**The effect of overweight and obesity on dyslipidemia. Cross-sectional study in Heart Center. Astana**

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**Влияние избыточного веса и ожирения на дислипидемию. Поперечное исследование в Центре Сердца. Астана**

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**Артық салмақ пен семіздіктің дислипидемияға әсері. Астана қаласындағы Жүрек орталығындағы көлденең зерттеу.**

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ORIGINAL ARTICLE

**THE EFFECT OF OVERWEIGHT AND OBESITY ON DYSLIPIDEMIA. CROSS-SECTIONAL STUDY IN HEART CENTER. ASTANA**

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**Abstract**

**Introduction:** Obesity has turned into a worldwide epidemic with increasing prevalence, that is associated with excess mortality and morbidity [1]. Obesity is a risk factor for many diseases including cardiovascular disease, the leading cause of death worldwide [2].

**Aim of the study:** This study was conducted to evaluate the association of obesity with dyslipidemia and hypertension among patients with low, medium and high risk of developing cardiovascular diseases

**Methods:** Cross-sectional study was conducted at the tertiary hospital in Astana, Kazakhstan. In total 227 participants included in this study.

**Results:** Student’s t test was performed to elicit association between body mass index (further – BMI) and lipid panel analysis such as cholesterol, triglycerides, low-density lipoprotein and high-density lipoprotein, where all p values found to be <0.0001. Consequently, there is a statistically significant association, and increased BMI is linked with higher lipids in the body. Obesity increases risk of atherosclerosis 2.97 times in comparison those who have a normal BMI. Obesity increases risk of coronary angioplasty with stenting 2.33 times in comparison those who did not undergo stenting procedure.

**Conclusion:** Atherogenic dyslipidemia is extremely common in obesity, both in the presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people

**Keywords:** *Obesity, Dyslipidemia, Cardiovascular risk factors, Сardiometabolic diseases*

**ВЛИЯНИЕ ИЗБЫТОЧНОГО ВЕСА И ОЖИРЕНИЯ НА ДИСЛИПИДЕМИЮ. КРОСС СЕКЦИОННОЕ ИССЛЕДОВАНИЕ В ЦЕНТРЕ СЕРДЦА. АСТАНА.**

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**Аннотация**

**Введение:** Ожирение превратилось в мировую эпидемию с растущей распространенностью, что связано с повышенной смертностью и заболеваемостью. Ожирение является фактором риска многих заболеваний, включая сердечно-сосудистые заболевания, ведущую причину смертности во всем мире.

**Цель исследования:** исследование проводилось с целью оценки связи ожирения с дислипидемией и артериальной гипертензией у пациентов с низким, средним и высоким риском развития сердечно-сосудистых заболеваний.

**Методы**: поперечное исследование было проведено в больнице третичного уровня в Астане, Казахстан. Всего в этом исследовании приняли участие 227 участников.

**Результаты:** t-критерий Стьюдента был проведен для выявления связи между индексом массы тела (далее – ИМТ) и анализом панели липидов, таких как холестерин, триглицериды, липопротеины низкой плотности и липопротеины высокой плотности, где все значения p оказались <0,0001. Следовательно, существует статистически значимая связь: увеличение ИМТ связано с более высоким содержанием липидов в организме. Ожирение увеличивает риск атеросклероза в 2,97 раза по сравнению с теми, у кого нормальный ИМТ. Ожирение увеличивает риск коронарной ангиопластики со стентированием в 2,33 раза по сравнению с теми, кто не подвергался процедуре стентирования.

**Заключение:** Атерогенная дислипидемия чрезвычайно распространена при ожирении как при наличии, так и при отсутствии выраженной инсулинорезистентности и, вероятно, является основным фактором повышенного риска сердечно-сосудистых заболеваний у этих людей.

**Ключевые слова:** ожирение, дислипидемия, сердечно-сосудистые факторы риска, кардиометаболические заболевания.

**АРТЫҚ САЛМАҚ ПЕН СЕМІЗДІКТІҢ ДИСЛИПИДЕМИЯҒА ӘСЕРІ. АСТАНА ҚАЛАСЫНДАҒЫ ЖҮРЕК ОРТАЛЫҒЫНДАҒЫ КӨЛДЕНЕҢ ЗЕРТТЕУ.**

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**Аңдатпа**

**Кіріспе:** семіздік өлім-жітім мен сырқаттанушылықтың жоғарылауымен байланысты таралуының өсуімен әлемдік эпидемияға айналды. Семіздік көптеген аурулардың, соның ішінде жүрек-қан тамырлары ауруларының қауіп факторы болып табылады, бұл бүкіл әлемде өлім-жітімнің негізгі себебі болып табылады.

**Зерттеу мақсаты:** Зерттеу жүрек-қан тамырлары ауруларының даму қаупі төмен, орташа және жоғары науқастарда семіздіктің дислипидемиямен және артериялық гипертензиямен байланысын бағалау мақсатында жүргізілді.

**Әдістері:** көлденең зерттеу Астанадағы (Қазақстан) үшінші деңгейлі ауруханада жүргізілді. Бұл зерттеуге барлығы 227 қатысушы қатысты.

**Нәтижелер:** студенттің t – критерийі дене салмағының индексі (бұдан әрі - ДСИ) мен холестерин, триглицеридтер, төмен тығыздықтағы липопротеидтер және жоғары тығыздықтағы липопротеидтер сияқты липидтер панелін талдау арасындағы байланысты анықтау үшін жүргізілді, мұнда барлық p мәндері <0,0001 болып шықты. Демек, статистикалық маңызды байланыс бар: ДСИ жоғарылауы организмдегі липидтердің жоғары болуымен байланысты. Семіздік атеросклероз қаупін қалыпты ДСИ-мен салыстырғанда 2,97 есе арттырады. Семіздік стенттеу процедурасынан өтпегендермен салыстырғанда коронарлық ангиопластика қаупін 2,33 есе арттырады.

**Қорытынды:** Атерогендік дислипидемия семіздікте инсулинге төзімділік болған кезде де, болмаған кезде де өте жиі кездеседі және бұл адамдарда жүрек-қан тамырлары ауруларының жоғары қаупінің негізгі факторы болуы мүмкін.

**Түйінді сөздер:** *семіздік, дислипидемия, жүрек-қан тамырлары қауіп факторлары, кардиометаболикалық аурулар.*

**Introduction**

Obesity is widespread in the industrialized world. Body mass index (BMI) is a common non-invasive anthropometric measure used as a indicator of fat mass to assess obesity. The World Health Organization and the American Heart Association (AHA) define obesity as a BMI greater than or equal to 30 kg/m22[1-3].

 Two billion people worldwide over 18 years of age, or approximately 30% of the world's population, are overweight or obese [4 - 6]. Studies conducted by the Kazakh Academy of Nutrition showed that the average prevalence of overweight and obesity among the adult population of Kazakhstan (15 years and older) was 29.7% in women and 33.9% in men; obesity was 25.8% in women and 15.3% in men. This means that more than half of the adult population of Kazakhstan (55.5% of women and 49.2% of men) are overweight or obese [7].

Overweight and obesity are responsible for more than 3.4 million deaths worldwide each year [8, 9]. The Association for Obesity Medicine has defined obesity as: "a serious, chronic, progressive, recurrent and treatable multifactorial, neurobehavioral disease in which increasing obesity contributes to adipose tissue dysfunction, resulting in adverse metabolic, biomechanical and psychosocial health consequences". It has been suggested that multiple mechanisms underlie the relationship between obesity and atherosclerosis, including abnormalities in lipid metabolism, insulin resistance, and inflammation [3, 10, 11]. Adipose tissue represents the largest reservoir of free cholesterol in the body. Adipocytes and adipose tissue store the largest amount of body lipids, including triglycerides and free cholesterol. Adipocytes and adipose tissue are endocrine and immune active. Adipocyte hypertrophy and excessive adipose tissue accumulation may contribute to the pathogenic effects of adipocytes and adipose tissue (adiposopathy), leading to abnormal levels of circulating lipids, with dyslipidemia being a major risk factor for atherosclerotic coronary heart disease [12]. Systemic inflammation and adipokine production by adipose tissue are important mechanisms for the adverse effects of obesity on the vascular wall [13]. Metabolic products, cytokines, and hormones released by adipose tissue can affect the liver by inducing changes in hepatic-derived lipoproteins, clotting factors and inflammatory factors that affect the atherogenic environment of the vessel wall. Visceral adipose tissue has access to the portal circulation and may be particularly important in this process. In addition, these same adipose tissue-derived factors have been shown to influence gene expression and cellular function of endothelial cells, arterial smooth muscle cells, and monocytes/macrophages. They represent the major cell types of the arterial wall and are key components to protect the homeostasis of the vessel wall [14].

There are many mechanisms by which obesity may affect systemic lipid and lipoprotein metabolism [15]. Increased production of fatty acids from adipose tissue in obesity with increased entry into the liver can lead to increased secretion of very low density lipoproteins, apolipoprotein B (apoB) and triglycerides. [15, 16, 17, 18]. Other factors secreted by adipose tissue may have adverse effects on circulating lipids. For example, in a study of white men with BMI values between 22 and 35 kg/m2, adiponectin was the most significant factor of plasma apoB very low density lipoprotein concentrations [19]. Tumor necrosis factor expression is upregulated in adipose tissue in obese patients and may have multiple effects on lipid metabolism through both paracrine effects on adipocytes and the liver [15,20,21].

Dyslipidemia is a widespread risk factor for coronary heart disease and an important feature of the metabolic syndrome. Obesity, especially visceral obesity, causes insulin resistance and is associated with dyslipidemia, impaired glucose metabolism, hypertension, which exacerbate atherosclerosis. Studies over the past 4 decades have consistently shown that the burden of dyslipidemia is very high in terms of morbidity, mortality, and medical costs. Dyslipidemia is an important risk factor for coronary heart disease (CHD), which is the leading cause of death worldwide. The World Health Organization estimates that dyslipidemia is associated with more than half of coronary heart disease cases worldwide and more than 4 million deaths per year [9]. The American Heart Association estimates that more than 100 million Americans - one-third of all Americans - have total cholesterol levels greater than 200 mg/dL and more than 34 million American adults have levels greater than 240 mg/dL, which is considered a high level requiring treatment [10]. Diabetes mellitus is closely associated with dyslipidemia, with people with DM(diabetes mellitus) having mean LDL levels greater than 140 mg/dL [11, 22].

**Aim of the study:** Obesity and dyslipidemia contribute to cardiovascular risk. This study was conducted to evaluate the association of obesity with dyslipidemia and hypertension among patients with low, medium and high risk of developing cardiovascular diseases

**Methods**

Cross-sectional study was conducted at the tertiary hospital in Astana, Kazakhstan. In total 227 participants included in this study. Inclusion criteria for the study were:

* Patients with high and very high cardiovascular disease risk according to American college cardiovascular disease (ASCVD) risk estimator
* Age ranges from 18 to 65 years old
* Gave consent to be included for the cross-sectional study

Exclusion criteria included the patients who did not give consent to participate to the study or had following diseases:

* History or currently have cancer
* Alcoholic steatohepatitis
* Viral hepatitis
* Asthma and/or COPD
* Heart failure with ejection fraction lower than 40%.

Demographic characteristics including age, gender, nationality, comorbidities, blood analysis results, instrumental analysis like ultrasound, computer tomography, liver ultrasound (fibroscan), echocardiography results were collected and analyzed to assess their potential influence on cardiovascular risk factors and outcomes.

For the categorical data set chi square test, and for the continuous data set student’s t test, two tailed were used. P values less than 0.05 were considered to be statistically significant. Odds ratio were calculated to find risk of atherosclerosis development in regards of obesity.

Patients all signed informed consent and the study was approved by the local ethical committee (approval number № 2023/01-008 from 05.07.2024.

**Results**

Out of 227 patients with high and very high risk of developing cardiovascular disease, 42.3% (n=96) to be female. Average weight for patients was 80.74 ± 15.3kg, while average body mass index (BMI) and body surface area (BSA) found to be 29.03 ± 5.17kg/m2 and 1.86c± 0.2m2, respectively. As mean BMI could be categorized as obese, hence we tried to break down patients on obesity stages depending on BMI:

* Overweight (not obese), if BMI is 25.0 to 29.9
* Class 1 (low-risk) obesity, if BMI is 30.0 to 34.9
* Class 2 (moderate-risk) obesity, if BMI is 35.0 to 39.9
* Class 3 (high-risk) obesity, if BMI is equal to or greater than 40.0.

Out of 227 patients, 58 (25%) had normal weigh, 86 (37.8%) were overweight, 54 (23.7%) had class 1 obesity, 12 (5.2%) had class 2 obesity and 6 (2%) had high risk or class 3 obesity. 190 (83.7%) had peripheral or brachiocephalic atherosclerosis. Moving to the blood analysis, mean total cholesterol level found to be 195.96 ± 43.86 mg/dL, further subdivided to low level lipoprotein (LDL) and high-density lipoprotein (HDL) which were calculated to be 132.67 ± 36.37 mg/dL and 49.18 ± 12.48. Furthermore, mean values for Non-HDL cholesterol was 146.45 ± 44.6 mg/dL and triglycerides was 143.02 ± 89 mg/dL. Regarding rest of the lipid panel analysis, mean Apo A was 1.29 ±0.63 mg/dL, mean Apo B was 1.089 ± 1.26 mg/dL and LP(a) 37.47 ± 50.29 mg/dL. Among the most frequently seen comorbidities were hypertension (72.6%) and diabetes mellitus type 2 (21.2%).

Student’s t test was performed to elicit association between BMI and lipid panel analysis such as cholesterol, triglycerides, LDL and HDL, where all p values found to be <0.0001. Consequently, there is a statistically significant association, and increased BMI is linked with higher lipids in the body.

**Table 1. Odds ratio of atherosclerosis for obese patients**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Obese | Non-obese | Total |
| Atherosclerosis present | 21 | 3 | 24 |
| Atherosclerosis absent | 127 | 54 | 181 |
| total | 148 | 57 | 205Odds ratio = 2.97 |

Obesity increases risk of atherosclerosis 2.97 times in comparison those who have a normal BMI (Table 2).

56.7% (127) of all patients did not have any intervention, 22.3% (50) patients had undergone coronary angioplasty with stenting, 12.3% (29) had coronary artery bypass grafting (CABG) surgery and lastly, 4% (9) underwent both percutaneous coronary intervention (PCI) and CABG procedure.

**Table 2. Odds ratio of percutaneous coronary intervention (PCI) for obese patients**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Obese | Non-obese | total |
| Stent | 41 | 9 | 50 |
| Have no stent | 84 | 43 | 127 |
| total | 125 | 52 | 177Odds ratio = 2.33 |

Obesity increases risk of coronary angioplasty with stenting 2.33 times in comparison those who did not undergo stenting procedure (Table 2).

**Discussion**

The robust body of literature extensively elucidates the well-established correlation between obesity and the progression of atherosclerosis. According to Lee et al.[23] increased BMI is associated with the increased risk of coronary artery calcification up to 1.4 times and the tendency could be seen from the resent Gil et al’s study .[24], where odds ratio for coronary artery disease development in obese patients was 1.491,2 [23, 24]. Our results obtained from the cross-sectional study was comparable, there was 2.97 times of increased risk for obese patients to develop atherosclerotic plaques. Moreover, interestingly, Dr. Henning [25] described in his paper from 2021, that increase in BMI above normal weight correlating with a 10% rise in risk for atherosclerosis and coronary heart disease.

Possible mechanism that explains atherosclerosis development in the particular subset of patients, could be due to the activation of adipokines/cytokines like leptin, resistin and inflammatory factor IL-6 leads to monocyte/macrophage infiltration into adipose tissue, promoting inflammation, oxidative stress, abnormal lipid metabolism, insulin resistance, and endothelial dysfunction, contributing to atherosclerosis.

To address both obesity and the associated inflammatory responses it triggers, various therapeutic avenues such as dietary adjustments, pharmaceutical interventions, and bariatric surgical procedures are explored, especially for individuals with body mass indexes surpassing 35-40 kg/m² when conventional lifestyle interventions prove ineffective. Furthermore, in obese patients grappling with conditions such as hypertension, a 10-year cardiovascular disease risk exceeding 7.5%, or prediabetes/diabetes, a comprehensive treatment approach involving antihypertensive agents, lipid-lowering medications, and glucose-lowering therapies is recommended [3, 22].

Further by focusing on the outcomes, there was at least twofold increased risk for obese patients to have either total occlusion or hemodynamically significant plaques in coronary artery (cover at least 70% of vessel diameter) further led to stenting of that vessel. Moreover, obesity is also associated with restenosis after coronary stenting, for instance Rana et al [26], there was 1.33 times higher risk in comparison with non-obese patients for the development of restenosis.

Potential limitations of this study include the absence of comparative analysis between the observed results on obesity-related atherosclerosis risk in healthy cohorts and the assessment of odds ratios within both subsets. Additionally, the sample size might not be sufficiently robust. Future investigations could explore the direct impact of waist-to-hip ratio or visceral fat on atherosclerosis development. Moreover, further research endeavors could delve into identifying potential genetic factors underlying atherosclerosis development, investigating whether these coincide with genes associated with obesity predisposition.

The strength of this study lies in its novelty as the first investigation to delineate the association between obesity and atherosclerosis development in Kazakhstan. Given the predominant Kazakh ethnicity of the study population, characterized by distinct dietary habits influenced by cultural traditions, it becomes imperative to contextualize these findings within a global perspective. Furthermore, the robust correlation observed between metabolic conditions such as obesity and subsequent cardiovascular disease underscores the potential impact on clinical decision-making, particularly regarding the initiation of preventive medication for hyperlipidemia in young obese patients, a matter subject to ongoing debate within the medical community.

Atherogenic dyslipidemia is extremely common in obesity, both in the presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people. A thorough understanding of the molecular mechanisms is crucial for further understanding the effects of obesity on lipoprotein metabolism and developing appropriate therapeutic approaches.

**Conclusion**

Atherogenic dyslipidemia is extremely common in obesity, both in the presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people. A thorough understanding of the molecular mechanisms is crucial for further understanding the effects of obesity on lipoprotein metabolism and developing appropriate therapeutic approaches.

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