Iran J Public Health, Vol. 44, No.12, Dec 2015, pp.1655-1661

Original Article

Prevalence of Null Genotypes of Glutathione S-Transferase T1 (*GSTT1*) and M1 (*GSTM1*) in Seven Iranian Populations

Gholamreza NASSERI, Tahereh ZAHEDI, Fatemeh MOUSAVI-KAZEROONI, *Mostafa SAADAT

Dept. of Biology, College of Sciences, Shiraz University, Shiraz, Iran

***Corresponding Author:** Email: saadat@shirazu.ac.ir

(Received 15 Feb 2015; accepted 11 Jul 2015)

Abstract

Background: Previous studies have revealed significant differences between populations for genotypic frequencies of glutathione S-transferase T1 (*GSTT1*) and M1 (*GSTM1*) polymorphisms. In order to find the frequency of the null genotypes of *GSTM1* and *GSTT1* in Iranian populations, the present study was carried out.

Methods: The total study subjects consisted of 1340 unrelated healthy Muslims/Iranian. From these 297, 200, 123, 168, 152, 200, and 200 individuals from Tabriz (East Azerbaijan Province; belong to Azaris), Yasuj (Kohgiluyeh-va-Boyerahmad Province; belong to Lurs), Abarku (Yazd Province; belong to Persians), Zahedan (Sistan-va-Balouchestan Province; belong to Balouchis), Zahedan (Sistan-va-Balouchestan Province; belong to Sistanis), Kermanshah (Kermanshah Province; belong to Kurds), and Gorgan (Golestan Province; belong to Turkmen) respectively. The genotypes were detected by multiplex PCR.

Results: The frequency of *GSTM1* null genotype among Azaris, Lurs, Persians, Balouchis, Sistanis, Kurds, and Turkmen was 43.8, 50.0, 52.0, 50.0, 51.3, 56.0, and 53.0%, respectively. There was no significant difference between these populations for the genotypic distribution of the *GSTM1* polymorphism (χ^2=8.47, df=6, *P*=0.206). The frequency of *GSTT1* null genotype among Azaris, Lurs, Persians, Balouchis, Sistanis, Kurds, and Turkmen was 18.2, 17.0, 29.3, 20.8, 17.8, 18.5, and 23.0%, respectively. There was very similarity between Azaris, Kurds and Lurs for the frequency of *GSTT1* genotypes (χ^2=0.17, df=2, *P*=0.916).

Conclusion: By comparing the frequency of *GSTT1* genotypes among Iranian populations, Caucasians and Asians, it is concluded that Azaris, Kurds and Lurs were similar to each other. Taken together, it is suggested that although Azaris are Turkish speaking belong to Caucasians.

Keywords: Iran, *GSTT1, GSTM1,* Population genetics

Introduction

Glutathione S-transferases (GSTs; EC 2.5.1.18), a superfamily of dimeric phase II metabolic enzymes, play an important role in the cellular defense system. In human, cytosolic GSTs have been divided into several families including mu and theta gene families. Genetic polymorphisms in genes encoding *GSTM1* (a member of class mu; OMIM: 138350), and *GSTT1* (a member of class theta; OMIM: 600436) have been well defined. The GSTM1-0 and GSTT1-0 alleles represent deletions of *GSTM1* and *GSTT1* genes, respectively and result in a loss of enzymatic activity (1, 2). A large number of association studies have been performed on *GSTM1* and *GSTT1* polymorphisms and susceptibility to several multifactorial traits (3-21). The prevalence of null genotypes of *GSTT1* and *GSTM1* varies in different ethnic groups (3, 22-24).

Over the past 4 decades, several reports were published in Iranian population genetics (21-36). They have investigated the distribution of some genetic polymorphisms of serum protein, red cell enzymes, and blood groups among Iranian populations (25-27). Iranian population is one of the most heterogeneous populations of the world (27). During 10 years ago, the frequencies of some genetic polymorphisms from several Iranian populations using DNA analysis have been reported (21-24, 28-36).

The Turkish-speaking Azaris is one of the most important Iranian ethnic groups. In addition, they are the major ethnic group in Republic of Azerbaijan, which borders Iran in the west north. They are living in several provinces of Iran including West and East-Azerbaijan, Ardabil and Zanjan. These provinces are located to west north of Iran. Azaris belong to Shiite sect of Muslims.

Lurs (the other Iranian ethnic group) distributed in several provinces, which mainly located in central, south-west and west parts of the country. Their language is a particular dialect of Persian. They are living in "Lorestan", "Chaharmahal va Bakhtiari", "Khuzestan", "Isfahan", "Fars", "Bushehr" and "Kohgiluyeh va Boyer-Ahmad" provinces. Traditionally, Lurs is divided into two majors groups named "Greater Lurs", and "Lesser Lurs". Greater Lurs includes "Chaharmahal-va-Bakhtiari", "Kohgiluyeh-va-Boyerahmad" and parts of "Fars", "Khuzestan" and "Isfahan" provinces. The lesser Lurs is more or less the area that is today known as the "Lorestan" province. Lurs belong to Shiite sect of Muslims.

The Turkish-speaking Turkmen is another most important Iranian ethnic group. In addition, they are the major ethnic group in Republic of Turkmenistan, which borders Iran in the East-north. They are living in Golestan province. Turkmen belong to Sunni sect of Muslims.

Balouchis and Sistanis are two Iranian ethnic groups living in Sistan-va-Balouchestan province (southeast Iran). In addition, Balouchis are living in several provinces of Pakistan and Afghanistan. Based on linguistic and historical studies these ethnic groups are related to Persians. Balouchis and Sistanis belong to Sunni and Shiite sect of Muslims, respectively.

Kurds are distributed in several countries, including Iran, Iraq, Turkey, and Syria. Their language is a particular dialect of Persian. Some populations of Kurds are belonging to Shiite sect and the others belong to Sunni sect of Muslims. Our participants belong to Shiite sect which living in Kermanshah (West of Iran).

Based on several facts (including population genetics, linguistic and historical studies) investigators believed that Kurds and Lurs are belong to Iranian gene pool. However, some investigators (especially who had history background) believe that Azaris belong to Turk gene pools. Turkish-speaking Azaris showed very similarity with Persians and other Caucasian populations for two genetic polymorphisms of insertion/deletion in intron 3 of *XRCC4* (rs28360071) and insertion/deletion on *ACE* (rs4646994) (35, 36).

Based on our knowledge, there is none published data about genetic polymorphisms of *GSTT1* and *GSTM1* in Iranian Azaris, Lurs, Kurds, Turkmen, Balouchis and Sistanis populations. In order to find the frequency of null genotypes of *GSTM1* and *GSTT1* in Iranian populations and comparing populations with each other, the present study was carried out.

Materials and Methods

Subjects

The total study subjects consisted of 297, 200, 123, 168, 152, 200, and 200 individuals from Tabriz (East Azarbaijan province; belong to Azaris), Yasuj (Kohgiluyeh-va-Boyerahmad Province; belong to Lurs), Abarku (Yazd Province; belong to Persians), Zahedan (Sistan-va-Balouchestan Province; belong to Balouchis), Zahedan (Sistan-va-Balouchestan Province; belong to Siatanis), Kermanshah (Kermanshah Province; belong to Kurds), and Gorgan (Golestan Province; belong to Turkmen) respectively. All individuals were healthy as assessed by medical history. Data on ethnicity were collected using a simple questionnaire including simple questions like the parental and grandparental ethnicity of each participant.

Participants that their mothers and fathers (and their grandparental) did not belong to same ethnic groups were excluded. Because *GSTs* polymorphisms showed significant association with several multifactorial diseases (3-21), we excluded the participants with positive history for diagnosed cancers, psychiatric disorders, asthma, cataract and cardiovascular diseases.

Written informed consent was obtained from each participant. This study was approved by the Shiraz University Ethics Committee. This work is carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for Ethical Principles for Medical Research Involving Human Subjects.

DNA extraction and genotyping analysis

Blood samples were obtained from the participants. Immediately after collection, whole blood was stored at -20 °C until use. Genomic DNA for PCR was extracted from whole blood. Genetic polymorphisms for *GSTT1* and *GSTM1* were detected by multiplex PCR as described previously (18). The absence of amplified product was consistent with the null genotypes of *GSTT1* and *GSTM1*. Successful amplification by □-globin specific primers confirmed the proper function of the PCR reaction.

A negative control containing all reagents but water instead of the DNA template was included to each amplification set. To test for contamination, negative controls (tubes containing the PCR mixture, without the DNA template) were incubated in every run. Any sample with ambiguous result due to low yield was retested and a random selection of 15% of all samples was repeated. No discrepancies were discovered upon replicate testing.

Statistical analysis

The difference in genotype frequencies between ethnic groups was determined using the Chi-square test of goodness of fit. Data analysis was performed using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) (version 11.5). A probability of $P<0.05$ was considered statistically significant.

Results

The frequency of *GSTM1* null genotype among Azaris, Lurs, Persians, Balouchis, Sistanis, Kurds, and Turkmen was 43.8, 50.0, 52.0, 50.0, 51.3, 56.0, and 53.0%, respectively (Table 1). There was no significant difference between these populations for the genotypic distribution of the *GSTM1* polymorphisms ($\chi^2=8.47$, df=6, $P=0.206$).

Table 1: Prevalence of *GSTT1* and *GSTM1* polymorphisms in different ethnic groups of Iranian populations

Ethnic		Number	%	Number	%
Azaris	297	54	18.2	130	43.8
Persians	123	36	29.3	64	52.0
Lurs	200	34	17.0	100	50.0
Balouchis	168	35	20.8	84	50.0
Sistanis	152	27	17.8	78	51.3
Kurds	200	37	18.5	112	56.0
Turkmens	200	46	23.0	106	53.0

*For distribution of the *GSTT1* polymorphism $\chi^2=10.26$, df=6, $P=0.114$

**For distribution of the *GSTM1* polymorphism $\chi^2=8.47$, df=6, $P=0.206$

The frequency of null genotype of *GSTT1* among Azaris, Lurs, Persians, Balouchis, Sistanis, Kurds, and Turkmen was 18.2, 17.0, 29.3, 20.8, 17.8, 18.5, and 23.0%, respectively (Table 1). Among study ethnic groups, Lurs showed very low frequency of *GSTT1* null genotype (17.0%). Other groups showed higher prevalence. The observed difference between populations for prevalence of *GSTT1* null genotype was not statistically significant ($\chi^2=10.26$, df=6, $P=0.114$). The prevalence

of *GSTT1* null genotype was higher in Persians, Balouchis and Turkmen in comparison with the other populations (Azaris, Lurs, Siatnis, and Kurds). There was very similarity between Azaris, Kurds and Lurs for the frequency of *GSTT1* genotypes (χ^2=0.17, df=2, *P*=0.916).

Table 2: Distribution of the *GSTT1* and *GSTM1* null genotypes in Asia and Europe

Country/ethnic	*GSTT1* (%)	*GSTM1* (%)	Ref.
Asian			
China	46.6	55.8	35
Japan	48.5	48.9	35
Republic of Korea	52.0	52.7	35
Singapore	42.6	47.6	35
Thailand	47.2	30.2	35
India	16.7	23.7	35
Mongolia	46.8	35.8	35
Turkey	22.5	36.7	35
Afghanistan (Pashtuns)	7.4	42.4	36
Afghanistan (Tajiks)	25.3	48.4	36
Afghanistan (Hazaras)	25.0	52.5	36
Afghanistan (Uzbeks)	29.0	40.3	36
Iran (Georgians, Feridonshahr)	15.7	46.3	28
Iran (Persians, Feridonshahr)	35.3	58.8	28
Iran (Persians, Shiraz)	24.8	49.6	27
Iran (Lurs, Yasuj)	17.0	50.0	Present study
Iran (Azaris, Tabriz)	18.2	43.8	Present study
Iran (Persians, Abarku)	29.3	52.0	Present study
Iran (Baluchis, Zahedan)	20.8	50.0	Present study
Iran (Sistanis, Zahedan)	17.8	51.3	Present study
Iran (Kurds, Kermanshah)	18.5	56.0	Present study
Iran (Turkmen, Gorgan)	23.0	53.0	Present study
Iran (Tehran)	33.3	48.5	21
Iran (Persians, Tonekabon)	15.0	41.6	31
Iran (Kurds, Kermanshah)	15.7	52.8	32
Europe			
Italy	17.9	49.8	35
Slovakia	18.3	50.8	35
Spain	22.2	49.4	35
Portugal	25.5	53.5	35
Netherland	20.3	47.1	35
Poland	17.3	49.8	35
Greece	10.5	47.6	35
Germany	17.3	50.9	35
France	17.3	50.9	35
Hungary	13.8	47.0	35
Denmark	11.9	53.9	35
Belgium	16.1	51.4	35
Finland	12.4	46.4	35
Sweden	14.0	54.0	35

Discussion

Table 2 shows the prevalence of *GSTT1* and *GSTM1* null genotypes in several populations. The null genotype of *GSTT1* showed specific geographical distribution (37). Overall, the frequency of *GSTT1* null genotype showed distinct differences in Caucasians and Asians.

It has low prevalence in north of Europe and increase from north to south and west to east of Europe. The same trends were present in Asia (3, 37). Based on the published data Korean and Japanese populations have high frequency of the null genotype of *GSTT1* (37).

Our present findings showed that the prevalence of *GSTT1* null genotype among Azaris is very similar to other Iranian populations such as Persians, and Iranian Georgians (Firidonshahr, Isfahan Province, Iran) (3-5, 23).

On the other hand, the frequency of *GSTT1* null genotype among Azaris (18.2%) showed similarity with the prevalence of null genotype of *GSTT1* among Tajiks (25.3%) and Pashtuns (7.4%) (Afghanistan) (38) and other Caucasian populations (3, 22, 23, 37). Allelic frequencies of other genetic polymorphisms such as angiotensin-converting enzyme (39) and *CYP2D6* (40) in Iranian Azaris showed similarity with Persians and Caucasians and revealed significant differences with the east-Asians populations. Taken together, it might be suggested that Azaris belong to Caucasians. Therefore, Azaris are Turkish speaking and not Turkish origin. Based on the allelic frequencies for several genetic polymorphisms, which reported form Turkey seems more similarity with Caucasian populations than East Asian populations (3, 22, 28, 29, 37). Based on prevalence of alleles of HLA polymorphisms, it is reported that Turks and Germans were equally distant to Mongolian populations, which are confirming the lack of strong genetic relationship between the Mongols and the Turks despite the relationship of their languages (41). Therefore, we believe that peoples living in Turkey also are Caucasians. It is self-evident that Iranian Azaris and Turkish people mixed with Mongolian and east-Asian people. Linguistically it is probable that Mongolian language and Turkish loosely belong to same family language. Mongolia is the original homeland of both Turks (such as Seljuks) and Mongols. In addition, we know that during several centuries that migration of Turk elements occurred into the Azaris territories and other parts of Iran and Afghanistan (like great Khorasan). It is interesting that prevalence of *GSTT1* null genotype among Azaris, Kurds and Lurs is more similar to Caucasians than Persian of Abarku. Finally based on our recent studies on two genetic polymorphisms of insertion/deletion in intron 3 of *XRCC4* (rs28360071) and insertion/deletion on *ACE* (rs4646994), Azaris showed very similarity with other Iranian populations and Caucasians (35, 36), which confirmed our suggestion.

Conclusion

Based on our knowledge, there is no published report from Republic of Azerbaijan for frequency of GSTs polymorphisms. Therefore, now, it is impossible to determine differences between the gene pools of Iranian Azaris and Republic of Azerbaijan. By comparing the frequency of *GSTT1* genotypes among Iranian populations, Caucasians and Asians, it is concluded that Azaris, Kurds and Lurs were similar to each other.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgments

The authors are indebted to the participants for their close cooperation. This study was supported by Shiraz University. The authors declare that there is no conflict of interests.

References

1. Harada S, Misawa S, Nakamura T, Tanaka N, Ueno E, Nozoe M (1992). Detection of *GST1*

gene deletion by the polymerase chain reaction and its possible correlation with stomach cancer in Japanese. *Hum Genet,* 90:62-64.
2. Pemble S, Schroeder KR, Spencer SR, Meyer DJ, Hallier E, Bolt HM, Ketterer B, Taylor JB (1994). Human glutathione S-transferase theta (*GSTT1*): cDNA cloning and the characterization of a genetic polymorphism. *Biochem J*, 300:271-276.
3. Saadat M (2006). Genetic polymorphisms of glutathione S-transferase T1 (*GSTT1*) and susceptibility to gastric cancer: a meta-analysis. *Cancer Sci,* 97:505-509.
4. Saadat M, Ansari-Lari M (2007). Genetic polymorphism of glutathione S-transferase T1, M1 and asthma, a meta-analysis of the literature. *Pak J Biol Sci*, 10:4183-4189.
5. Ansari-Lari M, Saadat M, Hadi N (2004). Influence of *GSTT1* null genotype on the offspring sex ratio of gasoline filling station workers. *J Epidemiol Community Health*, 58:393-394.
6. Zintzaras E (2009). Glutathione S-transferase M1 and T1 genes and susceptibility to chronic myeloid leukemia: a meta-analysis. *Genet Test Mol Biomarkers*, 13:791-797.
7. Wang B, Huang G, Wang D (2010). Null genotypes of *GSTM1* and *GSTT1* contribute to hepatocellular carcinoma risk: evidence from an updated meta-analysis. *J Hepatol*, 53:508-518.
8. Zhang ZJ, Hao K, Shi R, Zhao G, Jiang GX, Song Y, Xu X, Ma J (2011). Glutathione S-transferase M1 (*GSTM1*) and glutathione S-transferase T1 (*GSTT1*) null polymorphisms, smoking, and their interaction in oral cancer: a HuGE review and meta-analysis. *Am J Epidemiol*, 173:847-857.
9. Gao LB, Pan XM, Li LJ, Liang WB, Bai P, Rao L, Su XW, Wang T, Zhou B, Wei YG, Zhang L (2011). Null genotypes of *GSTM1* and *GSTT1* contribute to risk of cervical neoplasia: an evidence-based meta-analysis. *PLoS One*, 6:e20157.
10. S˘antl Letonja M, Letonja M, Ikolajevic-Starãevic JN, Petrovic D (2012). Association of manganese superoxide dismutase and glutathione S-transferases genotypes with carotid atherosclerosis in patients with diabetes mellitus type 2. *Int Angiol*, 31:33-41.
11. Saadat M, Saadat I, Saboori Z, Emad A (2004). Combination of *CC16*, *GSTM1*, and *GSTT1* genetic polymorphisms is associated with asthma. *J Allergy Clin Immunol*, 113:996-998.
12. Saadat M, Mobayen F, Farrashbandi H (2007). Genetic polymorphism of glutathione S-transferase T1: a candidate genetic modifier of individual susceptibility to schizophrenia. *Psychiatry Res*, 153:87-91.
13. Hu G, Yao W, Zhou Y, Hu J, Shi Z, Li B, Ran P (2008). Meta- and pooled analyses of the effect of glutathione S-transferase M1 and T1 deficiency on chronic obstructive pulmonary disease. *Int J Tuberc Lung Dis,* 12:1474-1481.
14. Wang J, Zou L, Huang S, Lu F, Lang X, Han L, Song Z, Xu Z (2010). Genetic polymorphisms of glutathione S-transferase genes *GSTM1*, *GSTT1* and risk of coronary heart disease. *Mutagenesis,* 25:365-369.
15. Saadat M, Farvardin-Jahromi M (2006). Occupational sunlight exposure, polymorphism of glutathione S-transferase M1, and senile cataract risk. *Occup Environ Med*, 63:503-504.
16. Sun L, Xi B, Yu L, Gao XC, Shi DJ, Yan YK, Xu DJ, Han Q, Wang C (2010). Association of glutathione S-transferases polymorphisms (*GSTM1* and *GSTT1*) with senile cataract: a meta-analysis. *Invest Ophthalmol Vis Sci*, 51:6381-6386.
17. Masoudi M, Saadat I, Omidvari S, Saadat M (2009). Genetic polymorphisms of *GSTO2*, *GSTM1*, and *GSTT1* and risk of gastric cancer. *Mol Biol Rep,* 36:781-784.
18. Mohammadynejad P, Saadat I, Ghanizadeh A, Saadat M (2011). Bipolar disorder and polymorphisms of glutathione S-transferases M1 (*GSTM1*) and T1 (*GSTT1*). *Psychiatry Res*, 186:144-146.
19. Sun F, Chen Y, Xiang Y, Zhan S (2008). Drug-metabolising enzyme polymorphisms and predisposition to anti-tuberculosis drug-induced liver injury: a meta-analysis. *Int J Tuberc Lung Dis*, 12:994-1002.
20. Borst L, Buchard A, Rosthøj S, Wesolowska A, Wehner PS, Wesenberg F, Dalhoff K, Schmiegelow K (2012). Gene dose effects of *GSTM1*, *GSTT1* and *GSTP1* polymorphisms on outcome in childhood acute lymphoblastic leukemia. *J Pediatr Hematol Oncol*, 34:38-42.
21. Mandegary A, Rostami S, Alimoghaddam K, Ghavamzadeh A, Ghahremani MH (2011). Glutathione-S-transferase T1-null genotype predisposes adults to acute promyelocytic leu-

kemia; a case-control study. *Asian Pac J Cancer Prev*, 12:1279-1282.
22. Saadat M, Saadat I (2012). Prevalence of G6721T polymorphism of *XRCC7* in an Iranian population. *EXCLI Journal,* 11:93-97.
23. Rafiee L, Saadat I, Saadat M (2010). Glutathione S-transferase genetic polymorphisms (*GSTM1*, *GSTT1* and *GSTO2*) in three Iranian populations. *Mol Biol Rep* 37:155-158.
24. Saadat M, Zendeh-Boodi Z (2008). Association between genetic polymorphism of *GSTT1* and depression score in individuals chronically exposed to natural sour gas. *Neurosci Lett*, 435:65-68.
25. Amirshahi P, Sunderland E, Farhud DD, Tavakoli SH, Daneshmand P, Papiha SS (1989). Serum proteins and erythrocyte enzymes of populations in Iran. *Hum Hered*, 39:75-80.
26. Amirshahi P, Sunderland E, Farhud DD, Tavakoli SH, Daneshmand P, Papiha SS (1992). Population genetics of the peoples of Iran I. Genetic polymorphisms of blood groups, serum proteins and red cell enzymes. *Inter J Anthrop*, 7:1-10.
27. Papiha SS, Amirshahi P, Sunderland E, Farhud DD, Tavakoli SH, Daneshmand P (1992). Population genetics of the people of Iran II. Genetic differentiation and population structure. *Inter J Anthrop,* 7:11-18.
28. Saadat M, Farhud DD (2005). Frequency of genetic polymorphism of the gene encoding 16KDa Clara cell secretory protein (*CC16*) in Shiraz, Iran. *Iran J Public Health,* 34:27-30.
29. Mohamadynejad P, Saadat M (2008). Genetic polymorphisms of *XRCC1* (at codons 194 and 399) in Shiraz population (Fars province, southern Iran). *Mol Biol Rep*, 35:669-672.
30. Zendeh-Boodi Z, Saadat M (2008). Genetic polymorphism of *GSTT1* may be under natural selection in a population chronically exposed to natural sour gas. *Mol Biol Rep*, 35:673-676.
31. Ansari BS, Vasudevan R, Mirinargesi M, Patimah I, Sabariah AR, Pasalar P, Bakhshi A (2009). Lack of Association of glutathione S-transferase gene polymorphisms in Iranian prostate cancer subjects. *Am J Biochem Biotechnol*, 5:30-34.
32. Nomani H, Mozafari H, Mohamadzadeh-Ghobadloo S, Zohreh Rahimi Z, Vaisi-Raygani A, Rahimi MA, Haghi A, Keshavarz AA (2011). The association between *GSTT1*, *M1*, and *P1* polymorphisms with coronary artery disease in Western Iran. *Mol Cell Biochem*, 354:181-187.
33. Nafissi S, Saadat I, Saadat M (2011). Genetic polymorphisms of glutathione S-transferase Z1 in an Iranian population. *Mol Biol Rep,* 38:3391-3394.
34. Bazrgar M, Karimi M, Fathzadeh M, Senemar S, Peiravian F, Shojaee A, Saadat M (2008). Apolipoprotein E polymorphism in Southern Iran: E4 allele in the lowest reported amounts. *Mol Biol Rep,* 35:495-499.
35. Fallahzadeh-Abarghooei L, Zahedi T, Mirabedi F, Saadat M (2015). Alleleic prevalence of intron 3 insertion/deletion genetic polymorphism of DNA double-strand break repair gene *XRCC4* in four Iranian populations. *Egypt J Med Hum Genet*, 16:215-218.
36. Saadat M (2015). Distribution of *ACE* insertion/deletion (I/D) polymorphism in Iranian populations. *Mol Biol Res Commun*, 4:63-66.
37. Saadat M (2007). *GSTM1* null genotype associated with age-standardized cancer mortality rate in 45 countries from five continents: an ecologic study. *Int J Cancer Res*, 3:74-91.
38. Saify K, Saadat I, Saadat M (2012). Genetic polymorphisms of glutathione S-transferase T1 (*GSTT1*) and M1 (*GSTM1*) in selected populations of Afghanistan. *Mol Biol Rep,* 39:7855-7859.
39. Abdi-Rad I, Bagheri M (2011). Angiotensin-converting enzyme insertion/deletion gene polymorphism in general population of west Azarbaijan, Iran. *Iran J Kidney Dis*, 5:86-92.
40. Kouhi H, Hamzeiy H, Barar J, Asadi M, Omidi Y (2009). Frequency of five important *CYP2D6* alleles within an Iranian population (Eastern Azerbaijan). *Genet Test Mol Biomarkers*, 13:665-670.
41. Machulla HK, Batnasan D, Steinborn F, Uyar FA, Saruhan-Direskeneli G, Oguz FS, Carin MN, Dorak MT (2003). Genetic affinities among Mongol ethnic groups and their relationship to Turks. *Tissue Antigens*, 61:292-299.