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The relationship between elevated Body Mass Index, exhaled nitric oxide, vitamin D serum concentration, and asthma control: a cross-sectional pilot study

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Numerous studies have demonstrated an association between obesity and asthma. The link between vitamin D deficiency and uncontrolled asthma has been shown in several papers.
Objectives. The aim of this study was to evaluate the relationship between increased BMI and other indicators (body composition, lipid accumulation product, and Body Adiposity Index), serum level of Vitamin D, and asthma control.
Material and methods. The study was conducted on 63 adults with asthma. Atopy was confirmed by skin prick tests. Body composition, BMI, BAI, LAP, forced expiratory volume in one second (FEV_1), and fraction of exhaled nitric oxide (FeNO) were measured for the study subjects. All patients completed the Asthma Control Test and International Physical Activity Questionnaire.
Results. The groups with BMI ≤ 25 and BMI > 25 were uniform in age and daily dose of inhaled corticosteroids. In men without atopy, independent of BMI, a negative correlation was found between vitamin D and FeNO. A negative correlation was observed between BAI and FeNO in all women. In the men without atopy, vitamin D levels were significantly lower than in the women without atopy, independent of BMI. The women with atopy and BMI > 25 had a lower mean ACT score than the women with atopy and BMI ≤ 25.
Conclusions. The obesity indicators BAI and LAP better describe the influence of obesity on asthma control in women than BMI. Women with a BMI of > 25 have worse asthma control assessed by ACT score than women with normal BMI. In men without atopy, regardless of BMI, an increase in vitamin D level reduces airway inflammation assessed by FeNO.
Key words: vitamin D, Body Mass Index, asthma.

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Background

Bronchial asthma is a heterogeneous disease that affects approximately 300 million people worldwide. Current descriptions of asthma phenotypes are based on heterogeneity in physiological, pathological, and molecular abnormalities, as well as on demography and clinical course [1]. One of the phenotypes is asthma with obesity. Based on American data, 25.7 million people suffer from bronchial asthma in the USA, and 34.9% of the general American population is obese [2]. Worldwide in 2016, more than 1.9 billion adults were overweight, and 650 million were obese [3]. Obesity is associated with an elevated risk of several diseases, including type 2 diabetes, coronary heart disease, brain stroke, some cancers, and asthma [4]. The influence of obesity on asthma is complex. Obesity mechanically impairs breathing – leading to mild restriction – and moderates the immune system, which results in systemic inflammation. Comorbidities like sleep apnea, esophageal reflux, and type 2 diabetes mellitus are more common in obese asthmatic patients than in patients within the normal weight range [5, 6]. In the group of obese patients, there are more women, the quality of life is lower, asthma exacerbations are more frequent, and the response to inhaled corticosteroids is worse. The mechanism of the association between Body Mass Index (BMI) and asthma in women is unknown. It may be partially explained by the fact that for a given BMI, women have a greater percentage of body fat than men, and that hormonal influences may also play a role [7].

The BMI is currently the best available anthropometric estimate of overweight and adiposity for public health purposes. The World Health Organization regards a person with a BMI of less than 18.5 as underweight, with a BMI equal to or greater than 25 overweight, and with a BMI above 30 to be obese [8]. Because BMI depends on weight and height, it ignores variation in physical characteristics. An elevated BMI is an imperfect indicator for assessing the risk of developing cardiovascular or metabolic diseases. The waist-to-hip ratio (WHR) has been used as a measure of health and the risk of developing serious health conditions. WHR is used as a measure of obesity. It also indicates abdominal obesity when a waist-to-hip ratio is above 0.90 for males and above 0.85 for females. Together with body fat percentage, WHR has been found to be a more efficient predictor of mortality in elderly people [9]. Lipid accumulation product (LAP) has been reported to be a marker of visceral fat and metabolic syndrome. LAP is an index which combines waist circumference (WC) and triglyceride level (TG) to reflect lipid accumulation. Unlike the BMI, the LAP describes lipid

over-accumulation, which might better predict the incidence of cardiovascular disease in adults. LAP combines anatomical and physiological changes associated with lipid over-accumulation in adults [10]. The Body Adiposity Index (BAI) is another method that estimates the degree of adiposity in humans. The BAI relies on height and hip measurements [11]. There are two main approaches in assessing body composition (the ratio between free fat mass, FFM, and fat mass, FM): physicochemical methods and imaging. The former measures the amount of body water using, for example, bioelectrical impedance analysis. Computed tomography and magnetic resonance imaging (MRI) can be used to precisely measure FM and FFM.

Vitamin D has demonstrated a potent immunomodulatory effect through its receptor (Vitamin D Receptor) on numerous immune cells, like T lymphocytes, macrophages, and dendritic cells. Vitamin D deficiency has been linked to an increase in the incidence of respiratory diseases, including asthma. Vitamin D deficiency is defined as a serum concentration of less than 20 ng/ml (50 nmol/l), while vitamin D insufficiency is defined as a serum concentration between 21 and 29 ng/ml (50–70 nmol/l) [12]. In the last twenty years, the link between vitamin D deficiency and impaired lung function has been reported in several papers. Only some studies, though, have confirmed that vitamin D supplementation leads to an improvement in asthma control or a reduction in exacerbation, and the data is inconsistent [13].

Objectives

The aim of the study was to evaluate the relationship between increased body mass, as assessed by BMI and other indicators (body composition, waist-to-hip ratio, LAP, and BAI), serum level of vitamin D, and clinical course of asthma.

Material and methods

Population

The study was conducted on a group of adult patients diagnosed and treated at least 18 months before being enrolled in the study. The Ethics Committee of Wrocław Medical University approved the study, and all patients provided written informed consent before participating. The patients had a diagnosis of asthma that was confirmed and documented by a specialist in allergology or pulmonology. All patients received a treatment grade of 3 or 4 according to the Global Initiative for Asthma (GINA): a medium or high dosage of inhaled corticosteroids (ICS) and a constant dosage of long-acting β_2-agonist (LABA) and leukotriene receptor antagonist at least three months prior to entering the study. Daily doses of ICS (budesonide, fluticasone, ciclesonide, and beclometasone) taken by the study subjects were calculated for equivalent doses of beclometasone HFA (hydrofluoroalkane propellant). In the two months prior to participation in the study, none of the participants was taking supplementary vitamin D. The exclusion criteria included the following: a history of bariatric surgery, any disease that influences vitamin D serum concentration, a history of systemic corticosteroids in the last 12 months, disability causing difficulty walking, and any other acute or uncontrolled disease.

Data collection

The following parameters were assessed: age, sex, weight, and height measured without shoes and outer clothing (stadiometer Radwag WPT-150), waist and hip circumference, and smoking status. BMI was calculated by dividing weight in kilograms by height squared in meters (kg/m^2).

The patients completed the Asthma Control Test (ACT). The possible scores range from 5 to 25 (the higher the score, the better the asthma control). An ACT score of > 19 indicates well-controlled asthma [14]. The patients completed the Polish version of the International Physical Activity Questionnaire (IPAQ). Average daily sitting and walking times, measured in minutes, in the week before the study were also taken into consideration in the analysis.

Every patient underwent spirometry using a Vitalograph 6800 Pneumotrack Spirometer (Vitalograph GmbH, Germany). Forced expiratory volume in 1 second (FEV_1), presented as a percentage of the normal value, was used in order to assess respiratory function. The measurements were performed between 8:00 a.m. and 10:00 a.m. before administration of the morning ICS and LABA.

Nitric oxide (NO) was measured in exhaled breath in parts per billion and is recorded as the fraction of exhaled nitric oxide (FeNO). The measurements were performed using a portable analyzer, the NObreathFeNo Monitor (Bedfont® Scientific Ltd., England) in accordance with ATS/ERS guidelines [15]. The results are expressed in parts per billion (ppb). Blood samples were obtained from every patient for triglyceride, total IgE, and serum 25-hydroxyvitamin D concentrations. Skin prick tests for the 12 standard aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae, Alternaria, Cladosporium*, cat, dog, hamster, grasses, birch, hazel, alder, and mugwort) were performed (Allergopharma GmbH, Germany) in compliance with the applicable procedures.

Measurements of the circumference of the waist and hips, in cm, were performed according to WHO recommendations, and the WHR was calculated for every patient [16]. The Lipid Accumulation Product was calculated using the formula LAP = (waist circumference [WC] in cm - 65) × trigliceryde [TG] in mmol/l for men and (WC in cm - 58) × TG in mmol/l for women.

The Body Adiposity Index (BAI) was calculated as (100 × hip circumference in m / height in m x √height in m) - 18. Body composition was estimated using bioelectrical impedance analysis with a TANITA MC-780 S MA body composition analyzer (Tanita Ltd. Japan). The following adiposity markers were taken into consideration in the analysis: body fat percentage (FAT%), body fat mass in kg (fat mass), visceral fat rating in kg, and fat free mass in kg (FFM). The patients were advised to fast for at least 4 hr prior to testing, to refrain from physical activity for 8 hr prior to testing, and to avoid taking diuretics at least 24 hr before testing.

Statistical analysis

Statistical analysis was performed with STATISTICA version 13 (StatSoft, Inc. Tulsa, USA) and Microsoft Excel. Normal distribution was proved for quantitative parameters using the Kolmogorov–Smirnov test with Lilliefors correction and the Shapiro–Wilk test. In the study population, all quantitative variables – age, BMI, asthma, ACT, and FEV_1 – presented normal distributions. Means (M), standard deviations (SD), minimum values (Min.), and maximum values (Max.) were calculated for all measurable parameters. Analysis of variance in ranks was used to determine the statistical significance of differences in means between the groups for parameters presenting normal distribution and homogeneity of variance. Values of $p < 0.05$ were considered statistically significant. For groups with small numbers without a normal distribution (IgE serum concentration), Spearman's rank correlation coefficient was used. Pearson correlations was used for the other parameters with normal distributions.

Results

Out of the 63 outpatients included in the study, 19 had a normal weight (BMI ≤ 25) and were assigned to Group A. The other 44 patients with increased weight (BMI > 25) comprised Group B. There were no current smokers in either group. Both groups were uniform in terms of age (A: 43.03 ± 15.52 years vs

B: 52.85 ± 19.93; $p > 0.05$). The general characteristics of the study participants are presented in Table 1. The mean BMI in Group A was significantly greater than Group B (22.38 ± 2.48 vs 30.12 ± 5.05, respectively; $p = 0.01$). The mean dosage of ISC was 755.55 ± 170.18 mcg, calculated for beclomethasone HFA; there were no significant differences between the groups (A: 715.79 ± 214.12 vs B: 772.73 ± 146.85; $p > 0.05$). Because LAP and FFR depend on gender to accurately act as markers of obesity phenotypes, the study population was divided into four groups based on gender and BMI:

- Group WA: women with a BMI of ≤ 25 ($n = 11$);
- Group WB: women with a BMI of > 25 ($n = 24$);
- Group MA: men with a BMI of ≤ 25 ($n = 8$);
- Group MB: men with a BMI of > 25 ($n = 20$).

Table 2 presents the subjects' characteristics by gender and BMI.

Table 1. Characteristics of the study participants

Total number: 63; Female: 35 (55.55%)

Variable	Mean	Median	Min.	Max.	SD
Age (years)	49.89	53.16	18.57	72.96	14.33
Height (m)	1.69	1.66	1.49	1.90	0.09
Weight (kg)	79.18	77.00	50.40	129.10	17.62
BMI (kg/m^2)	27.78	27.10	16.57	46.85	5.68
Visceral fat rating (kg)	8.86	9.00	1.00	18.00	4.44
FAT (%)	29.24	27.60	3.00	51.50	10.95
Fat mass (kg)	24.13	21.80	1.60	65.90	12.00
FFM (kg)	54.75	54.80	30.70	83.10	12.33
WHR	0.92	0.94	0.73	1.17	0.09
BAI (%)	28.99	27.39	17.51	49.33	6.70
LAP	46.48	36.40	22.80	199.36	37.76
FeNO (ppb)	29.07	21.50	1.00	132.00	25.92
FEV_1 (L)	2.22	2.07	0.84	4.15	1.02
FEV_1 % pred.	72.17	73.00	40.00	107.00	19.26
Vit. D (ng/ml)	23.97	22.00	7.30	56.60	12.32
IgE Total (IU/ml)	330.76	158.00	4.30	3340.00	507.30
ACT score	16.82	17.00	5.00	25.00	5.07
Sitting (minutes/day)	250.14	240.00	30.00	660.00	131.98
Walking (minutes/day)	90.00	74.25	10.00	400.00	67.89

p-values were calculated using a *t*-test. FEV_1 pred. – forced expiratory volume in 1 s, in percent of the predicted value.

Table 2. Subjects' characteristics by gender and BMI

Variable	WA (BMI ≤ 25)		WB (BMI > 25)		MA (BMI ≤ 25)		MB (BMI > 25)	
	$n = 11$		$n = 24$		$n = 8$		$n = 20$	
	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.
Age (years)	41.21 ± 13.02	41.97; 20,21; 60,92	54.72 ± 11.57	56.51; 27.03; 71,64	45.52 ± 19.12	51.88; 18.57; 65,26	50.60 ± 14,38	51.80; 21.64; 72.96
Height (m)	1.64 ± 0.04	1.63; 58; 1,71	1.61 ± 0.06	1.62; 1.49; 1.72	1.75 ± 0.05	1.76; 1.6; 1.83	1.78 ± 0.07	1.77; 1.67; 1.90
Weight (kg)	60.45 ± 7.29	59.40; 50.40; 73.00	82.70 ± 18.20	76.70; 61.50; 29,10	68.67 ± 9.57	68.60; 51.90; 82.00	89.46 ± 13.20	88.40; 70.30; 122.00
BMI (kg/m^2)	22.45 ± 2.23	22.56; 18.80; 25.00	31.69 ± 5.87	29.62; 25.69; 46.85	22.30 ± 2.94	23.21; 16.57; 24.91	28.23 ± 3.00	27.53; 25.50; 37.65
Visceral fat rating (kg)	3.54 ± 1.69	3.00; 1.00; 7.00	9.92 ± 3.09	9.00; 7.00; 18.00	6.75 ± 4.10	7.00; 1.00; 12.00	11.35 ± 4.36	12.00; 3.00; 18.00
FAT (%)	24.99 ± 8.24	25.70; 3.20; 33.20	40.23 ± 5.04	38.50; 33.90; 51.50	14.56 ± 6.87	16.50; 3.00; 22.20	24.24 ± 5.22	24.60; 12.70; 31.90
Fat mass (kg)	16.70 ± 3.89	17.70; 10.30; 23.80	33.89 ± 11.72	30.15; 21.8; 65.90	58.41 ± 5.21	57.75; 50.30; 66.80	21.93 ± 7.01	20.50; 10.10; 38.90
FFM (kg)	44.00 ± 4.78	44.00; 36.20; 51.90	47.77 ± 8.45	45.85; 30.70; 66.10	58.41 ± 5.21	57.75; 50.30; 66.80	67.57 ± 8.96	67.70; 50.90; 83.10
WHR	0.84 ± 0.07	0.84; 0.74; 0.97	0.93 ± 0.09	0.92; 0.78; 1.16	0.89 ± 0.07	0.90; 0.73; 0.97	0.98 ± 0.06	0.99; 0.84; 1.11
BAI (%)	26.56 ± 2.16	26.35; 23.22; 30.30	34.79 ± 6.81	34.07; 17.95; 49.33	22.40 ± 2.49	22.12; 18.52; 26.21	25.98 ± 3.45	25.79; 17.10; 32.07
LAP	19.74 ± 14.22	18.00; 0.64; 39.76	65.33 ± 47.25	46.12; 17.82; 199.36	22.87 ± 17,25	20.04; -1.50; 55.97	48.03 ± 25.20	47.07; 17.70; 110.08
FeNO (ppb)	27.36 ± 16.03	29.00; 7.00; 51.00	27.22 ± 24.39	16.00; 1.00; 83.00	19.71 ± 15.53	18.00; 6.00; 51.00	35.74 ± 34.13	26.00; 2.00; 132.00

Table 2. Subjects' characteristics by gender and BMI

Variable	WA (BMI ≤ 25)		WB (BMI > 25)		MA (BMI ≤ 25)		MB (BMI > 25)	
	n = 11		*n* = 24		*n* = 8		*n* = 20	
	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.	M ± SD	Med.; Min.; Max.
FEV_1 (L)	2.20 ± 0.74	2.30; 0.97; 3.53	1.74 ± 0.61	1.64; 0.76; 2.93	2.88 ± 0.65	2.66; 1.97; 4.06	2.72 ± 1.19	2.76; 1.41; 5.20
FEV_1 % predicted	78.50 ± 25.28	85.75; 40.00; 109.00	70.65 ± 19.55	69.27; 34.80; 109	76.49 ± 15.24	76.50; 50.50; 92.00	74.32 ± 24.24	79.15; 46.7; 110
Vit. D (ng/ml)	27.34 ± 14.68	27.70; 10,60; 56.60	28.13 ± 12.68	27.50; 7.30; 53.50	15.81 ± 6.34	14.70; 9.70; 28.70	20.39 ± 10.11	18.70; 9.00; 51.50
IgE total [IU/ml]	191.17 ± 199.22	66.00; 17.70; 481.00	297.75 ± 681.57	97.60; 4,30; 3340,000	401.22 ± 569.94	181.50; 20,90; 1722,00	418.95 ± 337.55	261.50; 59.00; 1260.00
ACT score	17.91 ± 5.73	18.00; 8,00; 25.00	14.37 ± 4.57	15.00; 5.00; 22,00	18.12 ± 5.51	20.50; 7.00; 24.00	18.65 ± 4.21	19.00; 9.00; 24,00
Sitting (minutes/ /day)	270.00 ± 168.11	240.00; 30.00; 540.00	256.62 ± 136.15	240.00; 30.00; 660.00	225.00 ± 105.15	240.00; 60.00; 360.00	241.50 ± 121.75	240.00; 30.00; 480.00
Walking (minutes/ /day)	82.93 ± 69.63	74.25; 10.61; 254.57	218.07 ± 115.78	70.12; 15.00; 360.00	72,93 ± 41.70	61,86; 14.14; 148.50	108.00 ± 68.44	99.00; 30.00; 270.00

In the study population, 39 patients had a positive skin prick test and an elevated total serum IgE concentration. In Group A, there were 9 atopic patients (47.4%) and in Group B there were 30 atopic patients (68.2%). There was no significant difference between the groups in terms of IgE serum concentration (Group A: 279.61 ± 339.66 vs B: 352.84 ± 550.04; $p < 0.05$). In the group of 24 patients without atopy, the total IgE concentration was significantly lower than the atopic patients (63.73 ± 49.33 vs 330.75 ± 507.30; $p < 0.001$).

Each study group was divided into two subgroups based on atopy: patients with atopy (A+ and B+) and those without atopy (A- and B-). An expanded version of Table 2 including atopic status is presented in Table 3.

After adjusting for gender, there was no correlation between BMI and any indicator of asthma control in the 63 participants, either for men (FEV_1: $r = -0.12$, $p = 0.13$; FeNO: $r = 0.25$, $p = 0.066$; ACT: $r = 0.11$, $p = 0.08$) or for women (FEV_1: $r = -0.01$, $p = 0.71$; FeNO: $r = -0.17$, $p = 0.13$; ACT: $r = 0.-17$, $p = 0.14$).

In the Men B+ group, the mean FEV_1 value was significantly higher than in the Men B- group ($p < 0.03$), but due to the small group population they were not analyzed.

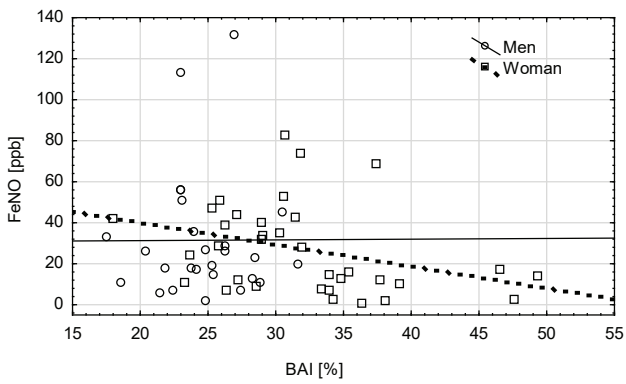
A negative correlation was observed between BAI and FeNO in all women ($r = -0.39$; Tables 1 and 2).

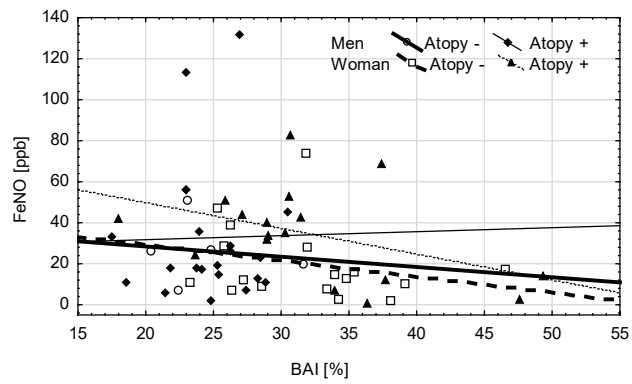
In men without atopy (Men A- and Men B-), a significant negative correlation was found between vitamin D and FeNO ($r = -0.9$; Table 3).

Vitamin D levels were significantly lower in men without atopy (Men A- and Men B-) than in women without atopy, independent of BMI (Women A- and Women B-; $p = 0.01$; Table 4).

In the Women B+ group, the ACT score was significantly lower than in the Women A+ group ($p = 0.03$) (Table 5).

In women with atopy, independent of BMI (Women A+ and Women B+), the average daily walking time correlated negatively with LAP ($r = -0.52$; Figures 1–5).





Figures 1 and 2. A negative correlation between BAI and FENO was observed in all female subjects ($r = -0.39$)

Table 3. Subjects' characteristics by gender, BMI, and atopy										
Group	*n*	Age (years)	BMI (kg/m^2)	Visceral fat (kg)	FAT (%)	WHR	FFM (kg)	BAI	LAP	FeNO (ppb)
		M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD
Men A-	4	57.31 ± 7.03	23.38 ± 2.22	9.25 ± 3.09	18.20 ± 5.44	0.93 ± 0.04	60.00 ± 4.59	23.04 ± 241	33.1 ± 16.11	28.00 ± 22.07
Men B-	2	52.85 ± 20.41	27.35 ± 2.61	10.50 ± 9.19	21.40 ± 12.30	0.93 ± 0.09	63.85 ± 7.85	28.22 ± 479	34.98 ± 0.31	23.50 ± 4.95
Men A+	4	33.73 ± 20.80	21.22 ± 3.48	4.25 ± 3.59	10.92 ± 6.73	0.85 ± 0.08	56.82 ± 595	21.76 ± 2.76	11.82 ± 10.48	13.50 ± 6.14
Men B+	18	50.35 ± 14.35	28.33 ± 3.09	11.44 ± 4.02	24.56 ± 4.53	0.99 ± 0.05	67.98 ± 9.18	25.73 ± 3.37	49.48 ± 26.21	37.18 ± 35.89
Women A-	6	41.32 ± 12.81	21.96 ± 2.01	3.50 ± 1.38	23.40 ± 11.05	0.87 ± 0.06	41.77 ± 3.25	26.07 ± 1.80	24.78 ± 16.25	19.17 ± 15.75
Women B-	12	55.11 ± 10.78	31.94 ± 6.03	10.42 ± 3.29	41.29 ± 4.67	0.94 ± 0.11	46.12 ± 9.83	35.34 ± 4.99	66.27 ± 53.34	20.45 ± 20.72
Women A+	5	41.08 ± 14.75	23.03 ± 2.57	3.60 ± 2.19	26.90 ± 2.96	0.81 ± 0.07	46.68 ± 525	27.16 ± 2.62	13.69 ± 9.59	37.20 ± 10.52
Women B+	12	54.33 ± 12.78	31.43 ± 5.97	9.42 ± 2.94	39.17 ± 5.37	0.91 ± 0.06	49.42 ± 6.83	34.25 ± 8.46	64.38 ± 42.66	33.42 ± 26.67

Group	n	FEV_1 (L)	FEV_1 (% pred.)	Vit. D (ng/ml)	IgE Total (IU/ml)	ACT score	Sitting (minutes/ /day)	Walking (minutes/ /day)
		M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD	M ± SD
Men A-	4	2.59 ± 0.46	75.65 ± 19.82	14.40 ± 4.40	81.45 ± 48.02	16.25 ± 6.90	240.00 ± 120.00	77.00 ± 58.60
Men B-	2	1.77 ± 0.51	50.95 ± 2.76	11.75 ± 2.90	164.50 ± 38.89	18.50 ± 4.95	360.00 ± 0.00	109.57 ± 85.00
Men A+	4	3.16 ± 0.76	77.32 ± 12.13	17.22 ± 8.31	721.00 ± 694.95	20.00 ± 3.74	210.00 ± 103.92	68.06 ± 23.70
Men B+	18	2.82 ± 1.21	76.92 ± 24.19	21.35 ± 10.20	447.22 ± 344.66	18.67 ± 4.28	228.33 ± 121.38	107.84 ± 69.36
Women A-	6	1.98 ± 0.76	72.17 ± 29.27	23.82 ± 8.12	47.33 ± 25.37	17.33 ± 6.50	235.00 ± 184.36	60.11 ± 53.63
Women B-	12	1.85 ± 0.68	77.22 ± 20.57	29.87 ± 11.79	49.22 ± 41.13	13.75 ± 4.07	315.00 ± 149.45	69.6 ± 21.3
Women A+	5	2.64 ± 0.50	92.08 ± 5.05	31.58 ± 20.38	363.78 ± 173.61	18.60 ± 5.32	312.00 ± 155.31	110.31 ± 82.51
Women B+	12	2.08 ± 0.55	79.52 ± 18.96	26.40 ± 13.82	546.27 ± 913.70	15.00 ± 5.12	198.25 ± 94.80	88.19 ± 104.62

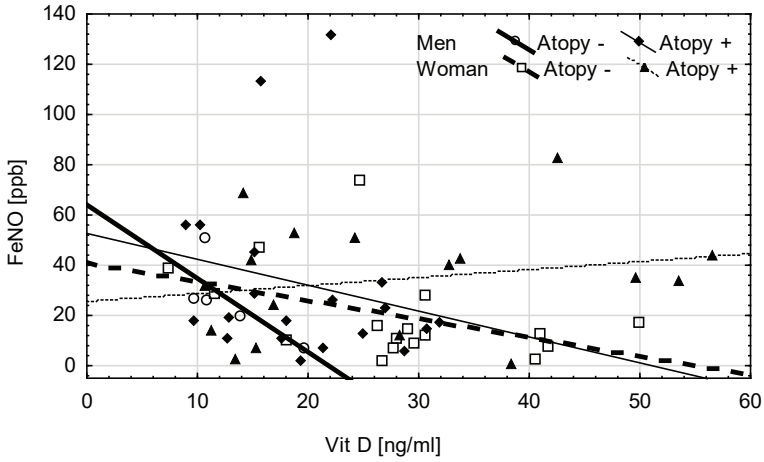


Figure 3. In men without atopy (Men A- and Men B-), a significant negative correlation was found between vitamin D serum concentration and FeNO (r = -0.9)

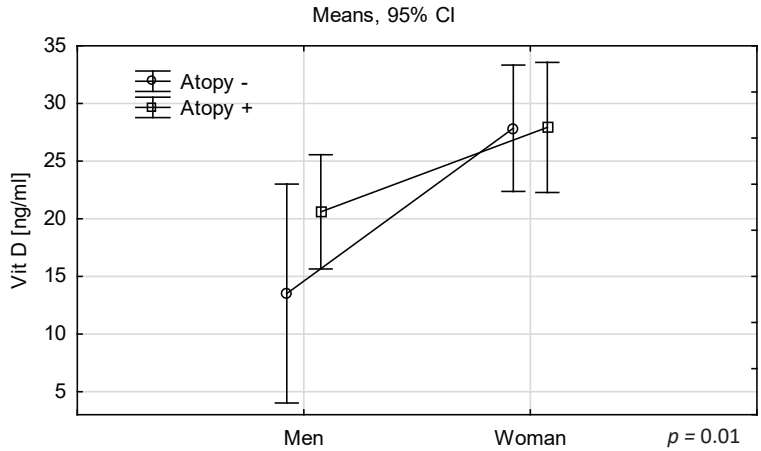


Figure 4. In men without atopy (Men A- and Men B-), vitamin D serum concentration was significantly lower than in women without atopy, independent of BMI (Women A- and Women A+). 95% CI – confidence interval

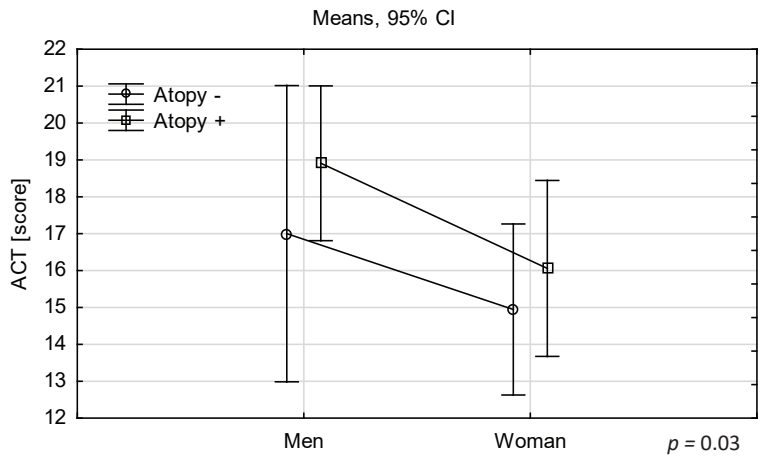


Figure 5. In the Women B+ group, there was a significantly lower ACT score than in the Women A+ group

Discussion

Body Mass Index is broadly used to categorize a person as being normal weight or obese. As a fat indicator, BMI has may limitations; it cannot distinguish muscle mass from fat mass, nor can it measure fat distribution. Because the negative influence of obesity on the course of bronchial asthma is associated with the mass of adipose tissue, additional indicators that take into account the amount and distribution of adipose tissue were used. Only one parameter was influenced by abdominal circumference and triglyceride concentration (BAI) – FeNO, a biomarker used to assess the severity of airway inflammation. In all women in the study, a significant inverse correlation was found between BAI and FeNO (r = -0.39). Because BAI takes into account hip circumference, it may be assumed that the distribution of adipose tissue in women is different from that in men and that it does not cause an increase in airway inflammation. Increased weight of visceral adipose tissue and LAP (parameters which describe adipose tissue distribution that are typical of men) had no influence on airway inflammation. In the group of men without atopy, independent of BMI, a high inverse correlation was observed between vitamin D concentration and FeNO (r = -0.9). No such correlation was observed in the group of women, nor in the group of men with atopy, regardless of BMI. In the group of women with elevated BMI and atopy, there was worse asthma control (assessed by ACT) when compared with the group of women with atopy and normal BMI (Woman B+ vs Woman A+; p = 0.047). Both results are consistent with the observations of Dias et al., who found that in allergic asthma

there is an elevated plasma level of leptin, an adipokine showing a positive correlation with cytokine activity (interleukins [IL-] 5, 6, and 17) and a negative correlation with the production of IL-10 by T cells, $CD4^+$ [17].

In patients with allergic asthma, $1,25(OH)_2D_3$ (calcitriol) was less effective at inhibiting the production of IL-5, IL-6, and IL-17 and the increase of IL-10 release than in healthy individuals. In obese patients with asthma, a deficiency of vitamin D was observed, which affected calcium homeostasis and may modulate the immune response. In a meta-analysis assessing the relationship between vitamin D and asthma control, it was shown that vitamin supplementation was associated with a reduction of asthma exacerbation by 27%. The protective effect was limited to patients with known vitamin D deficiency (< 30 ng/ml), in which an improvement in FEV_1 was also observed. Obesity through overproduction of leptin has a negative impact on the clinical course of allergic asthma. This negative effect may also be caused by a limited $CD4^+$ T response to vitamin D [18]. In our entire study population, only 15 patients (23.8% of the population) had vitamin D concentrations above 30 ng/ml, and no significant differences were observed in the concentrations between the study groups. It should be taken into account that vitamin D activity is controlled by its receptor (VDR), located in various cells. The role of vitamin D and VDR in obesity is not fully understood. Obesity can be caused by genetic disorders in which leptin, adipokine, and VDR genes are involved. The relationship between human VDR gene and obesity has been demonstrated in transgenic mice [19]. Also, in a group of obese men a correlation between low vitamin D concentration and the VDR polymorphisms TaqI and BsmI was observed [20]. An analysis of VDR gene polymorphisms in a group of 402 obese and 489 non-obese individuals showed that TaqI and Bsm-I minor allele polymorphisms are significantly more frequent in the obese individuals [21]. In another study on 309 patients with type 2 diabetes mellitus, no correlation was found between VDR gene polymorphisms compared to the control group [22]. The results of studies assessing the impact of the VDR gene polymorphism on obesity development are inconsistent and require further investigation.

Conclusions

Additional indicators of obesity – BAI and LAP – describe the influence of obesity on the degree of asthma control in women significantly better than BMI. Women with higher BMIs have worse asthma control, as assessed by ACT score, when compared to women with normal BMIs. In men without atopy, independent of BMI, an increase of vitamin D serum concentration reduces airway inflammation, as assessed by FeNO. A limitation to our study is the small sample size, especially in the groups with a BMI of ≤ 25. The presented research is pilot a study, and the study group will be expanded in the future.

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Tables: 3
Figures: 5
References: 22

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