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The Impact of Cationic Trypsinogen (PRSS1) Gene Polymorphism on the Prognosis of Acute Pancreatitis

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Abstract This article examines the impact of the Arg122His polymorphism in the PRSS1 gene on the incidence of acute pancreatitis. In the mechanism of acute pancreatitis development, environmental factors play an important role alongside genetic factors. Ethnic differences in the frequency distribution of alleles and genotypes of this gene's polymorphic variant were identified. Further advancement of molecular genetic research through studying the genetic basis of pancreatitis is crucial for developing new diagnostic methods and determining treatment strategies with an individualized approach to each patient.

Keywords Cationic trypsinogen (PRSS1), Gene polymorphism, Emergency abdominal conditions, Pathological reactions

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1. Introduction

Acute pancreatitis is one of the most pressing issues in modern medicine. For several years, it has ranked second, and in some regions even first, among urgent surgical diseases. In terms of growth rate, acute pancreatitis surpasses all other emergency abdominal conditions [1,4,5]. Along with the increasing number of patients with acute pancreatitis, there is a trend towards a higher proportion of fatal cases. The persistently high mortality rate in acute pancreatitis is associated with the complex, multi-level pathogenesis of the disease, and some mechanisms of pathological reactions remain unclear to this day [2,4,6,8].

One of the most advanced areas in the study of acute pancreatitis is the investigation of genetic predisposition factors for severe forms of the disease. Currently, several mutations have been identified that are considered the main factors of hereditary predisposition to pancreatitis. For instance, due to a mutation in the cationic trypsinogen gene (PRSS1), trypsinogen becomes resistant to autolysis and prone to mild autoactivation, which can lead to the development of genetically determined acute pancreatitis. A mutation in the pancreatic secretory trypsin inhibitor gene (SPINK1) disrupts trypsin inactivation in pancreatic tissues, resulting in the activation of pancreatic enzymes, proteolytic necrosis of pancreatic tissues, and lysis of venule walls [3,7,9].

At present, numerous studies are dedicated to the genetic aspects of pancreatitis; however, in clinical practice, a spectrum of genetic polymorphisms suitable for comprehensive diagnosis of pancreatitis has not been established. The literature often contains conflicting information about the role of specific polymorphisms in the pathogenesis of pancreatitis and the importance of their detection. There are also discrepancies between the research findings of European and Asian scientific centers. Therefore, determining the optimal diagnostic spectrum of genetic polymorphisms allows for timely prediction of acute pancreatitis development.

The aim of our study was to predict and improve treatment outcomes for acute pancreatitis by evaluating the clinical significance of cationic trypsinogen (PRSS1) gene polymorphisms.

2. Materials and Methods

This study was conducted in the surgical department of Republican Clinical Hospital No. 1 and in the molecular

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genetics department of RGIAM. To address these issues, we analyzed diagnostic and treatment measures in 68 patients hospitalized with acute pancreatitis of various etiologies.

To conduct the study, we formed standardized groups based on age and gender, depending on the diagnostic and treatment methods used. Patients were divided into two groups: - main group (n=68), patients with clinical signs of acute pancreatitis; - control group (n=70), healthy individuals, in whom the Arg122His polymorphism in the PRSS1 gene was studied.

The control group consisted of 38 healthy men (n=38) and 32 women (n=32) aged 25 to 66 years (mean age 56.7 ±8.4). The age of patients in the main group ranged from 29 to 75 years (mean age 57.3 ±9.3 years). Of these, 37 (52.2%) were women and 31 (47.8%) were men. Thus, the compared groups of patients were similar in sex distribution (main group: 37 men, 31 women; control group: 38 men, 32 women; χ^2= 0.018, p=0.89) and age (56.7 ±8.4 and 57.3 ±9.3; t=0.048, df=146, p=24.17), and these compared groups did not differ significantly from each other in the aforementioned parameters ($p<0.05$).

The diagnosis of acute pancreatitis is established based on the presence of at least two of the following signs, excluding other surgical pathologies: typical clinical presentation (severe belt-like pain unrelieved by antispasmodics, uncontrolled vomiting, history of alcohol consumption, spicy food intake, or cholelithiasis, etc.); characteristic ultrasound findings: enlargement, decreased echogenicity, and blurred contours of the pancreas; presence of free fluid in the abdominal cavity; hyperenzymeemia (hyperamylasemia or hyperlipasemia) exceeding the upper limit of normal by three times or more.

Samples used for genetic typing were obtained from whole peripheral venous blood. Materials were collected using vacuum tubes with EDTA-K3 anticoagulant applied to the wall. DNA extraction for the analysis of whole blood leukocytes was performed using the "DNA-express-blood" reagent of Russian manufacture (LLC "NPF "Litex," Moscow).

Data analysis was conducted using the "STATISTICA" version 6.0 statistical package, adhering to the principles and requirements of statistical processing of material in biological and medical research.

3. Research Results and Discussion

The PRSS1 gene is located on the long arm of chromosome 7 (location 7q34) and consists of 5 exons encoding cationic trypsinogen (or trypsinogen 1). Cationic trypsinogen comprises 2/3 of the total pancreatic trypsinogen. To date, more than 20 different mutations in the PRSS1 gene have been described, most of which in heterozygous form lead to the development of an autosomal dominant variant of pancreatitis. In this section, we studied the Arg122His polymorphism of the PRSS1 gene.

The study began by examining whether the molecular-genetically studied groups conformed to Hardy-Weinberg equilibrium. The frequency distribution of gene polymorphism genotypes in patients with acute pancreatitis and in the general sample of the Uzbek population corresponded to Hardy-Weinberg equilibrium ($p > 0.05$).

Table 1. Analysis of the study results on the effect of Arg122His polymorphism in the PRSS1 gene on the incidence of acute pancreatitis

Polymorphism		allele, genotype	Main group (n = 68)		Control group (n = 70)		χ^2, p, OR (95% CI)
			n	%	n	%	
Arg122His in the PRSS1 gene	Allele	Arg	133	97,8	139	99,3	χ^2= 1,1, p =0,3; OR= 0,32 (0,03- 3,1)
		His	3	2,2	1	0,7	
	Genotype	Arg/Arg	65	95,6	69	98,6	χ^2= 1,1, p =0,3; OR= 0,31 (0,03- 3,1)
		Arg/His	3	4,4	1	1,4	
		His/His	0	0	0	0.0	

Table 2. Analysis of the study results on the influence of the Arg122His polymorphism in the PRSS1 gene on the frequency of alcoholic (alimentary) acute pancreatitis

Polymorphism		allele, genotype	Main group (n = 68)		Control group (n = 70)		χ^2, p, RR, OR (95% CI)
			n	%	n	%	
Arg122His in the PRSS1 gene	Allele	Arg	55	94,8	139	99.3	χ^2= 4,12, p =0,042; RR=2,64 (1,44-4,9); OR= 7,6 (0,77- 3,1)
		His	3	5,2	1	0.7	
	Genotype	Arg/Arg	26	89,7	69	98,6	χ^2= 3,84, p =0,0499; RR=2,6 (1,4-5); OR= 7,4 (0,74- 74,1)
		Arg/His	3	10,3	1	1,4	
		His/His	0	0	0	0	

Table 3. Influence of PRSS1 (Arg122His) gene polymorphism on the morphological type of acute pancreatitis

Groups	Genotype frequency, %			Allele frequency, %	
	Arg/Arg	Arg/His	His/His	Arg	His
Healthy (n = 70)	69 (98,6%)	1 (1,4%)	0	139 (99,3%)	1 (0,7%)
Acute edematous pancreatitis (n = 45)	44 (64,7%)	1 (1,5%)	0	89 (65,4%)	1 (0,7%)
Sterile and purulent pancreatic necrosis (n = 23)	21 (30,9%)	2 (2,9%)	0	44 (32,4%)	2 (1,5%)
P*	χ^2=0,1; p=0,75; RR=1,2, OR=1,6			χ^2=0,1; p=0,75; RR=1,2, OR=1,6	
P**	χ^2=2,93; p=0,09; RR=2,9, OR=6,6			χ^2=2,88; p=0,09; RR=2,8, OR=6,3	
P***	χ^2=1,51; p=0,22; RR=2,1, OR=4,2			χ^2=1,48; p=0,22; RR=2, OR=4	

p - difference between healthy individuals and patients with acute edematous pancreatitis; p** - difference between healthy individuals and patients with sterile and infected pancreatic necrosis; p*** - difference between patients with acute edematous pancreatitis and patients with sterile and infected pancreatic necrosis*

Analysis of the distribution of genotype and allele frequencies in the control group showed that the frequency of the Arg allele was 99.3%, and the frequency of the His allele was 0.7%. Homozygotes for the Arg allele (genotype Arg/Arg) constituted 98.6% (n=69) of patients, while heterozygotes (genotype Arg/His) accounted for 1.4% (n=1) of patients. The homozygous genotype His/His was not observed in either the patient group or the control group (Table 1).

Analysis results based on the study of polymorphic markers of the PRSS1 gene (Arg122His) showed that the allele (χ2= 1.1, p =0.3; OR= 0.32 (0.03-3.1)), and the probability of genotype influence proved to be statistically insignificant. This indicates the almost complete absence of the role of PRSS1 (Arg122His) genotype polymorphism in the development of acute pancreatitis.

However, when these indicators were studied separately only in patients with alcoholic (alimentary) etiology, different results were obtained (Table 2).

The obtained results show that although the PRSS1 gene polymorphism (Arg122His), which is the main focus of this study, does not have significant importance in the development of acute pancreatitis overall, it plays a statistically significant role (p<0.05) in acute pancreatitis of alcoholic (dietary) etiology.

At the genotype level of the PRSS1 (Arg122His) gene polymorphism in the main group with acute pancreatitis of alcoholic etiology, the Arg/Arg homozygote was found in 26 (89.7%) cases, and the Arg/His heterozygote in 3 (10.3%) cases. Comparison with the control group showed that the probability of acute pancreatitis of alcoholic etiology is significantly higher (χ2= 3.84, p =0.0499), with the relative risk (RR) 2.6 times higher and the odds ratio (OR) 7.4 times higher.

According to the obtained results, the probability of acute pancreatitis of alcoholic etiology also showed high values at the allele level: the probability was significantly higher (χ2= 4.12, p =0.042), the relative risk (RR) was 2.64 times higher, the odds ratio (OR) was 7.6 times higher, the risk in the exposed group (Risk in Exposed) was 75%, the risk in the unexposed group (Risk in Unexposed) was 28.4%, and the overall risk (Overall Risk) was 29.3%.

Consequently, although the Arg122His polymorphism in the PRSS1 gene does not significantly affect the overall indicators of acute pancreatitis, it has a high probability of being involved in the occurrence of acute pancreatitis of alcoholic (dietary) etiology.

One of the main aspects of our research was to study the influence of the investigated gene polymorphisms on the morphological type of acute pancreatitis.

First, we examined the influence of the PRSS1 (Arg122His) gene polymorphism on the morphological type of acute pancreatitis (Table 3).

Table 3 shows the differences between morphological types of acute pancreatitis for the PRSS1 (Arg122His) gene polymorphism. The probability of acute edematous pancreatitis did not differ significantly at the genotype and allele level (χ2=0.1; p=0.75; RR=1.2, OR=1.6; Risk in Exposed=50%, Risk in Unexposed=38.9%, Overall Risk=39.1% and χ^2=0.1; p=0.75; RR=1.2, OR=1.6; Risk in Exposed=50%, Risk in Unexposed=39%, Overall Risk=39.1%). Nevertheless, the probability of this condition was 1.6 (OR) times higher, and the diagnostic value was 50%. There were practically no differences between the genotype and allele.

The study of the probability of sterile and infected pancreatic necrosis in the PRSS1 gene (Arg122His) polymorphism at the genotype and allele levels also did not yield sufficiently reliable results (χ^2=2.93; p=0.09; RR=2.9, OR=6.6). However, it was found that the probability indicators of sterile and infected pancreatic necrosis were somewhat higher than in acute edematous pancreatitis (OR=6.6; Risk in Exposed=66.7% and OR=1.6; Risk in Exposed=50%).

A comparative study of the PRSS1 gene (Arg122His) polymorphism in acute edematous pancreatitis and sterile and infected pancreatic necrosis yielded low indicators both at the genotype and allele levels (χ^2=1.51; p=0.22; RR=2.1, OR=4.2; Risk in Exposed=66.7%, Risk in Unexposed= 32.3%, Overall Risk=33.8% and χ^2=1.48; p=0.22; RR=2, OR=4; Risk in Exposed=66.7%, Risk in Unexposed=33.1%, Overall Risk=33.8%).

Based on the above, it can be concluded that the PRSS1 (Arg122His) gene polymorphism significantly affects the occurrence of acute pancreatitis (p<0.05), but does not have a significant effect on its morphological forms ($p>0.05$). However, it increases the likelihood of necrotic changes several times (OR=6.6).

4. Conclusions

Thus, in the mechanism of acute pancreatitis development, environmental factors play an important role alongside genetic factors. To date, the role of the PRSS1 gene polymorphism (Arg122His), which is involved in the mechanism of pancreatitis development, has been determined. Ethnic differences have been identified in the distribution of allele and genotype frequencies of this gene's polymorphic variant. Further development of molecular genetic research through studying the genetic basis of pancreatitis is crucial for developing new diagnostic methods and determining treatment strategies with an individualized approach to each patient. The PRSS1 gene polymorphisms (Arg122His) we studied have varying effects on the development of acute pancreatitis, its contributing factors (alcohol), and the course of the disease. Notably, the PRSS1 (Arg122His) gene polymorphism plays a significant role in the development of acute pancreatitis in cases of alcoholic pancreatitis.

REFERENCES

[1] Arif, A.; Jaleel, F.; Rashid, K. Accuracy of BISAP score in prediction of severe acute pancreatitis. Pak. J. Med. Sci. 2019, 35, 1008–1012.

[2] Minaga K, Watanabe T, Hara A, et al. Identification of serum IFN-α and IL-33 as novel biomarkers for type 1 autoimmune pancreatitis and IgG4-related disease. Sci Rep 2020; 10: 14879.

[3] Mofidi, R.; Du_, M.;Wigmore, S.; Madhavan, K.; Garden, O.; Parks, R. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br. J. Surg. Inc. Eur. J. Surg. Swiss Surg. 2006, 93, 738–744.

[4] Shul'pekova Yu. O., Kardasheva S. S., Okhlobystin A. V., Ivashkin V. T. The role of genetic factors in the development and progression of pancreatitis. Pediatric Nutrition. 2020; Vol. 18, No. 3. pp. 19-28.

[5] Tarasenko S. V., Natal'skiy A. A., Bogomolov A. Yu., Bakonina I. V., Kadykova O. A., Andrianova K. V. Genetic polymorphisms as predisposing factors for chronic pancreatitis. Experimental and Clinical Gastroenterology. 2018; Vol. 159, No. 11. pp. 38-43.

[6] Toth, E.; Maleth, J.; Zavogyan, N.; Fanczal, J.; Grassalkovich, A.; Erdos, R.; Pallagi, P.; Horvath, G.; Tretter, L.; Balint, E.R.; et al. Novel mitochondrial transition pore inhibitor N-methyl -4-isoleucine cyclosporin is a new therapeutic option in acute pancreatitis. J. Physiol. 2019, 597, 5879–5898.

[7] Vasudevan, S.; Goswami, P.; Sonika, U.; Thakur, B.; Sreenivas, V.; Saraya, A. Comparison of Various Scoring Systems and Biochemical Markers in Predicting the Outcome in Acute Pancreatitis. Pancreas 2018, 47, 65–71.

[8] Watanabe T, Yamashita K, Arai Y, et al. Chronic fibroinflammatory responses in autoimmune pancreatitis depend on IFN-α and IL-33 produced by plasmacytoid dendritic cells. J Immunol 2017; 198: 3886-3896.

[9] Wu, B.U.; Johannes, R.S.; Sun, X.; Tabak, Y.; Conwell, D.L.; Banks, P.A. The early prediction of mortality in acute pancreatitis: A large population-based study. Gut 2018, 57, 1698–1703.