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1 МАХСУС СОН

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CHANGES IN THE CYTOKINE PROFILE IN PATIENTS WITH SILICOSIS IN COMBINATION WITH CORONARY HEART DISEASE AND ARTERIAL HYPERTENSION

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ABSTRACT
This article is devoted to improving the quality of early diagnosis of dust diseases of the lungs, the development of which is associated with exposure to dust aerosols of varying degrees of fibrogenesis. According to the author, the definition of the factors of humoral immunity allows you to set features of the emergence, course, and progression of dust diseases of the lungs, which will improve the quality of early diagnosis, the strategy to optimize primary and secondary prevention in this disease, to predict the course of the disease, to reduce the number of disabling forms.
Keywords: fibrogenic dust, silicosis, neutrophil elastase, endothelial dysfunction, endothelin-1, lipid spectrum.

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ИЗМЕНЕНИЕ ЦИТОКИНОВОГО ПРОФИЛЯ У БОЛЬНЫХ СИЛИКОЗОМ В СОЧЕТАНИИ С ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА И АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

АННОТАЦИЯ

Статья посвящена улучшению качества ранней диагностики пылевых заболеваний легких, развитие которых связано с воздействием пылевых аэрозолей различной степени фиброгенности. Определение факторов гуморального иммунитета позволяют установить особенности возникновения, течения, и прогрессирования пылевых заболеваний легких, что позволит улучшить качество ранней диагностики, стратегию оптимизации первичной и вторичной профилактики этого заболевания, прогнозировать течение болезни, уменьшить число инвалидизирующих форм.

Ключевые слова: фиброгенная пыль, силикоз, нейтрофильная эластаза, эндотелиальная дисфункция, эндотелин-1, липидный спектр.

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KORONER YURAK KASALLIGI VA ARTERIAL GIPERTENZIYA BILAN BIRGALIKDA SILIKOZ BILAN OG'RIGAN BEMORLARDA SITOKIN PROFILINING O'ZGARISHI

ANNOTATSIYA

Maqola chang o'pka kasalliklarini erta tashxislash sifatini yaxshilashga bag'ishlangan bo'lib, ularning rivojlanishi turli darajadagi fibrogenlik darajasidagi chang aerozollari ta'siri bilan bog'liq. Gumoral immunitet omillarini aniqlash chang o'pka kasalliklarining paydo bo'lishi, kechishi va rivojlanishining xususiyatlarini aniqlashga imkon beradi, bu erta tashxislash sifatini, ushbu kasallikning birlamchi va ikkilamchi profilaktikasini optimallashtirish strategiyasini yaxshilaydi, kasallikning borishini bashorat qiladi, kasallik va nogironlik shakllari sonini kamaytiradi.

Kalit so'zlar: fibrogen chang, silikoz, neytrofil elastaz, endotelial disfunktsiya, endotelin-1, lipid spektri.

Relevance. Cardiovascular diseases (CVDs), the most common of which are arterial hypertension and ischaemic heart disease, occupy the main place in the structure of mortality and disability of the working population [4-8],

Despite preventive measures, miners’ occupational bronchopulmonary diseases are very high. At the same time, miners are exposed to high risk of developing occupational and production-related diseases, especially the cardiovascular system. However, mechanisms of etiology, pathogenesis, and features of the course of cardiovascular diseases at high professional risk employees, some questions of this problem remain poorly studied. The question of searching for optimal prognostication of circulatory system disease development concerning the influence of harmful production factors when developing prognostic methods remains open. In this connection, this article is devoted to assessing medical and biological parameters of health, working in the mining industry, and probabilistic assessment of negative consequences of the influence of working environment factors on the cardiovascular system of workers in contact with fibrogenic dust.

One of the most significant problems in professional pulmonology is the issue of improving the quality of early diagnosis of pulmonary dust diseases, the development of which is associated with exposure to dust aerosols of varying degrees of fibrogenicity. System approach to early diagnostics in dusty lung diseases will contribute to timely diagnosis and help predict the development and course of respiratory and hemodynamic disorders, facilitating timely treatment of such complications as cardiopulmonary insufficiency and chronic pulmonary heart. In this regard, a differentiated approach to the study of working conditions in the mining industry, based on real production situations, using a wide range of medical and biological indicators of the health of workers, probabilistic assessment of the negative effects of the working environment factors on the health of workers in this sector is necessary [6-10].

According to the immunological theory of pneumoconiosis, silicosis is now believed to be impossible without the phagocytosis of silica particles by macrophages. Macrophage death is the first and obligatory step in silico nodule formation. The rate of macrophage death has been shown to be proportional to the cytotoxicity of the production dust. Proteolytic enzymes such as metalloproteinases and elastase, released from damaged macrophages, also contribute to the destruction of lung structures. The inflammatory phase is accompanied by reparative processes in which growth factors stimulate the production and proliferation of mesenchymal cells. Uncontrolled mechanisms of neoangiogenesis and epithelialization lead to the development of fibrosis. In addition, fibrogenic dust particles independently activate pro-inflammatory cytokines. The important role of tumour necrosis factor-α (TNF-α) interleukin (IL)-8 in silicosis development has been established. The immunological status in silicosis has been shown to be characterized by an increase in myeloperoxidase, IL-8,TNF-α. [1,2,3.9,10].

The aim of the study is to assess the features and interrelation of markers of pulmonary fibrosis of dust etiology and endothelial dysfunction in silicosis patients combined with coronary heart disease and arterial hypertension, as well as to establish their influence on the development of long-term cardiovascular events to develop a prognostic model.

Materials and methods: We studied the condition of 126 patients diagnosed with silicosis of I, II, III stages (ICD-10 code: J62) who worked at different objects of Almalyk mining and smelting plant (AGMK) and were treated in the clinic of occupational diseases of Research Institute of Sanitary, Hygiene and Occupational Diseases of Ministry of Health. The average age was 39,6±1,2 years, duration of the disease was more than 10 years. In patients (with various degrees of silicosis combined with IBS and arterial hypertension), the immunological investigation was carried out - 82 patients with first-stage silicosis (predominantly interstitial form), 37 patients with second-stage silicosis (nodular form), 7 patients with third stage silicosis (nodular form). The obtained data were compared with 20 healthy workers of industrial enterprises and institutions who had no contact with occupational hazards at work, without signs of respiratory, cardiovascular and immune system lesions, recognized as healthy according to comprehensive examination. The diagnosis of the disease (a form of pathology, clinical features) was verified following clinical protocols for diagnosing and treating occupational diseases).

Laboratory tests were carried out at the Central Diagnostic Laboratory of the multidisciplinary clinic of the Tashkent Medical Academy. Immunoenzyme tests were performed on a Rayto analyzer using reagents Endotelein-I, neutrophil elastase, myeloperoxidase from “Elabscience” (America), TNF-a, Interleukin-8 from “Vector Best” (Russia). Biochemical studies of creatinine kinase and lipid profile were performed using reagents from “HUMAN” (Germany) on the automatic biochemical analyzer Mindray BS-380.

Results and discussion:. The study of an occupational route found that the largest percentage of workers were sinkers (28%). (Table 1.)

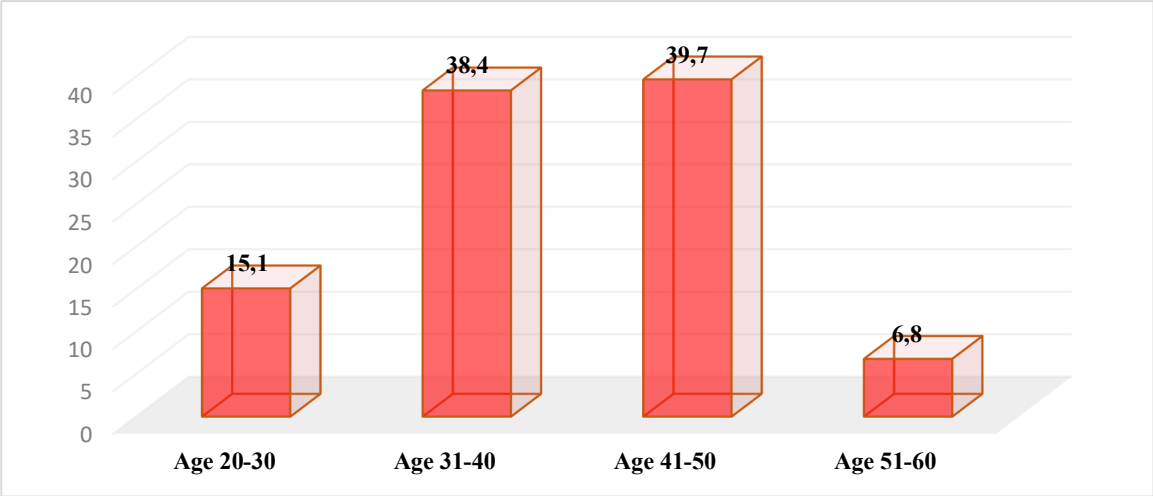
Table 1.

Occupational distribution of workers with detected silicosis

№/п	Occupation	Number, abs.
1	Pathfinders	35
2	Blasters	15

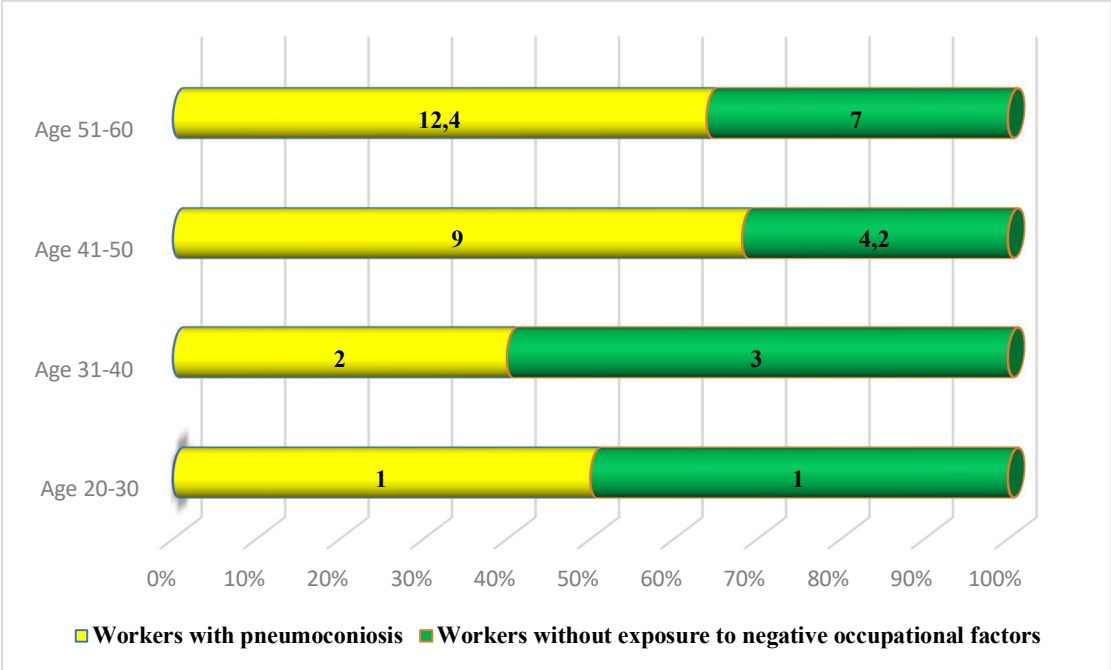
3	Plumbers	10
4	Electric locomotive driver	13
5	Drilling machine operator	17
6	The Fixers	9
7	Deliverers	7
8	Underground workers	10
9	Miners	10
	Total:	126

Most workers surveyed were aged 41-50 years, with a share of almost 40% (see Pic. 1).



Pic. 1. Distribution by the age of workers with identified silicosis (%)

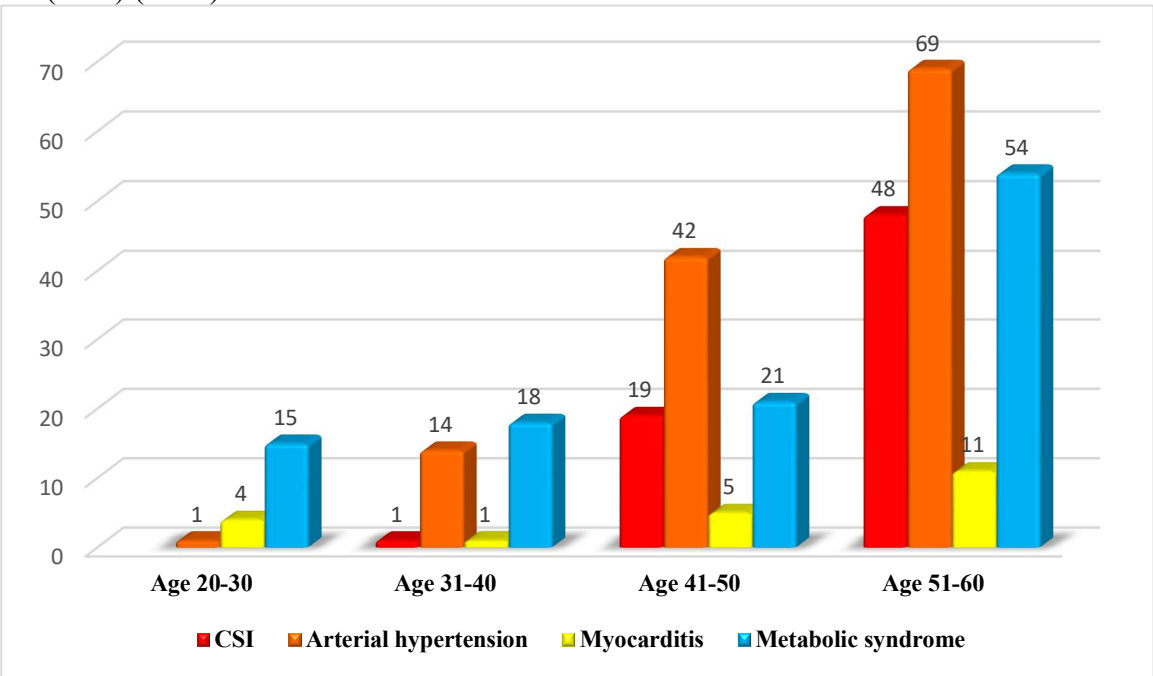
When exposed to harmful factors at work, the risk of CVD more than doubles (Pic.2).



Picture 2. Incidence of cardiovascular disease among workers with and without silicosis (%)

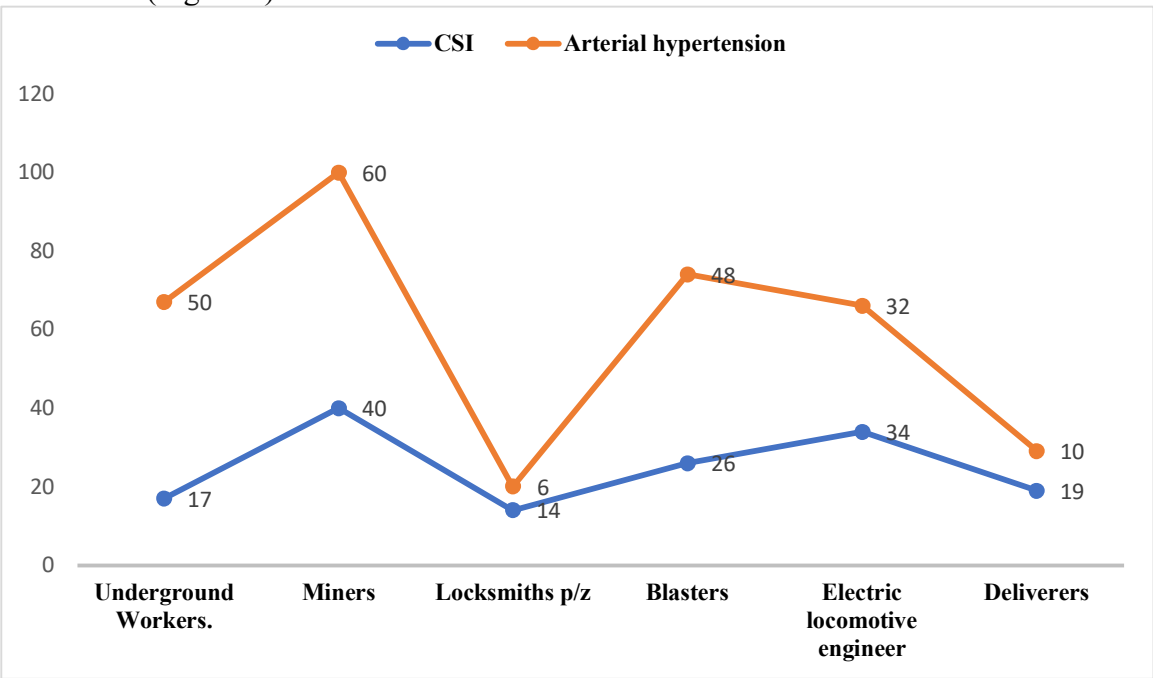
Cardiovascular diseases have recently shown an increasing and rejuvenating trend. A significant increase in the incidence of AH and CHD was most often observed in groups of people over 50 years of age. The study confirms the high incidence of IHD (about 48%) among miners of the oldest working age (51-60 years). At the same time, the work experience in the industry is 10 years or more. The increase in the incidence of CHD is traceable to the aging of workers. It is associated with the length of work experience due to cases of angina and myocardial infarction. The incidence of AH is significantly higher than CHD by almost 1.5 times among miners of most working

age (69%). With IBS and AH also occurs the development of metabolic syndrome among silicosis workers (54%) (Pic.3).



Pic. 3. Distribution of patients with cardiovascular diseases by age group (%)

The results show the prevalence of AH and CHD among miners at Almalyk mine, who work underground, which is 40% and reliably higher than among surface miners. It has been found that AH is diagnosed in underground miners as early as 30-39 years of age, whereas it occurs later among surface workers (Figure 4).



Pic. 4. Occupational distribution of workers with identified CHD and AH (%)

The clinical course of silicosis is aggravated by AH and is a predictor of hemocirculatory disorders, which lead to marked hemodynamic disorders, which determine the severity of the course, progression of the disease and loss of professional ability to work.

When studying endothelial dysfunction in patients with silicosis combined with CHD and AH, we found reliable increased content of cellular endothelial markers - Interleukin-8, TNF-a,

Endothelin-1 and MPO, respectively, changes of lipid spectrum, atherogenicity, creatine kinase (cardiac fraction) (P<0.05) (Fig.5).

When studying lipid metabolism disorders in patients with silicosis combined with CHD and AH, we found a significant increase of lipid, creatine kinase (cardiac fraction) - UX, Tr, HDL-C, LDL-C, HDL-C, AT and CK-MB (P<0.05) (Fig.6).

As a result of serum examination in patients with pneumoconiosis (in silicosis due to silica dust exposure), we found that myeloperoxidase level was significantly increased compared to the control group (p<0,05). In the groups of patients with silicosis combined with arterial hypertension, a significant increase in the vasopressor factor endothelin-1 was revealed, indicating a pronounced impairment of the vasomotor function of the endothelium with predominant vasoconstriction. Marked damage to the vascular wall in silicosis patients combined with AH was indicated by high blood levels of endothelin-1, TNF-α, interleukin 8, indicating the secretion of proteases damaging the endothelium, causing local inflammatory reactions and extracellular fibrosis, leading to to decreased elastic properties of blood vessels and, therefore, increased risk of cardiovascular complications.

Conclusions:

1. The differentiated approach to studying working conditions in the mining industry is necessary, proceeding from real industrial situations, using a vast complex of biomedical parameters of working health, probabilistic estimation of negative consequences of the influence of working environment factors on the health of the workers of this sector.
2. When providing medical supervision and rehabilitation measures for miners with pulmonary dust pathology, an account of associated circulatory system diseases (arterial hypertension and coronary heart disease) should be taken, which aggravate occupational pathology.
3. Reduction of risk of occupational disease development in mining and metallurgical manufactures is possible at the expense of carrying out actions of technological, sanitary, and technical character, and also maintenance of a high level of medical service, early diagnostics, rehabilitation and secondary prevention.
4. Considering the influence of harmful production factors on the risk of circulatory system diseases, such as long-term work experience in dusty underground conditions, and high levels of dustiness in the working area, it is necessary to recommend stopping work in contact with industrial aerosols and underground conditions when reaching a certain harmful work experience, dust load or when developing professional pathology of respiratory organs.

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