

Open Access Article

Ann. Acad. Med. Siles. (online) 2023; 77: 217-225 eISSN 1734-025X DOI: 10.18794/aams/166423 www.annales.sum.edu.pl

PRACA ORYGINALNA ORIGINAL PAPER

Comparison of course of infections and antibiotherapy in patients with and without diabetes mellitus - one center experience

Porównanie przebiegu infekcji oraz zastosowanej antybiotykoterapii u pacjentów chorych na cukrzycę i bez cukrzycy – doświadczenie jednego centrum medycznego

> Maria Stec¹, Agata Suleja¹, Wiktoria Kuczmik¹, Aleksandra Mroskowiak¹, Miktoria Kuczmik¹, Miktoria Kuczmik¹, Aleksandra Mroskowiak¹, Miktoria Kuczmik¹, Miktoria Kuczmik Maciei Migacz² Michał Holecki²

¹Students' Scientific Club at the Department of Internal Medicine, Autoimmune and Metabolic Diseases, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland ²Department of Internal Medicine, Autoimmune and Metabolic Diseases, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

ABSTRACT

INTRODUCTION: Infections affect all patients, including those with diabetes mellitus (DM), which can determine the course of infection. The aim of the study was to compare the course and treatment of infection in patients with DM and without DM.

MATERIAL AND METHODS: 180 medical records of patients hospitalized in 2021 at the Department of Internal Medicine, Autoimmune and Metabolic Diseases in Katowice, with infections were analyzed. The analysis included age, sex, clinical diagnosis, DM treatment, antibiotic therapy, and laboratory parameters. The Statistica program was used for statistical analysis.

RESULTS: The most prevalent reasons for hospitalization in both groups were: pneumonia in the course of COVID-19 (35.5% DM vs 33.7% non-DM) and urinary tract infections (26.3% DM vs 19.2% non-DM). Significantly more non-DM patients required polyantibiotic treatment (69.7% DM vs 89.4% non-DM). The most frequently used antibiotics were β-lactams (59.2% DM vs 57.7% non-DM). In-hospital mortality was 20% (21% DM vs 19.2% non-DM). The length of hospitalization was 1–35 days, the median in the whole group was 9 days (10 days DM vs 8 days non-DM). Both the initial and terminal CRP concentrations were analyzed. The median of the initial value was 71.6 (72.3 DM vs 66.2 non-DM) and the median of the terminal value was 17.15 (17.9 DM vs 15.3 non-DM). The glucose concentration on admission was assessed with the median 123.5 mg/dL (156 mg/dL DM vs 107 mg/dL non-DM).

CONCLUSIONS: Many DM complications are well known, yet the course and treatment of infection do not differ significantly in patients with DM and without DM. Despite that, each patient should be considered individually, so the chosen treatment constitutes an optimized therapy.

KEYWORDS

diabetes, infections, antibiotic therapy

Received: 06.03.2023

Revised: 15.04.2023

Accepted: 22.05.2023

Published online: 04.12.2023

Address for correspondence: Maria Stec, Students' Scientific Club at the Department of Internal Medicine, Autoimmune and Metabolic Diseases, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland, Medyków 14, 40-572 Katowice, tel. +48 32 789 43 01, e-mail: mariaannastec@gmail.com



This is an open access article made available under the terms of the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0) license, which defines the rules for its use. It is allowed to copy, alter, distribute and present the work for any purpose, even commercially, provided that appropriate credit is given to the author and that the user indicates whether the publication has been modified, and when processing or creating based on the work, you must share your work under the same license as the original. The full terms of this license are available at https://creativecommons.org/licenses/by-sa/4.0/legalcode.

Publisher: Medical University of Silesia, Katowice, Poland



STRESZCZENIE

WSTĘP: Zakażenia występują u wszystkich pacjentów, w tym także u chorych na cukrzycę (*diabetes mellitus* – DM), której współwystąpienie może jednak determinować przebieg zakażenia. Celem pracy było porównanie przebiegu i leczenia infekcji u chorych z DM i bez DM.

MATERIAŁ I METODY: Analizie poddano dokumentację medyczną 180 pacjentów hospitalizowanych w 2021 r. w Klinice Chorób Wewnętrznych, Autoimmunologicznych i Metabolicznych w Katowicach z powodu infekcji. W analizie uwzględniono wiek, płeć, rozpoznanie kliniczne, metodę leczenia DM, antybiotykoterapię i parametry laboratoryjne. Do analizy statystycznej wykorzystano program Statistica.

WYNIKI: Najczęstszymi przyczynami hospitalizacji w obu grupach były: zapalenie płuc w przebiegu COVID-19 (35,5% DM vs 33,7% bez DM) oraz infekcje dróg moczowych (26,3% DM vs 19,2% bez DM). Istotnie więcej pacjentów bez DM wymagało leczenia z użyciem wielu antybiotyków (69,7% DM vs 89,4% bez DM). Najczęściej stosowanymi antybiotykami były β-laktamy (59,2% DM vs 57,7% bez DM). Śmiertelność wewnątrzszpitalna wyniosła 20% (21% DM vs 19,2% bez DM). Czas hospitalizacji wynosił 1–35 dni, mediana w całej grupie wyniosła 9 dni (10 dni w przypadku DM vs 8 dni bez DM). Analizowano zarówno początkowe, jak i końcowe stężenie CRP. Mediana wartości początkowej wyniosła 71,6 (72,3 DM vs 66,2 bez DM), a mediana wartości końcowej 17,15 (17,9 DM vs 15,3 bez DM). Mediana stężenia glukozy przy przyjęciu wynosiła 123,5 mg/dL (156 mg/dL DM vs 107 mg/dL bez DM).

WNIOSKI: Wiele powikłań DM jest dobrze znanych, jednak przebieg i leczenie infekcji nie różnią się istotnie u pacjentów z DM i bez DM. Mimo to do każdego pacjenta należy podchodzić indywidualnie, tak aby wybrane leczenie stanowiło zoptymalizowaną terapię.

SŁOWA KLUCZOWE

cukrzyca, infekcje, terapia antybiotykowa

INTRODUCTION

Infections in patients with diabetes mellitus (DM) are believed to be more frequent and have a poorer clinical prognosis, which may be partially explained by a decreased T cell-mediated immune response or an impaired neutrophil function [1,2,3]. Persistent hyperglycemia may increase the number of inflammatory mediators produced by adipocytes and macrophages. Chronic inflammation may result in the damage of pancreatic beta cells, hence insufficient insulin production, resulting in hyperglycemia, which modulates immune cell function [4,5]. However, despite common belief, the link between DM and an increased susceptibility to infection is generally not supported by strong evidence.

DM describes a group of metabolic disorders characterized by a high level of glucose and it constitutes a tremendous worldwide health problem [1].

The prevalence of DM has been increasing in recent decades in all age groups and has risen rapidly in recent years mainly due to a sedentary lifestyle, unhealthy diet, obesity and minimal physical activity [2,3]. The International Diabetes Federation (IDF) estimated the global prevalence to be 151 million in 2000, yet it increased up to 537 million in 2021 [4,5] with over 61 million affected patients in Europe and 2.68 million affected patients in Poland [6].

According to meta-analyses and the SABRE prospective population-based study, DM is associated with double the risk of coronary heart disease, ischemic stroke and death attributed to other vascular causes [7,8] with significantly higher mortality in South Asians and African Caribbeans. Other cardiovascular diseases related to DM include ischemic heart disease, heart failure, coronary artery disease and atherosclerosis, the latter two being the most prevalent [9].

In addition to cardiovascular complications, DM is associated with a higher incidence and severity of infectious diseases. The more frequent infections in diabetic patients result from a dysfunction of the immune system conductive to a hyperglycemic environment, including neutrophil dysfunction, depression of the antioxidant system and humoral immunity. Complications such as micro- and macro-angiopathies, neuropathy, a decrease in the antibacterial activity of urine, motility disorders of the gastrointestinal and urinary tract, as well as immunological disorders, result in a higher number of medical interventions in these patients [10]. Furthermore, diabetic patients, especially those with uncontrolled DM have alterations in delayed healing, resulting in a more severe case of the infection and a poorer prognosis [11].

DM disrupts immunity on all levels, including the complement system, inflammatory cytokines and antibodies.

Complement system

The complement system is the main pillar of humoral immunity. It consists of a variety of serum and surface proteins, which induce the opsonization and phago-cytosis of microorganisms by means of macrophages and neutrophils, hence resulting in the lysis of these microorganisms [12]. One of the components of the complement system is C4. It plays a role in the activation of classical and lectin complement cascades, resulting in the neutralization of pathogens. In diabetic patients, the C4 serum concentration is significantly lower than in non-diabetic patients. Thus, DM patients are more prone to microbial infections [10,13].



Inflammatory cytokinesis

In hyperglycemic diabetic patients, the resting interleukin concentrations remain consistently elevated. Thus, in stimulation tests, cytokine production is impaired as a consequence of tolerance induced by prolonged hyperglycemia. As a result, the mononuclear cells and monocytes of people with diabetes secrete less interleukin 1 (IL-1) and IL-6 in response to lipopolysaccharide stimulation [10,14].

Antibodies

In patients with type II diabetes, the level of glycation of immunoglobulins corresponds to the concentration of HbA1c, which is associated with a higher glycation of immunoglobulins in patients with uncontrolled or poorly controlled diabetes. Thus, a higher number of antibodies may be damaged in diabetic patients, resulting in a substandard immune response [11].

The overall effect of all these immune pathologies is an increased susceptibility to infections in patients with diabetes. Therefore, the aim of the presented study is to compare the clinical picture, course and treatment of infections in diabetic and non-diabetic patients.

Our primary objectives are to compare the clinical characteristics and course of the infections (including the history of diagnosis and treatment of DM, inhospital pharmacotherapy, signs and symptoms, laboratory tests) in patients with and without DM and analyze and contrast the antibiotic treatment of patients with and without DM during hospitalization.

MATERIAL AND METHODS

Study design

We used a cross-sectional study design as the type of observational study, which allows measurement of the outcome (course of the infection) and the exposures (the administration of antibiotic therapy) in the study participants at the same time. This design allows assessment of the prevalence of the outcomes and exposures in the clinic-based samples.

Setting

The primary analysis covered 1090 patients hospitalized at the Department of Internal Medicine, Autoimmune and Metabolic Diseases in Katowice between the 1st January 2021 and 31st December 2021. Initially, information was collected regarding the history of diabetes diagnosis and treatment as well as signs and symptoms, pharmacotherapy administered in the hospital and laboratory test results (including serum HbA1c concentration, glucose on admission, lipid profile, C-reactive protein – CRP, leukocytes, procalcitonin on admission and discharge, creatinine and estimated glomerular filtration rate – eGFR).

Participants

We retrospectively identified patients with a principal diagnosis of infection among all the patients hospitalized at the Department in Katowice, and from among this population, subjects fulfilling eligibility criteria were selected.

The eligibility criteria constituted both inclusion and exclusion criteria. The inclusion criteria were any infection. The exclusion criteria were a history of diagnosis of metabolic syndrome or oncological diseases. A total of 180 patients met the inclusion criteria and were included in the further analysis.

The patients were divided into two groups: with diabetes (N = 76, age 70.78 \pm years, glucose level 199.67 \pm 169.37 [mg/dL) and without diabetes (N = 104, age 62.27 \pm years, glucose level 116.25 \pm 44.33 [mg/dL]), based on the diagnosis of DM.

Bias

In order to minimize bias, the control group comprised patients hospitalized at the Department in Katowice between the 1st January 2021 and 31st December 2021, who fulfilled the eligibility criteria and had no diagnosis of DM. Thus, data regarding the compared groups was extracted from the same institution and within the same time frame, resulting in the minimalization of bias.

Study size

The number of patients hospitalized with a diagnosis of infection at the Department in Katowice during the study period determined the size of the analyzed population.

Statistical analysis

All the statistical analyses were performed using Statistica 10 PL software. The comparison between the control and the DM groups was made by the Mann--Whitney U test. Correlation coefficients R were obtained according to Spearman's rank correlation coefficient. p < 0.05 was considered statistically significant. The values are presented as means and standard deviations.

RESULTS

The characteristics of the analyzed groups are presented in Table I. Blood samples were collected from non-fasting patients upon admission to the hospital. 180 medical history records of patients were analyzed. The cohort was divided into 2 groups: patients with DM (n = 76) and patients without DM (n = 104). The patients were hospitalized from 1 up to 35 days. The median in the whole group was 9 days (10 days for the patients with DM and 8 in patients without DM). Regarding mortality (20% in the whole group, 21% for the group with DM and 19% without DM), the median hospital stay was 7 days (7.5 days for the patients with DM and 7 without DM; Figure 1).

The vast majority of the DM patients were treated with antidiabetic pharmacotherapy (80.5% prior to hospitalization and 85.7% in-hospital). The most prevalent treatment was insulin therapy (41.6% vs 59.7% in-hospital), metformin (31.2% vs 28.6%) and sylphonylurea (18.2% vs 9.1%) in patients prior to hospitalization and in-hospital respectively.

In the statistical analysis of the characteristics such as the duration of hospitalization, mortality, CRP level, leukocytes, procalcitonin (on admission and at discharge) of the studied group, no statistical correlation was found between the DM and non-DM populations (Table I).

Table I. Characteristics of studied groups

······································				
Anthropometric parameters	DM (N = 76)	non-DM (N = 104)		
1	2	3		
Sex				
male [n] female [n]	44.74% (34) 55.26% (42)	57.69% (60) 42.31% (44)		
Age [y]	70.77 ±13.13	62.27 ± 17.75		
BMI [kg/m ²]	28.90 ± 8.57	26.62 ± 5.86		
Body mass [kg]	80.27 ± 19.21	78.05 ± 19.90		
Height [cm]	166.21 ± 8.92	170.85 ± 10.17		
Mortality [n]	21.05% (16)	19.23% (20)		
Duration of hospitalization [days]	10.68 ± 6.78	8.69 ± 5.02		
Non-fasting glycaemia on admission [mg/dL]	199.67 ± 169.37	166.25 ± 44.33		
Altered lipid profile	20.19% (21)	21.15% (22)		
CRP on admission [mg/L]	92.65 ± 77.78	93.85 ± 81.80		
CRP at discharge [mg/L]	40.03 ± 52.64	38.85 ± 58.63		
Leukocytes on admission [10 ³ /µL]	11.18 ± 7.82	10.42 ± 5.96		
Leukocytes at discharge [10³/µL]	9.61 ± 7.75	10.33 ± 5.93		
Procalcitonin on admission [ng/mL]	4.32 ± 10.52	2.37 ± 8.12		
Procalcitonin at discharge [ng/mL]	0.63 ± 1.59	1.27 ± 3.65		

		cd. tab. I	
1	2	3	
Creatinine [mg/dL]	1.50 ± 1.44	1.26 ± 1.07	
eGFR [mL/min]	35.51 ± 13.33	30.46 ± 13.49	
Pneumonia in the course of COVID-19	35.55% (27)	33.65% (35)	
Urinary tract infections	26.32% (20)	19.23% (20)	
Pneumonia	14.47% (11)	15.38% (16)	
C. difficile infection	9.21% (7)	13.46% (14)	
Diverticulitis	0% (0)	7.69% (8)	
Urosepsis	5.26% (4)	6.73% (7)	
Sepsis	6.58% (5)	4.08% (5)	
H. pylori infection	6.58% (5)	2.88% (3)	
Cholecystitis	3.95% (3)	5.77% (6)	
Acute tubulointerstitial nephritis	3.95% (3)	1.92% (2)	
Acute pancreatitis	1.32% (1)	3.85% (4)	
Colitis	1.32% (1)	2.88% (3)	
Abdominal abscess	0% (0)	2.88% (3)	
Urethritis	2.63% (2)	0% (0)	
Gastritis (other than <i>H. pylori</i> infection)	0% (0)	1.92% (2)	
Esophagitis	1.32% (1)	0.96% (1)	
Pericarditis	1.32% (1)	0% (0)	
Yersiniosis	0% (0)	0.96% (1)	
Perirectal abscess	0% (0)	0.96% (1)	
Meningitis	0% (0)	0.96% (1)	
Myocarditis	0% (0)	0.96% (1)	
β-lactams	59.2% (45)	56.73% (59)	
Quinolones	40.79% (31)	41.34% (43)	
Nitroimidazoles	28.95% (22)	26.92% (28)	
Glycopeptides	17.11% (13)	21.15% (22)	
Sulphonamides	9.21% (7)	3.85% (4)	
Macrolides	2.63% (2)	8.65% (9)	
Fosfomycin	5.26% (4)	1.92% (2)	
Aminoglycosides	1.31% (1)	5.77% (6)	
Rifampicin	3.95% (3)	1.92% (2)	
Linezolid	0% (0)	3.85% (4)	
Lincosamides	0% (0)	2.88% (3)	
Tetracycline	0% (0)	1.92% (2)	
Polymyxin	0% (0)	1.92% (2)	
Rifaximin	0% (0)	1.92% (2)	
Penicillin	0% (0)	0.96% (1)	

DM – diabetes mellitus; BMI – body mass index; CRP – C-reactive protein; eGFR – estimated glomerular filtration rate; COVID-19 – coronavirus disease 2019; C. difficile – Clostridium difficile; H. pylori – Helicobacter pylori.



Fig. 1. Dispersion of patient death rate during hospitalization; DM – diabetes mellitus.

The most frequent reasons for hospitalization in both groups were: pneumonia in the course of coronavirus disease 2019 (COVID-19; 35.5% of diagnoses in DM patients and 33.7% in non-DM ones), urinary tract infections (26.3% diagnosed in DM patients and 19.2%

Table II Reasons for hospitalization

in non-DM ones), pneumonia (14.5% of diagnoses in DM patients and 15.4% in non-DM ones), *Clostridium difficile* (*C. difficile*) infection (9.2% of diagnoses in DM patients and 13.5% in non-DM ones) and others (Table I, II).

Reason for hospitalization (from most common)			
with DN	1	without DM	
pneumonia in course of COVID-19	35.5%	pneumonia in course of COVID-19	33.7%
urinary tract infections	26.3%	urinary tract infections	19.2%
pneumonia	14.5%	pneumonia	15.4%
C. difficile infection	9.2%	C. difficile infection	13.5%
H. pylori infection	6.6%	diverticulitis	7.7%
sepsis	0.0%	urosepsis	6.7%
urosepsis	5.3%	cholecystitis	5.8%
kidney inflammation cholecystitis	3.9%	sepsis	4.8%
		pancreatitis	3.8%
acute pancreatitis colitis esophagitis pericarditis		abscess in the abdomen <i>H. pylori</i> infection colitis	2.9%
	1.3%	gastritis (other than <i>H. pylori</i> infection) urethritis	1.9%
		yersiniosis	
		perirectal abscess	
		meningitis	1%
		esophagitis pericarditis	

DM - diabetes mellitus; COVID-19 - coronavirus disease 2019; C. difficile - Clostridium difficile; H. pylori - Helicobacter pylori.

The compared groups do not show any particular differences; however, minor differences can be found. It was observed that the DM patients were more likely to suffer from pneumonia in the course of COVID-19

than the non-DM patients (35.5% vs 33.7%). Moreover, the diabetic group was more often hospitalized due to urinary tract infections than the non-diabetic group (26.3% vs 19.2%). Pneumonia was slightly more frequent in the non-DM patients (15.4% vs 14.5%) and *C. difficile* infection was also more common among the non-diabetic patients (13.5% vs 9.2%; Table I). There was no significant difference between the sexes in the incidence of the particular infections. β -lactams was the most frequently prescribed antibiotic in both groups. It were received by 59.2% of diabetic

patients and 56.7% of non-diabetic patients. Third-generation cephalosporin was the most often chosen with 66.7% and 85%, respectively, followed by quinolones (40.8% vs 41.3%; Table I, III).

The need for more than 1 type of antibiotic treatment occurred in 69.7% of the DM patients and 89.4% of the non-DM patients (Figure 2).

Antibiotic (from most common)					
with DM		without DM			
β-lactams	59.2%	β-lactams	56.73%		
quinolones	40.8%	quinolones	41.3%		
nitroimidazoles	28.9%	nitroimidazoles	26.9%		
glycopeptides	17.1%	glycopeptides	21.6%		
sulphonamides	9.2%	macrolides	8.7%		
fosfomycin	5.3%	aminoglycosides	5.8%		
rifampicin	3.9%	linezolid sulphonamides	3.8%		
macrolides	2.6%	lincosamides	2.9%		
aminoglycosides	1.3%	tetracycline polymyxin fosfomycin rifaximin	1.9%		
		penicillin	1%		

DM – diabetes mellitus.



Fig. 2. Number of antibiotics used in treatment; DM – diabetes mellitus.

The initial and terminal CRP values were analyzed. The median baseline value was 71.6 mg/L (72.3 mg/L in the patients with DM and 66.2 mg/L in the patients without DM) and the median of the final value was 17.15 mg/L (17.9 mg/L in the patients with DM and 15.3 mg/L in the patients without DM). The differences were not significant (p = 0.952 at baseline and p = 0.580 at end). Similarly, the initial and final leukocyte values were measured. The median baseline value was $8.61 \times 10^3/\mu$ L ($8.56 \times 10^3/\mu$ L in the patients with DM and $8.78 \times 10^3/\mu$ L in the patients without DM) and the

median final value was 17.15 ($7.55 \times 10^{3}/\mu$ L in the patients with DM and $8.64 \times 10^{3}/\mu$ L in the patients without DM). The differences were not significant (p = 0.906 for baseline and p = 0.140 for final). We also analyzed each major disease separately in each group and there were not significant differences either.

The glucose values were also compared. The median was 123.5 mg/dL (156 mg/dL in the patients with DM and 107 mg/dL in the patients without DM). There was a significant difference between the glycemia values (p < 0.01; Table IV).



Table IV. Differences in patients with and without DM

Patients		
with DM	without DM	
most common antibiotic: β-lactams (59.2%)	most common antibiotic: β-lactams (57.7%)	
death: 21%	death: 19.2%	
glucose value: 156 mg/dL	glucose value: 107 mg/dL	
CRP value: initial 72.3; terminal 17.9	CRP value: initial 66.2; terminal 13.3	
length of hospitalization: 10 days	length of hospitalization: 8 days	

DM – diabetes mellitus; CRP – C-reactive protein.

DISCUSSION

Despite the wide and common preventive awareness, hyperglycemia and hypoglycemia are still major challenges in modern medicine. Hyperglycemia is associated with the risk of infections, cardiovascular events and even higher mortality during hospitalization. All these factors may prolong the patient's stay in hospital, which was one of the results in our study as well [15,16]. What is more, according to World Health Organization (WHO) data, 537 million people worldwide suffer from diabetes. It is estimated that by 2030 it will be the 7th leading cause of death [2].

The first large study which compared the infection risk in diabetic and non-diabetic patients was published in Ontario in 1999. It compared 513 749 patients in each group. In both groups, 51.7% of the patients were men. While the study found no differences between men and women, it showed that diabetic patients were more likely to die from infection, 1% for diabetic patients and 0.6% for non-diabetic patients (p < 0.0001) [17,18,19]. In comparison, our study showed a completely opposite trend. It contained 53% men. 1090 records were analyzed but only 180 patients with infections were included. Of the 180 cases, 76 were diabetic (42%) and 104 non-diabetic (68%), 21% deaths were observed in the diabetic group and 19% in the non-diabetic group (p = 0.763), hence the difference was not significant.

However, according to Zoppini et al. [20], mortality in diabetic patients peaked in younger patients (30--64 years) and declined afterwards. This idea aligns with our results – the DM cohort was generally older than the non-DM cohort, thus mortality could have been lower in the analyzed diabetic patients.

The Ontario study also indicated that the most common infection among diabetic patients was upper respiratory tract infection (61.8% of all cases). This was followed by cystitis (11.9%), pneumonia (10.7%) and cellulitis (10%). On the other hand, the least common were human immunodeficiency virus (0.12%), appendicitis (0.13%) and peritonitis (0.20%) [19].

Our results also prove that respiratory infections are the most common conditions. It should be emphasized that the study covered a year full of COVID-19 cases. The diabetic patients in our study suffered the most from pneumonia in the course of COVID-19 (35.5%),

urinary tract infections (26.3%) and pneumonia per se (14.5%). Nevertheless, the least common were acute pancreatitis, colitis, esophagitis and pericarditis (all together 1.3%).

The COVID-19 epidemic has also changed the patterns. It was observed that during the 28-day follow-up period, the in-hospital death rate was much higher for individuals with a newly developed type 2 diabetes (T2D) or with pre-existing T2D compared to nondiabetic patients (7.8% vs 2.7%). Furthermore, T2D subjects were more likely to develop complications such as acute respiratory distress syndrome (ARDS; 16.9% vs 7.2%), septic shock (3.8% vs 1.0%) and disseminated intravascular coagulation (DIC; 0.5% vs 0.2%). There was no difference in the symptoms, such as cough or fever, between the DM and non-DM groups, but the diabetic patients were characterized by more frequent albuminuria and a higher serum level of CRP and leukocytes [21,22]. Nonetheless, our study did not show those tendencies; mortality was not higher in the DM group (24% vs 26.5%), we did not observe significantly greater inflammation markers or an elevated proportion of complications either.

It was also stated that patients with both urinary tract infection and diabetes presented a more severe course of infection. We also performed an isolated analysis of this group of patients but found no significant difference [23].

C. difficile infection is seldom associated with diabetes but tends to occur more frequently in often-hospitalized DM patients [24]. Interestingly, in our study the incidence of *C. difficile* infection was higher in the non-DM cohort (13.5% vs 9.2%). Nevertheless, according to Meier et al. [25], the infection may be more frequent in patients with a lower body mass index (BMI) and without diabetes.

Although the frequent occurrence of infections in patients with DM is often claimed, it has never been fully explained. The review of the available literature done by Knapp [26] highlights that it is not certain if DM itself predisposes to infections. The author states that it is important to remember that diabetes is a complex disorder which often occurs with other diseases. For this reason, it is not clear if DM makes patients more likely to suffer from infections. The impact of DM on immune response is still debated – a variety of studies support this thesis, but there are still



studies suggesting an undisturbed inflammatory response [16,26].

Our results differ from those obtained in some studies; however, there is a limited number of studies covering this area, exploring infections and the course of the disease generally. Our paper is a part of the debate and in our opinion, another clinical trial should be conducted.

Limitations

Our study also has several limitations. The first is the lack of HbA1c determination in every patient. Another is the small study group where some of the patients were admitted to hospital urgently, so fasting blood glucose was not measured. It should also be remembered that our study was conducted during the COVID-19 pandemic; some patients were transferred to other wards and temporary hospitals, so we could not collect data from the entire period of infection.

CONCLUSIONS

Hyperglycemia plays an important role in the inflammatory process and adversely affects the progression of diabetes complications. Diabetic patients are susceptible to various types of infection, and glycemic control is a prerequisite for effective infection control. The degree and duration of hyperglycemia seem to be of greater prognostic importance. This in turn means that achieving optimal diabetes control is paramount, which can translate into a better prognosis in severe infection, and that each patient needs to be treated individually so that the chosen treatment is an optimized, effective therapy.

Our study revealed that patients from the DM group presented a similar course of infections, were hospitalized for a comparable period of time and were treated with similar types of antibiotics in comparison with the non-DM group. Also, their prognosis in mortality was similar.

Author's contribution

Study design – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak, M. Migacz, M. Holecki
Data collection – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak
Data interpretation – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak, M. Migacz, M. Holecki
Statistical analysis – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak
Manuscript preparation – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak, M. Migacz, M. Holecki
Literature research – M. Stec, A. Suleja, W. Kuczmik, A. Mroskowiak, M. Migacz, M. Holecki

REFERENCES

1. Baena-Díez J.M., Peñafiel J., Subirana I., Ramos R., Elosua R., Marín-Ibañez A. et al. Risk of cause-specific death in individuals with diabetes: A competing risks analysis. Diabetes Care 2016; 39(11): 1987–1995, doi: 10.2337/dc16-0614.

2. Cho N.H., Shaw J.E., Karuranga S., Huang Y., da Rocha Fernandes J.D., Ohlrogge A.W. et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res. Clin. Pract. 2018; 138: 271–281, doi: 10.1016/j.diabres.2018.02.023.

3. Shaw J.E., Sicree R.A., Zimmet P.Z. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract. 2010; 87(1): 4–14, doi: 10.1016/j.diabres.2009.10.007.

4. International Diabetes Federation. IDF Diabetes Atlas, 1st edn. Brussels, Belgium 2000.

5. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium 2021.

6. Topor-Madry R., Wojtyniak B., Strojek K., Rutkowski D., Bogusławski S., Ignaszewska-Wyrzykowska A. et al. Prevalence of diabetes in Poland: a combined analysis of national databases. Diabet. Med. 2019; 36(10): 1209–1216, doi: 10.1111/dme.13949.

7. Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010; 375(9733): 2215–2222, doi: 10.1016/s0140-6736(10)60484-9.

8. Abu-Ashour W., Twells L., Valcour J., Randell A., Donnan J., Howse P. et al. The association between diabetes mellitus and incident infections: a systematic review and meta-analysis of observational studies. BMJ Open Diabetes Res. Care 2017; 5(1): e000336, doi: 10.1136/bmjdrc-2016-000336.

9. Tillin T., Hughes A.D., Mayet J., Whincup P., Sattar N., Forouhi N.G. et al. The relationship between metabolic risk factors and incident cardiovascular disease in Europeans, South Asians, and African Caribbeans: SABRE (Southall and Brent Revisited) – a prospective population-based study. J. Am. Coll. Cardiol. 2013; 61(17): 1777–1786, doi: 10.1016/j.jacc.2012.12.046.

10. Casqueiro J., Casqueiro J., Alves C. Infections in patients with diabetes mellitus: a review of pathogenesis. Indian J. Endocrinol. Metab. 2012; 16(Suppl 1): S27–S36, doi: 10.4103/2230-8210.94253.

 Peleg A.Y., Weerarathna T., McCarthy J.S., Davis T.M. Common infections in diabetes: pathogenesis, management and relationship to glycaemic control. Diabetes Metab. Res. Rev. 2007; 23(1): 3–13, doi: 10.1002/dmrr.682.
 Flyvbjerg A. Diabetic angiopathy, the complement system and the tumor necrosis factor superfamily. Nat. Rev. Endocrinol. 2010; 6(2): 94–101, doi: 10.1038/nrendo.2009.266.

13. Wang H., Liu M. Complement C4, infections, and autoimmune diseases. Front, Immunol, 2021: 12: 694928, doi: 10.3389/fimmu.2021.694928.

14. Geerlings S.E., Hoepelman A.I. Immune dysfunction in patients with diabetes mellitus (DM). FEMS Immunol. Med. Microbiol. 1999; 26(3–4): 259–265, doi: 10.1111/j.1574-695x.1999.tb01397.x.

15. Khazai N.B., Hamdy O. Inpatient diabetes management in the twenty-first century. Endocrinol. Metab. Clin. North Am. 2016; 45(4): 875–894, doi: 10.1016/j.ecl.2016.06.013.

16. Gupta S., Koirala J., Khardori R., Khardori N. Infections in diabetes mellitus and hyperglycemia. Infect. Dis. Clin. North Am. 2007; 21(3): 617–638, doi: 10.1016/j.idc.2007.07.003.

17. van Niekerk G., Davis T., Patterton H.G., Engelbrecht A.M. How does inflammation induced hyperglycemia cause mitochondrial dysfunction in immune cells? Bioessays 2019; 41(5): 1800260, doi: 10.1002/bies.201800260.

18. Atreja A., Kalra S. Infections in diabetes. J. Pak. Med. Assoc. 2015; 65(9): 1028–1030.

19. Shah B.R., Hux J.E. Quantifying the risk of infectious diseases for people with diabetes. Diabetes Care 2003; 26(2): 510–513, doi: 10.2337/diacare.26.2.510.

20. Zoppini G., Fedeli U., Schievano E., Dauriz M., Targher G., Bonora E. et al. Mortality from infectious diseases in diabetes. Nutr. Metab. Cardiovasc. Dis. 2018; 28(5): 444–450, doi: 10.1016/j.numecd.2017.12.007.

21. Zhu L., She Z.G., Cheng X., Qin J.J., Zhang X.J., Cai J. et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-

-existing type 2 diabetes. Cell Metab. 2020; 31(6): 1068–1077.e3, doi: 10.1016/j.cmet.2020.04.021.

22. Guo T., Shen Q., Ouyang X., Guo W., Li J., He W. et al. Clinical findings in diabetes mellitus patients with COVID-19. J. Diabetes Res. 2021; 2021: 7830136, doi: 10.1155/2021/7830136.

 Fünstück R., Nicolle L.E., Hanefeld M., Naber K.G. Urinary tract infection in patients with diabetes mellitus. Clin. Nephrol. 2012; 77(1): 40–48, doi: 10.5414/cn107216.

24. Davies K., Lawrence J., Berry C., Davis G., Yu H., Cai B. et al. Risk factors for primary Clostridium difficile infection; results from the

observational study of risk factors for Clostridium difficile infection in hospitalized patients with infective diarrhea (ORCHID). Front. Public Health 2020; 8: 293, doi: 10.3389/fpubh.2020.00293.

Rospitalized patients with interver dramtical (RCFIID). Front: Fubile Franking 2020; 8: 293, doi: 10.389/fpuble.2020.00293.
25. Meier K., Nordestgaard A.T., Eid A.I., Kongkaewpaisan N., Lee J.M., Kongwibulwut M. et al. Obesity as protective against, rather than a risk factor for, postoperative Clostridium difficile infection: a nationwide retrospective analysis of 1,426,807 surgical patients. J. Trauma Acute Care Surg. 2019; 86(6): 1001–1009, doi: 10.1097/TA.000000000002249.

26. Knapp S. Diabetes and infection: is there a link? A mini-review. Gerontology 2013; 59(2): 99–104, doi: 10.1159/000345107.