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## ABSTRACT

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# THE RELATIONSHIP BETWEEN CHRONIC HEPATITIS C VIRUS AND DIABETES MELLITUS

**Relevance.** Chronic hepatitis C (CHC) and type 2 diabetes mellitus (T2DM) are among the most common and serious problems in modern medicine. Hepatitis C virus (HCV) affects millions of people worldwide and leads to significant socioeconomic consequences and remains one of the main causes of chronic liver diseases such as fibrosis, cirrhosis and hepatocellular carcinoma (HCC).

**Objective.** To analyze the relationship between HCV infection and the development of type 2 diabetes mellitus, with an emphasis on pathophysiological mechanisms, clinical outcomes and the effect of antiviral therapy on glucose metabolism and insulin resistance (IR).

Materials and methods. Scientific articles, studies, and statistical data from PubMed, Karger, RKI, Onlinelibrary, CDC, Ecdc, and the Ukrainian Center for Public Health databases were analyzed. Methods of systematic literature review and comparative analysis of clinical outcomes were used.

**Results.** The relationship between HCV and the development of T2DM was analyzed with an emphasis on pathophysiological mechanisms, clinical outcomes, and the effect of antiviral therapy on glucose metabolism and IR.

The pathophysiological mechanisms that determine the relationship between these diseases are discussed. Particular attention is paid to IR as a key factor in the development of diabetes mellitus in patients with HCV. Studies confirm that HCV directly affects insulin signaling pathways in liver cells and muscles, causing a systemic inflammatory process that disrupts glucose metabolism.

The article presents statistics on the prevalence of T2DM among patients with CHC. It is noted that the prevalence of diabetes among patients with hepatitis is significantly higher than in the general population. The impact of direct-acting antiviral drugs (DAAs), which help to improve metabolic control, reduce blood glucose levels and reduce the need for insulin therapy, is highlighted. The need for further studies to

assess the long-term effects of HCV treatment on glucose metabolism is emphasized, as well as the importance of developing new therapeutic approaches for the treatment of patients with coexisting HCV and T2DM.

**Conclusions.** Chronic HCV infection and T2DM are closely related pathophysiologic conditions with significant clinical consequences. HCV contributes to the development of IR, which is a key mechanism of diabetes development in these patients and is provoked by the virus, disrupts glucose metabolism even in patients without classical risk factors such as obesity or metabolic syndrome. DAAs have proven to be highly effective in achieving a sustained virologic response, which contributes to a significant improvement in glycemic control. These drugs not only eliminate the virus, but also reduce the level of IR, which improves metabolic parameters in patients with T2DM. Virus eradication can reduce or eliminate the need for insulin therapy, improving the quality of life of patients.

**Keywords:** chronic viral hepatitis C, type 2 diabetes mellitus, insulin resistance, antiviral therapy, glucose metabolism, morbidity, health.

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## ВЗАЄМОЗВ'ЯЗОК МІЖ ХРОНІЧНИМ ВІРУСНИМ ГЕПАТИТОМ С ТА ЦУКРОВИМ ДІАБЕТОМ

**Актуальність.** Хронічний гепатит С (ХГС) та цукровий діабет 2 типу (ЦД2) є одними з найбільш поширених та серйозних проблем у сучасній медицині. Вірус гепатиту С (ВГС) вражає мільйони людей у всьому світі та призводить до значних соціально-економічних наслідків та залишається однією з головних причин розвитку хронічних захворювань печінки, таких, як фіброз, цироз та гепатоцелюлярна карцинома (ГЦК).

**Мета.** Аналіз взаємозв'язку між ХГС та розвитком ЦД2 типу, з акцентом на патофізіологічні механізми, клінічні наслідки та вплив противірусної терапії на метаболізм глюкози та інсулінорезистентність (ІР).

**Матеріали і методи.** Проаналізовано наукові статті, дослідження та статистичні дані, висвітлені у базах даних PubMed, Karger, RKI, Onlinelibrary, CDC, Ecdc, Центру громадського здоров'я. Застосовано методи систематичного огляду літератури та порівняльного аналізу клінічних результатів.

**Результати.** Проаналізовано взаємозв'язок між ХГС та розвитком ЦД2 з акцентом на патофізіологічні механізми, клінічні наслідки та вплив противірусної терапії на метаболізм глюкози та ІР.

Розглянуто патофізіологічні механізми, що зумовлюють зв'язок між цими захворюваннями. Особливу увагу приділено ІР, як ключовому фактору розвитку цукрового діабета у пацієнтів із ХГС. Дослідження підтверджують, що ВГС безпосередньо впливає на сигнальні шляхи інсуліну у клітинах печінки та м'язах, спричинюючи системний запальний процес, який порушує метаболізм глюкози.

Представлено статистику поширеності ЦД2 серед пацієнтів із ХГС. Зазначено, що поширеність діабету серед хворих на гепатит значно перевищує показники у загальній популяції. Висвітлено

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вплив противірусних препаратів прямої дії (ППДД), які сприяють покращенню метаболічного контролю, зниженню рівня глюкози у крові та зменшенню потреби в інсулінотерапії. Акцентується увага на необхідності подальших досліджень для оцінки довгострокових наслідків лікування ХГС на метаболізм глюкози, а також на важливості розробки нових терапевтичних підходів для лікування пацієнтів із поєднаним ХГС і ЦД2.

**Висновки.** ХГС та ЦД2 тісно пов'язані патофізіологічними станами, що мають суттєві клінічні наслідки. ВГС сприяє розвитку ІР, яка є ключовим механізмом розвитку діабету серед цих пацієнтів і спровокована вірусом, порушує метаболізм глюкози навіть у хворих без класичних факторів ризику, таких як ожиріння чи метаболічний синдром. ППДД довели високу ефективність у досягненні стійкої вірусологічної відповіді, що сприяє значному покращенню глікемічного контролю. Ці препарати не лише елімінують вірус, але й знижують рівень ІР, що дозволяє покращити метаболічні показники у пацієнтів із ЦД2. Ерадикація вірусу дозволяє зменшити або скасувати потребу в інсулінотерапії, покращуючи якість життя пацієнтів.

**Ключові слова**: хронічний вірусний гепатит С, цукровий діабет 2 типу, інсулінорезистентність, противірусна терапія, метаболізм глюкози, захворюваність, здоров'я.

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## INTRODUCTION

Chronic hepatitis C (CHC) and type 2 diabetes mellitus (T2DM) are among the most common and serious problems in modern medicine [1, 2]. HCV remains one of the main causes of chronic liver diseases such as fibrosis, cirrhosis and hepatocellular carcinoma (HCC) [3]. Hepatitis C virus (HCV) affects millions of people worldwide and leads to significant socioeconomic consequences [4]. Diabetes mellitus in patients with HCV differs from classical T2DM, as new immunological data suggest that diabetes in these patients may be associated with autoimmune processes that resemble the mechanisms of type 1 diabetes mellitus (T1DM). Treatment of CHC with interferon-alpha (IFN-α) can activate T cells and other components of the immune system, promoting autoimmunity in the pancreas, which increases the risk of diabetes in patients with HCV [5]. HCV is associated with an increased risk of developing T2DM, regardless of the severity of liver disease. The risk of T2DM is higher in patients with cirrhosis due to HCV compared to patients with CHC alone [6].

According to the World Health Organization (WHO), about 325 million people worldwide are living with chronic infection caused by hepatitis B virus (HBV) or hepatitis C virus (HCV). About 1.34 million deaths are recorded from viral hepatitis – this number is comparable to the number of deaths from tuberculosis and HIV. However, while the death rate from tuberculosis and HIV is decreasing, the number of deaths from viral hepatitis is increasing. According to the WHO, the total number of people living with hepatitis C reaches 71 million, and about 1 million new cases are registered annually [1, 2, 7]. The HCV problem is particularly relevant in European countries, where there are different trends in the dynamics of the virus spread over the period 2018–2021 [8, 9].

The prevalence of hepatitis C (HC) in European countries varies, showing both downward trends in the number of new cases and upward trends in the number of new cases. In Ukraine, the number of HCV cases tends to increase: in 2018, 51848 cases were officially under surveillance, and in 2021, 92,591 cases were already under surveillance [10]. In Poland, the number of HCV cases decreased from 3442 in 2018 to 1244 in 2021, indicating a decrease in the number of infected people [11]. In Germany, the situation remains relatively stable: 5,268 new cases were reported in 2018 and 5,489 in 2021 [12]. In the Czech Republic, there has been a slight decline in the number of new cases of HS: from 932 in 2017 to 770 in 2020 [13]. In contrast, the United States of America has seen positive trends, with the number of infected people decreasing from 123,312 in 2019 to 107,300 in 2021, as a result of effective national screening and treatment programs [14].

The dynamics of CHC prevalence in these countries

highlights different approaches and results in the fight against HCV, which emphasizes the importance of adapting national strategies to combat this infection.

T2D is another global epidemic with a steadily increasing number of cases. As of 2021, according to the International Diabetes Federation, there were more than 537 million people with type 2 diabetes worldwide, and this number is projected to reach 643 million by 2030 [15]. In Ukraine, according to the Ukrainian Center of Endocrinology, about 1.3 million people with T2DM were registered in 2019, which emphasizes the need for increased attention to this disease [16].

HC remains a serious global problem. In Ukraine, the incidence of new cases of HCV increased from 8.86 per 100 thousand people in 2022 to 14.99 per 100 thousand in 2023 [17], while the overall incidence of HCV in Ukraine is one of the highest in the world, ranging from 3.1% to 3.5% according to various estimates [18, 19].

HC is accompanied by significant endogenous intoxication and contributes to metabolic disorders, chronic inflammation, atherosclerosis, which increases the risk of coronary heart disease (CHD), arterial hypertension (AH), and cardiovascular complications. Patients with CHC and cardiovascular disease have a decrease in platelet and red blood cell counts, an increase in the level of rods and other inflammatory markers. Progression of hepatic fibrosis (especially F4) is associated with increased cardiovascular risks [20, 21].

Studies show that HCV is significantly associated with an increased risk of developing T2DM. A systematic review and meta-analysis of 33 articles confirmed that HCV infection increases the risk of T2DM regardless of the severity of liver disease [22].The cumulative prevalence of T2DM among patients infected with HCV is 19.67%, which is significantly higher than the global prevalence of T2DM in the general population, which is 8.5%.The highest prevalence rates of T2DM among patients with HCV infection are observed in Africa (27.72%), Asia (20.73%), North America (16.64%) and Europe (15.02%) [22, 23].

The main mechanisms of the link between HCV and T2DM are the direct effect of viral proteins on insulin receptors and the induction of IR through proinflammatory cytokines TNF-α. Experimental studies confirm that the HCV core protein induces insulin resistance by modifying signaling pathways. Differences in regional access to health care and behavioral factors such as physical activity and nutrition also influence the prevalence of T2DM among patients with CHC.

The highest rates of T2DM in Africa may be due to poorer access to CHC treatment.

The methodology of the study included a meta-analysis of 40 studies involving 14,765 participants from different regions, including Asia, Europe, North America and Africa.The systematic review was conducted in accordance with the PRISMA standard, which confirms the high prevalence of T2DM among patients with CHC, which is significantly higher than in the general population [22, 23].

**The purpose** of this review is to analyze the relationship between chronic HCV infection and the development of type 2 diabetes mellitus, with a focus on pathophysiological mechanisms, clinical outcomes, and the impact of antiviral therapy on glucose metabolism and insulin resistance.

**MATERIALS AND METHODS**

We used scientific articles and studies covered in the PubMed database. Ukrainian Center for Public Health, Karger, RKI, Onlinelibrary, CDC, Ecdc. Particular attention was paid to studies that investigated the relationship between HCV and T2DM, as well as the effectiveness of direct-acting antiviral therapy (DAA) in the treatment of CHC in patients with T2DM. Articles published from 2010 to 2023 were analyzed using the methods of systematic literature review, comparative analysis of clinical outcomes, and meta-analysis to ensure the relevance and accuracy of the findings.

**RESULTS**

It is known that patients with CHC have an increased risk of developing T2DM. According to studies, the risk of developing diabetes among people with hepatitis is 2–3 times higher than among uninfected individuals or those infected with hepatitis B. One of the main mechanisms of diabetes development in patients with CHC is IR [24].

HCV causes IR, even in patients who do not have obesity or other risk factors of metabolic syndrome. The virus directly affects insulin signaling pathways in liver cells and extrahepatic tissues, such as skeletal muscle, by disrupting protein kinase B (Akt) and insulin receptor substrate (IRS), which reduces tissue sensitivity to insulin. In addition, infected hepatocytes secrete inflammatory mediators that impair glucose metabolism. The main mechanisms by which HCV contributes to the development of IR and T2DM are impaired insulin signaling, fat accumulation in the liver, and systemic inflammation [25–27].

IR is a key mechanism of diabetes development in HCV infection and is observed in 70% of patients. The virus affects insulin sensitivity both directly, through disruption of signaling pathways, and indirectly through inflammatory processes caused by cytokines [28].

Liver steatosis (ST) is observed in 42–73% of patients with CHC and is more common in HCV genotype 3, where it is a direct consequence of

infection. ST is associated with impaired lipid metabolism, in particular through activation of transcription factors (SREBP-1c) and decreased β-oxidation of fatty acids. This contributes to the accumulation of triglycerides in the liver and exacerbates IR. There is a bidirectional relationship: ST enhances IR through inflammatory processes caused by cytokines (TNF-α), while IR promotes fat accumulation in the liver. In addition, ST is a cardiometabolic risk factor that increases the risk of cardiovascular disease, including atherosclerosis and heart failure [29].

HCV infection inhibits the insulin signaling pathway by affecting key elements of insulin signaling, such as IRS-1 and IRS-2. This effect disrupts the transmission of insulin signals to hepatocytes, which reduces their ability to absorb glucose. In addition, HCV reduces the expression of glucose transporter (GLUT2) in hepatocytes, which disrupts normal glucose metabolism in the liver [30].

ST is common in patients with CHC and is an important factor in the development of IR. The accumulation of triglycerides in the liver disrupts glucose and lipid metabolism, increasing gluconeogenesis and reducing the ability of the liver to utilize glucose. This further exacerbates IR and increases the risk of developing diabetes [31].

Chronic HCV infection causes systemic inflammation, which contributes to the development of IR. The virus activates proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), which leads to a disruption of the insulin signaling pathway. TNF-α inhibits the phosphorylation of the insulin receptor and reduces the activity of IRS-1/-2 proteins, impairing tissue sensitivity to insulin. An increase in TNF-α concentration correlates with a deterioration in carbohydrate metabolism (increased glucose levels, decreased insulin secretion) [32]. In patients with CHC without diabetes, significantly elevated levels of TNF-α, CXCL-10 and the IR index (HOMA-IR) were found compared to the control group. HOMA-IR was positively correlated with HCV viral load and levels of TNF-α and CXCL-10, confirming their involvement in the development of IR. TNF-α is a potent proinflammatory cytokine that disrupts insulin signaling, and CXCL-10 is involved in inflammatory processes and may affect metabolic disorders due to chronic inflammation. These mechanisms may explain the link between HCV and the development of T2DM. TNF-α levels correlate with the severity of inflammation in CHC, increasing the risk of developing T2DM, which is observed in 14.5–33% of patients with this disease, even without cirrhosis. In animal models using transgenic mice, it has been demonstrated that inhibition of TNF-α improves insulin sensitivity, which confirms the role of this factor in the pathogenesis of IR in CHC [33, 34].

HCV significantly affects glucose metabolism, contributing to the development of IR, which is common among patients with CHC. The most severe IR is observed in patients with genotype 1 and 4 viruses, while genotype 3 is associated with lower levels of IR [28, 35, 36]. HCV genotypes also play an important role, with genotypes 1 and 4 being more strongly associated with IR, which complicates treatment and increases the risk of fibrosis [37].

The prevalence of T2DM among patients with CHC (NC-HCV+) is higher than in the general population and patients with chronic hepatitis B (NC-HBV+). The relative risk of developing T2DM for patients with CHC is significantly higher than in the control group and among people with chronic hepatitis B. Patients with CHC and diabetes have a specific clinical phenotype: they usually have a lower body mass index (BMI) and LDL cholesterol level compared to those with diabetes as part of the classical metabolic syndrome, indicating unique metabolic features[35].

Treatment of CHC with DAAs contributes to a significant improvement in glycemic control, increased insulin sensitivity, and reduced inflammation and fibrosis. This allows in some cases to reduce the dose of antidiabetic drugs in patients with T2DM. In people without diabetes, HCV elimination reduces the risk of de novo T2DM by 21%, and in patients with T2DM, it reduces glycated hemoglobin (HbA1c) levels.

DAAs have significantly changed the approach to HCV treatment, and their effectiveness in achieving sustained virologic response (SVR) has become a key factor in reducing the risk of virus-related complications, including the development of IR and diabetes [27, 38]. Studies confirm that the presence of T2DM does not affect the effectiveness of HCV eradication with DAA-based regimens. In particular, studies have shown that T2DM does not affect the achievement of SVR with sofosbuvir regimens. However, diabetes was associated with reduced efficacy of boceprevir regimens [39].

HCV directly affects pancreatic β-cells, disrupting insulin signaling pathways, leading to impaired insulin sensitivity and increased risk of developing T2DM. Hepatogenic diabetes, as a separate form of T2DM, is associated with CHC and is characterized by impaired insulin secretion and sensitivity, contributing to the development of liver fibrosis and increasing the risk of HCC [36]. There are two types of IR in CHC: metabolic (associated with obesity) and viral (caused by exposure to HCV proteins such as NS5A). DAA-based therapy (NS5A and NS5B inhibitors) has been shown to be highly effective in the treatment of CHC, improving

glycemic control and reducing insulin requirements in patients with T2DM [40].

The development of T2DM in patients with CHC is associated with an increased risk of serious complications. One of the most serious is the progression of liver damage, including cirrhosis and HCC. Comparative analysis of cytokines has shown that in people with CHC, T2DM and their combination, there is a change in the levels of such molecules as β-NGF, CXCL1, CXCL9, adiponectin and IL-18. These molecules can work as markers to assess disease progression and the risk of complications. In particular, β-NGF indicates the progression from CHC to cirrhosis and HCC, and IL-18 and glucagon are associated with metabolic syndrome and diabetes. Elevated levels of CXCL1 and CXCL9 may indicate inflammation and fibrosis of the liver, which also increase the risk of HCC [41, 42].

T2DM is associated with an increased risk of developing HCC in patients with liver disease, including CHC. In these patients, the risk of HCC increases, especially if the hemoglobin A1c level exceeds 7.0%. Early treatment of CHC before the onset of glucose metabolism disorders can reduce the risk of HCC [42].

During the period of interferon (IFN)-based therapy, IR reduced the effectiveness of achieving SVR. Antidiabetic drugs, such as pioglitazone and metformin, did not always improve the results of SVR, while statins showed better efficacy. However, IR does not have such a significant impact with DAA-based regimens as with IFN therapy [37].

CHC in patients with T2DM is associated with a higher risk of cardiovascular complications, including hypertension, coronary heart disease, and stroke. IR contributes to elevated blood lipids, which increases the risk of atherosclerosis and cardiovascular disease [6, 46]. In addition, patients with CHF and T2DM are more likely to have kidney complications, including diabetic nephropathy. This increases the risk of developing renal failure requiring dialysis or kidney transplantation. In addition, patients with diabetes are more likely to have visual complications, such as diabetic retinopathy, which can lead to blindness [41, 47].

Studies have shown that T2DM is a powerful risk factor for HCC in patients with cirrhosis, even after treatment of CHC and achievement of SVR. For patients with cirrhosis and T2DM, the risk of developing HCC increases 7-fold compared to those without diabetes, with an annual risk of 7.9% during the first two years after SVR, but after 2 years this risk decreases significantly to 1.9% per year [44].

Risk factors for HCC include the severity of fibrosis before treatment, in particular Metavir stages F3 and F4, IR, and hyperinsulinemia, which contribute significantly to the progression of liver disease. Other factors, such as patient age, low albumin and platelet counts, also correlate with an increased risk of developing HCC [45].

The impact of treating HCV is significant, as achieving SVR reduces IR and improves biochemical parameters of liver function. In patients without cirrhosis, the risk of developing HCC after achieving SVR is extremely low, which calls into question the need for continued intensive follow-up in this group [37].

The use of DPP-4 inhibitors in patients with T2DM and chronic HCV infection is associated with a reduced risk of HCC. Prolonged treatment (more than 1.5 years) and high cumulative doses of drugs reduce the risk of HCC. The mechanism of action includes a decrease in viral load, suppression of inflammation, and activation of immune surveillance by increasing the level of the chemokine CXCL10 [48].

At the same time, HCV is a risk factor for the development of IR and T2DM, with up to 70% of patients with HCV having IR and 33% developing T2DM. Treatment of HCV can improve insulin sensitivity and reduce the risk of progression of liver fibrosis and HCC. However, the effect of DAAs on IR remains controversial, as some studies have shown improvement in fasting glucose levels, while other studies have not confirmed a significant effect on HbA1c or IR [39].

The use of DAAs allows achieving SVR in more than 95% of these patients, which leads to a significant improvement in the glycemic profile. Virus eradication helps to reduce the insulin resistance index (HOMA-IR), improve glucose metabolism, and reduce blood glucose and glycated hemoglobin (HbA1c) levels [27, 47, 49].

For example, in the case of a 38-year-old patient with T2DM and CHC (genotype 1b), after a 12-week course of elbasvir and grazoprevir, her HbA1c decreased from 13.2% to 5.7%, despite the absence of diet and drug treatment of diabetes. This underscores the importance of early treatment of CHC to improve glycemic control [50].

The methodology and results of the study demonstrate the importance of using the glucose tolerance test (OGTT) to more accurately assess changes in glucose metabolism in patients with CHC. More than 50% of patients had impaired glucose metabolism, and 17% were diagnosed with previously undiagnosed T2DM. After treatment with PPPD, there was a significant improvement in insulin sensitivity, a decrease in plasma glucose levels and the HOMA-IR index, especially in patients with initially high IR values. This contributed to a rapid improvement in

glucose metabolism, emphasizing the importance of virus eradication for the restoration of normal insulin pathways [44].

A unique case is that of a patient on long-term insulin therapy (MDI) who was able to completely stop insulin after achieving SVR without worsening glycemic control. Although previous cases demonstrated the possibility of reducing insulin doses, complete insulin withdrawal was rare and could worsen glycemic control. HCV eradication eliminates the disruption of insulin signaling and IR, which allows for normalization of C-peptide and glycemic levels [51].

Although DAAs have shown short-term improvements in glycemic control, long-term studies indicate a possible increase in HbA1c levels several years after treatment. It has been shown that 3 years after treatment, HbA1c levels may rise again in some patients, requiring further monitoring and measures to maintain a normal glycemic profile [52].

DAAs lead to viral eradication, which improves metabolic control. Studies have shown that HCV affects the expression of the glucose transporter (GLUT2) in hepatocytes, which may explain the impaired glucose metabolism in these patients. It also helps to restore normal hepatocyte function, which improves glucose metabolism in the body [53].

HCV eradication under DAAs helps reduce the risk of cardiovascular complications, including coronary heart disease, stroke, and renal failure. Individuals who have achieved SVR show a significant reduction in the risk of end-stage renal disease, which is supported by numerous studies. Among 1395 HCV-infected patients with T2DM, 52% were treated with antiviral drugs, of whom 75% achieved SVR. The risk of acute coronary syndrome, renal failure, stroke, and retinopathy was significantly reduced in recuperates with SVR compared to untreated patients. In addition, DPIs help improve the function of pancreatic β-cells responsible for insulin production. This has a positive effect on the overall glucose metabolism in the body, which reduces the need for insulin or other antidiabetic drugs [54].

**CONCLUSIONS**

There are more than 70 million people infected with the hepatitis C virus worldwide. At the same time, more than 537 million people suffer from type 2 diabetes. A significant number of patients with chronic hepatitis C also have type 2 diabetes, which may indicate a close relationship between these two diseases.

CHC and T2DM are closely related pathophysiological conditions with significant clinical consequences. HCV contributes to the development of IR, which is a key mechanism for the development of diabetes in these patients, provoked by the virus, disrupts glucose metabolism even in individuals without classical risk factors.

The prevalence of T2DM among patients with HC is significantly higher than among people with other chronic liver diseases. DAAs have shown high efficacy in achieving SVR, which contributes to a significant improvement in glycemic control. These drugs not only eliminate the virus, but also reduce the level of IR, which improves metabolic parameters in patients with T2DM, reduces or eliminates the need for insulin therapy, improving the quality of life of patients.

## PROSPECTS FOR FUTURE RESEARCH

Despite the fact that the results suggest a possible close relationship between CHC and T2DM, further research is needed to determine the most effective treatment strategies for this category of patients. Studying the mechanisms that affect IR in the setting of CHC is important for the development of new therapeutic approaches and improvement of treatment of patients with T2DM. Further research is also needed on the effect of DAAs on the function of pancreatic β-cells and the possibility of full recovery of the metabolic profile after achieving SVR.

## AUTHOR CONTRIBUTIONS

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ARTIFICIAL INTELLIGENCE DISCLOSURE

This publication was prepared without the use of artificial intelligence tools.

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