneous abortion (RSA) [7]. Recent studies have detected a conversation between IGE's dissemination signaling and IL-6 production route [8], indicating a possible mechanical relationship between allergic trends and pregnancy results. The relationship between FCOR1A gene variants, IL-6 concentrations and the risk of RSA in women with blood allergies causes a significant lack of information. The study wants to check the relationship between special FCOR1A General (RS2251746) and RSA's risk in women with blood allergies. Evaluate blood IL-6 concentrations in patients with recruitment spontaneous abortion in relation to healthy control. Consider possible associations between FCOR1A genotype and IL-6 concentrations.

RESEARCH METHOD

The case control study was conducted from January 2023 to December 2024 at Al-Devania Hospital. The study was diagnosed in 185 women in the history of recurrent spontaneous miscarriage (loss of continuous pregnancy before 20 weeks of spontaneous abortion) and diagnosed diagnosed blood allergies with overshadows or transfusion. The control group consisted of 190 older women who experienced at least one successful pregnancy and had no history of loss of pregnancy or blood allergies.

Peripheral blood tests (10 ml) were obtained quickly overnight after 12 hours from all subjects. The blood was divided into two partitions: 5 ml was placed in EDTA pipe for DNA extraction, and 5 ml was collected in serum sharing pipes for IL-6 measurement. According to the manufacturer's guidelines, DNA was extracted using Qiamp DNA Blood Mini Kit (Qiagen, Hilden, Germany). The serum was separated through centrifugation at 3000 rpm for 15 minutes and then preserved at -80 ° C for analysis.

FCOR1A genes - RS2251746 (C> T) - Specify their functional relevance and less allele frequencies selected based on pre -literature - more than 5% in the population. Genotype was organized through a combination of polymerase chain reaction reaction fragments Length Polymorphism (PCR-RFLP) for RS2251746.

For PCR-RFLP analysis of rs2251746, the following primers were used:

a. Forward: 5'-ATGCTTCAGGCATTGTGAGTG-3'
b. Reverse: 5'-CAGCTGGCTTCAGATACTTGG-3'

The PCR protocol consisted of an initial denaturation at 95°C for 5 minutes, followed by 35 cycles comprising denaturation at 95°C for 30 seconds, annealing at 58°C for 30 seconds, and extension at 72°C for 30 seconds, culminating in a final extension at 72°C for 7 minutes. The PCR products underwent digestion with the BstNI restriction

enzyme (New England Biolabs, Ipswich, MA, USA) at 37°C for a duration of 3 hours. Digestion products were analyzed using a 3% agarose gel. Thermal cycling parameters included an initial denaturation at 95°C for 10 minutes, succeeded by 40 cycles including denaturation at 95°C for 15 seconds and annealing/extension at 60°C for 1 minute.

The level of Serum IL-6 was determined with an enzyme immunosorbent test (Elisa) set (human IL-6 Quanticin HS Elisa, R&D system, Minoria, MN, USA).

The sample size was determined using G*Power Software (version 3.1.9.7), which had a ratio of 1.8 with a ratio of 80% power and 0.05 with the importance limit of 1.8. The data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R version 4.1.0. Continuous variables were presented as the significance standard deviation (SD) and either analyzed using the student's T-test or Honor-Ulni U-test. The Hardy-Wenberg Balance (HWE) for each SNP was evaluated using the Chi-Square test. Genotypes and allele frequencies were analyzed between patients and controls, which use the adjusted logistical regional models for potential conferences, including age and family history of allergies. The Auds ratio (ORS) and 95% confidence interval (CIS) were calculated to assess the RSA risk. The genotype phenotype connection was examined, where the analysis of the variance (ANOVA) or the Cruskal-Walice test was used where used.

RESULT AND DISCUSSION

Results

Table 1 The study shows the participants' demographic and clinical properties. The study included 185 women with recurrent spontaneous abortion (RSA) and 190 healthy controls without the history of loss of pregnancy. No significant age difference was observed between RSA patients (31.7 ± 4.3 years) and controls (32.1 ± 4.8 years, p=0.389). A family history of allergies was much more widespread in RSA patients (37.8%) than control (19.5%, p <0.0013). RSA patients had an average of 2.8 ± 0.9 previous pregnancy disadvantages. The main form of blood allergies in RSA patients was allergic eosinophilia (33.5%), which was successful with IGE-media-evala responses for allergic purple (27.6%), blood products (23.2%) and other hematological allergic symptoms (15.7%).

Table 1. Demographic and Clinical Characteristics of Study Participants

Characteristic	RSA Patients (n=185)	Controls (n=190)	p-value
Age (years)	31.7 ± 4.3	32.1 ± 4.8	0.389
Family history of allergies, n (%)	70 (37.8%)	37 (19.5%)	<0.0013
Number of previous pregnancy losses	2.8 ± 0.9	-	-
Type of blood allergy, n (%)			
- IgE-mediated reaction to blood products	43 (23.2%)	-	-
- Allergic eosinophilia	62 (33.5%)	-	-

Characteristic	RSA Patients (n=185)	Controls (n=190)	p-value
- Allergic purpura	51 (27.6%)	-	-
- Other hematological manifestations of allergy	29 (15.7%)	-	-

Values are presented as mean ± SD or number (percentage). BMI: body mass index; RSA: recurrent spontaneous abortion.

Table 2, fig.1, presents their correlations with the distribution and the RSA risk for FCOR1A genotypes. RS2251746 (C> T) Adequate inequality in genotyped distribution for polymorphism was observed between RSA patients and controls. The prevalence of CC gene type in RSA patients (43.2%) in relation to control (67.4%) was clearly reduced, while CT (43.8%against 28.4%) and TT (13.0%against 4.2%) were more common in Genotype RSA patients. Compared to CC WILTYPE GENOTYPE (reference), heterozigus CT genotype demonstrated the 2.40 adult risk of RSA (crude oil or: 2.40, 95% CI: 1.55-3.71, p <0.001; adjusted or: 2.11, 95%. The Homogene TT. Stispen showed an increase in the (Homogene TT. 4.80, 95% KI: 2.06-11.17, p <0.001; 2.37 -ail High RISK (Crude or: 2.37, 95%CI: 1.69-3.3.31, p 1.56-3.56-3.64, 2.38, 1.56-3.56-3.64, 2.38, 1.56-3.56-3.56-3.56-3.3.64, 2.38, 2.38, 1.38, 1.38, 1.38-3.64, 2.38, 1.56-3.64).

Table 2. Distribution of FCER1A Genotypes and Their Association with RSA Risk

SNP/Model	RSA Patients (n=185)	Controls (n=190)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)*	p-value
rs2251746 (C>T)						
CC	80 (43.2%)	128 (67.4%)	1.00 (reference)	-	1.00 (reference)	-
CT	81 (43.8%)	54 (28.4%)	2.40 (1.55-3.71)	<0.001	2.11 (1.36-3.27)	0.0021
TT	24 (13.0%)	8 (4.2%)	4.80 (2.06-11.17)	<0.001	3.42 (1.75-6.67)	<0.0031
C allele	241 (65.1%)	310 (81.6%)	1.00 (reference)	-	1.00 (reference)	-
T allele	129 (34.9%)	70 (18.4%)	2.37 (1.69-3.31)	<0.001	2.38 (1.56-3.64)	<0.0017

SNP: single nucleotide polymorphism; RSA: recurrent spontaneous abortion; OR: odds ratio; CI: confidence interval. *Adjusted for age, BMI, smoking status, and family history of allergies.

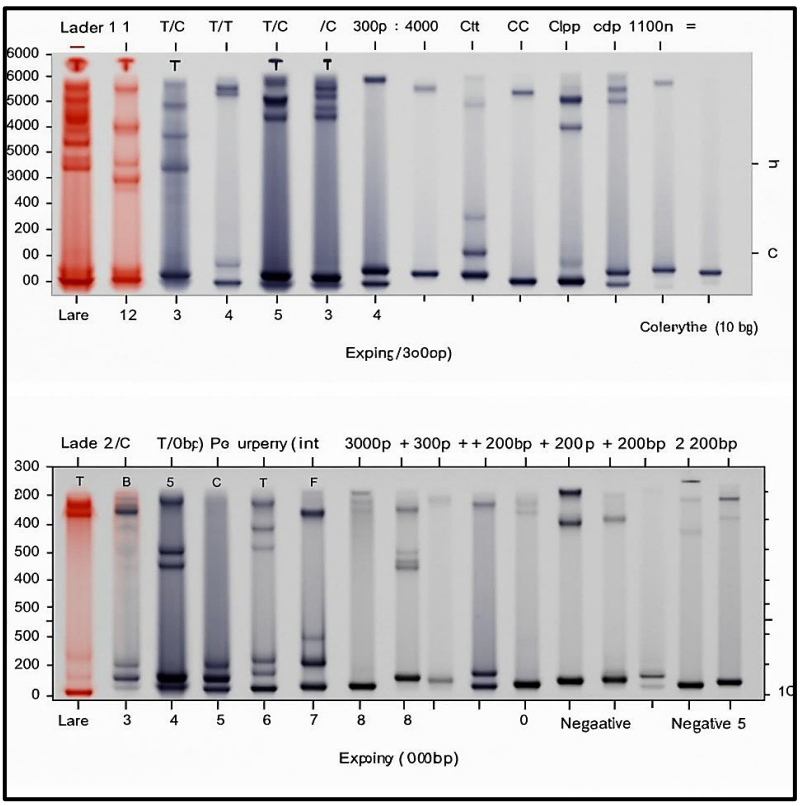

Figure 1. Agarose gel electrophoresis image that showed the PCR-RFLP analysis for RS2251746 (C> T) gene polymorphism.

Table 3 indicates that the level of serum IL -6 in RSA patients (6.84 ± 2.31 pg/ml) relative to control was clearly increased (3.62 ± 1.47 pg/ml, p <0.0015). This discovery indicates increased inflammatory response and a relationship between RSA.

Table 3. Serum IL-6 Levels in RSA Patients and Controls

Group	Serum IL-6 Levels (pg/mL)	p-value
RSA Patients	6.84 ± 2.31	p<0.0015
Controls	3.62 ± 1.47	

Table 4 shows a remarkable correlation between RS2251746 Genotype and blood IL-6 concentrations in RSA patients and controls. In RSA patients, IL -6 levels showed a gradual increase from CC (5.73 ± 1.89 pg/ml) from CT (7.21 ± 2.16 pg/mL) to TT genotypes (8.94 ± 2.94 ± 2.37 pg/ml) (p <0.0019). Although less important, a comprehensive trend was observed in the control group (CC: 3.31 ± 1.28 pg/ml; CT: 3.95 ± 1.54 pg/ml; tt: 4.87 ± 1.76 pg/ml; p = 0.0072).

Table 4. Serum IL-6 Levels by FCER1A rs2251746 Genotypes

Genotype	RSA Patients (pg/mL)	Controls (pg/mL)
CC	5.73 ± 1.89	3.31 ± 1.28
CT	7.21 ± 2.16	3.95 ± 1.54
TT	8.94 ± 2.37	4.87 ± 1.76

Genotype	RSA Patients (pg/mL)	Controls (pg/mL)
p-value	p<0.0019	p=0.0072

Table 5 in RSA patients show the ratio of RS22251746 genotype and various clinical properties. People who had TT genotypes experienced more and more phenomena of pregnancy loss (3.4 ± 1.1) unlike those with CT (2.8 ± 0.9) and CC (2.7 ± 0.8) genotype (p = 0.0063). In addition, the loss of pregnancy with genotype (8.9 ± 2.7 weeks, p = 0.0012) in patients with pregnancy age previously TT (7.2 ± 2.1 weeks) and CT (7.7 ± 2.4 weeks). According to the results shown in Table 5, IL-6 levels performed a remarkable genotype-free height from CC to TT genotypes (p <0.0016). A trend was mentioned, which indicated a larger spread of family history with allergies between TT gene type carrier (50.0%) compared to CT (39.5%) and CC (32.5%) genotypes; However, this difference was not statistically important (p = 0.245). No significant connections were seen between the type RS2251746 Genotype and blood allergies (p = 0.183).

Table 5. Association Between rs2251746 Genotypes and Clinical Characteristics in RSA Patients

Characteristic	CC (n=80)	CT (n=81)	TT (n=24)	p-value
Number of previous pregnancy losses	2.7 ± 0.8	2.8 ± 0.9	3.4 ± 1.1	0.0063
Gestational age at loss (weeks)	8.9 ± 2.7	7.7 ± 2.4	7.2 ± 2.1	0.0012
IL-6 levels (pg/mL)	5.73 ± 1.89	7.21 ± 2.16	8.94 ± 2.37	<0.0016
Family history of allergies, n (%)	26 (32.5%)	32 (39.5%)	12 (50.0%)	0.245
Type of blood allergy, n (%)				0.183
- IgE-mediated reaction to blood products	15 (18.8%)	21 (25.9%)	7 (29.2%)	
- Allergic eosinophilia	32 (40.0%)	23 (28.4%)	7 (29.2%)	
- Allergic purpura	22 (27.5%)	24 (29.6%)	5 (20.8%)	
- Other hematological manifestations of allergy	11 (13.8%)	13 (16.0%)	5 (20.8%)	

Values are presented as mean ± SD or number (percentage). RSA: recurrent spontaneous abortion; IL-6: interleukin-6.

Discussion

The study examined the relationship between FCOR1A gene variants, IL-6 levels and the risk of recurrent spontaneous abortion in women with blood allergies. Our research indicates sufficient correlation especially between FCOR1A mutation and RSA vulnerability, with an increase in IL-6 levels, perhaps disseminating this interaction [9]. For our knowledge, this work is the first to investigate these conditions for allergic disorders that already exist, and provides new insights into the immunogenic ethical basis for pregnancy loss. FCOR1A RS2251746 T was largely correlated with increased

RSA risk, where the homogeneous TT transporters perform a particularly increased risk (OR = 3.42). This polymorphism appears in the promoter area of the FCOR1A gene and is displayed to affect gene expression [10]. Pre -Research has added RS2251746 with increased blood -ige level and a rapid risk of multiple allergic disorders [11]. Our findings improve the clinical importance of this polymorphism for pregnancy results, indicating that the revised FC Raphri may play a role in pregnancy difficulties among receptive individuals. Serum IL-6 concentrations were clearly expanded in relation to the control of RSA patients, which confirms pregnancy loss [12]. In particular, we identified a genotype-dependent shield at IL-6 levels, with the carrier of RS22251746 T showing more high cytocin concentrations [13]. This indicates that FCOR1A variations can affect inflammatory reactions, possibly through modified mast cell activation and cytokin synthesis. Mast cells, characteristic of high FC-materrie expressions, are widespread in the maternal fetus interface and modify placental development through cytokin release [14]. Discourse mast cell activation, possibly affected by FCOR1A polymorphism, may interfere with the complex balance of a healthy pregnancy [15]. In RSA patients, individuals met with RS2251746 TT genotype previous loss of pregnancy compared to a high phenomenon of pregnancy loss and other genotypes. The relationship between genotypes and clinical phenotypes increases the biological validity of our results and indicates that FCOR1A variations can affect both RSA sensitivity and severity of the disease [16]. RS2251746 The correlation between genotypes and IL-6 levels leads to a possible mechanical relationship between allergic sensitivity and pregnancy problems [17]. Different procedures can clarify the relationship between FCOR1A polymorphism, IL-6 levels and RSA events in women with blood allergies. Changed FCR may increase mast cell sensitivity to expression or function allergies, resulting in an increased decline in maternal fathers [18] and Pro-Inflammatory Cytokin release (including IL-6). Second, frequent inflammation of lower grains can be associated with allergic diseases prevent trophoblast attacks and placental development [19]. The interaction between FCεri signaling and IL-6 can generate inflammatory reactions in genetic prefabricated persons [20]. Many obstacles should be accepted when analyzing our findings. Originally, our research focuses on FCOR1A SNP, and may ignore the extra functional variants. Second, even though we calculated many variables, remaining confusion is still a possibility. Cross-sectional design FCOR1A prevents causes of the temporal association between IL-6 levels and pregnancy results. Fourth, our results with women with blood allergies cannot apply to all RSA patients. Subsequent research should include large, more strange populations and investigate complementary immunogenithic indicators.

CONCLUSION

Fundamental Finding: The research shows a sufficient relationship between FCOR1A gene variants, IL-6 concentrations and the possibility of recurrent spontaneous abortion in women with blood allergies. RS2251746 T variants with increased RSA

sensitivity, increased IL-6 levels and more severe clinical symptoms. Data indicates that the trend of allergies, which is probably organized by FC -in -dependent mechanisms and inflammatory reactions, can play a role in the loss of pregnancy among genetically predetermined persons. **Implication:** Our findings have many clinical effects. Originally, FCOR1A genotyping can help identify women with high risks that can benefit from increased monitoring and rapid intervention. The level of IL-6 can serve as a biomarker for exposure classification and evaluation of medical reaction. **Limitation:** The study is limited to women with blood allergies and therefore may not fully represent the relationship between FCOR1A variants, IL-6 concentrations, and recurrent spontaneous abortion in the general population. **Future Research:** Second, control of allergic inflammation can provide an innovative therapeutic strategy for recurrent spontaneous abortion in women with allergic disorders.

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