Interleukin-10 Gene Polymorphisms in Coronary Artery Disease from Visakhapatnam

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Abstract

Introduction: Coronary Artery Disease (CAD), also called Coronary Heart Disease or (CHD) is caused by the narrowing of the large blood vessels that supply the heart with oxygen. It is the third leading cause of mortality worldwide and is associated with 17.8 million deaths annually. Coronary artery disease prevalence increases after 35 years of age in both men and women. CAD is a multifactorial disease including multiple genetic and environmental factors and their interactions. The production of IL-10 is thought to be genetically controlled and hence IL-10 polymorphisms may be a crucial factor in the differential production of this protein and thus, determination of polymorphisms can be beneficial in predicting the probability of incidence of CAD.

Aim: The aim of the present study was to investigate the association of IL-10 (G1082A) and IL-10 (C592A) gene polymorphisms in CAD patients and Controls from Visakhapatnam city.

Materials and Methods: A total of 400 samples (200 CAD patients and 200 controls) were included in the present study and genotyping was accomplished by using PCR – RFLP technique. Data was analyzed by SPSS 19 software.

Results: The, G allele and C allele frequencies of IL-10 (G1082A) and IL-10 (C592A) gene polymorphisms were higher in Controls than CAD patients, whereas, A allele and A allele frequencies were higher in CAD patients than Controls. The GG and CC genotype frequencies of IL-10 (G1082A) and IL-10 (C592A) gene polymorphisms were higher in Controls than CAD patients, whereas, GA+AA and CA+AA genotype frequencies were higher in CAD patients than Controls.

Conclusions: It was concluded from the present study that the allelic frequencies of chi-square p-values shows association with IL-10 (G1082A) gene polymorphism and lack of association was found in IL-10 (C592A) gene polymorphism and genotype frequencies of odds ratio p-values were found to be statistically significant with IL-10 (G1082A) and insignificant with IL-10 (C592A) genes polymorphisms in the study population.
Keywords: Coronary artery disease, Coronary Heart Disease, Interlukin-10, Polymerase Chain Reaction, Restriction Fragment Length Polymorphism.

INTRODUCTION:

Coronary Artery Disease (CAD), also called Coronary Heart Disease or (CHD) is caused by the narrowing of the large blood vessels that supply the heart with oxygen. These are called coronary arteries. Arteries that have become extremely narrow can cause shortness of breath and chest pain during physical activity. If a coronary artery suddenly becomes completely blocked, it can result in a heart attack. CAD can also lead to other health problems like heart failure or heart rhythm problems. Various treatments can be used to reduce the symptoms and the risk of complications.

Coronary artery disease accounts for approximately 6,10,000 deaths annually (estimated 1 in 4 deaths) and is the leading cause of mortality in the United States (Friede et al., 1996). It is the third leading cause of mortality worldwide and is associated with 17.8 million deaths annually (GBD, 2017; Lloyd-Jones et al., 2010; Nichols et al., 2014; Writing Group Members, 2008). Coronary artery disease prevalence increases after 35 years of age in both men and women. CAD is a multifactorial disease including multiple genetic and environmental factors and their interactions.

Interleukin-10 has a complex and predominantly opposing roles in inflammation and plays a major role in suppressing immune and inflammatory responses (Blake & Ridker, 2002). Its effects are directed mainly against functions of mononuclear cells, T lymphocytes and polymorphonuclear leukocytes. The best documented of these polymorphisms are the IL-10 gene promoter polymorphisms -1082G/A, -819C/T and -592C/A (de Jong et al., 2002; Koss et al., 2000). The human IL-10 gene is located on chromosome 1 and has been mapped to the junction between 1q31 and 1q32 (Eskdale et al., 1997; Kim et al., 1992). IL-10 is a member of the immunoregulatory cytokine family. Many studies have indicated that polymorphisms in the IL-10 gene are correlated with pathogenesis of coronary artery disease in different populations and however, the results remain conflicting (Blagodatskikh et al., 2010; Elsaid et al., 2014; Guo et al., 2012; Koch et al., 2001; Liu et al., 2013; Ren & She, 2015). Therefore, an attempt was made in the present study to find out the Interlukin-10 genes polymorphisms responsible for the occurrence of CAD in Visakhapatnam city.

MATERIALS AND METHODS:

The present study was carried out with 200 CAD patients (119 males and 81 females) from care hospital, Visakhapatnam and 200 age and sex matched controls (119 males and 81 females) above 20 years from Visakhapatnam city, during the period 2019-2020. The study was approved by the institutional ethical committee for blood sample collection. The information content was obtained from each participant before collecting the blood sample for evolution of molecular parameters.
Collection of blood samples:

About 5 ml of blood was drawn intravenously using the disposable sterilized syringes and collected in test tubes containing 0.2 ml of 15% EDTA as anticoagulant solution. The contents of the tubes were mixed thoroughly and kept in thermos flask containing the ice cubes. The blood samples collected were carefully brought to the Human Genetics Laboratory of Andhra University immediately for molecular analysis.

Molecular Analysis

DNA extraction:

The genomic DNA was extracted from peripheral blood by using salting out method. Genotyping was performed by polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) technique.

Statistical Analysis:

The data was analyzed by using Statistical Package of Social Sciences Software program (SPSS) 19 was used for calculating genotype and allele frequencies. Chi-square analysis was used to test for allele frequencies and odds ratio analysis was used to test for genotype frequencies in comparison of patients and healthy control groups. P value ≤ 0.05 considered statistically significant.

Results:

Table 1: Genotypes and allelic frequencies of IL-10 (G1082A) and IL-10 (C592A) gene polymorphisms in CAD patients and Controls

<table>
<thead>
<tr>
<th>Genotypes and Alleles</th>
<th>CAD patients N=200%</th>
<th>Controls N=200%</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10(G1082A)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG</td>
<td>76 (38.00%)</td>
<td>116 (58.00%)</td>
<td>1</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>GA</td>
<td>104 (52.00%)</td>
<td>77 (38.50%)</td>
<td>0.4851</td>
<td>0.3210 -0.7331</td>
<td>0.000**</td>
</tr>
<tr>
<td>AA</td>
<td>20 (10.00%)</td>
<td>7 (3.50%)</td>
<td>0.2293</td>
<td>0.0925 -0.5686</td>
<td>0.001**</td>
</tr>
<tr>
<td>G</td>
<td>256 (64.00%)</td>
<td>309 (77.25%)</td>
<td>Chi-square value 16.925</td>
<td>0.000**</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>144 (36.00%)</td>
<td>91 (22.75%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-10 (C592A)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>89 (44.50%)</td>
<td>101 (50.50%)</td>
<td>1</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>CA</td>
<td>90 (45.00%)</td>
<td>86 (43.00%)</td>
<td>0.8420</td>
<td>0.5585 -1.2695</td>
<td>0.4117</td>
</tr>
<tr>
<td>AA</td>
<td>21 (10.50%)</td>
<td>13 (6.50%)</td>
<td>0.5455</td>
<td>0.2582 -1.1526</td>
<td>0.1123</td>
</tr>
<tr>
<td>C</td>
<td>268 (67.00%)</td>
<td>288 (72.00%)</td>
<td>Chi-square value 2.359</td>
<td>0.000**</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>132 (33.00%)</td>
<td>112 (28.00%)</td>
<td></td>
<td></td>
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</tbody>
</table>

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant.
Table-1 shows that the genotype frequency of GG (58.00%) was higher in controls than CAD patients (38.00%) whereas, the frequency of genotype GA (52.00%) was higher in CAD patients than Controls (38.50%). The genotype frequency of AA (10.00%) was higher in CAD patients than Controls (3.50%). The odds ratio p-values of genotypes GA and AA were found to be statistically significant. The frequency of G allele was 64.00% in CAD patients and 77.25% in Controls. The A allelic frequencies in CAD patients and Controls were 36.00% and 22.75% respectively. The chi-square p value reveals that IL-10 (G1082A) gene polymorphism shows association with CAD.

The genotype frequency of CC (50.50%) was higher in Controls than CAD patients (44.50%) whereas, the frequency of genotype CA (45.00%) was higher in CAD patients than Controls (43.00%). The genotype frequency of AA (10.50%) was higher in CAD patients than Controls (6.50%). The odds ratio p-values of genotypes CA and AA were found to be statistically insignificant. The frequency of C allele was 67.00% in CAD patients and 72.00% in Controls. The A allelic frequencies in CAD patients and Controls were 33.00% and 28.00% respectively. The chi-square p-value reveals that IL-10 (C592A) gene polymorphism does not shows association with CAD.

Table 2: IL-10 (G1082A) gene polymorphism and its interaction with IL-10 (C592A) in CAD patients and Controls

<table>
<thead>
<tr>
<th>IL-10 (G1082A) GG v/s CAD patients N=200%</th>
<th>Controls N=200%</th>
<th>Odds ratio 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10 (C592A)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>33 (16.50%)</td>
<td>67 (33.50%)</td>
<td>1</td>
</tr>
<tr>
<td>CA</td>
<td>48 (24.00%)</td>
<td>51 (25.50%)</td>
<td>0.507</td>
</tr>
<tr>
<td>AA</td>
<td>06 (3.00%)</td>
<td>2 (1.00%)</td>
<td>0.136</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IL-10 (G1082A) GA+AA v/s IL-10 (C592A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
</tr>
<tr>
<td>CA</td>
</tr>
<tr>
<td>AA</td>
</tr>
</tbody>
</table>

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant

Table 2 represents the IL-10 (G1082A) gene polymorphism and its interaction with IL-10 (C592A) in CAD patients and Controls. It is evident that the GG genotype of IL-10 (G1082A) gene polymorphism was statistically significant with CA and AA genotype of IL-10 (G592A) gene polymorphism and the GA and AA genotype of IL-10 (G1082A) gene polymorphism was statistically insignificant with IL-10 (C592A) gene polymorphism.
Figure 1: PCR – RFLP of Gel Electrophoresis pattern of IL-10 G1082A by using restriction enzyme *BseR1*

Lane M: 100 bp ladder
Lane: 3, 5 showing GG (homozygous wild type) genotype with 477 bp
Lane: 1, 4, 7 showing GA (heterozygous) genotype with 477 bp, 377 bp & 100 bp
Lane: 2, 6 showing AA (homozygous mutant) genotype with 377 bp & 100 bp

For IL-10 G1082A, the PCR product yielded a 477 bp, which on digestion with enzyme *BseR1* produced a homozygous, wild type allele (GG) was identified by the presence of one 477 bp. The heterozygous allele (GA) was identified by 477 bp, 377 bp & 100 bp, while homozygous mutant allele (AA) was identified a 377 bp & 100 bp.

Figure 2: PCR – RFLP of Gel Electrophoresis pattern of IL-10 C592A by using restriction enzyme *RsaI*

Lane M: 100 bp ladder
Lane: 2, 5 showing CC (homozygous wild type) genotype with 412 bp
Lane: 3, 6, 7 showing CA (heterozygous) genotype with 412 bp, 236 bp & 176 bp
Lane: 1, 4 showing AA (homozygous mutant) genotype with 236 bp & 176 bp

For IL-10 C592A, the PCR product yielded a 412 bp, which on digestion with enzyme *RsaI* produced a homozygous, wild type allele (CC) was identified by the presence of one 412 bp. The
heterozygous allele (CA) was identified by 412 bp, 236 bp & 176 bp, while homozygous mutant allele (AA) was identified a 236 bp & 176 bp.

**DISCUSSION:**

In most cases, coronary artery disease has a multifactorial genetic basis, involving a number of genes and environmental factors, which are interacting to determine whether or not the disease will develop as well as its severity (Freitas et al., 2008). Genetic factors differ in various populations. Among these, Interleukins (ILs) IL-6 and IL-10 genes polymorphisms have received extensive attention and have been proposed as a CAD risk factors.

Interleukins-10 is widely viewed as an anti inflammatory mediator and is thought to play a critical role in a number of pathophysiological conditions like atherosclerosis and its acute complications. Therefore, IL-10 gene appears to be a good candidate for coronary artery disease studies. Some studies have shown inconsistent results on this IL-10 gene promoter polymorphisms and cardiovascular diseases (Densem et al., 2003; Kube et al., 1995; Turner et al., 1997).

In the present study, the frequency of G allele was 64.00% in CAD patients and 77.25% in controls. The A allelic frequencies in CAD patients and controls were 36.00% and 22.75% respectively. The chi-square p-value reveals that IL-10 (G1082A) gene polymorphism shows association with CAD. The genotype frequency of GG (58.00%) was higher in controls than CAD patients (38.00%) whereas, the frequency of genotype GA (52.00%) was higher in CAD patients than controls (38.50%). The genotype frequency of AA (10.00%) was higher in CAD patients than controls (3.50%). The odds ratio p-values of genotypes GA and AA were found to be statistically significant.

In the present study, the frequency of C allele was 67.00% in CAD patients and 72.00% in controls. The A allelic frequencies in CAD patients and controls were 33.00% and 28.00% respectively. The chi-square p-value reveals that IL-10 (C592A) gene polymorphism does not shows association with CAD. The genotype frequency of CC (50.50%) was higher in controls than CAD patients (44.50%) whereas, the frequency of genotype CA (45.00%) was higher in CAD patients than controls (43.00%). The genotype frequency of AA (10.50%) was higher in CAD patients than controls (6.50%). The odds ratio p-values of genotypes CA and AA were found to be statistically insignificant.

The results of (Muhammad et al., 2012), show that in Pakistani population, IL-10 haplotypes have no association with cardiovascular disease susceptibility as previously reported in Japanese (Oda et al., 2007), German (Koch et al., 2001; Koch et al., 2003) and Caucasian patients(Densem et al., 2003; Perrey et al., 1998). In Pakistani CAD patients, IL-10 -1082 GG is frequent in patients while IL-10
G1082A is the genotype, which showed negative association with disease. It was reported by (Blanco et al., 2008) that IL-10 -1082 G does not have any role in transcription of IL-10 gene by its own. A study of (Ma larstig et al., 2008), on 3634 individuals predicts that genetic effect of these Single Nucleotide Polymorphisms (SNPs) on IL-10 plasma level was relatively small. A study on large number of 3634 patients from Sweden favor the (Blanco et al., 2008) statement, IL-10 G1082A showed no association with CAD but IL-10 plasma level were high in patients then control. Patients with high IL-10 showed high death rate in myocardial infraction as compared with patients having low IL-10 plasma level (Ma larstig et al., 2008). In contrast, the studies of (Anguera et al., 2002; Tziakas et al., 2003) showed elevation of IL-10 serum level associated with decreased risk of coronary events. Previously IL-10 -1082 GG was high in healthy in North Italy (Lio et al., 2004) and showed no significant association in studies from France (Donger et al., 2001), Japan (Oda et al., 2007), South Italy (Lio et al., 2004), Germany (Koch et al., 2001) and Caucasian population (Perrey et al., 1998).

The study of (Elsaid et al., 2014) shows the frequency distribution of Interleukins-10 (G1082A) in CAD patients was significantly different, as compared to controls and G allele being more frequent in CAD patients than A allele. Therefore, presence of G allele or homozygosity of G allele of IL-10 (G1082A) might be associated with an increased prevalence of CAD. This finding was in good agreement with the study of (Blagodatskikh et al., 2010) suggesting that these polymorphisms are associated with a high risk of developing hypertension, unstable angina, Myocardial Infarction (MI) and CAD. A previous study of (Malarstig et al., 2006) has also reported similar results. On the other hand, study of (Koch et al., 2003) has found that polymorphisms of the genes for IL-10 do not represent genetic markers, indicating the risk of restenosis, death or MI after coronary stenting. Also, it is found that frequency distribution of IL-10 (G1082A) is not significantly different in the Mexican patients than control subjects (Fragoso et al., 2011).

The human Interleukins-10 gene contains three important gene locus mutations upstream of the transcription start site including IL-10 (G1082A), (C819T) and (C592A) (Kim et al., 1992; Turner et al., 1997). Previous studies have demonstrated that the IL-10 gene is affected by these upstream polymorphisms (Eskdale et al., 1998; Koch et al., 2001; Lio et al., 2004; Turner et al., 1997) and however, the results have been inconsistent. (Turner et al., 1997) reported that the three single base pair substitutions in the IL-10 gene promoter were correlated with IL-10 protein production in vitro. In the study of (Eskdale et al., 1998) suggested that a haplotype of IL-10 was associated with the highest overall IL-10 secretion and that the levels of secreted IL-10 could vary in humans according to the genetic composition of the IL-10 locus. However, more recent reports have demonstrated elevated levels of IL-10 associated with promoter polymorphisms (Assis et al., 2014; Heiskanen et al., 2010).
Several previous studies have reported the association between Interleukins-10 gene polymorphisms and CAD risk, but these results have also been controversial (Elsaid et al., 2014; He et al., 2014; Jin et al., 2013; Yu et al., 2012). (Elsaid et al., 2014) conducted a case-control study in an Indian population and reported that the C allele of IL-6 -174G/C (rs1800795) and the G allele of IL-10 (G1082A) (rs1800896) were associated with an increased risk of CAD. (Yu et al., 2012) conducted a study in a Korean population and reported that the IL-10 C592A and C819T gene polymorphisms might be associated with ischemic heart disease. However, in the study of (He et al., 2014) in a Chinese population, it was reported that IL-10 gene polymorphism was not correlated with the risk of CAD. In contrast, in a meta analysis of (Wang et al., 2012), fourteen case-control studies with a total of 5006 patients and 3968 controls, it was reported that the IL-10 G1082A gene polymorphism might be associated with an increased overall risk of CAD, especially in Caucasians. The results of (Yang et al., 2015) suggested that the IL-10 G1082A (rs1800896) polymorphism was associated with an increased risk of CAD. The discrepancy between these studies might be caused by differences in populations, study design and sample size.

Previous studies have reported an association between polymorphisms in the IL-10 gene and the development of cardiovascular disease (Elsaid et al., 2014; Jin et al., 2013; Karaca et al., 2011; Lin et al., 2014; Yu et al., 2012) and however, the results of these studies have been inconsistent. (Jin et al., 2013), in a study comprising 249 patients and 132 unaffected controls selected from a Chinese population, reported an association between the IL-10 C592A polymorphism and increased risk of coronary heart disease. On the other hand (Elsaid et al., 2014), conducted a case-control study with 108 Egyptian patients with coronary artery disease and 143 healthy subjects, reported that the G allele of IL-10 G1082A was associated with an increased prevalence of coronary artery disease. Meanwhile (Lin et al., 2014), reported a correlation between polymorphisms in the IL-10 gene (IL-10 G1082A) and the development of coronary artery aneurysm in a Taiwanese population (Lin et al., 2014). However, other studies have reported inconsistent results.

(Karaca et al., 2011) discovered an association between the IL-10 G1082A polymorphism and the development of coronary heart disease, while IL-10 T819C and C592A did not. A meta-analysis of (Chao et al., 2014) comprising sixteen studies suggested that the IL-10 G1082A polymorphism was associated with an increased risk of atherosclerosis. (Wang et al., 2012), in a meta analysis of six case-control studies conducted in a Caucasian population, suggested that the A allele of IL-10 G1082A contributed to increased risk of coronary heart disease. In the study of (Xu & Liu, 2015), the A allele of IL-10 G1082A was correlated with increased risk of coronary artery disease. The AA and GA+AA genotypes of the IL-10 G1082A polymorphism were found to be associated with an elevated risk of coronary artery disease. The discrepancies among the above results may be attributed to ethnic variations, differences in the source of patients and sample size and to chance.
(Wu et al., 2016) attempted to estimate the relationship between the Interleukins-10 G1082A and C592A genetic polymorphisms and CAD risk and they discovered a correlation between the CC genotype and C allele of IL-10 G1082A and increased CAD risk in the Chinese population. Moreover, the IL-10 C592A polymorphism had no association with development of CAD.

In regards to the role of Interleukin-10 G1082A and C592A polymorphisms in CAD risk, several previous studies have reported conflicting results (Blagodatskikh et al., 2010; Elsaid et al., 2014; Koch et al., 2001; Ren & She, 2015; Yang et al., 2015). (Blagodatskikh et al., 2010) evaluated the association of the IL-10 G1082A genetic variation with the development of CAD in a Russian population and discovered that IL-10 G1082A genetic polymorphism could influence the risk of CAD. (Ren & She, 2015) done a study in a Chinese population and revealed that IL-10 G1082A is correlated with an increased risk of CAD. However, some studies reported inconsistent results. (Guo et al., 2012) observed that IL-10 G1082A was unlikely to be a significant biomarker to CAD susceptibility in the Han Chinese population. (Koch et al., 2001) carried out a study in a German 998 patients with CAD and 340 control subjects and did not reported correlation of IL-10 G1082A and C592A polymorphisms with the risk of CAD. Further studies with larger scale samples are required to validate these findings.

In the hospital based case-control study of the (Liang et al., 2016), they assessed the role of IL-10 G1082A gene polymorphism (rs1800896) in the development of CAD. Their results indicated that IL-10 G1082A polymorphism is associated with an increased risk of CAD. Several studies reported an association between IL-10 G1082A polymorphism and the development of coronary artery diseases and however, the results were inconclusive (Elsaid et al., 2014; Guo et al., 2012; Li et al., 2015; Ren & She, 2015). (Li et al., 2015) conducted a case-control study in the Chinese population and did not find any association between IL-10 G1082A polymorphism and the risk of coronary artery diseases.

The distribution of Interleukin-10 G1082A and C592A genotypes as well as allele frequencies were not significantly different between patients with Coronary Heart Diseases (CHD) and the controls in the study of (Karaca et al., 2011) which was in agreement with many previous studies (Donger et al., 2001; Koch et al., 2001; McGlinchey et al., 2004). There are many studies evaluating the effect of gene polymorphisms on the occurrence of CHD in younger ages (≤45 years old) (Atherosclerosis, Thrombosis, and Vascular Biology Italian Study Group, 2003; De Caterina et al., 2011; Isordia-Salas et al., 2010; Isordia-Salas et al., 2010).

In the study reported by (Koch et al., 2001) allele frequencies, genetic distributions and frequencies of allele combinations for IL-10 G1082A, C819T and C592A promoter polymorphisms were similar between patients with MI, coronary artery disease patients and matched controls. (Donger et al., 2001) also investigated the genotypes of the same three IL-10 promoter polymorphisms and allele frequencies in 1107 patients with MI and their results suggested no association between IL-10
polymorphisms and increased risk of MI. In the study of (McGlinchey et al., 2004) examined polymorphisms in the promoter regions of the pro inflammatory cytokine IL-6 (-174G/C), anti inflammatory cytokines IL-10 (G1082A) genes in the susceptibility to Ischemic Heart Disease (IHD). They demonstrated that the genotypes of these polymorphisms and allele frequencies were not associated with IHD in Irish population. On the other hand, no significant difference between CHD and IL-10 C592A polymorphism has been found in a study of (Hsueh et al., 2009). (Trompet et al., 2007) performed a genetic association study of four IL-10 promoter single nucleotide polymorphisms (A4259G, G1082A, C592A and G2849A) with coronary and cerebrovascular events in participants at risk for vascular disease. They found that the -592C/A polymorphism in the promoter region of the IL-10 gene was associated with coronary events. Genotype -592AA was reported to reduce IL-10 production in cultures of peripheral blood mononuclear cells treated with interferon (Mallat et al., 1999). The AA genotype was associated with lower IL-10 production in both patients and healthy controls (McGlinchey et al., 2004).

Studies have been conducted in subjects from different ethnicities worldwide suggesting its diverse role in the pathogenesis of CAD. The PROSPER study conducted in Ireland, Scotland and Netherlands on 5,804 subjects revealed a significant risk association with the coronary events (Trompet et al., 2007). Similarly in study (Fragoso et al., 2011) carried out on 389 Mexican patients with Acute Coronary Syndrome (ACS) and 302 healthy controls a highly significant p-value was observed. Another epidemiological study of (Xie et al., 2013) carried on 1652 Chinese individuals, reports significantly associated with ischemic stroke even after controlling for covariates. In context to North Indian population, (Madeshiya et al., 2017) carried out a study on 384 patients and 386 controls and found the mutant allele A of IL-10 -592C > A polymorphism to be higher among the cases (40.1%) when compared to controls (34.2%) and the dominant model showed an association with the disease. But in the study of (Kaur et al., 2018), they observed only a marginal difference in the minor allele frequency among controls and cases (35.8% v/s 36.8%) and a protective association was seen in dominant model whereas risk association was reported in recessive model showing that two copies of the mutant alleles are required for the disease manifestation.

In contrast to their findings, the meta analysis by (Xuan et al., 2016), systematic review with meta analysis, trial sequential analysis, medicine, 2016, showed no relationship of this polymorphism and CVD risk. Similarly, no significant association between the IL-10 C592A polymorphism and CAD risk was observed by (Koch et al., 2001; Wang et al., 2015; Yao et al., 2016). However a study carried out in Kolkata, India by (Biswas et al., 2014) on 500 MI patients and 500 controls revealed no association of mean plasma levels of IL-10 and the three genotypes. Such differences in results might occur due to the different populations being studied, different criteria for the selection of patients and control subjects, difference in the sample sizes and different techniques used for genotyping the samples.
Genetic polymorphisms may have different effects on protein development based on the type of tissue and cell. Therefore, more studies are required to examine the role of IL-10 gene alleles in the development of CAD. IL-10 is just a single player among genes involved in atherosclerosis and thus play a minor role in the complex molecular pathways in CAD. Future studies are expected to examine with larger populations to find better understand the disease.

CONCLUSIONS

It was concluded from the present study revealed that the allelic frequencies of chi-square p-values shows association with IL-10 (G1082A) and lack of association was found in IL-10 (C592A) gene polymorphisms and genotype frequencies of odds ratio p-values were found to be statistically significant with IL-10 (G1082A) and insignificant with IL-10 (C592A) gene polymorphism in study population.

Gene-Gene interaction conclusions reveal that, the GG genotype of IL-10 (G1082A) gene polymorphism was statistically significant with CA and AA genotype of IL-10 (G592A) gene polymorphism and the GA and AA genotype of IL-10 (G1082A) gene polymorphism was statistically insignificant with IL-10 (C592A) gene polymorphism.

REFERENCES


