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Interleukin-18 gene promoter polymorphisms and recurrent spontaneous abortion

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Abstract

Background: IL-18 is a multifunctional cytokine capable of inducing either Th1 or Th2 polarization depending on the immunologic milieu. IL-18 is detected at the materno-fetal interface very soon in early pregnancy. Two polymorphisms in the promoter region of the IL-18 gene at positions of –607 and –137 appear to have functional impacts.

Objective: This study attempts to evaluate the frequency of these two polymorphisms in the IL-18 gene promoter in patients with recurrent spontaneous abortion (RSA) and normal pregnant women.

Subjects and methods: One hundred and two RSA patients and 103 healthy pregnant women were enrolled in this study. Single nucleotide polymorphisms of the IL-18 gene at positions –607 (C/A) and –137 (G/C) were analyzed by the sequence-specific PCR method.

Results: There was no significant association between the allele, genotype, and haplotype frequencies of the two single nucleotide polymorphisms (SNPs) in the IL-18 gene promoter and RSA.

Conclusion: The results of this study showed that IL-18 gene promoter polymorphisms at positions –607 and –137 did not confer susceptibility to RSA in southern Iranian patients.

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1. Introduction

Recurrent spontaneous abortion (RSA), the occurrence of three or more consecutive pregnancy losses in the first trimester, occurs in approximately 1% of pregnant women worldwide. A series of etiological factors responsible for RSA are divided into the embryologically driven causes (abnormal embryonic karyotypes) and maternally driven ones affecting the endometrium and/or placenta (luteal phase defect, hyperprolactinemia, hyperhomocysteinemia, uterine anomalies, coagulation disorders, autoimmune

diseases, endocrine disorders, and endometrial defects) [1]. Despite these well-established pathophysiological mechanisms, the exact underlying etiology is still poorly understood in up to 50% of RSA cases. Recent studies shed light on the immune mechanism as a cause of a proportion of these idiopathic pregnancy losses [1–4].

Production of cytokines and the distribution of the immune cells during pregnancy appeared to be critical in pregnancy outcome [1–4]. Interleukin (IL)-18, initially known as an interferon (IFN)- γ inducing factor, is a member of the IL-1 cytokine family, which is produced by a variety of immune and non-immune cells. It is a unique cytokine capable of enhancing either Th1 or Th2 differentiation depending on the immunologic milieu. It also augments the cytotoxic actions of natural killer and CD8+ T cells [5,6].

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