RELATIONSHIP OF TNF-α-308, IL-10-1082 GENE POLYMORPHISMS WITH THE SEVERITY AND SUSCEPTIBILITY OF RHEUMATIC HEART DISEASE

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Background

Acute rheumatic fever is an inflammatory disease developing after upper respiratory tract infection with group A streptococci and its most important complication is rheumatic heart disease. Recent studies emphasize the importance of IL-10 and TNF-α gen polymorphism in the pathogenesis. There are limited numbers of studies reporting TNF-α-308 and IL-10-1082 gene polymorphism may induce susceptibility to rheumatic heart disease. Gene polymorphisms change depending on race, and in Turkey there is no study on IL-10-1082 gene polymorphism in the patients with ARA. However, there are only two studies on TNF-α-308 of which results were conflicting. The aim of our study is to determine the frequency of IL-10-1082 A/G and TNF-α-308 G/A gene polymorphism in Turkish population and to investigate the relationship between these polymorphisms and rheumatic heart disease.

Methods

In this case-control study, the relationship between G/A polymorphisms in TNF-α-308 gene, A/G polymorphism in IL-10-1082 gene and rheumatic heart disease and valvular involvement. A total 57 patients with rheumatic heart disease and 99 healthy controls were included.

Results

The rate of TNF-α-308 gene polymorphism was %3,1 in healthy subjects and this polymorphism was not observed in patients with rheumatic heart disease. In healthy subjects, the frequency of IL-10-1082 gene polymorphism was higher than the patients with rheumatic heart disease.

There was no relation between TNF-α-308 genotype and allele distribution with valvular involvement (p>0.05). IL-10-1082 G/G and A/G genotypes were seen more frequent in patients with multiple valvular disease but there was no statistical significance (p>0.05).

Discussion

TNF-α is a cytokine that plays a crucial role on the pathogenesis of the rheumatic fever. The studies conducted in Mexico and Brazil have reported the relation between TNF-α-308 polymorphism and rheumatic heart disease.

Table 1. Allele and genotype frequencies of TNF-α-308 and IL-10-1082 in patients and controls

	Patients	Controls	P	OR	95% CI
TNF-α-308	**(n=57)**	**(n=97)**			
Genotypes					
GG (%)	45 (78.9)	64 (66)		1.0 (ref)	
AG (%)	12 (21.1)	30 (30.9)	NS	0.569	0.263-1.230
AA (%)	0	3 (3.1)	NS	0.202	0.010-4.017
Alleles					
A (%)	12 (10.5)	36 (18.6)	NS	0.516	0.257-1.039
G (%)	102(89.5)	158 (81.4)	NS	1.937	0.963-3.897
IL-10-1082	**(n=54)**	**(n=82)**			
Genotypes					
GG (%)	5 (9.3)	9 (11)	NS	0.654	0.196-2.180
AG (%)	21 (38.9)	40 (48.8)	NS	0.618	0.298-1.283
AA (%)	28 (51.9)	33 (40.2)		1.0 (ref)	
Alleles					
A (%)	77 (71.3)	106 (64.6)	NS	1.359	0.803-2.299
G (%)	31 (28.7)	58 (35.4)	NS	0.736	0.435-1.245

OR= Odds ratio; 95% CI=95% confidence intervals; NS=not significant.

Moreover, they also found out that in the patients with multivalvar disease, the frequency of the TNF-α-308 *A/A* polymorphism has increased. There are only two studies in Turkey about the relationship of which the results are in conflict. In this study, no relations between TNF-α-308 polymorphism and rheumatic heart disease were detected. In the literature, there is only one study conducted on the *IL-10-1082* polymorphism in the patients with rheumatic heart disease who have demonstrated a positive relation in between. On the other hand, in this study, we couldn't observe any significant relations.

Table 2. Allele and genotype frequencies of TNF-α-308 and IL-10-1082 in patients with different valve damage

	SVL	MVL	P	OR	95% CI
TNF-α-308	**(n=26)**	**(n=31)**			
Genotypes					
GG (%)	21 (80.8)	24 (77.4)	NS	0.816	0.225±2.961
AG (%)	5 (19.2)	7 (22.6)	NS	1.225	0.338±4.443
AA (%)	0	0			
Alleles					
A (%)	5 (9.6)	7 (11.3)		1.196	0.356±4.019
G (%)	47 (90.4)	55 (88.7)		0.836	0.249±2.808
IL-10-1082	**(n=25)**	**(n=29)**			
Genotypes					
GG (%)	1 (4)	4 (13.8)	NS	4.610	0.456±46.673
AG (%)	9 (36)	12 (41.4)	NS	1.538	0.492±4.808
AA (%)	15 (60)	13 (44.8)		1.0 (ref)	
Alleles					
A (%)	39 (78)	38 (65.5)	NS	0.536	0.227±1.267
G (%)	11 (22)	20 (34.5)	NS	1.866	0.789±4.413

OR= Odds ratio; 95% CI=95% confidence intervals; SVL= single valvular lesions (mitral or aortic); MVL= multivalvular lesions; NS=not significant.

Conclusions

There was no relationship between TNF-α-308, IL-10-1082 gene polymorphisms and rheumatic heart disease or valvular involvement in the study population (p>0.05).

TNF-α-308 polymorphisms are silent and may become important only with some certain HLA allels.

Studies checking both cytokine polymorphism and HLA alleles are needed.