Clinical And Morphological Parallels Between Helicobacter-Associated Gastroduodenal Disease and Fatty Liver Disease (FLD) (Literature Review)

Oybek Hasanov Gafurovich	Assistant Professor, Samarkand State Medical University
Rakhmonova Mokhigul Shodikulovna	319 group of the Faculty of Medicine Samarkand State Medical University
Tokhirjonova Aziza Tokhirjon qizi	319 group of the Faculty of Medicine Samarkand State Medical University
Sangirova Fotima Abdurakhmon kizi	319 group of the Faculty of Medicine Samarkand State Medical University

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease; its detection in the general population has reached global proportions. Although the disease has a relatively mild course in its early stages, the development of non-alcoholic steatohepatitis, cirrhosis and hepatocellular carcinoma during its natural course leads to a worse long-term prognosis. A growing body of evidence suggests that NAFLD has a complex, multifaceted aetiology involving many factors, including genetic factors. In this review we focus on a genetic component of NAFLD, namely the role of PNPLA3 gene polymorphisms in the development and course of the disease as well as its progression states such as nonalcoholic steatohepatitis, cirrhosis and hepatocellular carcinoma.

Keywords: Non-alcoholic fatty liver disease, morphological parallels, helicobacter-associated, gastroduodenal disease, fatty liver

Introduction. Non-alcoholic fatty liver disease (NAFLD) is currently the most common cause of liver disease in developed countries. The prevalence of NAFLD is 20-35% of the general population [1]. NAFLD has a wide range of clinical and physical symptoms and can manifest histologically as simple steatosis and non-alcoholic steatohepatitis (NASH), which includes steatosis, lobular inflammation, hepatocyte balloon dystrophy with or without fibrosis [2]. Although simple steatosis usually has a benign prognosis, NASH is much more likely to progress to fibrosis, cirrhosis and hepatocellular carcinoma (HCC) (3). The precise mechanisms responsible for the development and progression of NASH are currently a matter of debate. There is increasing evidence that genetic factors, as well as environmental factors, play an important role in the progression of NAFLD [4-6]. The PNPLA3 (Patatin-Like Phospholipase Domain Containing 3) gene, also known as adiponutrin, is located on chromosome 22 and encodes a protein composed of 481 amino acids that is expressed mostly in stellate liver cells, hepatocytes and retinal cells. The protein encoded by adiponutrin is a member of the patatin-like phospholipase family and has hydrolase activity against triglycerides, acyltransferase activity against lysophosphatidic acid, and esterase activity against retinol palmitate. Substitution of

isoleucine for methionine at position 148 of the amino acid sequence results in loss of these functions and accumulation of triglycerides and retinol palmitate in the liver [7, 8]. Association of the PNPLA3 gene with NAFLD. In 2008, S. Romeo et al. [5] conducted a study including 2111 participants of different nationalities. Using the method of genome-wide association analysis, the authors of the study were the first to identify the polymorphism of the PNPLA3 gene I148M (rs738409 C>G) and identified a higher susceptibility to NAFLD in carriers of this mutation. In addition, the researchers noted an association between adiponutrin and elevated serum alanine aminotransferase (ALT) levels in Hispanics. A 2009 study by S. Sookoian et al. [9] confirmed the conclusions drawn by S. Romeo et al. and additionally showed that adiponutrin carriage not only increases susceptibility to the disease according to histological findings. The greatest changes were observed in homozygotes for the rs738409 G allele. More severe steatosis and higher values of ALT and aspartate aminotransferase (AST) were observed in this category of study participants. Similar results have been reported by other authors (10,11). These results have been summarised in meta-analyses [12, 13]. However, a number of studies found no association between the presence of this gene and aminotransferase levels [14, 15]. For example, in a study by K. Kantartzis et al. [16] including 130 men and 200 women aged 16-69 years old, despite the presence of more severe steatosis, carriers of two rs738409 G alleles did not have higher values of aminotransferases in comparison to other groups. As NAFLD is closely related to the metabolic syndrome, several researchers have attempted to link the rs738409 G-allele to parameters defining the metabolic syndrome. Indeed, some authors have observed an association between PNPLA3 I148M and insulin resistance and decreased plasma triglyceride levels in obese patients and those of Asian origin [16-18]. However, the vast majority of studies have shown that PNPLA3 I148M does not correlate with manifestations of the metabolic syndrome [5, 11, 16, 19, 20]. For example, in a study by E.K. Speliotes et al. [11], which included 592 participants of European origin with NAFLD, found no associations of PNPLA3 I148M with body mass index, triglyceride, high-density lipoprotein and low-density lipoprotein levels and type 2 diabetes mellitus (DM). In 2011. S. Sookoian et al. [13] conducted a systematic review covering 16 studies to assess the strength of the effect of the rs738409 G allele on susceptibility to NAFLD and the severity of its course. This analysis demonstrated that homozygotes for the rs738409 G-allele tend to have a more pronounced accumulation of fat in the liver and have a more aggressive course of the disease compared with heterozygotes and homozygotes for the rs738409 C-allele. However, all included studies showed no significant differences between genotypes with regard to body mass index, glucose and insulin levels, and insulin resistance index. At the same time, some studies have found that PNPLA3 I148M significantly influences the development and severity of fibrosis in patients with NAFLD [10, 12, 22, 23]. For example, in 2010. L. Valenti and colleagues [10], in an analysis of polymerase chain reaction (PCR) results from 591 patients with histologically confirmed NAFLD, noted that homozygotes for the rs738409 G allele were more likely to have NASH and progressive liver fibrosis compared to heterozygotes and homozygotes for the rs738409 C allele. This association was observed irrespective of the severity of the metabolic syndrome. Similar data were obtained in a study by Y. Rotman et al. [12] in a cohort of 894 adults and 223 children with established NAFLD. The PNPLA3 I148M gene had a strong association with histological parameters of an aggressive course of the disease (inflammation, Mallory bodies, fibrosis) [12]. Furthermore, in a study in which genotyping and liver elastography were performed in 899 patients of European origin with chronic liver disease, M. Krawczyk et al. [2] were able to establish a significant association between PNPLA3 I148M and decreased liver elasticity. More importantly, the association between the gene and the development of liver fibrosis was seen not only in adults, but also in children. For example, in a

prospective study including 149 Italian children and adolescents with NAFLD confirmed by biopsy, perivenular fibrosis was observed in 31% of patients with the rs738409 CC genotype, in 48% of patients with the rs738409 CG genotype and in 74% of patients with the rs738409 GG genotype. The prevalence of periportal fibrosis was found to be inversely related to rs738409 G allele carriage and was 26% in patients with the rs738409 CC genotype, 18% in patients with the rs738409 CG genotype and 9% in patients with the rs738409 GG genotype. This correlation was independent of the severity of concomitant factors [13].__ In 2014, the results of a meta-analysis covering data from 9915 patients participating in 24 studies were published. The aim of this systematic review was to assess the effect of PNPLA3 I148M on liver fibrosis and HCC. The authors found a statistically significant association between PNPLA3 I148M and advanced liver fibrosis in patients with NAFLD. They also noted that, according to nine studies (2937 patients) included in the analysis, PNPLA3 I148M was associated with an increased risk of HCC in patients with NASH and with alcoholic cirrhosis [14]. In 2014, in Thailand, A. Khlaiphuengsin et al. [5] conducted a study including 388 patients with HCC of various etiologies; the authors retrospectively investigated the effect of the PNPLA3 polymorphism on the development of HCC of viral and non-viral etiology. The researchers concluded that the gene polymorphism increased the risk of HCC formation in patients with alcoholic liver disease and NASH, but not in patients with chronic viral hepatitis. In particular, the prevalence of the rs738409 GG genotype was comparable between patients with HCC of viral etiology and a control group, whereas the frequency of the rs738409 GG genotype was twice as high in patients with HCC in the NASH outcome than in the HCC associated with viral liver disease and control groups [5]. Of note, there is also evidence to date that PNPLA3 I148M demonstrates potential sex dimorphism in relation to susceptibility to NAFLD [11, 13]. In an analysis of a cohort with NASH, E.K. Speliotes et al. [11] observed that the effect of PNPLA3 I148M on the histological characteristics of NAFLD was greater in women than in men. This finding is supported by the results of a meta-regression analysis, which demonstrated a negative correlation between male gender and the effect of PNPLA3 I148M on liver fat content [13].

Literature:

1. Azimov M. I., Shomurodov K.E. A technique for Cleft Palate Repair. Journal of research in health science. Vol. 1, No. 2, 2018, pp. 56-59.
2. Khamdamov B.Z. Indicators of immunocitocine status in purulent-necrotic lesions of the lover extremities in patients with diabetes mellitus.//American Journal of Medicine and Medical Sciences, 2020 10(7) 473-478 DOI: 10.5923/j.ajmm.2020.-1007.08 10.
3. M. I. Kamalova, N.K.Khaidarov, Sh.E.Islamov,Pathomorphological Features of hemorrhagic brain strokes, Journal of Biomedicine and Practice 2020, Special issue, pp. 101-105
4. Kamalova Malika Ilkhomovna, Islamov Shavkat Eriyigitovich, Khaidarov Nodir Kadyrovich. Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 2020. 2(10), 53-59
5. Khodjieva D. T., Khaydarova D. K., Khaydarov N. K. Complex evaluation of clinical and instrumental data for justification of optive treatment activites in patients with resistant forms of epilepsy. American Journal of Research. USA. № 11-12, 2018. C.186-193.
6. Khodjieva D. T., Khaydarova D. K. Clinical and neuroph clinical and neurophysiological ch ogical characteristics of teristics of post-insular cognitive disorders and issues of therapy optimization. Central Asian Journal of Pediatrics. Dec.2019. P 82-86

7. Sadriddin Sayfullaevich Pulatov. (2022). Efficacy of ipidacrine in the recovery period of ischaemic stroke. World Bulletin of Public Health, 7, 28-32.
8. Tukhtarov B.E., Comparative assessment of the biological value of average daily diets in professional athletes of Uzbekistan. Gig. Sanit., 2010, 2, 65–67.
9. Исмоилов, О., Камалова, М., Анваршед , Т., & Махмудова , С. (2021). Кратко об анатомо-физиологических особенностяхстопы и применение некоторых комплексных упражнений для устранения плоскостопия. Зб1рникнауковихпрацъ SCIENTIA. вилученоіз https: //oj s .ukrlogos. in.ua/index.php/scientia/article/view/ 9999
10. Ergashovich, K. B., & Ilhomovna, K. M. (2021). Morphological Features of Human and Rat Liver and Biliary Tract Comparisons (Literary Review). *International Journal of Discoveries and Innovations in Applied Sciences*, *1*(4), 27–29.
11. Камалова, М., Исмоилов, О., Азимова, А., Бекмуродова, Д., & Исматова, С. (2021). Варианты конституции тела человека. *Збірник наукових праць scientia*.
12. Маматкулов Б., Камалова М., Аширов М. Причины, механизмы повреждения, основные типы переломов пяточной кости //Збірник наукових праць SCIENTIA. – 2021.
13. Kamalova M., Khaidarov N., Shomurodov K. Microscopic examination of brain tissue in hemorrhagic stroke in uzbekistan //Матеріали конференцій МЦНД. – 2021.
14. Kamalova, M., Ismatova, S., Kayumova, S., Gulomova, S., & Akhmedova, J. (2021). Blood supply to the shoulder and forearm muscles in the human foetus. *Збірник наукових праць ΛΌΓΟΣ*.
15. Khaidarov Nodir Kadyrovich, Shomurodov Kahramon Erkinovich, &Kamalova Malika Ilhomovna. (2021). Microscopic Examination OfPostcapillary Cerebral Venues In Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 3(08), 69–73.