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Original Article

Relationship between rs605059 and rs676387 Polymorphisms of HSD17B1Gene with Recurrent Abortion In Iranian Population

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Abstract

Recurrent abortion of the fetus can be said to the occurrence of three or more than three recognizable abortion that happens before the twentieth week of pregnancy. This study was studied with aim of investigating the relationship of HSD17B1 gene with recurrent abortion with selection of 80 subjects with a history of recurrent spontaneous abortion and unknown cause as patients group and 80 subjects without a history of recurrent abortion and having at least two successful fertility as the control group and totally 160 personsin Iranian population. The rs605059 and rs676387 polymorphisms of HSD17B1 gene were analyzed with the PCR-RFLP method. The findings of this study showed that in rs676387 polymorphism of HSD17B1 gene was seen in T allele in 8.125% and 37.5% of patients with recurrent spontaneous abortion and population control respectively. This is despite the fact that more than 91% of patients and of 62.5% of healthy individuals had G allele. In this genomic region of GG and GT genotypes were observed in 84% and 16% of patients and 37.5% and 50% of the control group respectively. In addition the TT genotype was found in 12.5% of healthy mothers, but was not seen in none of the patients. The results of this study showed that in the rs605059 genomic region of HSD17B1 gene, A allele was seen in 40% of patients population and only about 12% of the healthy mothers. In the other hand, G allele was observed in 60% of patients and more than 88% of the control group. Results also showed that GG and AA genotypes were about 51.25% and more than 31% in the patients population and 77.5% and about 1% in a population of healthy mothers, respectively. Statistical test results showed that for the rs676387 and rs605059genomic regions of HSD17B1 gene, there was a statistically significant difference between allelic and genotypic frequencies of patients and control population and existence ofG and A alleles in the genomic regions of rs676387 and rs605059 were associated with increased risk of recurrent abortion. These results indicated the relationship of rs676387 and rs605059 areas with susceptibility to recurrent abortion.

Key words: Recurrentabortion, HSD17B1 gene, Polymorphism

INTRODUCTION

Recurrent abortion of the fetus is defined the occurrence of three or more than three recognizable abortion that happens before the twentieth week of the last menstrual cycle or before reaching the fetus weight to 500 grams [22,24,27]. Recurrent abortion can be seen in two forms of primary and secondary form. Primary recurrent abortion refers to cases that patients have not experienced giving birth to a live child. However, in secondary recurrent abortion, there is a history of at least one live child. Studies have shown that the risk of loss of pregnancy after spontaneous abortion is 24%, followed by two spontaneous abortion is 30%, followed by 3 spontaneous abortion is 35% and after 4 recurrent spontaneous abortion is 40% [4, 6]. According to studies carried out in different parts of the world, about 10% to 15% of pregnancies lead to abortion. The occurrence of abortion is a good thing to prevent the birth of abnormal children and other problems and is potentially useful, but if it is repeated more than two times, it has found pathologic aspect and it requires investigation and appropriate treatment [11, 20, 30].

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Recurrent abortion affects 2% to 5% of pregnant women[25]. Several factors are involved in the pathogenesis of recurrent abortion. 50% of recurrent abortion include anatomical, immunological, genetic and endocrine causes and environmental factors. However, in about half the cases, the cause of abortion is uncertain [3,10, 26]. On average, about 17% to 20% of women with recurrent abortion have an endocrine disorder [9]. The most important endocrine factors that cause recurrent abortion include luteal phase defect, polycystic ovarian syndrome, diabetes, thyroid and prolactin secretion disorders [4, 12, 29]. The role of steroid hormones of estrogen and progesterone during pregnancy has been proven. Studies have shown that the amount of these hormones during pregnancy increases [21]. Progesterone prepares the endometrium for blastocyst implantation and controls the development of endometrium. Estradiol increased before ovulation carries out proliferation and differentiation of uterine epithelial cells, that progesterone subsequently causes proliferation and differentiation of stromal cells. Progesterone influences on the endometrium through specific receptors that their expression is controlled by estrogen [18]. HSD17B1 gene is located on 17q11-q21 chromosome. This gene usually occurs only in the placenta,breast epithelial cells and endometrium. The product of this gene is an enzyme called 17-beta-hydroxy steroid dehydrogenase type 1 (HSD17B1 or 17β-HSD1) that regulates different biological activities, especially in the case of steroid hormones [17]. The rs676387 region is one of the most important areas of polymorphic HSD17B1 gene and its distance from the farthest polymorph identified 318 base pairs. This area is located in intron 4 of HSD17B1 gene [16]. Perhaps the rs605059 polymorphism that is located in 313 codon and 6 exon and at 1954 nucleotide from the start of transcription of HSD17B1 gene and the glycine amino acid converts to serine amino acid known the most important and most famous area of the polymorphic gene [7, 8, 16, 19]. Although there is no doubt about the importance of HSD17B1 gene on process that leads to staying healthy or abortion, our knowledge about the role of this gene and enzyme which is coded by it is increasing day by day. Khaleghparast and colleagues in 2011 were examined the relationship between C677T and A1298C polymorphisms in MTHFR gene with recurrent abortion. Two MTHFR gene polymorphisms were studied with polymerase chain reaction and PCR products enzyme digestion with restriction endonuclease enzymes. There was interaction between two C677T and A1298C polymorphisms. 17 persons of the case group and 5 persons of the control group were heterozygous for the C677T polymorphism. The T mutant allele frequency in women with abortion was more than women in the control group. A1298C polymorphism frequency among women with recurrent abortion and women in the control group was 63.3% and 50%. The obtained results in this study showed that none of the MTHFR polymorphisms, can not explain the cause of recurrent abortion in women. Shakarami and colleagues in 2013 studied the relationship between spontaneous abortion and Plasminogen Activator Inhibitor-1 gene polymorphism (PAI-1) in Iranian patients. In this study for (4G/5G) PAI-1 polymorphism, the frequency of 4G mutant allele in women with recurrent abortion obtained 42% and for women in the control group obtained 30%, respectively, which it represents a significant increase of 4G allele in the patient population to the control group. Results of 4G/4G genotype with 17% frequency in the patient group and 5% in the control group showed a significant increase 4G/4G genotype in patients group. According to the results, it seems women with recurrent abortion faced with 4G allele and 4G/4G genotype more. Abbasi Rad and colleagues in 2013 compared the area of 3279A/C polymorphism of Foxp3 gene in women with recurrent abortion and control group. The findings of this study showed that the frequency of three CC, AC and AA genotypes in patients with recurrent abortion was 58.8%, 25% and 16.2% respectively and in control group was 52.2%, 21.2% and 26.2%. Statistical analysis showed that there was no significant differences in genotype frequency of 3279 place of Foxp3 gene between the control group and women with recurrent abortion. Ahmadi and colleagues in 2013 studied the relationship of GSTM1 gene polymorphism and abortion in Guilan province. This study was case-control in which genomic DNA extraction was performed from the blood of 80 patients with abortions and 100 healthy persons for controls. PCR analysis was performed in two stages: Internal Standard-Controlled PCR and Nested PCR. The results showed that 37.5% of cases with abortion had GSTM1 null genotype and 12% removal was observed in healthy subjects. Distribution of active GSTM1 genotypes showed a significant difference in patient and control groups, so that the frequency of AA or AO genotypes for GSTM1 gene was 88% for patients and was 15% for the control group. They concluded that GSTM1 gene homozygous deletion in Guilan women is probably a risk factor for spontaneous abortion. Jaber and Sharif in 2014 studied the relationship between functional polymorphisms of interleukin-21 gene (rs2055979 G/T and rs13143866 A/G) and Foxp3 gene (rs2232365 A/G and rs3761548 A/C) with recurrent abortion. The population included 100 patients with recurrent abortion and 100 healthy people with no history of recurrent abortion, all of whom were selected from Palestinian women in the Gaza Strip. In this study, PCR-RFLP method was used to determine the genotype of subjects. The findings showed that the gene and genotype frequencies for interleukin-21 gene polymorphisms were not statistically

different between patients and control group. This fact rejected the possibly of interleukin-21 gene polymorphisms relationship with abortion in the studied population. The frequency of gene and genotype for rs2232365 A/G and rs3761548 A/C polymorphisms of Foxp3 gene were different in patients and control group which represents the association of these polymorphisms with the risk of recurrent abortion. Chen and colleagues in 2015 by studying the effect of Plasminogen Activator Inhibitor-1 gene polymorphisms (PAI-1) on the risk of recurrent abortion showed that there was a relationship between the -675 G/A (4G/5G) polymorphism area of this gene and recurrent abortion. However, no association was observed between polymorphism of genomic region -844G/A of PAI1 gene and the risk of recurrent abortion. Xu and colleagues in 2015 examined the relationship between vascular endothelialgrowth factor (VEGF) gene polymorphisms and risk of recurrent abortion in 11 populations from different parts of the world. A total of 1832 patients with recurrent abortion and 2271 normal subjects were evaluated. Statistical analysis showed that of rs1570360, rs3025039, rs2010963 and rs3025020 genomic regionspolymorphism of VEGF gene were associated with the risk of recurrent abortion.

MATERIALS AND METHODS

In this study, 80 patients were selected with a history of unexplained recurrent abortion with unknown cause as patient group and 80 persons as control group and were studied. All experiments of this research were performed in the laboratory of medical genetics doctor MohammadReza Bazrafshani (Kerman). At first, in order to prevent clotting of sampled blood, 1ml EDTA 10% was added to 10ml of blood. Then 9ml of Cell LysisBuffer (CLB) solution was poured in a test tube and 3ml of whole blood were added to it. This was done to lubricate of cells. Then samples were centrifuged at around 2500 rpm for 10 minutes. After centrifugation the supernatant was discarded and the remaining sediment was kept at the bottom of the tube. Then 5ml of TKM1solution was added to the remaining sediment to break lymphocyte cell walls and its contents release to extract DNA. The tube was centrifuged at 2500 rpm for 10 minutes and then the supernatant was discarded. This time a white precipitate remained at the end of the tube. Then to remove proteins from the environment and to obtain purer DNA, on white deposit remained at the end of the tube, the amount of 1.5mlTKM2solutionwith 100 µlSodium Dodecyl Sulfate (SDS)-10% was added and the tube was placed within the water bath for 30 minutes at 65 ° C. After the solution was almost transparent in tube, 570 µl of NaCl-6 M was added to it, and it was centrifuged at 2900 rpm for 10 minutes. Then, 4ml of 96% cold alcohol was poured in a sterile test tube and after centrifugation the supernatant was added to a tube containing 96% alcohol. In next step, the door of the tube was blocked with parafilm and the tube was shaken gently to form the DNA in it. Then in 1.5ml micro tubes, 1ml of 70% alcohol was poured and the formed DNA in the tube gently transferred with pipette tip to micro tubes. Then micro tubes were centrifuged at 12000 rpm for 5 minutes. After the end of centrifugation white sediment were seen at the bottom of micro tubes. The supernatant was discarded and micro tubes with open doors were put in the area for 10 to 15 minutes for drying. At the end, the amount of 300 µl of Tris- EDTA (TE) that is the liquid holder for DNA was added the deposition. Then micro tubes were incubated in the incubator overnight at 37° C to dissolve DNA completely. The next day, DNA was ready to use for polymerase chain reaction. For HSD17B1 gene, for each sample three polymerase chain reaction were done by using thermo cycler instruments and with specific primers for the rs676387 and rs605059 regions. Characteristics of primers and restriction enzymes used to determine HSD17B1 gene polymorphisms is shown in Table 1. Program of PCR for rs605059 region includes denaturation for 5 min at 95 ° C and then 32 cycles of 30 seconds at 94 ° C, 40 seconds at 60 ° C (to connect primer), 40 seconds at 72 ° C and finally 10 minutes at 72 ° C, respectively. Program of PCR for rs676387 region also includes denaturation at 95 ° C for 5 minutes and then 30 cycles of 30 seconds at 95 ° C, 30 seconds at 58.5 ° C (to connect primer), 30 seconds at 72 ° C and 72 ° C for 10 minutes at the end.

After the end of polymerase chain reaction, amplified products were digested by restriction enzymes. BtsI enzyme was used to for the rs605059 region polymorphism and the BclI enzyme was used to identify the polymorphism of the rs676387 region. Operating temperature for BtsI and

Table 1: Restriction enzymes, primers sequences and their connection temperature to detect HSD17B1 gene polymorphisms

Region	Primers sequence	Connection temperature	Restriction enzymes	Length of parts
rs605059	Sense: 5'-ATGCACCGGGAAGTGTTC -3' Antisense: 5'-GATGGGGGTCTCACTGTGTT -3'	60	BtsI	A: 396 G: 105, 291
rs676387	Sense: 5'-ACACCTTCTCCATGAAGGCGGTGTG -3' Antisense: 5'-CCGCGTTTCAAATGTTCTGGTGATC -3'	58.5	BclI	G: 190 T: 75, 115

BclI enzymes were55 ° C. Restriction enzymes and DNA product size after digestion have been shown in Table 1. To do this task, the amount of 10 µl of PCR product was added to 3 µl of enzyme buffer, and 10 units of that enzyme (approximately 0.5 µl) and 17.5 µl of distilled water and it was placed for 4 hours in a water bath at a temperature of 55 ° C. Then by disabling the enzyme at 95 ° C, digested products were electrophoresed in 2% agarose gel. After electrophoresis of the samples, the agarose gel was transferred to the vessel containing 0.5µg/ml ethidium bromide and it remained in it for 20 minutes. After data collection, the analysis was performed using SPSS v.19 software. Genotypic and allelic frequencies distribution comparison were performed using the chi-square test. In all tests, the level of 5% probability was considered as significant level.

RESULTS

DNA pattern of population control subjects and patients with recurrent abortion for the rs676387 region of HSD17B1 gene was shown in Figures 1 and 2. Population control and patient genotype for this genomic region in were proposed in Tables 2 and 3. In the rs676387 area of HSD17B1 gene, in the presence of T allele, the presence of BclI restriction enzyme, Polymerase chain reaction products were cut and two pieces and finally two DNA bands with molecular weights of 75 and 115 bp were seen. But in the presence of G allele, BclI restriction enzyme failed to cut in DNA piece of PCR amplified from the incision and thus in gels resulting from sample electrophoresis, a single band of 190 bpwas seen. Accordingly, TT genotypes with the dual-band of 75 and 115 bp and GG genotypes with a 190 bp were detected. In the GT genotypes, all three bands of 75, 115 and 190 bp were seen. The findings showed that the T allele was observed at 8.125% and 37.5% of patients with recurrent abortion and population control. However, 91.875% of patients with recurrent abortion and 62.5% of healthy individuals had G allele. Statistical tests showed that for the rs676387 region of HSD17B1 gene there was a difference between G and T alleles frequency in a population of patients with recurrent abortion and population control in the 1% probability level.

The frequency of genotypes showed that 67 persons (83.75%) of tested patients and 30 persons (37.5%) of the control group were carrying the GG genotype. The 16.25%

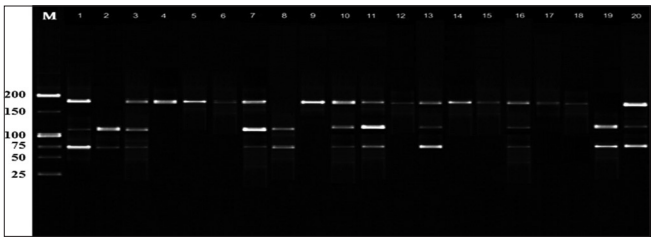

Figure 1: The DNA pattern of population control for the rs676387 region of HSD17B1 gene

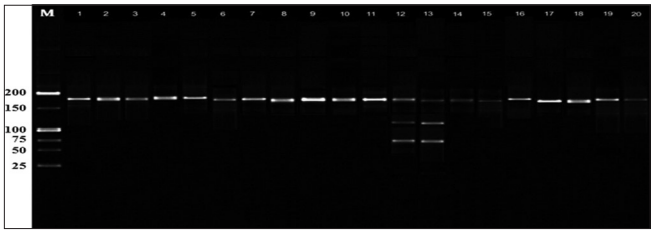

Figure 2: The DNA pattern of patients population with recurrent abortion for the rs676387 region of HSD17B1 gene

Table 2: Genotype of control group for the rs676387 genomic region of HSD17B1 gene

Person	Genotype	Person	Genotype	Person	Genotype	Person	Genotype
1	GT	21	GT	41	GT	61	GG
2	TT	22	GT	42	TT	62	GG
3	GT	23	GT	43	GT	63	GG
4	GG	24	GG	44	GG	64	GG
5	GG	25	GT	45	GG	65	GT
6	GG	26	GT	46	GG	66	GG
7	GT	27	GG	47	GT	67	GG
8	TT	28	GT	48	TT	68	TT
9	GG	29	GT	49	GG	69	GG
10	GT	30	GT	50	GT	70	GG
11	GT	31	GT	51	GT	71	TT
12	GG	32	TT	52	GG	72	GT
13	GT	33	GT	53	GT	73	GT
14	GG	34	GT	54	GG	74	GT
15	GG	35	GT	55	GG	75	GT
16	GT	36	GT	56	GT	76	GG
17	GG	37	GT	57	GT	77	GG
18	GG	38	GT	58	GT	78	GT
19	TT	39	GT	59	GG	79	GG
20	GT	40	TT	60	TT	80	GT

(13 persons) of the patients with recurrent abortion and 50% (40 persons) of the control group had GT genotype. The important point was that none of the patient population were not carrying the TT genotype. This is despite the fact that 10 persons (12.5%) of the control group had TT genotype. The results showed that all statistical tests including test that homozygous and heterozygous were present in it (TT, GT, GG), a test that only homozygous was present (GG, TT) and test compound by TT, GG + GT and GG, GT + TT, had a difference in probability level of 1% between the population of patients with recurrent abortion and control group. According to these results, in general, we can say that in the studied population, there was a difference in probability level of 1% between the genotypic frequencies of rs676387regionof HSD17B1 gene and the risk of recurrent abortion. The genotype for studied control group and patients with recurrent abortion for the rs605059 genomic region of HSD17B1 gene has proposed in Tables 4 and 5.DNA pattern of some control group and the patient has shown in Figures 3 and 4. In the study, in the presenceof A allele, restriction enzyme could not make change polymerase chain reaction of the product and so only a single band of 396 bp was shown. However, in the presence of G allele, BtsI restriction enzyme was cut PCR product and result in two pieces 291 and 105 bp. So AA, GG and AG genotypes were observed one, two and

Table 3: Genotype for patients with recurrent abortion of the rs676387 genomic region of HSD17B1 gene

Person	Genotype	Person	Genotype	Person	Genotype	Person	Genotype
1	GG	21	GG	41	GG	61	GG
2	GG	22	GG	42	GG	62	GG
3	GG	23	GT	43	GG	63	GG
4	GG	24	GG	44	GG	64	GT
5	GG	25	GT	45	GG	65	GG
6	GG	26	GG	46	GG	66	GG
7	GG	27	GG	47	GG	67	GG
8	GG	28	GG	48	GG	68	GG
9	GG	29	GG	49	GG	69	GG
10	GG	30	GG	50	GG	70	GG
11	GG	31	GG	51	GT	71	GG
12	GT	32	GG	52	GG	72	GG
13	GT	33	GT	53	GT	73	GG
14	GG	34	GG	54	GG	74	GG
15	GG	35	GG	55	GG	75	GG
16	GG	36	GT	56	GG	76	GT
17	GG	37	GT	57	GG	77	GG
18	GG	38	GG	58	GG	78	GG
19	GG	39	GG	59	GG	79	GT
20	GG	40	GG	60	GG	80	GT

Table 4: Genotype of control group for the rs605059 genomic region of HSD17B1 gene

Person	Genotype	Person	Genotype	Person	Genotype	Person	Genotype
1	GG	21	GG	41	AG	61	GG
2	AG	22	GG	42	GG	62	GG
3	GG	23	GG	43	GG	63	AG
4	GG	24	GG	44	GG	64	GG
5	GG	25	AG	45	GG	65	GG
6	GG	26	GG	46	GG	66	AG
7	GG	27	AG	47	GG	67	GG
8	GG	28	GG	48	GG	68	GG
9	GG	29	GG	49	GG	69	GG
10	GG	30	GG	50	GG	70	GG
11	AG	31	AG	51	GG	71	GG
12	AG	32	AG	52	GG	72	GG
13	GG	33	GG	53	GG	73	GG
14	GG	34	GG	54	GG	74	GG
15	GG	35	GG	55	AG	75	AG
16	GG	36	AG	56	GG	76	GG
17	GG	37	AA	57	GG	77	GG
18	GG	38	AG	58	AG	78	GG
19	GG	39	GG	59	GG	79	AG
20	GG	40	GG	60	AG	80	GG

Table 5: Genotype of patients with recurrent abortion for the rs605059 genomic region of HSD17B1 gene

Person	Genotype	Person	Genotype	Person	Genotype	Person	Genotype
1	GG	21	GG	41	AA	61	GG
2	GG	22	GG	42	AA	62	GG
3	GG	23	GG	43	AA	63	GG
4	GG	24	GG	44	AA	64	GG
5	GG	25	GG	45	AG	65	GG
6	GG	26	GG	46	AG	66	AG
7	GG	27	GG	47	GG	67	GG
8	AA	28	GG	48	AG	68	GG
9	AA	29	AA	49	GG	69	GG
10	AA	30	AG	50	GG	70	GG
11	AA	31	GG	51	AA	71	AG
12	AA	32	AA	52	AA	72	GG
13	AG	33	AA	53	AA	73	AA
14	AA	34	AA	54	AA	74	AG
15	AG	35	AA	55	AA	75	AA
16	GG	36	GG	56	AG	76	GG
17	AG	37	GG	57	GG	77	GG
18	AA	38	GG	58	GG	78	AG
19	AA	39	GG	59	AG	79	GG
20	GG	40	AA	60	GG	80	AG

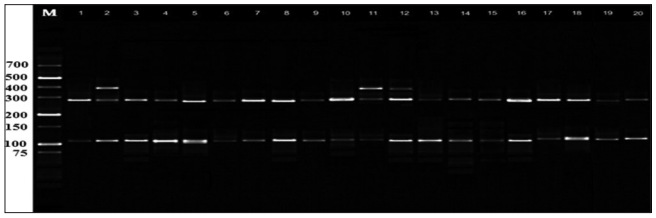

Figure 3: The DNA pattern of control group for the rs605059 region of HSD17B1 gene

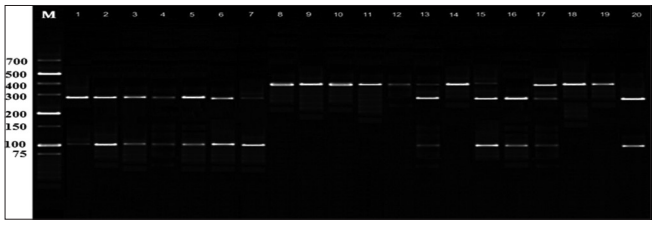

Figure 4: The DNA pattern of patients with recurrent abortion for the rs605059 region of HSD17B1 gene

three bands, respectively.

The results of this study showed that for the rs605059 genomic region of HSD17B1 gene, A allele was observed at 11.875% of the control group. However, this allele existed in 40% of patients with recurrent abortion. Also, G allele at this genomic region was observed in 60% of the patients that this allele was observed in the control group more than 88% of persons. Statistical tests showed that there was a difference in the 1% possibility levelbetweenallelic frequencies in the two populations studied, and these frequencies were associated with the talent of recurrent abortion. The findings showed that in a population of patients, AA, AG and GG genotypes were observed in 25 persons (31.25%), 14 persons (17.5%) and 41 persons (51.25%), respectively. However, the AA, AG and GG genotypes made up the 1.25% (1 person), 21.25% (17 persons) and 77.5% (62 persons) of the control group. Results of testing different combinations of genotypic (AA, AG, GG and GG, AA and AA, GG + AG and GG, AG + AA), showed that genotypic frequencies between the two populations were at 1% statistical difference. According to these results, in general, we can say that statistical analysis showed that in the studied population there was a correlation between genotypic and allelic frequencies of the rs605059 genomic region of HSD17B1 gene and the risk of recurrent abortion.

DISCUSSION

Based on the results, in the rs676387 region, TT genotype was not observed in a population of patients with recurrent abortion. Also for the rs605059 genomic region, AA genotype was observed only in one person in the control group. The results of this study showed that there was a significant difference between genotypic and allelic frequencies of the rs676387 genomic region of HSD17B1 gene in a population of patients with recurrent abortion and healthy mothers. That's about 92% of patients had a G allele. More than 83% of patients had GG genotype. This is despite the fact that even one person of subjects with TT genotype were not patients. T allele frequency in a population of patients was only 8.125%. As a result, in the studied population, existence of G allele has been caused increased susceptibility to recurrent abortion. Since the research about the relationship of rs676387 polymorphism of HSD17B1 gene with recurrent abortion and other

uterine diseases has not been done, there was no possibility to compare the results. Several studies have shown that the rs676387 region is one of the most important areas of the HSD17B1 polymorphic gene has relationship with the risk of some diseases. The findings showed that the frequency of A and G alleles in a rs605059 genomic region of HSD17B1 gene were not the same between patients with recurrent abortion and control group and two populations had difference in this aspect. Thus, most patients had carried A allele, and G allele was more common among the control group. Statistical tests showed that for this genomic region, there was a significant difference in genotypic frequencies in a population of patients and control group. AG genotype existed in 17.5% and 21.25% of patients with recurrent abortion and the control group, respectively. However, in a population of patients with recurrent abortion, 25 persons had AA genotype and this genotype was observed only in one person of the control group. The frequency of GG genotype in the control group, was 26.25% more than the population of patients. All of these results showed that in the Iranian population, rs605059 polymorphism of HSD17B1 gene was associated with recurrent abortion disease and presence of A allele was associated with increased susceptibility to this disease. Tsuchiya and colleagues in 2005 examined the relationship between rs605059 polymorphism with the risk of endometriosis in a population of 138 healthy subjects and patients. The results showed that the presence of A allele at this genomic region was associated with an increased risk of endometriosis. Lamp and colleagues in 2011, in another study, examined the relationship between polymorphisms of HSD17B1, ESR1, ESR2, CYP19A1 and PGR genes with the risk of endometriosis. The findings also showed that A allele in the rs605059 region of HSD17B1 gene was associated with an increased risk of endometriosis. On the other hand, Cong and colleagues in 2012 examined the relationship between polymorphisms of HSD17B1 and HSD17B2 genes with the incidence of uterine tumors among 338 healthy women and women with uterine tumor. The findings showed that all threegenomic regions in the evaluated population were polymorphism and AA genotypic frequency and A allelic were significantly higher in the patients compared to healthy people. In another study, Ntostis and colleagues in 2015 studied the relationship of rs605059 regionpolymorphism of HSD17B1 gene with the risk of recurrent abortion in the population consisted of 138 patients with a history of recurrent abortion 3 times and 140 persons of the control group. The results showed that the frequency of AA, AG and GG genotypes in the population of patients were 0.22%, 0.45% and 0.33% and in control group were 0.37%, 0.41% and 0.22%, respectively. Also, the frequency of A allele in the patients population and control group were0.44% and 0.57%, respectively. However, the G allele frequency in the population of people with recurrent abortion and healthy individuals were estimated 0.56% and 0.43% respectively. Statistical analyzes showed that in this population there was a difference of genotypic and allelic frequencies between the healthy persons and patients with recurrent abortion and therefore rs605059 region polymorphism of HSD17B1 gene was associated with recurrent abortion. One of the main tasks HSD17B1 gene is encoding the 17b-hydroxy steroid dehydrogenase type1 enzyme. This enzyme has a special role in the conversion of estrone to estradiol and this case can be a good justification for the relationship of polymorphisms for this gene with recurrent abortion. So polymorphism of rs605059 and rs676387 genomic regions of HSD17B1 gene can be used as markers for identification of mothers that have more prone to recurrent abortion. But of course, the results of this study are only valid for the studied population and to be able to use this polymorphism of the genomic regions as genetic markers, this results must be approved on other researches that done on other populations.

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