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Effects of IL-1 receptor antagonist *intron 2* gene polymorphisms on recurrent pregnancy loss in Iranian population.

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Abstract

Introduction: Recurrent Pregnancy Loss (RPL) is a heterogeneous disease which consisting of three or more successive abortions before 20 weeks of pregnancy. The cytokines that secreted by Th1 cells (IL-1, TNFα and IFNγ) were described as etiologic factors in RPL. The aim of this study was investigate to association between recurrent pregnancy loss and IL-1 receptor antagonist gene (*IL-1RN*) *intron 2* polymorphism (86-bp VNTR) in Iranian Azeri and Persian women.

Materials and methods: Genotype and allele distribution were studied in 280 Persian women (140 case and 140 control) and 200 Azeri women (100 case and 100 control). Case group were included women with least three RPL and control group were included healthy women with at least two successful deliveries. Genomic DNA was extracted from the whole blood and polymorphism analysis was performed by Polymerase Chain Reaction (PCR) method.

Results: No significant association was observed between *IL-1RN* 86-bp VNTR polymorphism in *intron 2* and RPL among Iranian Persian and Azeri women.

Conclusion: *IL-1RN* VNTR polymorphism may not be a genetic factor for RPL. However investigation of *IL-1RN* polymorphism was recommended in other populations and patients with recurrent pregnancy loss.

Keywords: *IL-RN*, Polymorphism, Recurrent pregnancy loss.

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Introduction

Recurrent Pregnancy Loss (RPL) is a multi-factorial syndrome consists of three or more successive abortions [1-3] and is a serious reproductive problem in 1-5% of reproductive age women [4,5]. The causes for this syndrome are very different, such as genetical, anatomical, chromosomal and endocrinological agents. Also environmental agents are important, which including disposal to ethylene oxide and lead [6]. In several conditions, RPL appear from immunological problems [7]. Since there is a reasoning about the suitable evaluation and treatment of cases experiencing this disease [8].

Anti-inflammatory immune response during pregnancy is normal and necessary for embryo conservation against maternal pro-inflammatory immune response [9]. The increased production of Th1 type cytokines, particularly IL-1, TNFα and IFNγ, due to allograft induced activation and release of material P during pregnancy, nitric oxide and other toxic material might be elevated, that in turn improve pregnancy loss chances [10,11].

The *IL-1* gene family has an important effect on inflammatory response. *IL-1* cluster has located within 430 kilo base area on the chromosome 2 (2q13-21) [12]. There are two types of cytokines family, including pro-inflammatory cytokines (IL-1α, IL-1β) and an anti-inflammatory material (IL-1Ra or *IL-1RN*) [12,13]. Human *IL-1RN* gene has been defined in the q14-q21 condition, which *intron 2* encompasses VNTR polymorphism with an 86-base pair and the VNTR sequence was repeated 2 to 6 times. Usually, there are 4, 2, 5, 3 and 6 repetition in allele 1 (*IL-1RN**1), allele 2 (*IL-1RN**2), allele 3 (*IL-1RN**3), allele 4 (*IL-1RN**4) and allele 5 (*IL-1RN**5),