Diabetes mellitus type 2 in hospitalized patients with chronic obstructive pulmonary disease

Evgeni Mekov, Yanina Slavova, Marianka Genova, Adelina Tsakova, Dimitar Kostadinov, Delcho Minchev, Dora Marinova

Diabetes mellitus (DM) affects 2-37% of patients with chronic obstructive pulmonary disease (COPD), with results being highly variable between studies. DM may also correlate with disease characteristics.The aim of this study was to examine the prevalence of DM and its correlation with comorbidities and COPD characteristics in patients with COPD admitted for exacerbation. 152 patients were studied for presence of DM. All of them were also assessed for vitamin D status and metabolic syndrome (MS). Data were gathered for smoking status and exacerbations during the last year. All patients completed CAT (COPD assessment test) and mMRC (Modified Medical Research Council Dyspnea scale) questionnaires and underwent spirometry. Duration of current hospital stay was recorded. 13.2% (20/152) of patients are taking medications for DM. Additional 21.7% (33/152) have newly discovered DM and 30.9% (47/152) have prediabetes. Only 34.2% of the studied patients do not have DM or prediabetes. 37% (40/108) of males have DM vs. 29,5% (13/44) of females (p=0.379). The prevalence of DM in this study is significantly higher when compared to an unselected Bulgarian population (12,8% in subjects over 45 years). 91% of patients with newly discovered diabetes had glycated hemoglobin (HbA1c)≥6,5% suggesting prolonged hyperglycemia. There is a correlation between the presence of DM and MS (p=0.008). The presence of DM is associated with more severe exacerbations (hospitalizations) during the previous year (p=0.003) and a longer hospital stay (p=0.006). DM is not associated with reduced quality of life and worse pulmonary function. The patients with COPD admitted for exacerbation are at great risk for impaired glucose metabolism which is associated with worse COPD characteristics. The majority of the patients in this study are unaware of having DM.

Diabetes mellitus type 2 in hospitalized COPD patients

Evgeni Mekov [1], Yanina Slavova [1], Marianka Genova [2], Adelina Tsakova [2], Dimitar Kostadinov [1], Delcho Minchev [1], Dora Marinova [1]

1 - Clinical Center for Pulmonary Diseases, SHATPD 'Sveta Sofia', Sofia, Bulgaria
2- Central Clinical Laboratory, UMHAT 'Alexandrovska', Sofia, Bulgaria

Abstract

Introduction: Diabetes mellitus (DM) affects 2-37% of patients with chronic obstructive pulmonary disease (COPD), with results being highly variable between studies. DM may also correlate with disease characteristics.The aim of this study was to examine the prevalence of DM and its correlation with comorbidities and COPD characteristics in patients with COPD admitted for exacerbation.
Material and methods: 152 patients were studied for presence of DM. All of them were also assessed for vitamin D status and metabolic syndrome (MS). Data were gathered for smoking status and exacerbations during the last year. All patients completed CAT (COPD assessment test) and mMRC (Modified Medical Research Council Dyspnea scale) questionnaires and underwent spirometry. Duration of current hospital stay was recorded.
Results: 13.2% (20/152) of patients are taking medications for DM. Additional 21.7% (33/152) have newly discovered DM and 30.9% (47/152) have prediabetes. Only 34.2% of the studied patients do not have DM or prediabetes. 37% (40/108) of males have DM vs. 29,5% (13/44) of females (p=0.379). The prevalence of DM in this study is significantly higher when compared to an unselected Bulgarian population (12,8% in subjects over 45 years). 91% of patients with newly discovered diabetes had glycated hemoglobin (HbA1c)≥6,5% suggesting prolonged hyperglycemia. There is a correlation between the presence of DM and MS (p=0.008). The presence of DM is associated with more severe exacerbations (hospitalizations) during the previous year (p=0.003) and a longer hospital stay (p=0.006). DM is not associated with reduced quality of life and worse pulmonary function.
Conclusions: The patients with COPD admitted for exacerbation are at great risk for impaired glucose metabolism which is associated with worse COPD characteristics. The majority of the patients in this study are unaware of having DM.

Funding: This manuscript is part of a PhD project, which is partially funded by Medical University – Sofia, Sofia, Bulgaria (grant number 15-D/2014, project number 22-D/2014).

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with significant extrapulmonary effects that may contribute to the severity in individual patients. By 2030, COPD will be the fourth cause of mortality worldwide. The extrapulmonary comorbidities influence the prognosis of the patients with COPD (1).

Diabetes mellitus type 2 (DM) is common in patients with COPD. According to the available studies the prevalence of DM in COPD patients varies between 2-37% (2). The prevalence of DM in COPD patients is increased when compared to a control group (3-8).

Available studies suggest that DM may have impact on quality of life (9), lung function (10-15), natural course of COPD (number of exacerbations) (3,16-21) as well as to affect comorbidities (22) in COPD patients. DM is also associated with arterial hypertension, hypovitaminosis D and metabolic syndrome (MS) (23-27).

Prevalence of DM in an unselected Bulgarian population aged 20-80 years is 9,6% and the prevalence of prediabetes is 3,7%. The prevalence of DM and prediabetes for participants over 45 years (the most common age group for the COPD patients) is 12,8% and 5,6% respectively (28). One Bulgarian study assessed prevalence of DM in COPD patients only anamnestically and yielded a prevalence of 11,1% (56). It can be expected that prevalence of DM in COPD patients hospitalized for exacerbation will be higher.

Many studies examine prevalence of DM in COPD patients (4,21,30-42) with results being highly variable between studies. There are not enough data to determine whether the results from these studies are applicable to specific subgroups of patients such as COPD patients admitted for exacerbation. COPD is increasingly divided in subgroups or phenotypes based on specific features and association with prognosis or response to therapy, the most notable being the feature of frequent exacerbations (43). We hypothesize that the prevalence of DM in COPD patients admitted for exacerbation is high and may have distinctive characteristics for this subgroup ('severe' exacerbator phenotype). The aim of this study is to find out the prevalence of DM in patients with COPD admitted for exacerbation and the correlations of presence of DM with comorbidities and COPD characteristics.

Material and methods

A total of 152 COPD patients hospitalized for exacerbation were studied for the presence of DM, prediabetes, MS and vitamin D deficiency and insufficiency using well-established criteria for:

- Presence of DM: fasting plasma glucose ≥7.0 mmol/L OR 2-h plasma glucose ≥11.1 mmol/L during an oral glucose tolerance test (OGTT) OR HbA1c≥6.5% OR on therapy (44);
- Presence of prediabetes: fasting plasma glucose 5.6-6.9 mmol/L OR 2-h plasma glucose 7.8-11.0 mmol/L during an OGTT OR HbA1c 5.7-6.4% (44);
- Presence of MS: at least 3 of the following: 1. Elevated waist circumference >102 cm in males, >88 cm in females; 2. Triglycerides >1.7 mmol/L (or on therapy); 3. HDL <1.0 mmol/L in males, <1.3 mmol/L in females (or on therapy); 4. Elevated blood pressure: systolic ≥130 and/or diastolic ≥85 mm Hg (or on therapy); 5. Fasting glucose >5.5 mmol/L (or on therapy) (45).
- Presence of vitamin D deficiency: 25(OH)D <25 nmol/L; vitamin D insufficiency: 25(OH)D 25-50 nmol/L; vitamin D sufficiency: >50 nmol/L (46,47).

The diagnosis of COPD was made according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria (1). Data were gathered for age, sex, smoking status and number of pack-years, number of bone fractures, therapy for arterial hypertension, therapy for DM, COPD therapy and number of exacerbations in the last year. The patients completed CAT and mMRC questionnaires and underwent pre- and post bronchodilatatory spirometry. Blood pressure was obtained

according to the American Heart Association Guidelines (48). A patient was considered as having arterial hypertension if taking antihypertensives.

The inclusion criteria were post bronchodilator spirometry obstruction defined as FEV1/FVC<0.70. All participants in this study signed informed consent.

The exclusion criteria were failure to comply with study procedures (no completed questionnaires, no medical and demographic information, no spirometry, no lab tests) or FEV1/FVC ratio >0.70 after administration of bronchodilator.

Smoking status

Every participant was classified according to smoking status (49):

Never smoker – never smoked a cigarette or who smoked fewer than 100 cigarettes in their entire lifetime.

Former smoker – smoked at least 100 cigarettes in their entire life but were not currently smoking.

Current smoker – had smoked at least 100 cigarettes in their entire life and were still smoking.

Numbers of pack-years were calculated using the formula:

Number of pack-years = years of smoking X number of daily smoked cigarettes/20

Anthropometric indices

Body weight and height were measured and the body mass index (BMI) was calculated by dividing weight by height squared (kg/m^2). According to BMI all patients were classified as underweight (<18,5), normal (18,5 – 24,99), overweight (25-29,99) and obese (>30). Waist circumference was measured at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest according to the WHO STEPS protocol (50). Hip circumference was measured around the widest portion of the buttocks (50). Body adiposity index (BAI) was calculated as:

$$\textit{Hip circumference} / (\textit{Height} \times \sqrt{\textit{Height}}) - 18$$

COPD exacerbations and duration of hospital stay

Data were gathered for number of severe exacerbations (hospitalizations) and moderate exacerbations (antibiotic or/and systemic steroid treatment without hospitalization due to worsening of pulmonary symptoms) (1) in the previous year. The duration of the current hospital stay was recorded.

Quality of life

Quality of life was assessed with the mMRC scale and CAT questionnaire. Patients were instructed that there were no right or wrong answers. All patients' questions were answered. Patients were classified according to GOLD as having less symptoms (CAT <10) and breathlessness (mMRC grade 0-1) and more symptoms (CAT ≥10) and breathlessness (mMRC grade ≥2). Because all patients were hospitalized due to exacerbation there were only group C (high risk, less symptoms) and group D (high risk, more symptoms) patients according to GOLD (1).

Pulmonary Function Testing

The spirometry was performed using Minispir® New spirometer (MIR - Medical International Research, Italy). Patients were instructed to withdraw using short-acting β2-agonists at least 6 hours, long-acting β2-agonist at least 12 hours, long acting muscarinic antagonist 24 hours and short acting muscarinic antagonist 12 hours before the spirometry (51). Post bronchodilator spirometry testing was performed 15-30 min after inhalation of 400mcg Salbutamol according to ERS/ATS recommendations (51). Pre- and post- values were obtained for: FVC, FEV1, FEV1/FVC, FEV6, FEV1/FEV6, PEF, FEF2575, FEV3, FEV3/FVC as well as the difference between post/pre values (delta values). GLI (Global Lungs Initiative) predicted values were used (GLI-2012). Patients' obstruction were classified according to the severity of airflow limitation based on post-bronchodilator FEV1 as follows: mild (≥80% predicted); moderate (80>FEV1≥50% predicted); severe (50%>FEV1≥30% predicted); very severe (<30% predicted) (1).

Blood samples and analyses

A venous blood sample was collected from each subject after a 12-hour fasting. Blood samples were taken as late as possible before discharging (usually on 6th or 7th day). Plasma glucose, triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and total cholesterol (tChol) were measured with a Roche COBAS INTEGRA® 400 plus analyzer and an enzymatic colorimetric assay and blood glucose was measured with an enzymatic reference method with hexokinase. Vitamin D was measured with Elecsys 2010 (Roche) and Electro-chemiluminescence immunoassay (ECLIA). Glycated hemoglobin (HbA1c) was measured with a NycoCard device and boronate affinity assay. For patients without established DM a 75g OGTT was performed with blood samples for glucose taken on first and second hour.

Statistical Analysis

Statistical analysis was performed with the SPSS for Windows software, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation and 95 Confidence intervals (95%CI) and categorical variables - as percentages. Chi-square test was used to determine the associations between categorical variables. Continuous variables were examined for normality by Shapiro-Wilk test. For normally distributed variables, differences between the groups were determined by independent-samples T test for two samples and analysis of variance (ANOVA) for more than 2 samples. Mann-Whitney U test was used for abnormally distributed variables with 2 samples and Kruskal-Wallis test for variables with more than 2 samples. Regression analyses were used to determine risk factors for presence of DM or the consequences of having DM. Significance value (p-value) was set at 0.05.

All patients signed informed consent. Medical University-Sofia Research Ethics Commission approved the study.

Results and discussion

Sample characteristics

A total of 152 COPD patients admitted for exacerbation were recruited from University Specialized Hospital for Active Treatment of Pulmonary Diseases 'Saint Sofia', Sofia, Bulgaria. Mean age of patients in this study was 65,1±9,9 years. 71,1% (108/152) were males, 28,9% (44/152) were females; mean post-bronchodilator FEV_1 was 55,34 ±19,5%. 15,8% from the patients were never smokers, 57,9% - former smokers and 26,3% - current smokers.

Prevalence of DM

13,2% (20/152) of patients are taking medications for diabetes. Additional 21,7% (33/152) have evidence of newly discovered DM and 30,9% (47/152) have prediabetes. Only 34,2% (52/152) of the studied patients do not have DM or prediabetes. 37% (40/108) of males have DM vs. 29,5% (13/44) of females but this difference is not statistically significant (p=0.379) (table 1).

Table 1. Presence of DM and prediabetes according to different factors

	% DM	P value	% prediabetes	P value
All	34,9		30,9	
Sex				
Male	37,0	P=0.379	34,3	P=0.163
Female	29,5		22,7	
Smoking status				
Never	29,2	**P=0.003**	37,5	P=0.510
Former	45,5		27,3	
Current	15,0		35,0	
Arterial hypertension				
Yes	41,9	**P=0.007**	27,6	P=0.188
No	19,1		38,3	
Vitamin D status				
>50 nmol/l	36,0	P=0.976	21,3	P=0.281
25-50 nmol/l	35,4		33,8	
<25 nmol/l	33,9		24,2	
MS				
Yes	52,6	**P=0.008**	26,3	P=0.478
No	28,9		32,5	
BMI				
Underweight	0	P=0.097	42,9	P=0.427
Normal	29,2		35,4	
Overweight	43,6		32,7	
Obese	35,7		21,4	
BAI				
Underweight	31,3	P=0.311	18,8	P=0.534
Normal	30,2		30,2	
Overweight	33,3		37,8	
Obese	50,0		28,6	
Quality of life				

CAT 0-9	28,0	P=0.430	32,0	P=0.898
CAT ≥10	36,2		30,7	
mMRC 0 or 1	30,2	P=0.376	30,2	P=0.886
mMRC ≥2	37,4		31,3	
FEV1				
FEV1>50%	36,3	P=0.659	30,8	P=0.961
FEV1<50%	32,8		31,1	

According to the available studies the prevalence of DM in COPD patients varies between 2-37% (table 2). This study found relatively high prevalence of DM compared to previous studies (fig. 1). The prevalence of DM and prediabetes in our study is significantly higher when compared to the general Bulgarian population (12,8% and 5,6% respectively in subjects over 45 years) (28). The odds ratio for COPD patients admitted for exacerbation of having DM is 3.44 (95% CI 2.38-4.97), which is higher than previous reported (table 3). Prevalence of DM is high in Bulgaria (12,8%) and it is even higher in COPD patients admitted for exacerbation (34,9%).

Table 2. Prevalence of DM in patients with COPD

Authors	N	Studied population	Prevalence of DM
Almagro et al. (30)	N1=398 N2=606	Two studies of patients with COPD	**29.4%** **37%**
Antonelli et al. (31)	270	Patients with COPD	**14%**
Cazzola et al. (32)	15018	Patients with COPD	**18.7%**
Chang et al. (33)	495	Hospitalized patients with COPD	**10.5%**
Crisafulli et al. (34)	2962	Patients with COPD in pulmonary rehabilitation program	**14.4%**
Gudmundsson et al. (35)	416	Hospitalized patients with COPD	**10.6%**
Kobylianskii et al. (36)	616	Patients with COPD	**9.5%**
Mapel et al. (37)	N1=42565 N2=8507	Two databases of patients with COPD	**22%** **29%**
Mapel et al. (38)	200	Patients with COPD and controls	**11%**; no difference between groups
Parappil et al. (21)	172	Hospitalized patients with COPD	**22%**
Rubinsztajn et al. (39)	266	Died due to hospitalization patients with COPD	**20.7%**
Sidney et al. (4)	45966	Patients with COPD and controls	**1.6%;** OR 1.51 (CI 1.35-1.69)
Terzano et al. (40)	288	Hospitalized patients with COPD	**25.3%**
van Manen et al. (41)	290	Patients with COPD	**5%** In general population - 7%
Walsh et al. (42)	3000	Patients with COPD	**16%**

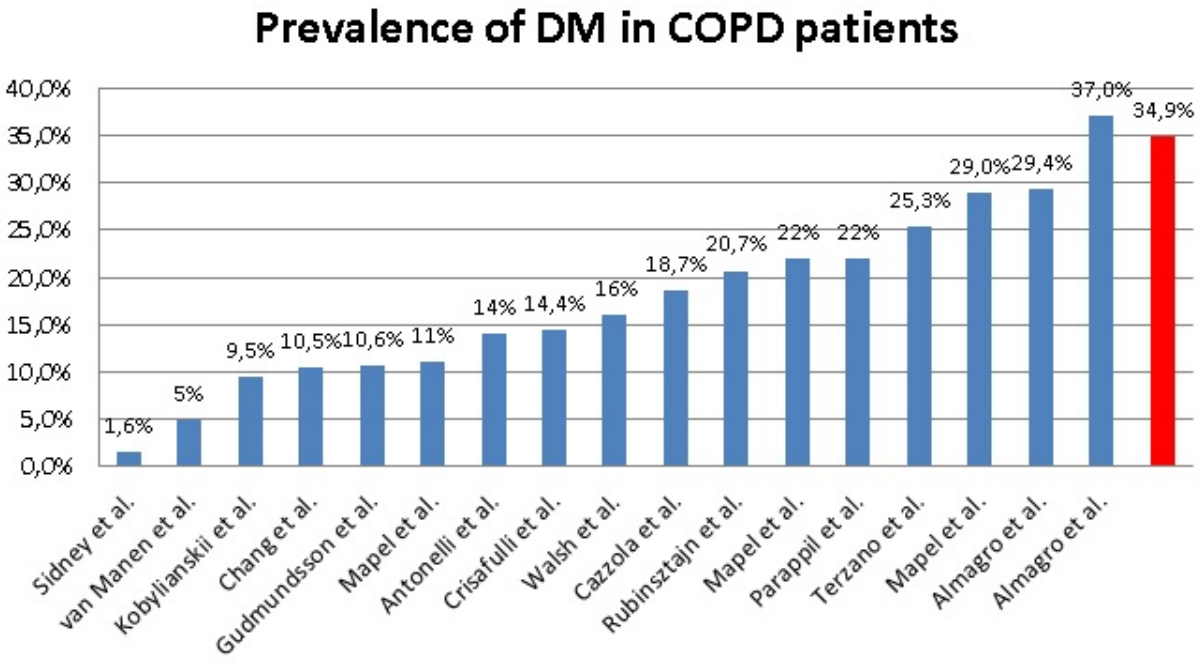

Fig. 1. Prevalence of DM in COPD patients

Table 3. Risk for development and presence of DM in COPD patients

Authors	N	Studied population	Results
Feary et al. (5)	1204100	General population >35 years	**OR 2.04** (95% CI 1.97 – 2.12)
Joo et al. (52)	2177	General population >40 years	No increase in risk of developing DM
Lee et al. (6)	16088	Patients with COPD and controls	**HR 1.41** (95% CI 1.23-1.63)
Mannino et al. (3)	20296	General population >45 years	**OR 1.5** (95% CI 1.1-1.9)
Rana et al. (7)	103614	Women	**RR 1.8** (95% CI 1.1–2.8)
Sidney et al. (4)	45966	Patients with COPD and controls	**OR 1.51** (95% CI 1.35-1.69)
Song et al. (8)	38570	Women	**RR 1.38** (95% CI 1.14–1.67)

When comparing the results only by medical history with the other Bulgarian study (29) which assess prevalence of DM in COPD patients, the data are similar – 11,1% vs 13,2%. But when lab tests are performed for DM the prevalence increased almost threefold. This stresses the need for active screening for the disease.

91% of patients with newly discovered diabetes had HbA1c ≥6,5% suggesting prolonged hyperglycemia. Fulfilled criteria for DM (in all and in newly discovered) are shown in table 4.

Table 4. Rate of fulfilled criteria for all and new DM.

	All DM	New DM
Blood glucose 0’ ≥7,0 mmol/l	24,5% (n=13)	15,2% (n=5)
Blood glucose 120’ ≥11,1 mmol/l	37,7% (n=20)	60,6% (n=20)

HbA1c ≥6,5%	75,5% (n=40)	90,9% (n=30)
On therapy	37,7% (n=20)	-

The patients with DM are significantly older (68,4 vs 63,3 years, p=0.002), including patients with new DM (68,1 vs 63,3 years, p=0.013). Presence of prediabetes is not associated with age (65,2 vs 61,6 years, p=0.068).

The prevalence results could be explained with differences between the populations in different studies (physical activity, diet, lifestyle etc.). For example, Bulgaria is low-income country, which may impact diet preferences and treatment choices. Second, the prevalence depends on the used criteria for DM (this study uses all of them, so it cannot be underdiagnosed). Not least, patients in this study had been hospitalized due to exacerbation, which represents the most severe group of COPD patients.

The COPD patients admitted for exacerbation are a risk group for DM and a screening should be considered. HbA1c have biggest sensitivity.

Lifestyle factors

According to another study smokers are 30-40% more likely to develop DM than nonsmokers and the risk increases with the number of pack-years (53). Our study did not find significant differences in prevalence of DM and prediabetes in neversmokers and eversmokers (former and current). However the prevalence of current smokers was higher in patients without DM (34,3 vs. 11,3%) while the prevalence of former smokers was lower (48,5 vs. 75,5%, p=0.003). Number of pack-years did not differ significantly according to the presence of DM (p=0.626). These results could be explained with smoke being the biggest factor in developing COPD and effect of developing DM could be reduced. Also lifestyle changes (quit smoking) in the presence of the two diseases should be considered.

Treatment with inhalatory corticosteroids (ICS) is not associated with higher prevalence of DM and prediabetes (p=0.742 and p=0.283 respectively) confirming the results by other authors (54).

Glycemic control (HbA1c) in patients with DM in this study did not differ between the seasons (p=0.196) as described by other authors (55), probably because of lower seasonal differences in physical activity as a consequence of limited pulmonary function.

Most of the patients with DM in this study are former smokers. Glycemic control did not differ between seasons.

Comorbidity results

COPD is a disease that affects mainly the lungs, but is characterized by systemic inflammation and a number of extrapulmonary manifestations. Only 1/3 of patients with COPD die due to respiratory failure. Main cause of death is lung cancer and cardiovascular complications (56).

The vast majority of patients with COPD have a vitamin D deficiency (57). Aside from its role in the metabolism of calcium and phosphorus, vitamin D is involved in the pathogenesis of multiple diseases, including DM, because it affects the secretion and the function of insulin (23). In our study vitamin D levels do not significantly differ in relation to presence of DM (31,89 vs 32,01 nmol/l, p=0.951). Presence of DM is also not related to vitamin D status (p=0.976) (table 1).

Two systematic reviews establish an increased risk of fractures in patients with DM (24,25). Although there are common risk factors that potentiate osteoporosis in patients with DM, MS and COPD, DM is an independent risk factor (26). However number of fractures in our study does not

significantly differ regarding the presence of DM (p=0.401) or prediabetes (p=0.673). Presence of at least one fracture also does not differ significantly in relation to presence of DM (p=0.396) or prediabetes (p=1.0).

Most patients with DM have MS, but the opposite is not necessarily true (27). In our study there is a correlation between the presence of DM and MS (p=0.008). 37,7% (20/53) from patients with DM have MS. Presence of arterial hypertension is related to the presence of DM (p=0.007). 83% (44/53) from patients with DM have arterial hypertension compared to 61,6% (61/99) from patients without DM. BMI and BAI does not differ significantly according to presence of DM (p=0.138 and p=0.078 respectively). There is also not significant difference in prevalence of DM in BMI and BAI groups (p=0.097 and p=0.311).

A logistic regression analysis was conducted to predict presence of DM in a relation to presence of other comorbidities. Presence of MS slightly improves the model (chi square = 6.818, p=0.009 with df = 1). Nagelkerke's R2 of 0.060 indicating a weak relationship. Odds ratio was 2,73. Presence of arterial hypertension is associated with similar results (chi square = 7.025, p=0.008 with df = 1, Nagelkerke's R2 = 0.070, odds ratio 3.046). Vitamin D status does not improve the model. DM is risk factor for presence of arterial hypertension (odds ratio 3.046, p=0.005).

The presence of DM is associated with presence of MS and arterial hypertension, but is not associated with vitamin D levels, vitamin D status, number of fractures, BMI and BAI.

Exacerbations results and duration of hospital stay

Hyperglycemia is associated with elevated glucose concentrations in tissues and bronchial aspirates (58) where it may stimulate infection by enhancing bacterial growth (59) and by promoting bacterial interaction with the airway epithelium (60). Hyperglycemia also impairs both innate and adaptive immunity, suppressing the host response to infection.

The presence of DM increase the risk of exacerbations almost two fold (16), the risk of hospitalization (3) and is associated with more serious deterioration which may prolong hospital stay (17-21). However one study found no effect of DM on the frequency of exacerbations (61).

Our study found a significant difference between the number of severe exacerbations according to the presence of DM and the duration of hospital stay (table 5, p=0.003 and p=0.006 respectively). The risk for severe exacerbation and duration of hospital stay are furthermore increased in COPD patients with untreated (new) DM (p=0.001 and p=0.026 respectively). Known (treated) DM is not associated with increased number of moderate, severe and total exacerbations (all p>0.05) but prolongs hospital stay (p=0.039). Prediabetes is not associated with increased risk of exacerbation and duration of hospital stay (table 5, all p>0.05).

Triglycerides and blood glucose levels in our study did not correlate with number of exacerbations as reported by other authors (62), nor did other MS components or MS itself (all p>0.05).

Table 5. Number of severe, moderate and total exacerbations in previous year and duration of hospital stay according to the presence of DM and prediabetes

	DM				
	All DM	New (Untreated) DM	Known DM	Prediabetes	No DM
Moderate exacerbations	0,64 (0,40-0,92)	0,52 (0,30-0,74)	0,85 (0,35-1,52)	0,53 (0,36-0,70)	0,72 (0,56-0,89)
Severe exacerbations	**2,13 (1,88-2,44)**	**2,24 (1,93-2,56)**	1,95 (1,47-2,45)	1,81 (1,52-2,12)	**1,72 (1,51-1,93)**
All exacerbations	2,77 (2,44-3,15)	2,76 (2,42-3,11)	2,80 (2,08-3,56)	2,34 (2,02-2,71)	2,43 (2,21-2,68)
Hospital stay (in days)	**7,85 (7,53-8,24)**	**7,97 (7,48-8,57)**	**7,65 (7,29-8,00)**	7,38 (7,12-7,67)	**7,33 (7,11-7,57)**

Linear regression showed presence of DM as risk factor for higher number of hospitalizations (R=0.189, r^2=0.036, p=0.020, B=0.415, 95% CI 0.067-0.762) and prolonged hospital stay (R=0.196, r^2=0.039, p=0.015, B=0.516, 95% CI 0.1-0.931).

DM is associated with increased number of severe exacerbations and longer hospital stay. This risk is further increased in untreated DM.

Quality of life results

Our study did not find difference between mMRC and CAT scores in relation to the presence of DM or prediabetes (table 6). Prevalence of DM is not significantly different between patients with less symptoms (CAT 0-9) and breathlessness (mMRC 0 or 1) compared to patients with more symptoms (CAT ≥10) and breathlessness (mMRC ≥2) (all p>0.05) (table 1). This is in contrast with the data about reduced quality of life in patients with DM (9) but may be explained with COPD having higher negative impact on quality of life than DM (physical limitation due to shortness of breath) (63) and ameliorating the effect in patients having the two diseases.

Table 6. Mean CAT score on every question and in total according to presence of DM

DM	Mean CAT score	N	P value
DM – no	CAT1 2,10	99	P=0.947
DM - yes	CAT1 2,15	53	
DM – no	CAT2 1,97	99	P=0.502
DM - yes	CAT2 2,13	53	
DM – no	CAT3 2,56	99	P=0.262
DM - yes	CAT3 2,83	53	
DM – no	CAT4 3,51	99	P=0.229
DM - yes	CAT4 3,70	53	
DM – no	CAT5 1,24	99	P=0.277
DM - yes	CAT5 1,51	53	
DM – no	CAT6 1,48	99	P=0.310
DM - yes	CAT6 1,75	53	
DM – no	CAT7 1,46	99	P=0.681
DM - yes	CAT7 1,60	53	
DM – no	CAT8 2,63	99	P=0.171
DM - yes	CAT8 2,94	53	

DM – no	Total CAT 16,95	99	P=0.230
DM - yes	Total CAT 18,62	53	

Regression analyses also showed that DM is not a risk factor for reduced quality of life (all p>0.05).

In this study the presence of DM is not associated with reduced quality of life.

Pulmonary function test (PFT) results

COPD is characterized by airway obstruction, which is not fully reversible. DM is associated with a reduction of lung volumes (10,11). Large epidemiological studies have found a correlation between lung volumes on one hand and duration of DM and the presence of complications on the other (12-15). It should be noted that some studies found no association between lung function and the presence of DM (64-66).

Our study did not find differences in FVC, FEV1, FEV6, PEF, FEF2575, FEV3 according to the presence of DM. It should be noted that FVC difference is almost significant (p=0.051). However, because of the latter there is significant difference in FEV1/FVC ratio (p=0.013) and FEV1/FEV6 ratio (p=0.033) (table 7). Prediabetes was not associated with impaired lung function (all p>0.05). However there is weak negative correlation between HbA1c and FVC (p=0.041, r=-0.166).

Table 7. Mean PFT values according to the presence of DM

DM	Mean PFT value	N	P value
No	FEV1 55,52%	99	P=0.882
Yes	FEV1 55,02%	53	
No	FVC 81,58%	99	P=0.051
Yes	FVC 72,62%	53	
No	FEV1/FVC 0,52	99	**P=0.013**
Yes	FEV1/FVC 0,57	53	
No	FEV6 74,80%	99	P=0.165
Yes	FEV6 68,42%	53	
No	FEV1/FEV6 0,57	99	**P=0.033**
Yes	FEV1/FEV6 0,61	53	
No	PEF 56,66%	99	P=0.688
Yes	PEF 54,43%	53	
No	FEF2575 37,96%	99	P=0.112
Yes	FEF2575 42,11%	53	
No	FEV3 67,29%	99	P=0.466
Yes	FEV3 63,42%	53	
No	FEV3/FVC 0,81	99	P=0.067
Yes	FEV3/FVC 0,84	53	

Untreated (new) DM is associated with significantly lower FVC (68,48 vs. 81,58%, p=0.008) and FEV6 (64,09 vs. 74,80%, p=0.027) when compared to patients without DM. Regression analysis showed that the presence of DM is risk factor for lower FVC (R=0.195, r^2=0.038, p=0.016, B=-8.953, 95% CI -16.214;-1,692).

There is no difference in prevalence of DM in patients with FEV1 <50%, when compared to patients with FEV1 >50% (p=0.659) or regarding GOLD stage (p=0.861) (table 1).

DM in our study is not associated with worsen pulmonary function. Untreated DM is associated with lower FVC.

Conclusions

This study finds high prevalence of DM (34,9%) in COPD patients admitted for exacerbation. DM is more prevalent in males, but the gender difference is not statistically significant. In this study most of the patients are former smokers and glycemic control does not differ between seasons.

The presence of DM is associated with presence of MS, more severe exacerbations (hospitalizations) during the previous year and longer hospital stay. DM is not associated with reduced quality of life, but is a risk factor for FVC.

Patients with COPD admitted for exacerbation are at great risk for impaired glucose metabolism which may impact natural course of COPD. 34,9% of them have DM and 30,9% have prediabetes. The majority of the patients in this study are unaware of having DM and a screening should be considered.

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