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METABOLIC DISORDERS IN PATIENTS WITH ONCOLOGIC PATHOLOGY

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ABSTRACT

Relevance: *Metabolic disorders often take on a systemic character. It affects carbohydrate, lipid, and hormonal metabolism. Moreover, these changes promote the development and aggravation of several pathologies. The prevalence of metabolic disorders, including obesity, is increasing worldwide and in Kazakhstan.*

The study focused *on the clinical characteristics of metabolic syndrome (MS) components in patients with cancer comorbidities.*

Methods: *The materials included medical records of cancer patients with MS – 35 people (main group) and non-cancerous patients with MS – 35 people (control group). MS was diagnosed with a combination of three symptoms: abdominal obesity, high blood pressure, and increased high-density lipoprotein cholesterol (HDL-C) levels. The data were analyzed and processed using the STATIS-TICA 10 software package. The significance criterion was $p<0.05$.*

Results: *All studied patients were diagnosed with abdominal obesity. Indicators analysis showed a significant difference in HDL-C concentration in the main and control groups: 3.8 mmol/L in cancer patients and 5.7 mmol/L in the controls. No significant difference in blood pressure was found.*

Conclusion: *The age of patients with MS evidences a threatening tendency to develop metabolic disorders in young and middle ages. A significantly lower concentration of LDL-C in cancer patients compared with the controls allows using this parameter to predict cancer]development in patients diagnosed with MS. Thus, HDL-C concentration could be used as a metabolic marker for pre-symptomatic diagnostics.*

Keywords: *metabolic syndrome (MS), cholesterol, diagnostic criteria, abdominal obesity, cancer.*

Introduction: Metabolic syndrome (MS) is a complex of metabolic disorders accompanied by hormone imbalance and several clinical pathologies. MS development often leads to the aggravation of several pathologies, such as oncological, hormonal, and cardiovascular. MS can be called "plethora" syndrome. Specialists of the World Health Organization (WHO) call it a new pandemic and predict a twofold increase in MS cases in the next 25 years [1-3].

Abdominal obesity (AO) is often the main criterion indicating MS development. Being overweight (according to WHO) is a problem for two billion adults on the planet, and about 600 million people are obese to varying degrees. It is expected that obesity will become an actual diagnosis for 73% of men and 63% of women in Europe by 2030 [4].

This problem is also relevant to the Asian region. Thus, from the data of a comprehensive population study in Kazakhstan, the prevalence of MS among Kazakhs is 38.5%, and among Uzbeks is 42.1%. The study showed dependence on national standards of lifestyle, nutrition, and traditions, as well as on professional activity: MS has affected 40.3% of public officers in Kazakhstan aged 35 to 70 years [1].

There is evidence of a correlation between the development of oncological pathologies and obesity in patients, particularly in pancreatic duct adenocarcinoma. However, experts suggest the dependence of 12 types of cancer on obesity, especially AO [4, 5]. However, obesity cannot be called the only trigger for oncopathologies. Genetic mutations, excess weight, hormonal disorders, eating disorders, chronic inflammation, and stress can be promoting agents [5]. At the same time, oncologists predict a constant increase in oncological diseases. Thus, by 2040 the number of new cases may increase by 47% and reach 28.4 million cases of registered oncopathologies per year, with breast cancer (BC) taking the lead [6]. Such trends require searching for new diagnostic approaches and agents that accompany, aggravate, and promote oncopathology.

The study focused on the clinical characteristics of metabolic syndrome (MS) components in patients with cancer comorbidities.

Materials and methods: The authors have conducted a one-time retrospective study based on the analysis of medical records of patients admitted in 2019 to the Marat Ospanov West Kazakhstan Medical University Medical Center oncology department, NJSC (Aktobe, the Republic of Kazakhstan).

From the total number of medical records provided for analysis (295), we have selected the records of patients diagnosed with concomitant pathology (oncology and MS). The study included data from 35 patients aged 37 to 54 years.

The control group consisted of 35 patients (38-47 years old) diagnosed with MS without oncological pathology, who were examined at polyclinic No. 1 and the family medicine clinic in Aktobe. Both groups were comparable in terms of gender: the main group consisted of 15 men and 20 women; the control included 13 men and 22 women.

In order to recognize MS in a patient, we focused on the recommendations of the All-Russian Scientific Cardiologist Society (ARSCS) for the diagnosis and treatment of metabolic syndrome (2009). According to these recommendations, MS was considered recognized in a patient at the combined presence of three criteria (Table 1) [7].

It should also be noted that ARSCS accepts the waist-to-hip ratio of more than 94 cm in men and more than 80 cm in women as the main criterion for recognizing MS in the adult population [7].

Table 1 – Criteria characterizing MS development in patients

No.	Indicators	Women	Men
1	Waist-to-hip ratio, cm	80 / 0.85	94 / 0.9
2	Body mass index, kg/m^2	Over 30	
3	Arterial hypertension, mm Hg Art.	130/85 or more	
4	Fasting glucose, mmol/L	5.6	
5	Fasting insulin, μIU/ml	2.6-24.9	
6	Triglycerides, mmol/L	Not more than 1.7	
7	Cholesterol-lipoproteins of low density, mmol/L	More than 3	
8	Uric acid in blood serum, μmol/l	150-350	210-420
9	Uric acid in urine, mmol/day	1.48-4.43	
10	Estradiol / testosterone, nmol/l	Less than 183	11.4-27.9
11	Glucose tolerance test with C-peptide	Positive	

Body mass index (BMI) was determined by the formula of a simple ratio of body weight (in kg) to height (in m) squared. According to WHO recommendations, being overweight is considered established at BMI ≥25. BMI ≥30 indicates the development of obesity and is one of the indicators for diagnosing MS [8], especially in combination with abdominal obesity (diagnosed by the ratio of waist to hips) [7].

In our study, we relied on the experience of international research teams and used a three-component MS diagnosis among cancer patients with AO, taking into account the level of blood pressure (BP) and the LDL-C concentration in the blood serum of the examined patients. We also compared the serum LDL-C concentration in the control and index groups (in combination with MS and oncopathology) for a deeper analysis of the effectiveness of this indicator.

The analysis of the data obtained was performed using the methods of descriptive and nonparametric statistics using the STATISTICA 10 software package. The data are presented as Me, Q1, Q3 (median, upper and lower quartiles). The statistical significance of differences between the two groups was tested using the Mann-Whitney u-test for independent populations. The critical level of significance was $p<0.05$.

Results: Analysis of the statistics of oncopathologies in patients with combined MS showed that lung cancer (13 cases) was typical for men aged 37-49 years, BC was recorded in women aged 39-49 – 15 cases, stomach cancer was recorded as in men (2 cases), and in women (5 cases) with MS (44-54 years age).

BMI was determined for all patients in the study and equaled or exceeded 30 in all cases. The waist-to-hip ratio also confirmed the MS development (Table 2).

Table 2 - Indicators indicating the MS development in the trial arms

Indicators	Index group, n = 35			Control group, n = 35			P
	Me	Q1	Q3	Me	Q1	Q3	
Waist, cm							
Men	97.0	96.0	102.0	97	96.0	102.0	0.000
Women	89.0	85.0	90.0	90.0	86.0	91.0	0.000
Systolic blood pressure, mm Hg.	140.0	135.0	140.0	140.0	135.0	142.0	0.457
Diastolic blood pressure, mm Hg	90.0	87.5	90.0	88.0	87.0	90.0	0.280
Cholesterol-lipoproteins of low density, mmol/L	3.8	3.5	4.0	5.7	5.6	6.0	0.000

The systolic and diastolic pressure ratio slightly exceeded the norm (140/88 mm Hg) in both trial arms. Differences in blood pressure in the cancer patients group and between groups were not found.

In our study, we used LDL-C levels as a component characterizing MS development. According to the ARSCS (2009) MS diagnosing criteria, an LDL-C concentration of more than 3 mmol/L in combination with other

criteria, such as BMI > 30, etc., indicates MS development in patients [7].

The lipid metabolism analysis showed that the control group was characterized by an increase in the LDL-C concentration in blood serum (Me - 5.7 mmol mmol/L [5.6-6.0]), while the indicators were lower (Me – 3.8 mmol/L [3.5-4.0], p=0.000) in cancer patients (Figure 1).

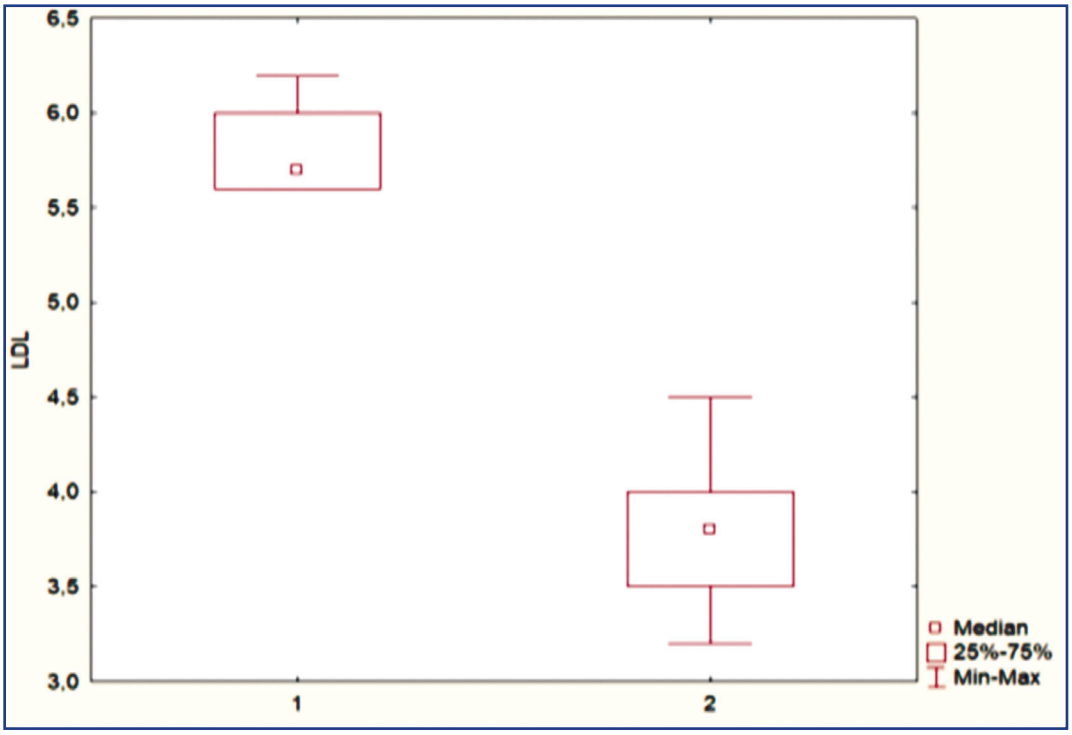

Figure 1 - The LDL-C concentration in the control (1) and index (2) groups

At the same time, LDL-C content in blood serum analysis in combination with registered oncopathology showed (with reliability p=0.000): for patients with oncopathology in the respiratory system – Me 3.9 [3.8-4.0], for patients with breast cancer – Me 3.8 [3.2-4.0] and 3.8 [3.4-3.8]. A comparative analysis of these subgroups of cancer patients showed a statistically significant difference (p<0.05) compared with the control group, where the LDL concentration ranged from 5.5 to 6.0 mmol/L.

Discussion: Oncological pathologies (in particular, lung cancer, colorectal cancer, cervical lesions, etc.) are persistently leading among the causes of death worldwide [9-10]. According to the statistics of oncological morbidity, lung cancer and stomach cancer in both sexes and breast cancer in women annually occupy the leading positions in the Aktobe region. Oncopathologies are often associated with AO, in particular, at waist circumference ≥94 cm in men and ≥80 cm in women; an increase in blood pressure, both systolic and diastolic; and a decrease in the LDL-C level [9].

It should be noted that BP control is an important monitoring aspect in preventing complications in oncological diseases and developing an individual approach to each oncological patient, especially in the case of overweight [10].

MS diagnosis is a combined procedure: the diagnosis is considered proven in the presence of three or more marker indicators [7]. Thus, a combination of the following indicators confirmed MS in our study: BMI > 30, determination of abdominal obesity, elevated blood pressure, and impaired triglyceride metabolism.

Analysis of morphometric body volumes of patients and blood pressure indicators did not reveal a significant difference between the groups: the groups were comparable in these indicators. At the same time, we noted that the control and index groups had significantly different levels of LDL-C concentration.

Comparison of the mean values in the control group (5.5-6.0 mmol/L) and cancer patients (Me 3.8-3.9 mmol/L) shows a significant difference between these groups both in general and in individual types of cancer (p<0.05). It should be noted that the normal LDL-C concentration is 2.8-5.2 mmol/L. However, this indicator cannot be regarded as independent but should be assessed in conjunction with the history, biochemical and hormonal blood markers, as well as the anthropometric characteristics of the patient [2, 7, 15]. The LDL-C increase can be observed in several diseases and often accompanies obesity, while this indicator decrease may cause a more detailed examination to be prescribed [7].

The literature provides conflicting data on the role of MS in cancer genesis. In 1986, R. Hiatt and B. Fireman made a multivariate analysis of the development and progression of 21 types of cancer, adjusted for race, education, bad habits, and BMI, in addition to the onset of menarche, parity, and menopausal status in women. No strong or consistent association was found between low choles-

terol and cancer development, except for an increased risk of lymphoma in men and cervical cancer in women [11].

Today, MS, particularly obesity, is gaining prevalence in the population of Kazakhstan, with women being more prone to obesity. The increase in children's BMI deserves special attention and concern [12, 13].

Some researchers reported an association between metabolic disorders and the development of oncological, particularly colorectal, lesions. At the same time, an oncological pathology development exacerbates metabolic disorders, creating a vicious pathological circle [14]. The same association was observed in breast cancer [15]. Metabolic changes due to hormonal surges during menopause trigger a range of pathologies [15, 16]. However, there is evidence that MS, being a consequence of several pathologies, including cardiovascular disorders, can only accompany oncological diseases or result from them [3, 14, 17].

Today, three types of screening are available in Kazakhstan: breast cancer detection in women of 40-70 years, colorectal cancer in men and women of 50-70 years, and cervical cancer in women of 30-70 years. Innovative technologies, particularly computed tomography, are being extensively introduced. These screenings focus on early pathology detection [18].

The dependence of the metabolic syndrome (in particular, the level of cholesterol, lipid metabolism as one of the markers) and the development of oncological pathology, in our opinion, requires additional study in the direction of finding opportunities for early cancer diagnosis of the logical mechanism for determination criteria (metabolic indicators) for the likelihood of oncological pathology genesis.

Conclusion: The age of cancer patients diagnosed with metabolic syndrome ranged from 37 to 54 years, while the age of the control group (non-cancer patients with metabolic syndrome) was slightly lower - from 38 to 47 years.

In the group of oncological patients, a significant decrease in the LDL-C concentration was noted in comparison with the control group (Me - 3.8 mmol/L versus Me - 5.7 mmol/L, respectively). Therefore, the LDL-C concentration can be used as a metabolic marker for the "pre-symptomatic" diagnosis of oncological diseases and a predictive indicator of oncological pathology development in patients with a diagnosed metabolic syndrome.

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ТҰЖЫРЫМ

ОНКОПАТОЛОГИЯСЫ БАР НАУҚАСТАРДАҒЫ МЕТАБОЛИКАЛЫҚ БҰЗЫЛЫСТАР

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Өзектілігі: *Көмірсулар, липидтер, гормондар метаболизмі бұзылуының әсері салдарынан жүйелі сипат алатын метаболизмдік өнімдердің күйреуі жиі кездеседі, және олардың ең бастысы, бірқатар патологиялардың дамуына және шиеленісуіне әкеледі. Зат алмасу бұзылыстары мен семіздіктің даму қарқынының пайыздық мөлшері Қазақстан аймағында, дүниежүзілік деректермен қатар арақатынаста барған сайын артып келе жатырғандығын аңғаруға болады.*

Зерттеудің мақсаты *– онкологиялық науқастарда біріктірілен метаболикалық синдром компоненті бар патологияларға клиникалық сипаттама беру.*

Әдістері: *Метаболикалық синдроммен (МС) біріктірілген онкологиялық патологиясы бар науқастардың саны 35 олар негізгі топты және МС диагнозы бар қатерлі ісік емес науқастар – 35 олар бақылау тобын құрады, зертеуде медициналық құжаттар деректері талданды. МС үш симптомның тіркесімі ретінде қарастырылды: семздік (іштің семіздігі), жоғары қан қысымы және жалпы холестерин мен жоғары тығыздықтағы липопротеиндердің (ХС-ТТЛ) деңгейлері. Алынған деректерді талдау және өңдеу STATISTICA 10 бағдарламасын қолдану арқылы жүзеге асырылды, маңыздылық критерийі $p<0,05$ болды.*

Нәтижелері: *Негізгі және бақылау топтарының ХС-ТТЛ деңгейі бойынша көрсеткіштерін талдау айтарлықтай статистикалық айырмашылықты көрсетті: онкологиялық науқастар үшін 3,8 ммоль/л; ал бақылау тобындағы емделушілерде 5,7 ммоль/л. Қан қысымында айтарлықтай айырмашылық анықталмады. Жас ерекшелігіне байланысты талдауда жас және орта жастағы науқастарда метаболикалық бұзылулардың болуын көрсетті: негізгі топтың орташа жасы 44,5 жасты, бақылау тобының - 42,0 жасты құрады.*

Қорытынды: *МС диагнозы қойылған онкологиялық және онкологиялық емес науқастар топтарындағы ХС-ТТЛ деңгейінің айтарлықтай айырмашылықтары анықталды, олар онкологиялық ауруларды диагностикалау алгоритмдерін құруда қолданылуы мүмкін: метаболикалық бұзылыстардың көрсеткіштері онкологиялық аурулардың ерте «клиникаға дейінгі» диагностикалық іздеу жолында ықтимал көрсеткіштер.*

Түйінді сөздер: *метаболикалық синдром, холестерол, диагностикалық белгілер, абдоминальды семіздік, қатерлі ісік.*

АННОТАЦИЯ

МЕТАБОЛИЧЕСКИЕ НАРУШЕНИЯ У ПАЦИЕНТОВ С ОНКОПАТОЛОГИЕЙ

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Актуальность: *Нарушение обмена веществ часто принимает системный характер, влияя на углеводный, липидный, гормональный обмен, а главное, приводя к развитию и усугублению ряда патологий. Частота метаболических нарушений и ожирения постоянно растёт как в масштабах Казахстана, так и в мире в целом.*

Цель исследования *– изучение клинической характеристики компонентного метаболического синдрома (МС) у пациентов с сочетанной онкопатологией.*

Методы: *Были проанализированы данные медицинских карт пациентов с онкологической патологией в сочетании с МС. Диагноз МС ставился на основании трёх симптомов: абдоминального ожирения, повышенного артериального давления и повышенной концентрации холестерола и липопротеидов низкой плотности (ХС-ЛПНП). Анализ и обработка полученных экспериментальных данных проведены с использованием пакета программ STATISTICA 10, критерий достоверности – $p<0,05$.*

Результаты: *У всех исследованных пациентов было диагностировано абдоминальное ожирение. Сравнение показателей основной и контрольной групп показало наличие достоверной разницы в концентрации ХС-ЛПНП: у онкологических больных – 3,8 ммоль/л, у пациентов контрольной группы – 5,7 ммоль/л. Достоверной разницы в показателях артериального давления выявлено не было.*

Заключение: *Возраст пациентов с МС свидетельствует об угрожающей тенденции развития метаболических нарушений у людей молодого и среднего возраста. Наличие достоверного снижения концентрации ХС-ЛПНП у онкологических пациентов в сравнении с контрольной группой позволяет использовать концентрацию ХС-ЛПНП в качестве предиктивного показателя развития онкологической патологии у пациентов с диагностированным МС. Следовательно, концентрацию ХС-ЛПНП можно использовать для «досимптоматической» диагностики онкологических заболеваний в качестве метаболического маркера.*

Ключевые слова: *метаболический синдром (МС), холестерол, критерии диагностики, абдоминальное ожирение (АО), рак.*

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