ISSN NO: 2770-2936
January 2025

Evaluation Of The Acetylation Process And Blood Lipid Profile In Patients With Chronic Periodontitis Associated With Hepatitis C

Abdiyusupova K.M., Khaydarov A.M., Khadzhimetov A.A., Khaydarova S.E.
(CRPKMR Ministry of Health of the Republic of Uzbekistan, Tashkent State Institute)

Abstract. The purpose of this study was to investigate the relationships between allelic variants of acetylation and the blood lipid profile in patients with chronic periodontitis associated with hepatitis C. Biochemical studies were conducted on 42 individuals aged 18–45 years (24 men and 18 women) diagnosed with chronic periodontitis associated with chronic hepatitis C. The acetylation phenotype in saliva and the blood lipid spectrum were studied. A higher prevalence of the disease was noted among patients with a slow acetylation phenotype in saliva, averaging 17% in the primary group. Patients with a slow acetylation phenotype demonstrated elevated triglyceride levels, which were accompanied by lower concentrations of cholesterol, high-density lipoproteins (HDL), and low-density lipoproteins (LDL) in the blood.
Keywords: chronic generalized periodontitis, hepatitis C virus, acetylation phenotype, blood lipid profile.

Introduction. Numerous studies have demonstrated that population research on phenotype determination significantly enhances the effectiveness of pharmacotherapy courses and reduces the incidence of side effects during treatment [4, 5, 9, 27]. In this regard, the study of acetylator phenotypes has garnered increasing interest in recent years, as acetylation processes play a central role in intermediary metabolism. Furthermore, recent research has shown that an individual's acetylator group can influence their susceptibility to liver diseases [11, 13, 18, 21].

Acetylation processes are pivotal in intracellular metabolism. For instance, oxidative decarboxylation of pyruvic acid, the synthesis and breakdown of fats, the synthesis of acetylcholine, steroids, and other compounds occur through acetylation [14, 15, 31, 37].

Acetylation is considered a genetically determined ability of the body to metabolize compounds containing amino groups. Depending on the acetylation rate, two groups are distinguished within the human population. One group includes individuals who metabolize test drugs at a high rate (rapid acetylation), while the other metabolizes at a low rate (slow acetylation) [17, 19, 20, 52].

It is well known that cholesterol levels in the blood depend on genetic factors and partially on dietary cholesterol intake. Cholesterol synthesis occurs in cells of nearly all organs and tissues, with significant quantities produced in the liver (80%), the wall of the small intestine (10%), and the skin (5%) [23, 24, 39]. Notably, the studies by Shevchenko O.V. et al. (2012) have shown that "slow" allelic variants of the NAT2 gene reduce the activity of the N-acetyltransferase enzyme, slowing the conversion of Acetyl-CoA into acetoacetyl-CoA and disrupting the multi-step cholesterol synthesis chain.

It is also important to highlight that lipid metabolism is deeply involved in the molecular mechanisms of the infectious cycle of hepatitis C virus [42, 43, 49]. This unique interaction between the hepatitis C virus and lipid metabolism provides an opportunity to thoroughly study the role of lipids at all stages of the viral infectious cycle, especially in periodontal disease manifestations. The acetylator phenotype of patients with chronic periodontitis associated with hepatitis C virus plays a significant role in these metabolic changes, potentially helping to better understand the role of certain lipids in cellular metabolism [33, 34, 36, 44, 51].

The aim of this study was to investigate the relationships between allelic variants of acetylation and the blood lipid profile in patients with chronic periodontitis associated with hepatitis C.

Materials and Methods. To achieve the study's objective, a biochemical investigation was conducted involving 42 individuals aged 18–45 years (24 men and 18 women) undergoing inpatient treatment at the Scientific-Practical Medical Center for Epidemiology, Microbiology, Infectious, and Parasitic Diseases in the 2nd Department of Chronic Viral Hepatitis, diagnosed with chronic hepatitis C. The study adhered strictly to the requirements of biomedical ethics, as outlined in the Geneva Convention on Human Rights (1997) and the Helsinki Declaration of the World Medical Association (2000), based on approval from the local ethics committee. All patients provided written informed consent to participate in the study.

ISSN NO: 2770-2936
January 2025

Inclusion criteria included a verified diagnosis of chronic viral hepatitis C identified through PCR testing using a test system, patients who had not used narcotics for the past six months, and those not undergoing antiviral therapy. Patients younger than 18 years, those with concomitant hepatitis B, D, or other liver diseases, HIV infection, a history of pulmonary tuberculosis, autoimmune or oncological diseases, and pregnant women were excluded from the study.

To determine the control values of the studied hemostasis system parameters, 16 practically healthy individuals aged 25–45 years, who gave informed consent and did not differ from the patients in terms of gender and age, were examined. These individuals had no history of viral hepatitis or other liver diseases based on clinical, biochemical, and serological findings.

All patients underwent a standard clinical and laboratory examination for liver pathology. The diagnosis of chronic hepatitis was based on clinical symptoms (liver pain, dyspeptic syndrome, asthenovegetative syndrome, hepatomegaly, jaundice) and laboratory syndromes (cytolysis, cholestasis, inflammation, and mild hepatic insufficiency). Detection of HCV RNA, viral genotype determination, and viral load levels were assessed using polymerase chain reaction (PCR). The glycemia, lipid profile (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], very low-density lipoprotein cholesterol [VLDL-C], triglycerides [TG]), and apolipoproteins A (ApoA1) and B (ApoB) were measured. Analyses were conducted using enzyme-linked immunosorbent assay (ELISA) with reagents and equipment from HUMAN. The atherogenic coefficient was calculated using the formula: (TC - HDL-C) / HDL-C.

Patients and control group participants took 0.5 g of sulfodimethoxine on an empty stomach. The levels of free and total sulfodimethoxine (SD) were determined using spectrophotometry at a wavelength of 400 nm. The acetylated SD level was calculated as follows: AS = TS - FS, where AS is acetylated SD, TS is total SD, and FS is free SD. The M-acetylation phenotype was determined as the acetylation rate of SD and calculated as the ratio of AS to TS in percentage terms.

The acetylation phenotype type (fast and slow acetylators) was assessed based on the percentage of acetylated sulfodimethoxine in the blood five hours after drug administration, following the method of B. Evans (1969) modified by L.N. Bulovskaya (1982). Individuals with ≥50% acetylation of sulfodimethoxine after five hours were classified as fast acetylators, and those with <50% as slow acetylators.

Statistical analysis of the results was performed using Microsoft Excel 2002. The mean value and standard error of the mean (M ± m) were calculated. The significance of differences for dependent and independent samples between two means was evaluated using Student's t-test. Differences between the compared indicators were considered significant at $p < 0.05$.

Results and Discussion

As shown in the results presented in Table 1, among the primary group of patients with chronic periodontitis associated with hepatitis C, a rapid acetylation type (acetylation intensity >50%) was observed in 36 patients, whereas slow acetylation (acetylation intensity <50%) was noted in 6 patients.

Table 1

Comparative Characteristics of Acetylation Intensity in Saliva Among Examined Patients

Indicator	Rapid Acetylation (n=36)	Slow Acetylation (n=6)
Acetylation Intensity, %	38.58 ± 3.24	61.42 ± 5.26

Analysis of serological diagnostics and acetylation types revealed that patients with very high acetylation levels in saliva often exhibited chronic periodontal inflammation associated with hepatitis C. The findings suggest that patients with low acetylator phenotype values experience a more pronounced clinical picture of the disease, characterized by clinical and laboratory signs of liver damage and hypersensitivity to medications. Patients with a slow acetylation type demonstrated a significantly higher risk of developing extrahepatic diseases and hypersensitivity complaints induced by hepatitis C. In contrast, those with a rapid acetylation type exhibited a lower reaction to commonly used dental medications. This condition may also contribute to insufficient lipid delivery by the liver and an imbalance in their blood content. Impaired lipid synthesis and transport disrupt the pathogenetic mechanisms of membrane permeability, resulting in inflammation and contact sensitization due to reduced antimicrobial protection of the oral mucosa.

The study of lipid metabolism parameters in 42 patients with chronic periodontitis associated with hepatitis C revealed the dynamics presented in Table 2. As evidenced by the data, rapid acetylators displayed dyslipidemia

ISSN NO: 2770-2936
January 2025

characterized by a significant yet minor increase in total cholesterol, low-density lipoproteins (LDL), and triglycerides compared to the control group. Conversely, this group showed a decrease in HDL levels.

Table 2

Lipid Metabolism Indicators in Patients with Chronic Periodontitis Associated with Hepatitis C

Indicator	Healthy Individuals (n=16)	Patients with Hepatitis C (n=42)	
		Rapid Acetylators (n=36)	Slow Acetylators (n=6)
Cholesterol (mmol/L)	4.68 ± 0.27	4.71 ± 0.31	3.39 ± 0.27*
HDL (mmol/L)	1.23 ± 0.12	1.19 ± 0.12	1.01 ± 0.11
LDL (mmol/L)	2.19 ± 0.14	2.31 ± 0.24*	2.08 ± 0.16
VLDL (mmol/L)	0.71 ± 0.05	0.97 ± 0.06*	1.18 ± 0.07*
Triglycerides (mmol/L)	1.12 ± 0.13	1.42 ± 0.15*	2.52 ± 0.24*

Note: *Significant differences at $p < 0.05$ relative to the comparison group.

In patients with a slow acetylator type, there was a significant reduction in cholesterol levels by 27.6%, HDL by 18%, and LDL by 5.1%. In contrast, these patients demonstrated an increase in VLDL levels by 66% and triglyceride concentration by 2.25 times.

We hypothesize that mutations in the NAT2 gene, leading to slow acetylation, impair cholesterol synthesis. Slow allelic variants of the NAT2 gene reduce the activity of the N-acetyltransferase enzyme, slowing the conversion of Acetyl-CoA into acetoacetyl-CoA and disrupting the multi-step cholesterol synthesis chain [7]. Gene polymorphisms in cholesterol metabolism may serve as crucial factors affecting cholesterol and VLDL levels, potentially influencing cholesterol's immunoregulatory effects on the skin.

Conclusions. Patients with chronic periodontitis associated with hepatitis C exhibit statistically heterogeneous acetylation activity, with a prevalence of the disease observed in 17% of patients with a slow acetylation type in saliva. In the peripheral blood of patients with chronic periodontitis associated with hepatitis C in the group with a slow acetylation type, elevated triglyceride levels were noted, accompanied by low concentrations of total cholesterol (TC), high-density lipoproteins (HDL), and low-density lipoproteins (LDL).

References

1. Aryamkina O.L., Briginyevich V.E., Vinogradova I.B., Klimova N.N., Mukhorin V.P., Nasyrov R.A. Extrahepatic manifestations of chronic viral hepatitis B and C // Russian Medical Journal. 2006. No. 1. P. 6–8.
2. Ignatova T.M. Natural course of chronic HCV infection / T.M. Ignatova // Russian Journal of Gastroenterology, Hepatology, Coloproctology. – 2002. – No. 2. – P. 20–30.
3. Sergeev Yu.V., Svechnikova E.V., Dudnik V.S. Extrahepatic manifestations of chronic viral hepatitis // Bulletin of Dermatology and Venereology. 2007. No. 4. P. 37–39.
4. Abduyusupova K.M., Alimov A.S. Periodontal status and features of dental therapy in patients with hepatitis C // Stomatologiya No. 3 (84), 2021, P. 51–57.
5. Abduyusupova K.M., Alimov A.S. Manifestations of periodontal diseases against hepatitis C // International Scientific-Practical Conference, Kursk, 2021, 1 CD-ROM. P. 101–103.
6. Antidze M.K. Evaluation of complex treatment of patients with chronic generalized periodontitis based on clinical and laboratory indicators: Dissertation. -M., 2013. -119 p.
7. Vavilova T.P., Ostrovskaya I.G., Medvedev A.E. Opportunities and prospects for studying hormones in saliva / Biomedical Chemistry. – 2014. – Vol. 60, Issue 3. – P. 295–307.
8. Khaydarov A.M. Clinical efficacy of periodontitis treatment in patients with hypothyroidism. Medical Journal of Uzbekistan, 2011, No. 1, P. 14–17.
9. Dombrovskaya Yu.A. Influence of age-related androgen deficiency on the development of periodontal and oral mucosa pathology / Yu.A. Dombrovskaya, A.V. Pechersky, V.N. Ellinidi, I.A. Samusenko, B.T. Moroz // Institute of Dentistry. - 2007. - Vol. 1, No. 34, P. 78–79.
10. Khaydarov A.M., Kamilov Kh.P., Muydinova M.Sh. Clinical evaluation of periodontal condition in patients with hypothyroidism, Medical Journal of Uzbekistan, 2011, No. 5, P. 18–20.
11. Yanushevich O.O., Syrbu O.N. The role of sex hormones in the pathogenesis of chronic generalized periodontitis (literature review) // Russian Dentistry. - 2014. - No. 7. - P. 3–7.

ISSN NO: 2770-2936
January 2025

12. Khaydarov A.M., Kamilov Kh.P. Dynamics of alveolar ridge mineralization during osteotropic therapy of periodontitis in patients with hypothyroidism. Scientific-Practical Journal "Doctor-Aspirant," 2011, No. 6.3(49), P. 490–495.
13. Khaydarov A.M., Rizaev J.A. Prevalence and intensity of dental caries in children living in ecological risk zones. Stomatologiya Journal, No. 3-4, 2014, P. 10–16.
14. Khaydarov A.M., Rizaev J.A., Rustamova D.A., Rizaev E.A. Study of periodontal disease intensity and prevalence based on patient surveys. Stomatologiya Journal, No. 1-2, 2015, P. 150–154.
15. Influence of female sex hormones on the adhesion of Candida albicans to buccal epithelium / E.G. Kravtsov, I.V. Anokhina, Ya.A. Rybass, N.P. Sachivkina, A.V. Ermolaev, S.B. Brodskaya // Bulletin of Experimental Biology and Medicine. – 2014. – No. 2. – P. 211–213.
16. Khaydarov A.M., Rizaev J.A. Fluoride Concentration in Water and Influence on Dental Diseases in Uzbekistan. World Healthcare Providers. 2015, USA. P. 4–6.
17. Khaydarov A.M. Local oral cavity immunity in children living in ecologically unfavorable areas. Stomatologiya Journal, No. 1, 2016, P. 12–16.
18. Khaydarov A.M. Prevalence and frequency of periodontal diseases in children living in cities with varying ecological conditions. Bulletin of the Tashkent Medical Academy, 2015, No. 4, P. 103–106.
19. Khaydarov A.M., Rizaev E.A. Prevalence of periodontal diseases among children and adults living in cities with varying ecological conditions. Medical Journal of Uzbekistan, No. 6, 2016, P. 77–80.
20. Khaydarov A.M. Influence of ecologically unfavorable factors on clinical and functional indices of the oral cavity in children. European Science Review, No. 7–8, Vienna-Prague, 2017, P. 76–78.
21. Mayansky, A.N., Zaslavskaya, M.I., Salina, E.V., Strogova, Yu.Yu., Rassanov, S.P., Malysheva, E.F. Adhesive reactions of buccal epithelial cells in indicating local and general homeostasis disorders // Nizhny Novgorod Medical Journal. – 2005. – No. 1. – P. 158–161.
22. Khaydarov, A.M., Muhamedov, I.M. Biology of the oral cavity in children living in Chirchik city // Journal of Research in Health Science. – No. 1, 2018. – P. 39–47.
23. Khaydarov, A.M., Olimov, A.B., Ahmadaliev, N.N. Quantitative analysis of microbiota in patients with orthopedic structures on dental implants using the real-time PCR method // International Journal of Pharmaceutical Research. – 2020. – P. 736–738.
24. Khaydarov, A.M., Olimov, A.B., Olimjonov, K.Zh. Study of conditionally pathogenic microorganisms using PCR in patients with orthopedic constructions on dental implants // Problems of Biology and Medicine Journal. – No. 1 (116), 2020. – P. 109–112.
25. Khaydarov, A.M., Akhmedov, A.A., Rizaev, Zh.A. Features of glycoprotein composition in oral fluid in athletes of cyclic sports // Problems of Biology and Medicine Journal. – No. 2 (118), 2020. – P. 24–26.
26. Khaydarov, A.M., Olimov, A.B., Nazarov, Z.Z., Mannanov, Zh.Zh. Comparative assessment of individual and professional hygiene effectiveness in dental implant prosthetics // Bulletin of Tashkent Medical Academy. – No. 1, 2021. – P. 176–179.
27. Muratova, S.K., Zhabriyeva, A.Zh., Khaydarov, A.M. Features of oral microcirculation against the background of chronic cerebral ischemia // Bulletin of Tashkent Medical Academy. – No. 4, 2021. – P. 161–163.
28. Abduyusupova, K.M., Khaydarov, A.M., Khadjimetov, A.A. The role of endothelial function regulation disorders in the development of exfoliative cheilitis // Biomedicine and Practice Journal. – Vol. 7, No. 6, 2022. – P. 268–277.
29. Abduyusupova, M. Kamola. Comparative analysis of the index informative value in the examination of periodontal diseases // European Journal of Molecular Medicine. – Vol. 1, No. 4, 2021. – P. 4–6.
30. Abduyusupova, K.M., Muminova, G.G. Comparative analysis of index informativeness in the examination of periodontal diseases // International Conference Europe, Science and We. – Europe, 2020. – P. 40–43.
31. Chen, J., Duan, Z.P., Bai, L., et al. Changing characteristics of blood coagulation factors and their correlation with coagulation status in different hepatic diseases // Zhonghua Gan Zang Bing Za Zhi. – 2012. – Vol. 20(3). – P. 206–210.

ISSN NO: 2770-2936
January 2025

32. Bilalova, A.R. Features of the hemostasis system in patients with chronic hepatitis and liver cirrhosis // Infectious Diseases. – 2015. – Vol. 13, Issue 3. – P. 37–45.
33. Morozov, Yu.A. Hemostasis system disorders in liver pathology and their diagnostics // Hemorrhagic Diatheses, Thromboses, and Thrombophilias. – 2014. – No. 14. – P. 162–174.
34. Abduyusupova, K.M., Khaydarov, A.M., Khadjimetov, A.A. Assessment of the hormonal background of saliva and blood in patients with inflammatory-destructive periodontal processes against the background of hepatitis C // Journal of Population Therapeutics & Clinical Pharmacology. – No. 30 (3), 2023. – P. 480–484.
35. Abduyusupova, K.M., Khaydarov, A.M., Mukhamedkarimova, S.R. Study of microbial contamination in periodontal pockets of patients with periodontitis associated with hepatitis C using PCR // Journal of Dentistry and Craniofacial Research. – Samarkand, Vol. 4, No. 1, 2023. – P. 63–67.
36. Aryamkina, O.L., Briginyevich, V.E., Vinogradova, I.B., Klimova, N.N., Mukhorin, V.P., Nasyrov, R.A. Extrahepatic manifestations of chronic viral hepatitis B and C // Russian Medical Journal. – 2006. – No. 1. – P. 6–8.
37. Spiegel, B.M., Younossi, Z.M., Hayes, R.D., et al. Impact of hepatitis C on health-related quality of life: a systematic review and quantitative assessment // Hepatology. – 2005. – Vol. 41. – P. 790–800.
38. Changes in cytokine status in chronic viral hepatitis B and C in children / Zhukova, E.A., Kaplina, N.A., Romanova, S.V., et al. // Cytokines and Inflammation. – 2009. – Vol. 8, No. 4. – P. 38–39.
39. Zhukin, A.S., Soloviev, S.V. Cytokine production and interferon therapy in patients with chronic viral hepatitis // Epidemiology. – 1999. – No. 5. – P. 27–29.
40. Abduyusupova, K.M., Muminova, G.G. Comparative analysis of index informativeness in the examination of periodontal diseases // International Conference Europe, Science and We. – Europe, 2020. – P. 40–43.
41. Abduyusupova, K.M., Alieva, M.A., Alyavi, M.N. Clinical and microbiological evaluation of chloride preparations in the complex treatment of periodontitis // Uzbek Medical Journal. – Vol. 3, Issue 3, 2022. – P. 51–54.
42. Abduyusupova, K.M., Khaydarov, A.M., Khadjimetov, A.A. Evaluation of coagulation system status in patients with periodontitis against hepatitis C // Medicine and Innovations. – No. 5, 2024.
43. Bostanci, V., Toker, H., Senel, S., Poyraz, O., Akpinar, A., Gorgun, E.P., Bakar, O. Evaluation of IL-1β, IL-1ra, and IL-10 levels and outcome of periodontal therapy in chronic periodontitis with familial Mediterranean fever // Clinical Oral Investigations. – 2017. – Vol. 21(1). – P. 469–475.
44. Makarov, V.K., Chainikova, E.A. Age-related lipid spectrum features in serum of patients with acute viral hepatitis A // Epidemiology and Infectious Diseases. – 2007. – No. 1. – P. 34–37.
45. Morozova, N.V. Study of the relationship between the NAT2 phenotype and chronic liver diseases // Dissertation Abstract. – Moscow, 2006. – P. 26.
46. Fadeenko, G.D. Fatty liver: etiopathogenesis, diagnostics, treatment // Modern Gastroenterology. – 2003. – No. 3(13). – P. 9–17.
47. Shevchenko, O.V., Bychkov, E.N., Svistunov, A.A., Borodulin, V.B., Saratsev, A.V., Losev, O.E., Kiselev, A.R., Posnenkova, O.M. Influence of NAT2 gene polymorphisms on cholesterol metabolism in patients with arterial hypertension // Fundamental Research. – 2012. – No. 7-1. – P. 219–223.