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PATHOGENETIC ASSESSMENT OF CLINICAL AND INSTRUMENTAL PARAMETERS OF THE LUNGS IN PATIENTS WITH DIABETES MELLITUS

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Abstract

Background: For the past two decades, many studies have investigated how diabetes mellitus (DM) affects the bronchopulmonary system, but the results have been inconsistent. Diabetes mellitus leads to metabolic disorders and lack of oxygen. And thus causes problems in the lungs and their vessels. One of the common diseases is increased ventilation of the lungs.

Aim of the study is to identify the features and characteristics of the effect of diabetes mellitus and its concomitant pathologies on the morphofunctional state of the respiratory system.

Materials and methods. The sample size was 395 people. A One Touch® glucose meter and a DCA-2000 MT analyzer were used for laboratory and diagnostic assessment of the patients' condition. C-peptide, hormone levels, and insulin resistance indices (Caro and HOMA-IR) were determined using standard laboratory techniques. Instrumental examinations included chest X-rays, computer spirometry, and bronchoscopy.

Results. Lung function disorders were found in the study sample of patients: from bronchial obstruction in type 1 diabetes to restrictive and perfusion disorders in combination with type 2 diabetes with coronary heart disease and obesity.

Conclusion. As a result of the study, it was found that diabetes mellitus is associated with various disorders of respiratory function, including restrictive and obstructive changes, as well as morphological changes in the lung tissue and vascular system. Ultrasound revealed a complex of destructive and inflammatory changes in the lungs.

Keywords: Type 1 and Type 2 Diabetes Mellitus, Abdominal Obesity, Bronchopulmonary Function, Pulmonary Ventilation, Spirometric Assessment, Metabolic Disturbances, Pulmonary Morphology.

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Резюме

ПАТОГЕНЕТИЧЕСКАЯ ОЦЕНКА КЛИНИКО-ИНСТРУМЕНТАЛЬНЫХ ПОКАЗАТЕЛЕЙ ЛЕГКИХ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ

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Введение: За последние два десятилетия было проведено множество исследований, посвященных изучению влияния сахарного диабета (СД) на бронхолегочную систему, но результаты были противоречивыми. Сахарный диабет приводит к

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нарушению обмена веществ и недостатку кислорода. И, таким образом, вызывает проблемы в легких и их сосудах. Одним из распространенных заболеваний является повышенная вентиляция легких.

Целью исследования является выявление особенностей и характерных черт влияния сахарного диабета и сопутствующих ему патологий на морфофункциональное состояние дыхательной системы.

Материалы и методы. Объем выборки составил 395 человек. Для лабораторной и диагностической оценки состояния пациентов использовались глюкометр One Touch® и анализатор DCA-2000 MT. С помощью стандартных лабораторных методов определяли уровень С-пептида, гормонов и индексы инсулинорезистентности (Caro и HOMA-IR). Инструментальные исследования включали рентгенографию грудной клетки, компьютерную спирометрию и бронхоскопию.

Результаты. В исследуемой выборке пациентов были обнаружены нарушения функции легких: от бронхиальной обструкции при сахарном диабете 1 типа до рестриктивных и перфузионных нарушений в сочетании с сахарным диабетом 2 типа с ишемической болезнью сердца и ожирением.

Вывод. В результате исследования было установлено, что сахарный диабет связан с различными нарушениями дыхательной функции, включая рестриктивные и обструктивные изменения, а также морфологические изменения в легочной ткани и сосудистой системе. УЗИ выявило комплекс деструктивных и воспалительных изменений в легких.

Ключевые слова: Сахарный диабет 1-го и 2-го типов, абдоминальное ожирение, Бронхолегочная функция, легочная вентиляция, спирометрическая оценка, Метаболические нарушения, морфология легких.

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Түйіндеме

ҚАНТ ДИАБЕТІМЕН АУЫРАТЫН НАУҚАСТАРДА ӨКПЕНІҢ КЛИНИКАЛЫҚ-АСПАПТЫҚ КӨРСЕТКІШТЕРІН ПАТОГЕНЕТИКАЛЫҚ БАҒАЛАУ

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Кіріспе: Соңғы екі онжылдықта көптеген зерттеулер қант диабетінің (ҚД) бронхопульмональды жүйеге қалай әсер ететінін зерттеді, бірақ нәтижелер сәйкес келмеді. Қант диабеті метаболизмнің бұзылуына және оттегінің жетіспеушілігіне әкеледі. Және осылайша өкпеде және олардың тамырларында проблемалар туғызады. Жалпы аурулардың бірі-өкпенің желдетілуінің жоғарылауы.

Зерттеудің мақсаты-қант диабеті мен оның қатар жүретін патологияларының тыныс алу жүйесінің морфофункционалды жағдайына әсерінің ерекшеліктері мен сипаттамаларын анықтау.

Материалдар мен әдістер. Іріктеме көлемі 395 адамды құрады. Пациенттердің жағдайын зертханалық және диагностикалық бағалау үшін One Touch® глюкоза өлшегіші мен DCA-2000 МТ анализаторы қолданылды. С-пептидтер, гормондар деңгейі және инсулинге төзімділік көрсеткіштері (Саго және HOMA-IR) стандартты зертханалық әдістермен анықталды. Аспаптық зерттеулерге кеуде Қуысының Рентгенографиясы, компьютерлік спирометрия және бронхоскопия кірді.

Нәтижелер. Пациенттердің зерттеу үлгісінде өкпе функциясының бұзылуы анықталды: 1 типті қант диабетіндегі бронх обструкциясынан жүректің ишемиялық ауруы мен семіздігі бар 2 типті қант диабетімен бірге шектеуші және перфузиялық бұзылуларға дейін.

Қорытынды. Зерттеу нәтижесінде қант диабеті тыныс алу функциясының әртүрлі бұзылыстарымен, соның ішінде шектеуші және обструктивті өзгерістермен, сондай-ақ өкпе тіндері мен тамыр жүйесіндегі морфологиялық өзгерістермен байланысты екені анықталды. Ультрадыбыспен өкпеде деструктивті және қабыну өзгерістерінің кешені анықталды.

Түйінді сөздер: 1 типті және 2 типті Қант диабеті, іштің семіздігі, бронхопульмональды функция, өкпені желдету, спирометриялық бағалау, метаболикалық бұзылулар, өкпе морфологиясы.

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Introduction

Studies on the impact of metabolic control on external respiratory function (ERF) show contradictory results [9], [10]. Some scientific papers say that the relationship between impaired sugar metabolism in the body (carbohydrate metabolism) and lung function (spirometric) is not always found in diabetes mellitus [18]. The duration of diabetes mellitus has a negative effect on the state of the

respiratory system. Many patients show both functional and morphological changes in lung tissue. This highlights the mutual effects of the respiratory system and the development of diabetes. [3, 7].

The reason is high sugar levels (hyperglycemia) shown in the Figure 1.

The figure shows the relationship between the effect of the glycemic index level and lung function.

Effect of Blood Sugar on Lungs	Impact on Lungs
High average blood sugar (increased HbA1c)	Reduced lung efficiency
Very high sugar levels (in animals)	Damage to lungs (increased bubbles in lung cells, collapse and swelling of alveoli)
Figure 1. The Relationship Between Blood Sugar Levels and Lung Function.	

Aim. To identify the features and characteristics of the effect of diabetes mellitus and its concomitant pathologies on the morphofunctional state of the respiratory system.

Materials and Methods. The studied sample of patients were DM patients, along with 49 individuals without chronic disease serving as controls. Participants were stratified into the following subgroups, according to Table 1.

Table 1.

Clinical subgroups.

	87 patients with type 2 DM (T2DM) and IHD	
	54 with IHD without T2DM (group X-IHD)	
395	153 with T2DM and obesity	
patients	ts 45 with obesity but no diabetes (group Co)	
	56 with type 1 DM (T1DM), and 24 healthy	
	controls (group C1)	

The average age of the T1DM group was 37.5±1.68 years, with disease duration of 11.43±0.32 years. In T2DM patients, the average age was 53.74±2.48 years, with a

disease duration of 9.2 ± 0.61 years. The average age in the T2DM + IHD group was 60.1 ± 2.98 years, and IHD duration was 10.7 ± 1.47 years. Effort angina class II was noted in 50% of patients, class III in 23%, class IV in 9%, and myocardial infarction in history in 18% of patients.

The following parameters of abdominal obesity, assessment of glycemia, glycated hemoglobin levels, lipid and protein metabolism, and liver enzymes were diagnosed for the study sample. The following equipment was used: One Touch® glucose meter, DCA-2000 MT analyzer. Methods: the colorimetric method and the Reitman and Frenkel methods.

All participants underwent a questionnaire for respiratory symptoms and a physical examination of the lungs. None of the patients had chronic lung diseases or respiratory complaints. Smoking was noted in some patients: 9.2% smoked regularly, 5.8% — sporadically.

The following instrumental, functional and radiation research methods were used (figure 2).

Chest X-rays

• Performed in two projections according to the standard procedure.

Computer Spirography

• External respiratory function was assessed using the automated spirometer "AD-02" (National Center for Occupational Hygiene and Occupational Diseases, Karaganda), operating on a Pentium-III system. Testing was performed in a fasting state, at rest, in a seated position, following standard interpretation guidelines [19]. Evaluated parameters included VC, FVC, FEV₁, FEV₁/FVC (Tiffeneau index), MEF25/50/75, MMEF25−75, and PEF. To assess bronchial reversibility, a Berotec inhalation test with repeat spirometry after 20 minutes was conducted; an increase of ≥15% indicated reversible obstruction [10], [20]. Results were compared to reference values from the 1986 All-Union Pulmonology Institute guidelines (Leningrad).

Fibrobronchoscopy

 Performed in the morning on an empty stomach under local anesthesia using a BF-P20 fibrobronchoscope (Olympus, Japan). Changes in the bronchial mucosa and the degree of inflammation were assessed according to the Lemoine IM classification (2002).

Statistical processing

• Methods of variational statistics were used: the mean (M), standard deviation (δ) and mean error (m) were calculated. To assess the significance of the differences, the Student's t-test was used. Correlation analysis was carried out using the Pearson and Spearman coefficients, their significance was checked using the t-test. The correlation coefficient r was calculated in Excel with the CORREL function.

Figure 2. Instrumental, functional and radiation research methods.

Results

No clinically evident signs of lung pathology were revealed during the examination. Slight percussion-

auscultatory changes were noted in 20.23% of patients: shortening of percussion sound — in 4.05% (DM1), 6.98% (DM2) and 9.25% (DM2+CHD); in 29.48%, prolonged

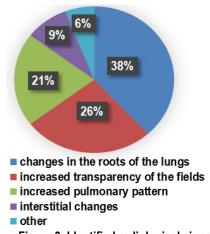
expiration was observed, mainly over the lower lobe of the right lung. Vesicular breathing with prolonged expiration was observed in 13.87% of cases, weakened — in 3.47%. Fluorography did not reveal any pathologies, while standard radiography in two projections revealed a number of changes detected in Figure 3.

These signs are regarded as a non-specific reaction of the bronchopulmonary system to chronic exposure

In patients DM2, the changes included: lung roots - 30.68%, increased transparency - 28.14%, increased pattern - 33.3%, interstitial changes - 22.22%, bulging of the pulmonary artery arch - 6.82%. In 10 patients, pleural adhesions were found, indicating previous pneumonia.

All values are shown in the Figure 4.

In the study group of patients with T2DM, pathological changes in the lungs were detected (Fig. 5) in 49%.





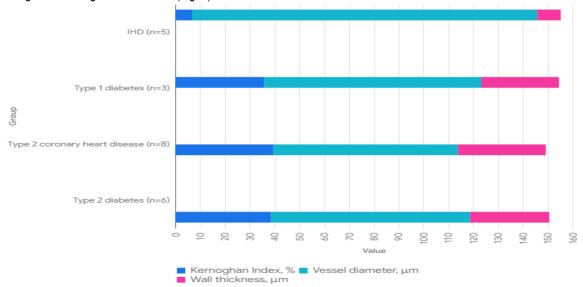


Figure 4. Morphometric Indices of Lungs in Patients with Diabetes.

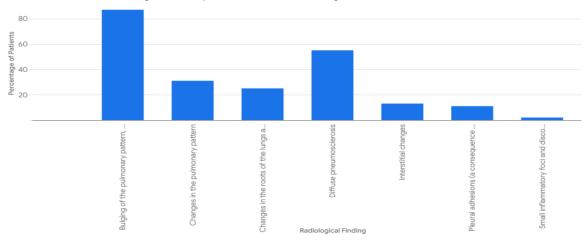


Figure 5. Lung Findings in Type 2 Diabetes.

According to Figure 6, diabetes mellitus affects the bronchopulmonary system. However, patients with concomitant diseases, such as cardiovascular pathology and thyroid diseases, were the most susceptible.

External Respiratory Function (ERF) Study in patients with diabetes mellitus (DM) revealed pulmonary ventilation disorders associated with the severity of DM. For the identified sample, determining lung ventilation disorders,

radiology, endoscopy, and PVD were performed. The results are shown in the figure 6.

FVD disorders were found in 23% of 175 patients, with a decrease in speed indicators and patency of the central airways. Illustrated below is a clustered bar graph displaying the quantitative values of various indices for each group, enabling a detailed examination of the data distribution and patterns (Figure 7).

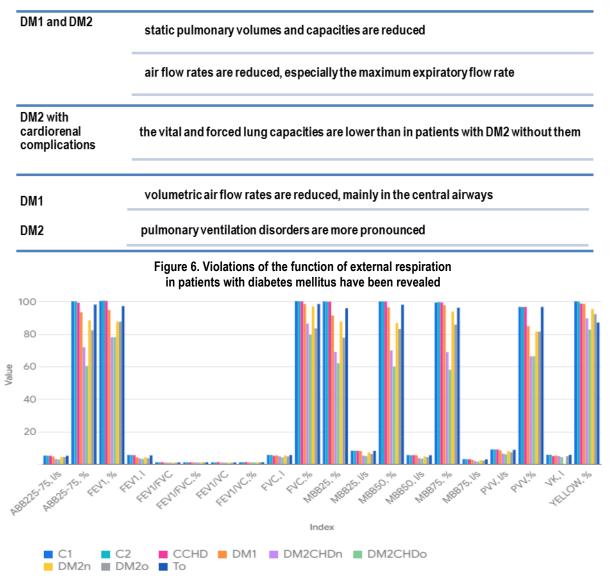


Figure 7. Comparative Analysis of Indices by Group.

The results of the Berotec test demonstrated that the bronchospastic component in the formation of respiratory disorders in severe type 2 diabetes mellitus plays a limited role, since a positive response was recorded only in 20% of patients. In 68% of patients with severe vascular complications, multiple respiratory function disorders were detected: FEV_1 , Tiffen index, and air flow

velocity decreased, involving both small and large bronchi.

Fiberoptic bronchoscopic characteristics of the state of the bronchial mucosa.

Bronchoscopy was performed for patients with type 1 and type 2 diabetes. Specific diffuse lesions of the bronchopulmonary system are shown in the figure 8.

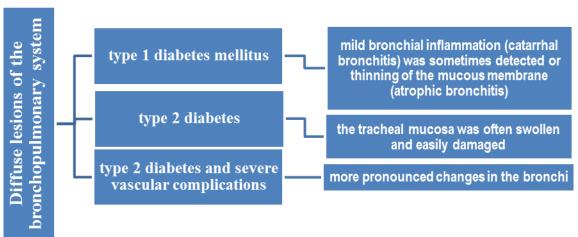
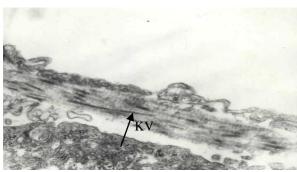


Figure 8. Revealed diffuse changes by bronchoscopy.

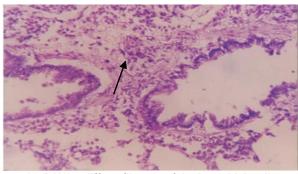
X-rays also showed that almost half of these patients have impaired patency of the small bronchi. This was confirmed by a trial with Berotec, a medicine that dilates the bronchi. Patients with diabetes mellitus, especially in combination with cardiovascular diseases, are more likely to show radiological signs of lung damage and impaired respiratory function. A positive bronchodilator test was recorded in 45% of patients, and signs of bronchial inflammation were found in 21%.

Pathological disorders of the lungs in patients with diabetes mellitus. Histological examination showed that

some patients with type 1 diabetes (23%) develop alveolitis, followed by the formation of alveolar fibrosis and microcystic tissue transformation. Structural changes of varying severity were observed at the level of blood vessels of the small circle of blood circulation, including thickening of the walls, hyperplasia of the muscular membrane and sclerosis, which indicates a progressive violation of pulmonary hemodynamics and an increase in vascular resistance (Figure 9).



a) (CD1) sclerosis of the interalveolar capillary wall.



b) (DM2) – diffuse fibrosis of the bronchial wall.

Figure 9. Pathomorphology of the lungs in DM patients.

In patients with type 2 diabetes mellitus (in 5-24.9% of cases), vascular lesions were generalized, manifested by significant narrowing of the vascular lumen, thickening of the vascular wall, destructive changes in the elastic membrane and pronounced hyperelastosis of venous structures. In some cases, endophlebitis in the interlobular veins was observed, indicating a chronic inflammatory process.

The most pronounced morphological changes in lung tissue were detected in patients with a combination of type 2 diabetes and cardiovascular pathologies. These patients had marked alveolar fibrous rearrangement, which led to impaired gas diffusion and the development of persistent hypoxemia. In conditions of pulmonary hypertension, the vascular walls showed pronounced swelling, plasma infiltration, structural deformation, and loss of barrier function due to endothelial damage. These processes increased the risk of hemorrhages and contributed to the destruction of the vascular bed.

Morphometric study of the lungs of patients with diabetes mellitus.

Morphometric analysis of the lungs of deceased patients (9 men and 8 women, mean age 67.4 ± 2.4 years) with type 1 and type 2 diabetes mellitus showed changes associated with atherosclerotic lesions (Figure 10).

It has been found that in people with diabetes, the small vessels in the lungs become narrower and their walls thicker. Because of this, the blood passes through them worse, and there is increased pressure in the lungs. This interferes with normal blood flow and makes it difficult for the lungs to function. The most pronounced changes are observed when type 2 diabetes mellitus is combined with coronary heart disease. Morphological signs of vascular remodeling in this category of patients indicate the formation of latent pulmonary arterial hypertension.

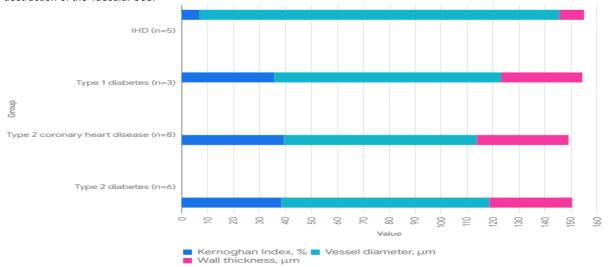


Figure 10. Morphometric indices of the lungs in patients with diabetes (autopsy material).

Discussion

According to comprehensive examination data, changes in the bronchopulmonary system were detected in 43.93% of cases in patients with DM. X-ray changes are more often detected than changes during physical examination, especially when DM2 is combined with coronary artery disease. In 68% of patients with DM2 in PS, disorders of the function of external respiration (LVEF) of restrictive, obstructive and mixed types were detected. The Berotec test showed a decrease in the significance of bronchial reactivity in DM, which indicates the predominance of sclerotic processes. Violations of FVD, in particular, a decrease in FEV1 and VVC, are considered as an independent risk factor for mortality in diabetes [1, 2, 5, 6, 8, 11-16, 18]. In the study [8], spirography indicators were more dependent on the state of metabolic control of carbohydrate metabolism in patients with T2DM. Obesity, diseases of the cardiovascular system, and the duration of the disease contributed to impaired bronchial patency. In addition, a 10% decrease in FEV1 was associated with a 12% increase in mortality among the surveyed.

The results of studies that have revealed a link between spirography and mortality make it possible to consider deterioration of respiratory function as an independent risk factor for mortality, and the determination of FEV1 and VVC as indicators of health status [11], including in diabetes [12], [13], [14]. It was found that VVC in diabetes mellitus decreases to a greater extent than FEV1.

The pathological process in DM involves the bronchopulmonary system, causing functional and morphological changes, including changes in the vessels of the small circle of blood circulation. In conditions of pulmonary hypertension, a compensatory venoarterial reaction and vascular restructuring occur.

The importance of closure-type vessels as regulators of blood supply in the pulmonary circulation in conditions of pulmonary hypertension plays an important pathogenetic role. The presence of a longitudinal muscle layer in the vessels of the closure type makes it possible to completely stop blood flow in one or another part of the microcirculatory bed and helps to change its direction.

Conclusions

38.4% of people with type 1 diabetes had breathing problems. This was manifested by the fact that the air passed worse through the respiratory tract, especially in large bronchi, and increased air resistance. 23.3% of people with type 2 diabetes had shallow breathing due to poor alveolar function. In some patients (21.3%), bronchial inflammation, deterioration of respiratory parameters and difficulty in gas exchange in the lungs were found.

The majority of patients with type 2 diabetes (62%) had both obstructive (difficulty getting air out) and restrictive (decreased lung volume) breathing disorders. They also had bronchial inflammation, a severe decrease in lung volume, and impaired blood flow in the lungs.

A deeper (microscopic) examination of the lungs of diabetic patients revealed alveolar damage, inflammation, scarring of tissue and destruction of the vascular membrane. This led to hemorrhages, edema, and vascular thickening in most cases.

Conflict of Interest. The authors declare that they have no conflict of interest.

Contribution of authors. All authors were equally involved in the writing of this article.

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