EFFECT OF THE SARS COV-2 VIRUS ON DIABETES SYMPTOMS, DIAGNOSTICS, AND TREATMENT

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ABSTRACT

Because COVID-19 has been recognised as one of the most important pandemics in the history of humankind, in recent years many scientists have investigated the effect of the disease on various aspects of mental and physical human health. This article presents a literature review regarding the effect of SARS CoV-2 infection on the symptoms, diagnostics, and treatment of diabetes. It discusses the effect of infection with virus SARS-CoV-2 on the course of type 1 and type 2 diabetes as well as the frequency of occurrence of the disease in patients affected by

COVID-19. Moreover, it presents information on the pharmacotherapy and way of providing services by doctors during the pandemic. According to the literature, infection with virus SARS CoV-2 causes a general inflammation of the organisms and numerous metabolic and hormonal disturbances, and therefore affects the course of diabetes. It may lead not only to serious metabolic complications in the course of early diabetes, but also to the development of the disease. It was determined that infection with COVID-19 in diabetes patients (mainly type 2) increases the risk of complications (such as acute respiratory failure, multi-organ failure, and death).

1. INTRODUCTION

COVID-19 is an infectious disease of the respiratory system caused by an infection with virus SARS-CoV-2. It was first described in 2019 in China. In March 2020, the disease gained the status of a pandemic – one of the most significant ones in the history of mankind [1]. As of 18 May 2023, the World Health Organisation announced a total of 766 440 796 diagnosed COVID-19 cases globally, including 6 932 591 deaths related to COVID-19. It is a highly contagious infection of the respiratory system. The symptoms and their intensity vary depending on the person – it may be asymptomatic or lead to a critical state or death.

Diabetes iso one of the most frequently occurring chronic diseases and constitutes a serious problem of social life [2], [3], [4]. Diabetes affects 422 million people worldwide [5]. According to the Ministry of Health, more than 2 million people in Poland currently have diabetes [6]. It is a metabolic disease resulting in disturbances in the production or abnormal function of insulin, and consequently hyperglycaemia [7]. Diabetes is directly related to the diet and lifestyle. It affects the functioning of various organs (such as eyes, brain, immune system, kidneys, or heart), and may contribute to their long-term damage [8].

Due to the constantly growing number of COVID-19 cases, numerous studies have been conducted in recent years, concerning both the course of the disease and its effect on various aspects of the physical and mental health in people. Because diabetes is considered a

civilisational disease, many researchers have undertaken studies on the effect of infection with virus SARS-CoV-2 on the course of diabetes or its development. Literature sources report that COVID-19 may lead not only to serious metabolic complications in the course of early diabetes, but also to higher incidence of this disease. According to Remuzzi and Remuzii [9], the average age of persons that died due to COVID-19 in Italy was 81, and more than two thirds of them were diagnosed with diabetes, cardiovascular disease, or cancer [9]. Prolonged time of treatment of patients with co-occurring diabetes was reported in China [10].

Moreover, numerous studies have shown that the relation between these diseases can be two-directional [11]. It may be directly related to the infection with virus SARS-CoV-2 resulting in increased release of cytokines and inflammatory mediators (and consequently an increase in insulin resistance and the related hyperglycaemia) [12]. The applied methods of treatment of the virus, however, can also affect glucose homeostasis in the blood [13]. For example, treatment with glycocorticosteroids (applied in patients affected by SARS CoV-2 with critical symptoms) contributes to the intensification of gluconeogenesis and an increase in insulin resistance, and therefore to higher glucose levels in the blood [14], [15]. The occurrence of SARS-CoV-2 may also lead to a decrease in the number of secretory vesicles in pancreas beta-cells (responsible for insulin secretion) and affect ACE2 receptors in pancreatic islets [16].

It is also worth mentioning that during the pandemic, diagnostics related to hospitalisation due to SARS-CoV-2 infection covered a range of tests, including blood glucose concentration, resulting in an increase in the detectability of diabetes. Personal appointments with general practitioner doctors were limited, and the best form of contact proved to be telemedicine.

This article presents a review of available literature regarding the effect of SARS CoV-2 infection on the symptoms, diagnostics, and treatment of diabetes.

FREQUENCY OF OCCURRENCE OF DIABETES IN COVID-19 PATIENTS

According to research, diseases most frequently co-occurring in COVID-19 patients include: obesity (39.4%) as well as hypertension and cardiovascular diseases (12.1%) [17]. Those diseases are in many cases related to type 2 diabetes [17]. Research shows that the frequency of occurrence oscillates at a level of 7-30%. Moreover, a greater share of hospitalisations, acute pneumonia, and morbidity is observed in these patients than healthy people [18]. It should be

emphasised that in patients hospitalised due to COVID-19 in intensive care units, the frequency of occurrence of diabetes is twice or even three times higher, and morbidity is approximately twice as high as in patients without diabetes [19].

COVID-19 AND TYPE 1 DIABETES

Type 1 diabetes (T1DM) is a genetic autoimmune disease that causes damage to beta-cells by autoreactive T lymphocytes (CD4^{+} and CD8^{+}). Hyperglycaemia alters the immunological response and triggers dysregulation of cytokines, leading to inflammation and procoagulation [20]. Not much research is available on the relation of type 1 diabetes to virus SARS-CoV-2. It may result from the fact that T1DM constitutes approximately 5% of all cases of diagnosed diabetes [20]. It may also be caused by the awareness of patients with diabetes regarding their increased susceptibility to infections and the related intensified prevention during the developing pandemic [21]. According to the literature, type 1 diabetes in persons affected by COVID-19 occurs with a frequency from 0.15% to 28.98% [22], [23]. The most frequent adverse reaction is diabetic ketoacidosis [23].

COVID-19 AND TYPE 2 DIABETES

Type 2 diabetes (T2DM) is mainly related to unhealthy lifestyle and inappropriate nutrition. In patients affected by both T1DM and T2DM, the prognosis in COVID-19 is considerably worse than in healthy persons [24]. Mechanisms explaining this phenomenon are still not thoroughly investigated. According to paper [25], they include the disturbance of neutrophile degranulation, complement system activation, and greater glucose concentration in the secretions in the respiratory tract, allowing for the intensification of the virus replication and pro-inflammatory cytokine response. The comparison of type 2 diabetes patients infected with virus SARS-CoV-2 with those without diabetes shows that persons with T2DM more frequently develop a more serious form of the disease, and show a considerable increase in inflammation markers such as C-reactive protein, procalcitonin, ferritin, lactate dehydrogenase, and D-dimers [26]. Research shows a greater risk of complications (acute respiratory failure, multi-organ failure, and death) in patients affected by both diabetes (mainly type 2) and COVID-19 [27]. According to Bode et al.

[28] patients with COVID-19 and diabetes with uncontrolled hyperglycaemia underwent longer hospitalisation and showed higher mortality.

DIABETIC KETOACIDOSIS

Diabetic ketoacidosis is a disturbance of the acid-alkaline balance in the organism, resulting in a decrease in blood pH below 7.35. It is caused by a sudden considerable insulin deficiency. Diabetic ketoacidosis is one of the most serious complications of diabetes where the presence of urinary ketones is characteristic. Research also shows that the disease is included in the most frequent hyperglycaemic complications in patients with diabetes infected with SARS-CoV-2, and in complications with the highest hospitalisation ratio [29]. Treatment of diabetic ketoacidosis in patients with COVID-19 takes a standard course, although it is sometimes necessary to apply higher insulin doses [30]. It is also very important to quickly apply anticoagulant therapy in patients with diabetic ketoacidosis and COVID-19, due to the considerably increased risk of thromboembolic events [31]. A consequence of diabetic ketoacidosis is dehydration and electrolyte disturbance. It is therefore necessary to properly hydrate and monitor the patient.

PATHOPHYSIOLOGY OF DIABETES AND COVID-19

ACE-2 is used as the main receptor for SARS-CoV-2 that permits penetration of the host cell [32]. The expression of ACE-2 occurs in various organs such as: lung alveoli, intestines, kidneys, heart, blood vessels, and pancreas [33], [34]. According to recent studies, its expression in the cells of pancreas islets is higher than in the lungs [18], [35]. Virus SARS-CoV-2 combines with ACE2 by means of S-glycoprotein, and then penetrates pancreas cells causing their dysfunction, consequently leading to hyperglycaemia [18], [35]. Through creating oxidation stress, acute hyperglycaemia in diabetes patients with COVID-19 results in inflammation, endothelial dysfunction, and thrombosis [36].

DIABETES PHARMACOTHERAPY IN COVID-19

The most frequently applied hypoglycaemic agent also most preferred by patients with type 2 diabetes affected by COVID-19 is metformin. Persons taking this medicine have shown considerable improvement of their state of health [37]. It is worth emphasising, however, that the side effect of the application of metformin can be the occurrence of lactate acidosis. This complication usually appears in patients with acute COVID-19, kidney dysfunctions, serious infections, or sepsis [38], [39].

Safe medicines in diabetes therapy during COVID-19 infection are DPP-4 inhibitors that are well tolerated and not related to the risk of hypoglycaemia [37]. As suggested by Iacobellis [40], they can also mitigate the effects of COVID-19 infection.

Another medicine applied in COVID-19 treatment in diabetes patients is sulfonylurea. It can be applied in patients that can regularly take food orally [41]. Sulfonylureas are not preferred during diabetes treatment in patients with serious COVID-19 due to the risk of hypoglycaemia [42].

Another popular group of medicines are flozins (SGLT2 inhibitors) that increase excretion of sodium and glucose with urine [13]. Their application can lead to dehydration [13]. The medicines are preferred in patients with mild COVID-19. It is not recommended to administer them in critical cases [39]. It should be emphasised that SGLT2 inhibitors can increase lactate concentration, simultaneously reducing intracellular pH, providing for their antiviral effect [43].

Diabetes pharmacotherapy in the course of COVID-19 also often covers GLP-1 agonists. Their application, however, increases the risk of occurrence of nausea and vomiting in patients, potentially leading to dehydration and aspiration pneumonia [44]. Due to this, the medicines are recommended for treatment of the mild and moderate form of COVID-19 [41]. In treatment of patients with an acute form of the disease, it is important to remember about their proper hydration and monitoring of their vital parameters [39].

Pioglitazone can be applied in mild and moderate COVID-19, but it should be avoided in patients in a critical state or with hepatic or heart impairment [41]. In COVID-19 patients hospitalised in severe general condition, the preferred first-line medicine is insulin [41]. The best

choice is to administer it intravenously, but in special cases, its subcutaneous application is possible [41], [13].

CORTICOSTEROIDS AND COVID-19

Steroids are drugs with proven effectiveness in COVID-19 treatment. According to research conducted in Great Britain, the application of dexamethasone contributes to the reduction of mortality in patients requiring oxygen therapy or mechanical ventilation [13], [45]. Corticosteroids show anti-inflammatory and immunosuppressive properties, hence they are frequently applied by doctors in both short- and long-term treatment. Unfortunately, they have many adverse effects such as hypertension, hypoglycaemia, or diabetes caused by steroid induced diabetes [46]. The dosing, treatment duration, relative strength, and accompanying infection affect the degree of hyperglycaemia, but the risk of hospitalisation due to uncontrolled blood sugar levels certainly increases in diabetes patients taking steroids [47].

DIABETES IN THE PERIOD OF THE COVID-19 PANDEMIC

It is commonly recognised that the lifestyle and diet of society underwent considerable changes during the COVID-19 pandemic. The conditions occurring during that time favoured reduced physical activity and affected the amount and quality of meals. A study conducted by Ghosh [48] showed that an increase in carbohydrates and fats intake in India during the pandemic reached 21% and 13%, respectively. According to the literature, lack of physical activity and changes in eating habits have a direct effect on the development of insulin resistance [49].

Moreover, the proliferating obesity could have contributed to the development of type 2 diabetes. Another important factor affecting the general state of health of society and causing worsening of the diet was strong stress due to the occurring situation related to the COVID-19 pandemic.

During the COVID-19 pandemic, the way of providing services by doctors also changed. Telemedicine became a popular form of conducting consultations. It affected both the blood glucose level diagnostics as well as access to medicines applied in diabetes treatment.

TELEMEDICINE AND DIABETES DURING THE COVID-19 PANDEMIC

Telemedicine, i.e. remote health care covering telephone calls, video calls, and applications, considerably facilitates communication between the doctor and patient [13]. In the period of the COVID-19 pandemic, it proved incredibly helpful in monitoring the course of diabetes, medical consultations related to the disease, and obtaining information regarding its treatment [50]. Telemedicine is an easy way to contact a doctor, particularly for young patients with type 1 diabetes [51]. Patients with type 2 diabetes are primarily older persons that do not use the internet or other technologies daily. Telemedicine services, however, also proved effective in that group of patients, allowing for better control of glycaemia than personal appointments in medical facilities [52]. According to literature sources, the application of telemedicine in comparison to standard health care correlates with a substantial decrease in glycosylated haemoglobin (HbA1c) [51]. It should be emphasised that a greater decrease in HbA1c has been recorded in patients with recently diagnosed diabetes and higher initial HbA1 (>8%).

SUMMARY

The effect of COVID-19 on the development and course of diabetes should be considered in several aspects: diagnostics of the disease during the pandemic, changes in the lifestyle of society caused by the pandemic, direct effect of SARS-CoV-2 infection on the functioning of the organism (such as dysfunction of pancreas β cells, general inflammation of the organism, metabolic and hormonal disturbances), and type of the applied treatment method. It is worth emphasising that the development of diabetes or aggravation of its effects can be caused by a combination of all the aforementioned factors.

SARS CoV-2 infection has an effect on the course of diabetes (it can lead to both serious metabolic complications in early diabetes and development of the disease). Diabetes in turn contributes to the aggravation of complications related to COVID-19 such as acute respiratory failure or multi-organ failure. Better understanding of the effect of infection with virus SARS-CoV-2 on the course and treatment of diabetes requires conducting further research.

DISCLOSURE

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As a review paper, our work does not present new data or analyses. Therefore, there are no specific datasets or data availability to report. The information and findings presented in this review are based on previously published studies, which can be accessed through their respective sources as cited in the reference section.

Conflict of Interest Statement

The authors declare that there are no significant conflicts of interest associated with this research work.

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