VER
Vascular & Endovascular Review

Frequency Of H.Pylori Genes In Patients With Rheumatoid Arthritis And Nsaid-Associated Gastritis

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ABSTRACT

This article examines the diagnosis and frequency of H. pylori genes in patients with rheumatoid arthritis who have taken NSAIDs. As part of the study, 69 patients were examined, who were divided into 2 groups: patients with gastropathy and patients without gastropathy. The study characterized H. pylori genotypes among patients using molecular genetic analysis. The frequency of H. pylori gene occurrence and their combinations in the examined patients were studied.

KEYWORDS: H.Pylori genotypes, gene combination, rheumatoid arthritis, gastropathy.

How to Cite: Tukhtaeva Nigora Khasanovna, Marufhanov Xamidjan Maxmudovich, Karimov Ma'ruf Shakirovich, Xabibullo Tulqinovich Nurmetov, Aida Abdiganiyevna Eshmurzaeva, Alimov Ulagbek Sadikovich, Mavlyuda Mahmudovna Azimova., (2025) Frequency Of H.Pylori Genes In Patients With Rheumatoid Arthritis And Nsaid-Associated Gastritis, Vascular and Endovascular Review, Vol.8, No.14s, 187-190.

INTRODUCTION

According to modern understanding, rheumatoid arthritis RA is an idiopathic autoimmune disease that proceeds as symmetrical erosive arthritis (synovitis), and also has various types of extra-articular manifestations [1,2]. It is not only a medical but also an economic problem, as it leads to a decrease in the quality of life, early disability, and increased mortality of patients [3-4].

Helicobacter pylori (H.P) is a gram-negative microaerophilic bacterium with spiral flagella, possessing urease activity [5]. MALT lymphomas, stomach and duodenal ulcers, chronic gastritis, and stomach tumors are interconnected with HP [6]. The frequency of HP spread is linked to the level of development of countries, as this infection is less common in developed countries and more common in developing countries. Regional and ethnic affiliations, a person's age, as well as socio-economic factors play a significant role in the development of the pathology. According to the WHO (World Health Organization) (2010), while in Sweden, H.P. was found in only 11% of cases among adults, in Brazil, Chile, Nigeria, Mexico, and India it reached 70-90% [7, 8]. Depending on the characteristics of the population and genotypes of H.P, not in all cases can diseases associated with H.P. develop [9, 10, 11, 12].

Intensive research on the bacterial human pathogen H.Pylori (N.R.) has been carried out since being first described in 1984

(Marshall and Warren, 1984; Marshall et al., 1985) as the pathogen infecting half of the world's population. Its genome sequence is very diverse and is a great tool for studying evolution and disease, to identify factors that lead to a greater risk of severe consequence and to search for novel therapeutic approaches. Isolated studies concerning the prevalence of various hypothesized H.R. virulence genes and their purported role in the pathogenesis of disease have also been performed [6-9]. The pathogenicity of N.R. has proved to be more complex, in that N.R. isolates have been found to be geographically highly variable, where some N.R. genotypes correlate with more severe clinical outcomes in one geographic area, but are characterized as almost harmless variants in other studied populations. On top of that, the differences between East Asian and Western strains support the hypothesis that variations in gastroduodenal pathology is determined by the complex interplay between host genetics, other environmental factors, and initial population compositions of different sets of H.R. virulence genes. The role of most N.R. Virulence genes is not yet consistently interpreted; however, information on their significance in pathogenesis and disease outcome has critically progressed during the last two decades. The chromosome encodes for a stre of urease genes, several cytotoxins and the cag pathogenicity island. Toxins: And also cytotoxin, which stretch cytotoxin, vacuolating cytotoxin (VacA), inducing apoptosis of host epithelial cells (cell death), and cytotoxin-associated antigen (CagA), affecting the pathway of the host cell signaling. CagA, a virulence factor, is injected into host cells via the type IV secretion system encoded by the pathogenicity island known as cag. A relationship between N.R. genes and development of gastritis, gastroduodenal ulcers, and stomach cancer in several studies has been analyzed[ ].

OBJECTIVE OF THE STUDY

The purpose of the study is to study the genotypes of H.R. in patients with RA using molecular genetic analysis.

A. Materials and Methods

The study examined 69 patients with rheumatoid arthritis who had complaints from the gastrointestinal tract. Patients received complex treatment (glucocorticoid, anti-inflammatory, basic drugs). Patients were divided into 2 groups: the first group consisted of 45 (66%) patients with gastropathy and the second group of 24 (34%) patients without gastropathy. All patients underwent clinical, laboratory-instrumental, molecular-genetic, chromatographic, and statistical research methods.

Molecular genetic studies included studying the frequency of H.R. genes occurrence in patients with and without gastropathy, the frequency of gastroduodenal pathology occurrence in RA patients with gastropathy, taking into account H.R. genotypes.

RESULTS

Studies of the frequency of H.P. genes among RA patients with and without gastropathy, verified in biomaterial using PCR, showed that 21 out of 45 (46.7%) RA patients with gastropathy and 4 out of 24 (16.7%) RA patients without gastropathy had a vacAs2 positive H.pylori genotype ($\chi 2$=6.1; P=0.01; OR=4.3; 95% CI 1.288-14.86), as well as 19 out of 45 (42.2%) RA patients with gastropathy and 4 out of 24 (16.7%) RA patients without gastropathy had a cagA positive H.pylori genotype ($\chi 2$=4.5; P=0.029; OR=3.6; 95% CI 1.073-12.45), 16 out of 45 (35.6%) RA patients with gastropathy and 5 out of 24 (20.8%) RA patients without gastropathy had an Ice2 positive H.pylori genotype ($\chi 2$ =1.6; P=0.2; OR=2.1; 95% CI 0.658-6.68). The values of the Ice1 and vacAm1 genes were statistically insignificant (Table. 1).

TABLE I. Combination of H. pylori genes in RA patients with and without gastropathy

H.P. genes.	Frequency of occurrence of H.Pylori genotypic variants (n=69)				Statistics
	Rheumatoid arthritis with gastropathies n=45		*Rheumatoid arthritis without gastropathy n=24*		
	N	*%*	*N*	*%*	
cagA	19	42.2	4	16.7	$\chi 2$=4.5; P=0.029; OR=3.6; 95% CI 1.073-12.45
Ice1	9	20.0	3	12.5	χ^2=0.6; P=0.4; OR=1.7; 95%CI 0.425-7.19
Ice2	16	35.6	5	20.8	$\chi 2$ =1.6; P=0.2; OR=2.1; 95% CI 0.658-6.68
vacAm1	17	37.8	7	29.2	χ^2 =0.5; P=0.5; OR=1.4; 95% CI 0.50- 4.28
vacAs2	21	46.7	4	16.7	χ^2=6.1; P=0.011; OR=4.36; 95% CI 1.288-14.86

Thus, when studying the frequency of H.P. gene distribution among RA patients with and without gastropathy, H.pylori vacAs2, cagA, Ice2 genes were found statistically significantly more frequently. The presence of the vacAs2 gene in the bacterium increases the risk of developing gastropathy by 4.4 times ($\chi2$=6.1; P=0.011; OR=4.36; 95% CI 1.288-14.86), the presence of the cagA gene in the bacterium increases the risk of developing gastropathy by 3.6 times ($\chi2$=4.6; P=0.03; OR=3.6; 95%CI 1.073-12.45) and the presence of the Ice2 gene in the bacterium increases the risk of developing gastropathy by 2.1 times ($\chi2$ =1.6; P=0.2; OR=2.1; 95% CI 0.658-6.68). VacAm1, vacAs2 genotypes were found in 42.2% of cases in RA patients with gastropathy and in 16.7% of cases in RA patients without gastropathy ($\chi2$=4.6; P=0.031; OR=3.6; 95% CI1.073-12.45). The combination of cagA, Ice2, vacAm1, vacAs2 occurred in 31.1% of cases in RA patients with gastropathy and in 4.2% of cases in RA patients without gastropathy ($\chi2$=6.7; P=0.011; OR=10.3; 95% CI 1.273- 84.75). The combination of Ice2, vacAm1, vacAs2 occurred in 24.4% of cases in RA patients with gastropathy and in 8.3% of cases in RA patients without gastropathy ($\chi2$=2.7; P=0.1; OR=3.6; 95% CI0.7191, 17.61).

The combination of the H.pylori Ice1, vacAm1, vacAs2 genotype occurred in 17.8% of cases in RA patients with gastropathy and in 8.3% of cases in RA patients without gastropathy ($\chi2$=1.1; P=0.3; OR=2.4; 95% CI0.462-12.22). The combination of cagA, Ice1 genes was statistically rare - 24.4% of cases in RA patients with gastropathy and 20.8% of cases in RA patients without gastropathy. The combination of cagA, Ice1, Ice2, vacAm1, vacAs2 ($\chi2$=0.2; P=0.6) (Table. 2.).

TABLE II. Combination of H. pylori genes in RA patients with and without gastropathy H.P. genes.

H.P. genes.	Frequency of occurrence of H.Pylori genotypic variants (n=69)				Statistics
	Rheumatoid arthritis with gastropathies n=45		*Rheumatoid arthritis without gastropathy n=24*		
	N	*%*	*N*	*%*	
cagA, Ice2, vacAm1, vacAs2	14	31.1	1	4.2	χ^2=6.7; P=0.011; OR=10.3; 95%CI 1.273- 84.75
Ice2, vacAm1, vacAs2	11	24.4	2	8.3	χ^2=2.7; P=0.1; OR=3.6; 95%CI0.7191, 17.61
cagA, Ice1	11	24.4	5	20.8	χ^2=0.1; P=0.7; OR=1.2; 95% CI0.371-4.069
vacAm1, vacAs2	19	42.2	4	16.7	$\chi2$=4.6; P=0.031; OR=3.6; 95% CI1.073-12.45
cagA, Ice1, Ice2, vacAm1, vacAs2	3	6.7	-	-	χ^2=0.2; P=0.6
Ice1, vacAm1, vacAs2	8	17.8	2	8.3	χ^2=1.1; P=0.3; OR=2.4; 95%CI0.462-12.22

CONCLUSION

Thus, in the study of H.pylori gene combinations in RA patients with and without gastropathy, H.pylori genotype combinations cagA, Ice2, vacAm1, vacAs2; vacAm1, vacAs2; Ice2, vacAm1, vacAs2 and Ice1, vacAm1, vacAs2. The presence of a combination of cagA, Ice2, vacAm1, vacAs2 in bacteria increases the risk of developing gastropathy by 10.4 times ($\chi2$=6.7; P=0.011; OR=10.3; 95% CI 1.273- 84.75), the presence of a combination of vacAm1, vacAs2 in the bacterium increases the risk of developing gastropathy by 3.6 times ($\chi2$=4.6; P=0.03; OR=3.6; 95%CI1.073-12.45), the presence of a combination of Ice2, vacAm1, vacAs2 increases the risk of developing gastropathy by 3.6 times ($\chi2$=2.7; P=0.1; OR=3.6; 95% CI0.7191, 17.61) and the presence of a combination of Ice1, vacAm1, vacAs2 increases the risk of developing gastropathy by 2.4 times ($\chi2$=1.1; P=0.3;

OR=2.4; 95% CI0.462-12.22).

According to the results of molecular genetic testing, in the presence of vacAs2, iceA2 and cagA genes and/or combinations of cagA, Ice2, vacAm1, vacAs2 in patients with RA N.R and NSAIDs; vacAm1, vacAs2; Ice2, vacAm1, vacAs2 increase the risk of erosion and ulceration of the stomach and duodenum. A thorough study of the pathogenicity factors of H.R., identification of the pathogen's genotypes, will allow for the identification of risk groups for RA patients with gastropathies, the creation of a therapy regimen, and the recommendation of measures for further monitoring of the pathology.

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