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RESEARCH ARTICLE

Clinical and paraclinical approach to community-acquired pneumonia in obese individuals

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ABSTRACT

Introduction. Obesity is a metabolic disease that presents a real challenge for the medical system due to the significant increase in the number of obese people in recent decades. Currently, 38% of the global population is overweight or obese. Obesity is an important risk factor for multiple chronic pathologies and lung infections, especially pneumonia. For obese subjects, chronic proinflammatory status due to an excess of fat cells is characteristic.

Material and methods. This prospective cohort study is based on clinical and laboratory examinations of patients hospitalized with community-acquired pneumonia in the Department of Internal Medicine at *Holy Trinity* Municipal Hospital, Chisinau, Republic of Moldova. The study included 210 patients with community-acquired pneumonia, divided into two groups: the base group (group 1) consisted of 105 patients with varying degrees of obesity, and the control group (group 2) consisted of 105 normal-weight patients. The research was conducted according to the principles of the Helsinki Declaration - WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The study was approved by the Research Ethics Committee of the *Nicolae Testemițanu* State University of Medicine and Pharmacy, with the issuance of favorable opinion no. 46 from March 27, 2018. All patients were examined clinically and paraclinically (radiological examination, pulse oximetry screening, complete blood count, erythrocyte sedimentation rate, fibrinogen, LDH, C-reactive protein, oxidative stress markers). The obtained data were statistically analyzed using Statistical Package for the Social Sciences (SPSS) version 20.

Results. According to the obtained data, the most common comorbidities associated with obesity were cardiovascular and metabolic diseases. The main symptom that prevailed in the obese was dyspnea (97%). Obese subjects showed more frequent signs of acute respiratory failure (86.7%), required oxygen therapy with an average duration of 7.62±6.23 days, showed increased serum levels of LDH (286.31±94.66 U/L) and C-reactive protein (66.08±71.44 mg/l), data that influenced the clinical course of pneumonia.

Conclusions. Patients with obesity and community-acquired pneumonia presented with infectious symptoms and acute respiratory failure, increased values of inflammatory markers, and required oxygen therapy more frequently compared to those of normal weight.

Keywords: pneumonia, obesity, clinical course, comorbidities.

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Key messages

What is not yet known on the issue addressed in the submitted manuscript

The clinical evolution, pro-inflammatory status, and oxidative stress in obese subjects with community-acquired pneumonia are not sufficiently known. Some studies reported more severe evolution of pneumonia in obese patients, while others mentioned contradictory data.

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The research hypothesis

Community-acquired pneumonia in obese individuals is manifested by a more severe clinical course, complications, and marked inflammatory syndrome in comparison with normal-weight subjects.

The novelty added by manuscript to the already published scientific literature

Our research results report the clinical course of community-acquired pneumonia, commonly associated comorbidities, and possible complications in obese patients. The research data may contribute to the clinical management of patients with different degrees of obesity and pneumonia as well as predicting prognosis.

Introduction

The global increase in the number of obesity cases represents one of the most serious challenges for the public health system, the medical system, but also for the entire society. In 1997, due to the increase in worldwide prevalence, obesity was declared an epidemic by the World Health Organization. According to the 2023 *World Obesity Atlas* report, currently, 38% of the global population is overweight or obese, with a body mass index (BMI) greater than 25 kg/m^2 [1]. By 2035, it is estimated that the global prevalence of overweight and obese people will reach up to 51% [2].

Obesity is a metabolic disease, the consequence of a long-term imbalance between food intake and energy consumption. This clinical nosology arises as a result of the complex interaction between genetic, environmental and psychosocial factors [3]. Moreover, obesity is an important risk factor for cardiovascular diseases, diabetes mellitus, cancer, and sleep apnea syndrome. Also, the accumulation of excessive adipose tissue can attenuate the host's local pulmonary defenses. This contributes to the predisposition of obese subjects to lung infections, especially community-acquired pneumonia (CAP) [4]. This is explained by the fact that adipose tissue is a dynamic structure directly involved in various metabolic processes like lipid storage, production of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β, IL-18), and hormone synthesis (leptin, adiponectin). White adipose tissue is mainly composed of preadipocytes, adipocytes, macrophages, dendritic cells, T cells, and B cells. Immune cells in adipose tissue maintain adipocyte integrity, metabolic function, and hormone sensitivity. Macrophages constitute up to 40–50% of all adipose tissue cells. In the obese, adipose tissue macrophages are transformed into proinflammatory (M1) macrophages that secrete proinflammatory cytokines. Due to adipocyte hypertrophy, adipose tissue hypoxia develops, which subsequently presents the source of activation of inflammatory processes. Consequently, systemic inflammation develops that compromises immune function, triggers changes in pro-inflammatory cells and oxidative stress, as well as increased susceptibility to infections, including pulmonary ones [5].

During the last years, due to the high prevalence among the general population, these two clinical entities (pneumonia and obesity), have garnered research interest in many clinical studies. Research data show that community-acquired pneumonia in obese subjects has a more severe clinical course, longer hospital stay, more expressed pro-inflammatory markers, more frequent complications, but also a higher mortality rate compared to normal-weight subjects. On the other hand, a series of meta-analysis studies present controversial data, such as obese patients hospitalized with pneumonia having better clinical results compared to normal weight or underweight individuals [6, 7].

Based on the literature data, but also considering that obesity has reached pandemic proportions and the evident role of associated comorbidities in the course of community-acquired pneumonia, we aimed to study clinical course, laboratory features, and comorbidities in community-acquired pneumonia in obese individuals compared to those with normal weight.

Material and methods

A prospective cohort study was conducted within the Department of Internal Medicine, Clinical Syntheses Discipline, *Nicolae Testemițanu* State University of Medicine and Pharmacy, with the clinical base at *Holy Trinity* Municipal Clinical Hospital, Chisinau, Republic of Moldova. The study included 210 patients with community-acquired pneumonia, divided into two groups: the base group (group number 1) constituted 105 patients with varying degrees of obesity, and the control group (group number 2) constituted 105 normal-weight patients. The research inclusion criteria were: age >18 years; the presence of clinical and radiological pulmonary consolidation syndrome; BMI for obese patients ≥ 30 kg/m^2 and BMI for normal-weight patients 18.5-24.9 kg/m^2.

The aim of the study was to assess the clinical course, laboratory findings, and comorbidities in community-acquired pneumonia in obese compared to normal weight patients.

The research was conducted according to the Principles of the Helsinki Declaration - WMA Declaration of Helsinki

- Ethical Principles for Medical Research Involving Human Subjects. The study was approved by the Research Ethics Committee of *Nicolae Testemițanu* State University of Medicine and Pharmacy, with the issuance of favorable opinion no. 46 from March 27, 2018.

All patients signed the agreement to participate in the study and were questioned about the history of the disease (the onset, presence of infectious signs, presence of respiratory symptoms). They were examined clinically and paraclinically (radiological examination, pulse oximetry screening, complete blood count, erythrocyte sedimentation rate, fibrinogen, LDH, C-reactive protein, oxidative stress markers). The clinical course of pneumonia was monitored during hospitalization.

The obtained data were statistically analyzed using Statistical Package for the Social Sciences (SPSS) version 20. Results were expressed as percentages for categorical variables and mean ± SD for continuous variables. Variable analysis was performed using descriptive statistics. The correlation analysis of the variables was performed using the non-parametric test Spearman's Rho. A p-value < 0.05 was considered statistically significant.

Results

The mean age of patients participating in the study was 64.4±12.5 years for group 1 and 65.2±13.04 years for group 2, with a p-value of 0.906. Males constituted 39 (37%) in group 1 and 65 (61.9%) in group 2, with a p-value of <0.001. Among the associated comorbidities, cardiovascular and metabolic diseases showed statistical significance: chronic heart failure - 97 (92%) vs 83 (79%); p=0.005, grade III arterial hypertension - 63 (60%) vs 14 (13.3%); p<0.0001, coronary heart disease - 89 (84%) vs 73 (69.5%); p=0.009; dyslipidemia - 66 (62.9%) vs 35 (33.3%); p<0.0001, chronic kidney disease - 20 (19.9%) vs 7 (6.7%), p=0.006; diabetes mellitus - 42 (40%) vs 17 (16.2%), p<0.0001: and metabolic syndrome - 102 (97.1%) vs 27 (25.7%), p<0.0001, comparing group 1 to group 2.

Classical onset of community-acquired pneumonia was characteristic for 26 (24%) obese cases vs 41 (39%) normal weight cases, p=0.191. Presenting complaints at admission were: infectious symptoms in 67 (63%) vs 55 (52.4%), p=0.198; chills in 26 (24%) vs 31 (29.5%), p=0.268; dry cough in 40 (38%) vs 51 (48.6%), p=0.082; cough with mucous sputum in 22 (21%) vs 13 (12.4%); and cough with mucopurulent sputum in 26 (24%) vs 20 (19%), p=0.107; dyspnea in 102 (97%) vs 85 (81%), p<0.001, pleural pain in 34 (32%) vs 30 (28.6%), p=0.327, in groups 1 and 2, respectively.

The clinical data assessment revealed accentuated vocal fremitus in 19 (18%) cases vs 67 (63.8%) cases, p<0.0001; dullness on chest percussion in 24 (22.9%) vs 73 (69.5%), p<0.0001 diminished vesicular murmur on lung auscultation in 86 (81.9%) vs 89 (84.4%), p=0.356, comparing group 1 compared to group 2. Respiratory rate > 30 breaths/minute was observed in 24 (22.9%) vs 9 (8.6%), p=0.004, and peripheral O_2 saturation <90% in 46 (43%) vs 29 (27.6%), p=0.010, in obese compared to normal weight patients. Typical pulmonary consolidation syndrome was observed in 20 (19%) cases in group 1 vs 69 (65.7%) cases in group 2, p<0.0001. A severe general condition was more common in group 1 patients compared to group 2 - 21 (20%) vs 15 (14.3%), p=0.302, as was the severe form of pneumonia - 34 (32.4%) vs 29 (27.6%), p=0.274.

On radiological examination, bilateral extension of the inflammatory infiltrate was observed in 78 (74.3%) cases in group 1 compared to 60 (57.1%) cases in group 2, p=0.062. Control radiological examination revealed infiltrate resolution in 61 (58.1%) cases in group 1 vs 67 (63.8%) cases in group 2, p=0.504.

The mean hospital stay was 12.35±5.76 days in group 1 vs 11.69±4.58 days in group 2, p=0.355, and the mean duration of antibacterial therapy was 14.1±5.56 days vs 12.8±4.75 days, p=0.087, group 1 versus group 2. Transfer to ICU was required in 15 (14.3%) cases vs 10 (9.5%) cases, p=0.287, and the length of stay in ICU was 8.1±3.2 days vs 5.0±0.5 days, p=0.483, group 1 versus group 2.

The need for non-invasive ventilation was observed in 22 (21%) cases in group 1 vs 9 (8.6%) cases in group 2, p=0.009. Invasive mechanical ventilation was applied in 4 (3.8%) patients in group 1 vs 2 (1.9%) patients in group 2, p=0.341. Oxygen therapy via nasal cannula or face mask was required in 97 (92.4%) cases in group 1 vs 75 (71.4%) cases in group 2, p<0.0001, and the mean duration of oxygen therapy was 7.62±6.23 days in group 1 vs 4.66±5.77 days in group 2, p=0.001.

Examination of pro-inflammatory markers revealed: leukocytes (10^9/L) 10.79±5.09 vs 10.49±4.47, p=0.654; neutrophils (%) 72.65±13.36 vs 74.31±12.74, p=0.361; LDH (Units/L) 286.31±94.66 vs 215.89±110.16, p=0.001; fibrinogen (g/L) 5.9±8.21 vs 6.08±8.34, p=0.890; erythrocyte sedimentation rate (mm/h) 31.75±18.19 vs 27.89±18.23, p=0.127; and C-reactive protein (mg/l) 66.08±71.44 vs 40.85±58.82, p=0.006, in groups 1 and 2, respectively.

Pro-oxidative stress markers were also assessed: advanced oxidation products (μM/l) 97.51±6.33 vs 80.39±49.20, p=0.033; malondialdehyde (μM/l) 19.40±0.87 vs 20.68±1.03, p=0.346; AGE-verperlisin-like (μM/l) 737.98±34.56 vs 725.51±58.56, p=0.855; AGE-pentosidine-like (μM/l) 577.92±31.48 vs 485.82±24.50, p=0.022; nitric oxide (μM/l) 45.24±0.81 vs 44.65±0.69, p=0.585, in group 1 versus group 2.

Anti-oxidative stress markers did not show statistical significance between the groups: total antioxidant capacity (CUPRAC method) (μM/L) 29.14±3.97 vs 26.33±3.70, p=0.606; total antioxidant capacity (ABTS method) (μM/L) 128.04±1.90 vs 124.52±1.96, p=0.201; catalase (μM/L) 37.07±1.78 vs 37.34±2.69, p=0.925; thiolic compounds (μM/L) 7.21±0.35 vs 6.84±0.33, p=0.448, in group 1 compared to group 2.

Table 1. Clinical findings of community-acquired pneumonia in obese patients compared with normal weight patients

Clinical manifestations of community-acquired pneumonia in obese	Group 1 (Patients with obesity and CAP), n, %	Group 2 (Normal weight patients with CAP), n, %	P
Dyslipidemia	66 (62.69%)	35 (33.3%)	p<0.0001
Metabolic syndrome	102 (97.1%)	27 (25.7%)	p <0.0001
Classic onset of CAP	26 (24%)	41 (39%)	p=0.019
Infectious symptoms	67 (63%)	55 (52.4%)	p=0.198
Dyspnea	102 (97%)	85 (81%)	p <0.0001
Dry cough	40 (38%)	51 (48.6%)	p=0.082
Cough with mucous sputum	22 (21%)	13 (12.4%)	p=0.107
Severity of pneumonia	34 (32.4%)	29 (27.6%)	p=0.274
Typical pulmonary consolidation syndrome	20 (19%)	69 (65.7%)	p <0.0001
Respiratory rate >30/min	24 (22.9%)	9 (8.6%)	p=0.004
Bilateral/multilobar extension of inflammatory infiltrate on chest X-ray examination	78 (74.3%)	60 (57.1%)	p=0.062
O2 therapy	97 (92.4%)	75 (71.4%)	p <0.0001
Non-invasive ventilation	22 (21%)	9 (8.7%)	p=0.009
Invasive ventilation	4 (3.8%)	2 (1.9%)	0.341
Length of hospitalization	12.3±5.7	11.6±4.5	0.355
Length of ICU stay	8.1±3.2	5.0±0.5	0.483

Note: *CAP- community-acquired pneumonia, ICU – intensive care unit*

Community-acquired pneumonia complications were observed in both groups: acute respiratory failure - 91 (86.7%) vs 65 (61.9%), p<0.0001; acute respiratory distress syndrome - 17 (16.2%) vs 6 (5.7%), p=0.013; pleural effusion - 22 (21%) vs 28 (26.7%), p=0.209; disseminated intravascular coagulation syndrome and sepsis - 3 (2.9%) vs 1 (1%), p=0.311; hypercatabolic state - 41 (39%) vs 51 (48.6%), p=0.105; pulmonary thromboembolism - 6 (5.7%) vs 2 (1.9%), p=0.140; and death - 4 (3.8%) vs 2 (1.9%), p=0.249; group 1 compared to group 2.

Correlational analysis showed a positive correlation of obesity with dyspnea (rs=0.25), the need for oxygen therapy and the duration of oxygen therapy (rs=0.27, rs=0.24), the association of mixed dyslipidemia (rs=0.29) and diabetes mellitus (rs=0.26), increased serum LDH (rs=0.32), and C-reactive protein (rs=0.20).

Discussions

According to the literature data, obesity is an important risk factor for multiple chronic diseases. For example, the Framingham Offspring study presents data showing that 78% of new cases of essential hypertension in men and 65% in women were attributed to excess body fat [8]. Another study, which included 82,882 women followed prospectively for 14 years, showed that BMI was the strongest risk factor for the development of hypertension, with obese women having an incidence nearly five times higher than those with normal BMI [9]. Up to 70% of patients with obesity are concomitantly diagnosed with dyslipidemia, frequently manifested paraclinically by elevated serum low-density lipoprotein (LDL) and reduced high-density lipoprotein (HDL) levels [10]. Obesity is directly associated with the presence of metabolic syndrome, with the prevalence of metabolic syndrome among the obese being 62.4% [11]. Moreover, obesity is a significant factor in the association with diabetes, such that 85.2% of patients with diabetes are obese [12]. We obtained similar data in our research, showing that metabolic and cardiac diseases positively correlate with obesity.

Although literature sources report controversial data regarding the course of community-acquired pneumonia severity, length of hospitalization, and need for ventilation, there are studies demonstrating that obese patients who develop community-acquired pneumonia have a more severe clinical course, a longer length of hospitalization, and require ventilation compared to normal-weight subjects [13, 14]. The presented research shows that, although without statistical difference, obese patients had a longer period of hospitalization, a longer period of antibiotic therapy, and a need for mechanical ventilation.

Recent pandemic studies reveal multiple data indicating that respiratory failure was more pronounced in obese subjects with community-acquired pneumonia [15, 16]. Our data demonstrate that obese patients presented with acute respiratory failure more frequently compared to those with normal body weight.

Obesity is an underlying condition for the development of lung infections, including pneumonia, by impairing lung function and contributing to a reduced degree of chronic inflammation. At the same time, obesity as an associated comorbidity contributes to increased mortality from pneumonia [17, 18]. Multiple studies examining patients with different BMI have concluded that obese people have a marked pro-inflammatory status compared to those who are normal weight or underweight. This is explained by significantly elevated serum values of C-reactive protein and other inflammatory markers in the obese group patients [19].

Data from another study show that obese subjects have elevated serum lactate dehydrogenase values, which correlate with metabolic syndrome and increase the risk of cardiovascular complications [20]. According to the results of our study, obesity cases had a positive correlation with elevated C-reactive protein (CRP) values (rs=0.20) and LDH values (rs=0.32), supporting the relationship between inflammatory status and a high body mass index.

The results of our study revealed no significant differences in pro-oxidative and anti-oxidative stress markers, except for advanced oxidation products and AGE-verperlisin like markers. Similar data were also observed in other research, which demonstrate a more pronounced pro-oxidant status in obese individuals compared to normal weight [21].

Pulmonary thromboembolism is a complication observed more frequently in obese subjects with community-acquired pneumonia. The main cause of pulmonary thromboembolism in obese individuals is endothelial injury and hypercoagulable states. Some studies report an increased risk of thromboembolism of up to 2.4 times in obese patients compared to those with a normal BMI. Another common complication among obese individuals with pneumonia is acute respiratory distress syndrome, due to a more pronounced pro-inflammatory status, a condition that was also observed in our study [22].

Conclusions

Patients with obesity and community-acquired pneumonia had complaints of dyspnea, tachypnea, infectious signs, elevated inflammatory marker values, and required oxygen therapy more frequently compared to normal weight patients.

The most common comorbidities associated with obese patients were chronic heart failure, coronary artery disease, hypertension, diabetes mellitus, and metabolic syndrome, all of which influenced the clinical course of community-acquired pneumonia.

Competing interests

None declared.

Authors' contributions

All the authors participated in the study design and contributed to drafting the manuscript. The authors critically reviewed the work and approved the final version of the manuscript.

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Patient consent

Obtained.

Ethics approval

The Research Ethics Committee of the *Nicolae Testemiţanu* State University of Medicine and Pharmacy approved the study (Minutes no. 46 from March 27, 2018).

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