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ORIGINAL ARTICLE

The biochemical effect correlated with pulmonary dysfunction and complications in obese patients

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ABSTRACT

Objective: Obesity, an epidemic metabolic disorder, is associated with various biochemical, inflammatory, oxidative and immunological pathways. We aimed to investigate the biochemical effect correlated with pulmonary dysfunction and complications in overweight and obese patients.

Material and Methods: We aimed to evaluate retrospectively the effect of biochemical parameters on pulmonary dysfunction and complications in 79 overweight and obese patients.

The correlative effect of biochemical values, including CRP, and spirometric measurements, such as forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1), on pulmonary dysfunction and complications in 79 overweight and obese patients seen in the outpatient clinic were evaluated. Body mass index (BMI), FEV1 and FVC, and total biochemistry values, including creatinine, AST, ALT and CRP values were correlated among each other.

Results: Low FVC levels, leukocytosis, high AST and ALT levels, and comorbidities of obesity are significantly associated with high BMI values by univariate analysis in these patients. Higher AST levels are significantly correlated with higher leucocyte counts, and both AST and ALT levels are significantly correlated with platelet counts.

Conclusion: We investigated the effect of biochemical parameters on pulmonary dysfunction and complications in obese patients. Obesity can be helpful to categorize high-risk patients with low FVC levels in the context of respiratory diseases and high AST and ALT levels for other comorbidities as steatohepatitis, diabetes mellitus and coronary artery disease. This study sheds light on future research on obese patients for prognosis of these diseases, because of their biochemical profile correlation with pulmonary dysfunction and complications.

Keywords: Biochemical parameters, pulmonary function, complications, obesity

INTRODUCTION

Obesity is an epidemic metabolic problem and defined as a body mass index (BMI) greater than 30 kg/m^2. The worldwide prevalence of obesity has increased gradually in the last years, with the major health and economic burdens, because of its comorbidities, such as malignancies, metabolic syndrome, diabetes mellitus (DM), steatohepatitis (MESH), hypertension (HT) and cardiovascular diseases (CAD) [1-3]. These complications are caused by mechanical changes and impairment of anti-oxidant mechanisms via adipocytes accumulation, especially in the chest and abdominal regions, and as well as adipocytes-derived pro-inflammatory cytokines like tumor necrosis factor-α (TNF-α), tumor growth factor (TGFβ), interleukin-1-β (IL-1β), and interleukin-6 (IL-6) [4,5].

Obesity, a preventable and treatable metabolic condition, is associated with chronic inflammation through the cascade of adipocytes-derived pro-inflammatory adipokines and adipokine-derived reactive oxygen species. Because of its complex pathophysiology, this condition has a high mortality and morbidity rate. In this metabolic process, there are both immune (immune cells) and non-immune (adipocytes) inflammatory changes via oxidative stress imbalance, which is triggered by genetic, epigenetic and environmental disturbances. Chronic inflammation is caused by activation of the innate immune system, which promotes a pro-inflammatory state and adipokine-derived oxidative stress, eventually systemic acute-phase response. Similar to other organs, chronic inflammation in the airways initiates the pathological process of respiratory diseases. This inflammatory process is ended up with an irreversible lipotoxic tissue damage, which induces chronic airway obstruction, bronchitis and systemic pulmonary dysfunction [6,7].

The mechanical effects of obesity on pulmonary physiology and the functional effect of adipose tissue as an endocrine organ producing chronic systemic inflammation via cytokines and effects on central respiratory control result in the comorbidity of obesity as pulmonary dysfunction. Obesity causes mechanical compression of the diaphragm, lungs, and chest cavity, which can lead to restrictive pulmonary damage. It also significantly interferes with respiratory function by decreasing lung volume, particularly the expiratory reserve volume and functional residual capacity. The ineffectiveness of the respiratory muscles reduces strength and increases pulmonary resistance. All these factors lead to inspiratory overload, which increases respiratory effort, oxygen consumption, and respiratory energy expenditure [8,9].

Besides chronic obstructive pulmonary disease (COPD), obesity plays a key role in the development of obstructive sleep apnea and obesity hypoventilation syndrome [10].

Recent literature has shown that obesity is associated with impaired pulmonary function and increased risk of respiratory diseases [6,10-21]. Bantula et al. and Zammit et al. indicated that asthmatic patients with obesity have severe disease, need intense treatment, harder to treat and have frequent acute attacks [5,6].

BMI and waist-to-hip ratio (WHR) are both inversely associated with lung function, as assessed by forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) [14]. By using inverse-variance weighting to estimate the causal association of BMI and BMI-adjusted WHR with FVC, FEV1, FEV1/FVC, and asthma, Liu et al. found that increased BMI is causally related to decreased FVC and FEV1, and increased BMI-adjusted WHR could lead to lower FVC value and higher risk of asthma. Higher BMI and BMI-adjusted WHR were suggested to be causally associated with higher FEV1/FVC [14].

Therefore, we aimed to pursue a better understanding of the causal relationship among obesity, pulmonary dysfunction and diseases, and investigate the biochemical effect correlated with pulmonary dysfunction and complications in obese patients.

MATERIAL and METHODS

This study is a retrospective study. Patients over the age of 18 who applied to Lokman Hekim Chest Diseases outpatient clinic between January 2018 and February 2024 and having BMI values of 20-24.99, 25-34.99 and higher than 30, which is equivalent to normal, overweight and obesity (respectively) were included in the study with an

ethical approval of Lokman Hekim University Ethical Committee Approval No: 2024/74. Patients under the age of 18 and pregnant, who have a history of malignancy, active systemic disease, collagen tissue disease, interstitial lung disease, COPD, obstructive sleep apnea, obesity hypoventilation syndrome and those who use drugs that could affect complete blood count and total biochemistry parameters were excluded from the study.

Obese patients over 18 years old and retrospective analysis of the files of patients admitted to the outpatient clinic. The files and résumés of these patients were examined. Pulmonary function tests were recorded from their files. The patients' admission complete blood counts and total biochemistry parameters, including creatinine, aspartate transaminase (AST) and alanine transaminase (ALT), and acute phase reactant as C-reactive protein (CRP) results were examined from their files.

We evaluated retrospectively the effect of biochemical parameters on pulmonary dysfunction and complications in 79 overweight and obese patients, compared with healthy weight people.

The correlative effect of biochemical values, CRP and spirometric measurements, such as FEV1, FVC and FEV1/FVC on pulmonary dysfunction and complications in obese patients seen in the outpatient clinic were evaluated. BMI, FEV1, FVC and CRP values and total biochemistry values were correlated among each other.

FEV1 (lt), FVC (lt) and FEV1/FVC levels were measured by spirometry.

In their initial blood tests, which were obtained at admission, following parameters were studied: White Blood Cells (WBC) numeric value (normal range 4.6-10.2 x10^3/μL), neutrophil numeric value (normal range 1800-7700/μL), lymphocyte numeric value (normal range 1500-4000/μL), platelet numeric value (normal range 142-450x10^3/μL), creatinine value (normal range 0.5-1.2 mg/dL), CRP value (normal range 0-0.5 mg/dL), ALT value (normal range 10-40 IU/L) and AST value (normal range 15-50 IU/L) [22].

WBC, neutrophil and lymphocyte counts were measured by fluorescent flow scatter [22]. Platelet counts were measured by electric impedance [22].

Serum creatinine levels were measured by alkaline picrate based assay (Beckman) [22].

Serum CRP levels were measured by nephelometric/ turbidometric method (Beckman) [22].

Serum ALT levels were measured by IFCC method-LDH without pyridoxal 5 phosphate (P5P) (UV without P5P) (Beckman) [22].

Serum AST levels were measured by IFCC method-MDH without P5P (UV without P5P) (Beckman) [22].

In order to determine the number of samples, a power analysis (α =0.05, β =0.80) was performed by taking a study with similar methodology and a sample size of n=75 was obtained [7], a total sample of 79 people was obtained at the end of the study.

Analysis was performed with the SPSS v.25 software. Significance was set at $p < 0.05$ for all comparisons/analyses. Continuous data were summarized with mean ± standard deviation values, categorical data were summarized with frequency (n) and relative frequency (%). Univariate comparisons for continuous data were performed with the Mann-Whitney U test due to the fact that parametric assumptions were not met for any of the comparisons or variable sets. Categorical data distributions were compared with the Pearson Chi-square or the Fisher's exact test depending on assumptions.

RESULTS

11 female (5 (BMI 20-24.99), 4 (BMI 25-34.99) and 2 (BMI higher than 35)) and 68 male (36 (BMI 20-24.99), 28 (BMI 25-34.99) and 4 (BMI higher than 35)) healthy weight, overweight and obese patients were included in our study (Table 1).

Median age were 59.12 (BMI 20-24.99), 56.87 (BMI 25-34.99) and 59.5 (BMI higher than 35) years old (Table 1).

Low FVC levels, high WBC counts (leukocytosis), high AST and ALT levels are significantly associated with high BMI values by univariate analysis in these patients (Table 1).

Comorbidities of obesity including hypertension (HT), diabetes mellitus (DM), Coronary arterial disease (CAD) are significantly associated with high BMI values, by univariate analysis (Table 1).

Table 1. Summary and comparison of patient characteristics with respect to Body mass index (BMI) groups by using univariate analysis of possible risk factors in 79 patients

		Body mass index			P value
		25-29.9	30-34.9	>35	
Sex	Female	5 (12.2%)	4 (12.5%)	2 (33.3%)	0.360
	Male	36 (87.8%)	28 (87.5%)	4 (66.7%)	
Age (years)		59.12 ± 7.28	56.87 ± 9.03	59.5 ± 13.13	0.514
FEV1 (%)		48.85 ± 14.38	51.75 ± 13.19	50.33 ± 10.33	0.577
FEV1 (L)		1.2 ± 0.43	1.27 ± 0.36	1.22 ± 0.35	0.583
FVC (%)		57.34 ± 6.86	59.59 ± 7.5	59.33 ± 9.31	0.278
FVC (L)		2.04 ± 0.65	2.17 ± 0.62	1.55 ± 0.57	0.050
FEV1/FVC		84.98 ± 8.6	84.13 ± 7.27	78.83 ± 5.56	0.108
WBC (mm^3)		9.29 ± 2.28	9.48 ± 2.35	12.19 ± 2.47	0.050
Platelet count (mm^3)		238.37 ± 106.48	228.66 ± 127.46	233 ± 46.59	0.700
Neutrophil count (mm^3)		6.16 ± 1.87	6.23 ± 1.98	7.33 ± 1.92	0.411
Lymphocyte count (mm^3)		1.39 ± 0.6	1.43 ± 0.57	1.39 ± 0.46	0.875
CRP (mg/L)		10 ± 13.16	8.26 ± 7.66	12.39 ± 10.06	0.433
Creatinine (mg/dL)		1.05 ± 0.52	1.16 ± 0.65	0.91 ± 0.27	0.734
CAD	No	36 (87.8%)	28 (87.5%)	1 (16.7%)	**<0.001**
	Yes	5 (12.2%)	4 (12.5%)	5 (83.3%)	
HT	No	30 (73.2%)	23 (71.9%)	1 (16.7%)	**0.018**
	Yes	11 (26.8%)	9 (28.1%)	5 (83.3%)	
DM	No	32 (78%)	27 (84.4%)	2 (33.3%)	**0.023**
	Yes	9 (22%)	5 (15.6%)	4 (66.7%)	
AST (IU/L)		22.8 ± 10.89*	33.08 ± 14.88	42.37 ± 7.48	**<0.001**
ALT (IU/L)		24.29 ± 11.12*	33.72 ± 15.1	49.33 ± 14.73	**0.001**

Continuous data reported as mean ± standard deviation, categorical data reported as n (%).

Continuous data comparisons performed with the Kruskal-Wallis test, categorical data compared with Pearson chi square test.

*Significantly lower compared to both other groups (Bonferroni correction).

FEV1: forced expiratory volume in 1 second, FVC: forced vital capacity, WBC: white blood cell count, CRP: c-reactive protein, CAD: coronary artery disease, HT: hypertension, DM: diabetes mellitus, AST: aspartate transaminase, ALT: alanine transaminase.

FEV1 levels are significantly correlated with older age, and FVC levels are significantly correlated with FEV1 levels (Table 2).

Lympocytes counts are significantly correlated with older age (Table 2).

Liver function parameters, such as AST and ALT levels, are significantly correlated with each other. AST levels are significantly correlated with WBC counts, and both AST and ALT levels are significantly correlated with platelet counts (Table 2).

DISCUSSION

Obesity is a metabolic disorder with high morbidity and mortality. This disorder is caused by the consequence of an excessive adipose tissue accumulation. M1 macrophages' infiltration in adipose tissue of obese patients as well as overexpression of inflammatory adipokines are the major causes of obesity-related chronic inflammation "metainflammation". The inflammatory process is triggered by adipose tissue-derived adipokines, such as increased pro-inflammatory leptin and decreased anti-inflammatory adiponectin levels, and increased levels of pro-inflammatory cytokines, such as IL-1β, IL-6, TNFα, and TGFβ. For instance, in asthma, pro-inflammatory cytokines, such as IL-4, IL-5, IL-13, and IL-33, maintain the lean state. Obesity increases asthma risk and severity. Macrophage activation, age and sex affects immunometabolism in obese asthma patients [23-25]. Weight loss reduces inflammation, so improves asthma prognosis and lung function [5,26].

Table 2a. Correlations among continuous variables (age, FEV1, FVC, FEV1/FVC and WBC) examined by using correlation analysis in 79 patients

		Age	FEV1	FVC	FEV1/FVC	WBC
Age (years)	r	1				
	p	.				
FEV1 (L)	r	-.253*	1.000			
	p	**.025**	.			
FVC (L)	r	-.204	.357**	1.000		
	p	.072	**.001**	.		
FEV1/FVC	r	-.136	.053	.076	1.000	
	p	.233	.642	.508	.	
WBC (mm^3)	r	-.099	.135	.164	.141	1.000
	p	.384	.236	.149	.215	.
Platelet count (mm^3)	r	-.071	-.018	.079	-.020	.118
	p	.531	.877	.488	.863	.300
Neutrophil count (mm^3)	r	.052	.151	.132	.080	.723**
	p	.652	.185	.246	.485	**.000**
Lymphocyte count (mm^3)	r	-.356**	.066	-.002	.058	.138
	p	**.001**	.562	.987	.609	.225
CRP (mg/L)	r	-.153	.053	-.043	-.037	.080
	p	.178	.642	.706	.748	.484
Creatinine (mg/dL)	r	-.198	.025	.026	.069	.029
	p	.081	.827	.823	.547	.803
AST (IU/L)	r	-.055	-.054	.012	-.107	.270*
	p	.628	.635	.918	.350	**.016**
ALT (IU/L)	r	-.101	-.002	-.041	-.096	.186
	p	.376	.988	.719	.401	.100

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Besides activation of pulmonary NLRP3 inflammasome causes increased infiltration and activation of neutrophils, resulting in NETosis, worsening pulmonary symptoms, decreased lung function, and increased steroid resistance in obese asthma patients [27].

Asthma and obesity are two diseases bridged by inflammation. In obesity-related metainflammation, adipocytes and M1 macrophages produce inflammatory cytokines including IL-6, TNF-α, IL-1β, and monocyte chemoattractant protein (MCP-1). By the trigger of NLRP3 activation, M1 macrophages can secrete pro-inflammatory cytokines such as IL-1β, IL-18, MCP-1, TNF-α, and IL-6 into the circulation [5]. Obesity increases airway hyperresponsiveness via the TNF-alpha pathway and treating obesity induces recovery [28]. Obese adipose tissue modulates proinflammatory responses of airway epithelial cells via neutrophilia and monocytosis [29]. Adipose tissue macrophage populations and inflammation are associated with systemic inflammation-related complications such as pulmonary dysfunction [30] and insulin resistance in obesity [31].

In our study, the synergistic effect of low FVC levels and leukocytosis, especially neutrophilia and monocytosis, are significantly associated with high BMI values by univariate analysis in overweight and obese patients without any pulmonary diseases (Table 1).

Additionally, the synergistic effect of low FVC levels and high AST and ALT values are significantly associated with high BMI values (Table 1). AST levels are significantly correlated with WBC counts (Table 2). Comorbidities of obesity including HT, DM and CAD are significantly associated with high BMI values (Table 1). As a summary of our study, obesity alone is associated with pulmonary dysfunction, leukocyte (monocyte and neutrophil) infiltration (possibly metainflammation) and liver dysfunction.

Table 2b. Correlations among continuous variables (platelet, neutrophil and lymphocyte count, CRP, Creatinine, AST and ALT) examined by using correlation analysis in 79 patients

		Platelet count	Neutrophil count	Lymphocyte count	CRP	Creatinine	AST	ALT
Age (years)	r							
	p							
FEV1 (L)	r							
	p							
FVC (L)	r							
	p							
FEV1/FVC	r							
	p							
WBC (mm^3)	r							
	p							
Platelet count (mm^3)	r	1.000						
	p	.						
Neutrophil count (mm^3)	r	.054	1.000					
	p	.634	.					
Lymphocyte count (mm^3)	r	.132	.051	1.000				
	p	.247	.652	.				
CRP (mg/L)	r	-.176	.054	.092	1.000			
	p	.120	.633	.421	.			
Creatinine (mg/dL)	r	-.011	-.006	-.044	.004	1.000		
	p	.924	.955	.701	.969	.		
AST (IU/L)	r	-.257*	.183	.155	-.071	-.095	1.000	
	p	**.022**	.106	.173	.536	.407	.	
ALT (IU/L)	r	-.309**	.110	.088	-.054	-.106	.881**	1.000
	p	**.006**	.336	.443	.635	.354	**.000**	.

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Obese patients have increased asthma risk, and obese asthmatic patients have more symptoms, more frequent and severe exacerbations, reduced response to several asthma medications, and decreased quality of life [26,32,33]. On the other hand, obesity related central airway collapse can be independent of asthma phenotype [34]. Airway mechanics can be altered in both obesity and/or asthma [35]. BMI has significant effects on all of the lung volumes [36-39], and the greatest effects were on functional residual capacity and expiratory reserve volume [40]. In addition, obesity decreases total respiratory system compliance primarily because of decreased lung compliance, with only mild effects on chest wall compliance. Obesity is associated with impaired gas transfer with decreases in oxygenation and varied but usually mild effects on diffusing capacity for carbon monoxide, while the carbon monoxide transfer coefficient is often increased [41].

Metabolically healthy obesity had better lung function [38]. Metabolically healthy obesity was associated with attenuated FVC and FEV1 decline in middle-aged people [38]. This shows the necessity for the synergistic effect of abnormal biochemical metabolism and pulmonary dysfunction on obesity, similar to our study.

The most important advantages of our study are: (1) All BMI levels are included in the study. (2) None of the patients had malignancy, active systemic disease, collagen tissue disease, interstitial lung disease, COPD, obstructive sleep apnea, obesity hypoventilation syndrome. Therefore, the direct influence of obesity on biochemical values and pulmonary dysfunction could be evaluated. (3) Since the number of studies conducted in mid-aged (median age= 58.5) overweight and obese people without any pulmonary disease is less, we think that our findings can contribute to the demonstration

of the correlative effect of biochemical values and pulmonary dysfunction in Turkish overweight and obese patients. However, some potential limitations should be considered when interpreting the results. First, the results cannot be generalized to the whole population, as it is a single-center study. Secondly, the small number of participants prevented detailed comparison of the correlative effect of biochemical values and pulmonary dysfunction; hence, it may have unfavorably affected the statistical analyses.

Besides the correlation between body fat and BMI is not constant. Therefore, assessing body fat distribution with measurements, such as waist circumference or waist-to-hip ratio may improve evaluation and diagnosis of obesity [42].

In conclusion, the synergistic effect of low FVC, high AST and ALT levels and leukocytosis may help predict the complications (comorbidities), such as respiratory diseases, HT, DM, CAD and MESH, in overweight and obese patients. Further studies are necessary to assess whether the correlative effect of biochemical values and pulmonary dysfunction can help explain the pathophysiological mechanisms of obesity-related inflammatory complications.

Author contribution

Study conception and design: ESG and BC; data collection: ESG and BC; analysis and interpretation of results: ESG and BC; draft manuscript preparation: BC. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Lokman Hekim University Ethical Committee (Approval No: 2024/74/23.02.2024).

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Conflict of interest

The authors declare that there is no conflict of interest.

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