American Journal of Medicine and Medical Sciences 2025, 15(3): 547-550
DOI: 10.5923/j.ajmms.20251503.12

Studying the Significance of IL-1, IL-6, IL-10 Gene Polymorphisms and Gene Interaction in Predicting Acute Pancreatitis

Tursunov Firdavs Nuriddinovich[1], Ismailov Uktam Safaevich[2], Boboev Kadirjon Tukhtabevich[3]

[1]Assistant, Department of Surgical Diseases and Family Medicine, Termez Branch of Tashkent Medical Academy, Termiz, Uzbekistan
[2]Doctor of Medical Sciences, Professor, Head of the Department of Surgical Diseases, Tashkent Medical Academy Tashkent, Uzbekistan
[3]Doctor of Medical Sciences, Professor, Republican Specialized Hematology Scientific and Practical Medical Center, Tashkent, Uzbekistan

Abstract This article provides information on the significance of interleukin gene polymorphisms and their interaction in predicting the development of acute pancreatitis, as well as on the combination of IL-1, IL-6, IL-10 genes that cause pancreatic necrosis.

Keywords Acute pancreatitis, Hereditary interaction, Gene polymorphism, Genetic mechanisms, Interleukin-1, Interleukin-6, Interleukin-10, and the mutual significance of genes

1. Introduction

Acute pancreatitis (AP) is one of the most common gastrointestinal diseases with variable characteristics, making it difficult to predict in its early stages [2]. In turn, despite the use of modern diagnostic methods for acute pancreatitis and contemporary conservative and surgical treatment approaches, mortality rates remain high, ranging from 7.5-15.2%, and reaching 40-70% in the destructive form. Mortality in the first week after hospitalization is associated with the development of multiple organ failure in 35-50% of cases [1]. Approximately 80% of patients develop mild to moderate pancreatitis. However, about 20% of patients develop severe acute pancreatitis, which leads to serious complications and a mortality rate of 20-30% [6]. To this day, severe acute pancreatitis remains unpredictable and difficult to manage with modern intensive therapy due to its progression and high mortality rates. Severe acute pancreatitis is often accompanied by serious complications, and the occurrence of these complications is frequently a significant reason for prolonging the duration of the illness, increasing hospitalization time, and raising mortality rates [3]. The APACHE II and SOFA scales significantly improve the treatment of patients with aseptic pancreatic necrosis using minimally invasive methods. No significant differences were observed in the group of patients with infected pancreatic necrosis [4]. Studying some research indicates that cytokine levels, including IL-1b, IL-6, IL-8, and IL-10, may be associated with the occurrence of early complications of acute pancreatitis (AP). Among them, IL-6 has a relatively good prognostic value. Identifying cytokines that are highly upregulated in the AP process during the current era of monoclonal antibodies and other targeted therapies may provide information for future directions in targeted therapy research. As cytokines are inexpensive, reproducible, and non-invasive markers of systemic inflammation, monitoring IL-6 levels within 48 hours after AP onset helps predict the clinical outcomes of these patients [7]. In pancreatitis, molecular genetic studies that identify the genetic basis of the disease play an important role in developing new approaches to treatment strategies and predicting the course of the disease for each individual [5].

Objective: To investigate the role of cytokine gene polymorphisms IL-1 (rs16944), IL-6 (rs1800795), and IL-10 (rs1800896) in the development of acute pancreatitis among the Uzbek population.

Received: Feb. 3, 2025; Accepted: Feb. 28, 2025; Published: Mar. 8, 2025
Published online at http://journal.sapub.org/ajmms

2. Materials and Methods

The study material consisted of 88 patients who were hospitalized with various forms of acute pancreatitis and had blood samples taken between 2021 and 2022 in the surgical departments of the Surkhandarya branch of the Republican Scientific Center for Emergency Medical Care, Tashkent City Clinical Hospital No. 7, and the Republican Scientific Center for Emergency Medical Care. For the control group, DNK from 81 practically (relatively or conditionally) healthy individuals was used from the DNK bank stored at the RSNPMCH (Republican Specialized Scientific and Practical Medical Center of Hematology). In the main group of patients, 50 (56.8%) were women and 38 (43.2%) were

men. The control group of 81 healthy individuals consisted of 39 (48.1%) men and 42 (51.9%) women. The age of patients in the main group ranged from 18 to 84 years. According to the World Health Organization (WHO) classification, we divided patients into 4 age groups. The 18-44 year age range comprised 36 (40.9%) patients, 45-60 years - 31 (35.2%), 61-74 years - 18 (20.5%), and 75 years and older - 3 (3.4%).

We categorized the patients in our study into subgroups according to the ATLANTA classification: 57 patients with acute edematous pancreatitis; 15 patients with sterile pancreatic necrosis; and 16 patients with infected pancreatic necrosis.

Venous blood samples were collected from all subjects for molecular genetic research. Genomic DNA was isolated using the standard phenol-chloroform extraction method. Genotyping of polymorphisms in the IL-1b (rs16944), IL-6 (rs1800795), and IL-10 (rs1800896) genes was performed on a CFX96 amplifier using TaqMan probes (Bio-Rad Laboratories, USA) through allele discrimination with real-time polymerase chain reaction, following protocols published in the literature. To verify the quality of genotyping, 10% of the samples were randomly selected as "working controls" and subjected to re-analysis, which yielded results identical to the original. The chi-square test and odds ratio (OR with 95% confidence interval (CI)) were employed to assess the allelic and genotypic associations of the studied gene polymorphisms with the risk of acute pancreatitis. Statistical analysis was performed using the Statistics 6.0 software ("StatSoft" USA). The level of statistical significance was set at $p<0.05$.

3. Research Results

Results of examining the polymorphism of the interleukin-1β T-511C (rs16944) gene.

Table 1. Distribution of frequencies of polymorphic markers of the IL-1β T-511C gene in patients with acute pancreatitis and in the population control group

Polymorphism		Allele, genotype	Main group (n=88)		Control group (n=81)		χ^2, p, OR (95% CI)
			n	%	n	%	
IL-1 (rs16944)	Allele	T	96	54,5	107	79,4	χ^2= 4.65, p = 0.031; OR= 0.62 (0.4- 0.96)
		C	80	45,5	55	20,6	
	Genotype	TT	25	28,4	35	43,2	χ^2= 4.04, p = 0.045; OR= 0.52 (0.28- 0.99)
		TC	46	52,3	37	45,7	χ^2= 0.73, p = 0.39; OR= 1.3 (0.71- 2.38)
		CC	17	19,3	9	11,1	χ^2= 2.18, p = 0.14; OR= 1.9 (0.8- 4.58)

The analysis results based on the study of polymorphic markers of the IL-1b gene showed that the allele IL-1b (rs16944) had a significantly higher probability of influencing the occurrence of acute pancreatitis ($\chi2$=4.65, p=0.031, OR=0.62; (0.4 - 0.96)). When examining this condition at the genotype level, the influence of the TT-dominant homozygous genotype of IL-1b (rs16944) was found to be highly significant ($\chi2$=4.04, p=0.045; OR=0.52 (0.28-0.99)). However, the analysis of heterozygous (TC) and recessive homozygous (CC) genotypes of IL-1b (rs16944) revealed that these genotypes have practically no role in the development of acute pancreatitis ($\chi2$= 0.73, p=0.39; OR=1.3 (0.71-2.38) and $\chi2$=2.18, p=0.14; OR=1.9 (0.8-4.58)).

Results of examining the Interleukin-6 C-174G (rs1800795) gene polymorphism.

Table 2. Distribution of frequencies of polymorphic markers of the IL-6 C-174G factor genes in patients with acute pancreatitis and in the population control group

Polymorphism		Allele, genotype	Main group (n=88)		Control group (n=81)		χ^2, p, OR (95% CI)
			n	%	n	%	
IL-6 (rs1800795)	Allele	C	127	72,2	99	61,1	χ^2= 4.65, p = 0.031; OR= 1.65 (1.04- 2.6)
		G	49	27,8	63	38,9	
	Genotype	CC	48	54,6	31	38,3	χ^2= 4.49, p = 0.034; OR= 1.94 (1.05- 3.58)
		CG	31	35,2	37	45,7	χ^2= 1.92, p = 0.17; OR= 0.65 (0.35- 1.2)
		GG	9	10,2	13	16	χ^2= 1.26, p = 0.26; OR= 0.6 (0.24- 1.48)

The results of the analysis, based on the study of polymorphic markers of the interleukin-6 gene, showed that the IL-6 C-174G allele ($\chi2$=4.65, p=0.031, OR=1.65; (1.04 - 2.6)) had a significantly higher probability of influencing the occurrence of acute pancreatitis. When studying this condition at the genotype level, the influence of the dominant homozygous genotype IL-6 C-174G CC was found to be highly significant ($\chi2$=4.49 p=0.034; OR=1.94 (1.05-3.58)). However, in the analysis of heterozygotes (CG) and recessive homozygotes (GG) of the IL-6 C-174G genotype, these genotypes were found to have practically no role in the development of acute pancreatitis ($\chi2$= 1.92, p=0.17; OR=0.65 (0.35-1.2) and $\chi2$=1.26, p=0.26; OR=0.6 (0.24-1.48)).

Results of examining the polymorphism of the interleukin-10 (rs1800896) gene.

Table 3. Distribution of frequencies of polymorphic markers of the IL-10 G-1082A (rs1800896) gene in patients with acute pancreatitis and in the population control group

Polymorphism		Allele, genotype	Main group (n=88)		Control group (n=81)		χ^2, p, OR (95% CI)
			N	%	n	%	
IL- 10 (rs1800896)	Allele	G	115	65,3	115	71	χ^2= 1.24, p = 0.27; OR= 0.77 (0.49- 1.22)
		A	61	34,7	47	29	
	Genotype	GG	41	46,6	42	51,8	χ^2= 0.47, p = 0.49; OR= 0.81 (0.44- 1.48)
		GA	33	37,5	31	38,3	χ^2= 0.01, p = 0.92; OR= 0.97 (0.52- 1.8)
		AA	14	15,9	8	9,9	χ^2= 1.36, p = 0.24; OR= 1.73 (0.68- 4.36)

The results of the analysis, based on the study of polymorphic markers of the interleukin-10 gene, showed that the probability of IL-10 G-1082A (rs1800896) ($\chi2$= 1.24, p = 0.27; OR= 0.77 (0.49-1.22)) influencing the occurrence of acute pancreatitis was statistically insignificant at the allele level. When examining this at the genotype level, it was found that the influence of IL-10 GG dominant homozygous ($\chi2$= 0.47, p=0.49; OR=0.81 (0.44-1.48)), GA heterozygous ($\chi2$=0.01, p=0.92; OR= 0.97 (0.52-1.8)), and AA homozygous ($\chi2$=1.36, p=0.24; OR=1.73 (0.68-4.36)) genotypes was also statistically insignificant, similar to the alleles.

Analysis of intergenic and gene-environment interactions in acute pancreatitis.

Table 4. Analysis of the association of paired combinations of genotypes IL-1b T-511C (rs16944), IL-6 C-174G (rs1800795), and IL-10 G-1082A (rs1800896) showed (p>0.05)

Genotype/allele	Patients with acute pancreatitis (n=88)		Healthy individuals (n=81)		p	OR
	n	%	n	%		
IL 1b (rs16944)+ IL 6 (rs1800795)	28	31,8	11	13,6	χ^2= 7.9, p = 0.005	OR= 2.97 (1.36- 6.46)
IL 1b (rs16944)+ IL 10 (rs1800896)	29	33	15	19,8	χ^2= 4.56, p = 0.033	OR= 2.16 (1.06- 4.42)
IL 6 (rs1800795)+ IL 10 (rs1800896)	17	19,3	11	12,6	χ^2= 1.05, p = 0.32	OR= 1.5 (0.67- 3.48)
IL 1b (rs16944)+ IL 6 (rs1800795)+ IL 10 (rs1800896)	14	15,9	7	8,8	χ^2= 2.05, p = 0.15	OR= 2 (0.76- 5.24)

4. Conclusions

Based on the data from our study, it has been determined that predicting the development of acute pancreatitis and pancreonecrosis using genetic analysis has a positive effect on treatment strategies. The study of gene polymorphisms of interleukin-1b T-511C (rs16944), interleukin-6 C-174G (rs1800795), and interleukin-10 (rs1800896) is recommended as a method for determining susceptibility to acute pancreatitis. Furthermore, carrying the T allele of the Interleukin-1b T-511C gene and the C allele of the IL-6 C-174G gene is a risk factor for the development of inflammatory pancreatic diseases, and their combination indicates a high likelihood of developing destructive forms of pancreatitis. The co-occurrence of genotypes of the Interleukin-1b T-511C and Interleukin-10 G-1082A gene polymorphisms plays a significant role in the development and prediction of acute pancreatitis and pancreonecrosis.

REFERENCES

[1] B.R. Abdullajanov, Clinical-epidemiological aspects of acute biliary pancreatitis and features of treatment-diagnostic tactics. Diss, 2020. Uzbekistan.

[2] Mederos MA, Reber HA, Girgis MD. Acute Pancreatitis: A Review. JAMA. 2021; 325(4): 382–390. doi:10.1001/jama.2020.20317.

[3] Nina Gliem, Christoph Ammer-Herrmenau, Volker Ellenrieder, Albrecht Neesse; Management of Severe Acute Pancreatitis: An Update. Digestion 29 June 2021; 102(4): 503–507. https://doi.org/10.1159/000506830.

[4] Rizaev E.A., Kurbanyiazov Z.B., Abdurakhmanov D.Sh. Differentiated approach to surgical treatment of severe acute pancreatitis with prediction of treatment results. Uzbek journal of case reports. 2024; 4(3): 6-11. https://doi.org/10.55620/ujcr.4.3.2024.1.

[5] Tursunov F.N., Ismailov U.S., Madatov K.A., Sharapov A.N., Matmuratov S.K. The role of some interleukins in the development of acute pancreatitis. O‘zbekiston xirurgiyasi №2 2024. 118-120.

[6] Chan KS, Shelat VG. Diagnosis, severity stratification and management of adult acute pancreatitis–current evidence and controversies. World J Gastrointest Surg 2022; 14(11): 1179-1197 [PMID: PMC9727576 DOI: 10.4240/wjgs.v14.i11.1179.

[7] Yao J, Zhang S, Zhou F, Zhuang M, Fei S. The relationship between inflammatory cytokines and in-hospital complications of acute pancreatitis. Immun Inflamm Dis. 2024; 12: e1203. doi:10.1002/iid3.1203.