

Pneumologia

Clinical-radiological features and oxidative stress in patients with community-acquired pneumonia and heart failure

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Abstract

English:

Background and Objective: Diagnosing community-acquired pneumonia (CAP) in patients with chronic heart failure (CHF) can be challenging. This study aimed to examine the clinical and paraclinical diagnostic characteristics, along with oxidative stress (OS) markers, in individuals suffering from both CAP and CHF.

Methods: A total of 210 patients were enrolled and divided into two groups: group 1 ($n = 105$) – patients with CAP associated with CHF and group 2 ($n = 105$) – patients with CAP without CHF.

Key Content and Findings: Worsening of dyspnoea was present in 98 (93.3%) patients in group 1, compared to group 2 – 73 (69.5%) patients, $P < 0.0001$. Bilateral extension of pneumonia was more frequent in group 1 compared to group 2: 63 (60.0%) patients versus 57 (54.3%) patients, respectively, $P = 0.515$. The presence of pleural effusion was more common in group 1 compared to group 2: 41 (39.0%) patients versus 14 (13.3%) patients, $P < 0.0001$. The total antioxidant activity (AAT), by CUPRAC method, had higher values in group 1 (6.70 ± 4.62) versus group 2 (4.99 ± 4.29), $P = 0.006$.

Conclusions: Bilateral extension of pneumonia, presence of pleural effusion, worsening of preexisting dyspnoea and the elevation of total antioxidant activity values (CUPRAC method) are useful tools in the early diagnosis of CAP in patients with CHF.

Keywords

community-acquired pneumonia • heart failure • oxidative stress

Particularitățile clinico-radiologice și stresul oxidativ la pacienții cu pneumonie comunitară și insuficiență cardiacă

Rezumat

Romanian:

Introducere: Diagnosticul pneumoniei comunitare (PC) pe fundalul insuficienței cardiace cronice (ICC) poate fi dificil. Scopul lucrării a fost de a analiza particularitățile clinice și paraclinice de diagnostic, precum și parametrii stresului oxidativ (SO), la pacienții cu PC și ICC.

Metode: În studiu au fost incluși 210 de pacienți, divizați în 2 loturi: grupul 1 ($n = 105$) – pacienți cu PC asociată cu ICC și grupul 2 ($n = 105$) – pacienți cu PC fără ICC.

Rezultate: Agravarea dispneei fost prezentă la 98 (93.3%) pacienți din grupul 1, comparativ cu grupul 2, unde aceasta a fost prezentă la 73 (69.5%) pacienți, $P < 0.0001$. Extinderea bilaterală a pneumoniei s-a întâlnit mai frecvent în grupul 1 comparativ cu grupul 2: 63 (60.0%) pacienți versus 57 (54.3%) pacienți, respectiv, $P = 0.515$. Prezența revărsatului pleural a fost mai frecvent întâlnită în lotul 1, comparativ cu lotul 2: 41 (39.0%) pacienți versus 14 (13.3%) pacienți, $P < 0.0001$. Activitatea antioxidantă totală (AAT), prin metoda CUPRAC, a avut valori mai mari în grupul 1 ($6,70 \pm 4,62$) versus grupul 2 ($4,99 \pm 4,29$), $P = 0,006$.

Concluzii: Extinderea bilaterală a pneumoniei, prezența revărsatului pleural, agravarea dispneei preexistente și elevarea valorilor activității totale prin metoda CUPRAC, sunt instrumente utile de diagnostic precoce a pneumoniei comunitare la pacienții cu insuficiență cardiacă cronică.

Cuvinte-cheie

pneumonie comunitară • insuficiență cardiacă • stres oxidativ

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Introduction

Community-acquired pneumonia (CAP) is a frequent cause for hospital admission that results in significant costs for the health care system and represents the most frequent cause of death of infectious origin. Almost 10% of patients hospitalised for CAP require admission to intensive care units, and mortality varies from 20% to 50% (1). Several risk factors are associated with severe progression in patients with CAP. The strongest associated risk factor is pre-existing cardiovascular disease. Moreover, patients with CAP older than 65 years tend to have higher rates of comorbidities, the most common being chronic congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus and stroke, as demonstrated during the Coronavirus-19 (COVID-19) pandemic (2, 3).

Chronic heart failure (CHF) is one of the most common chronic diseases, and the number of hospitalisations due to decompensated heart failure has tripled over the past 15 years (4). The diagnosis of CHF is a complex process and, in addition to clinical signs and symptoms, requires instrumental and laboratory data (electrocardiography, echocardiography and brain natriuretic peptides). The presence of clinical response to appropriate therapy also supports the diagnosis of CHF (5). The diagnosis of CAP can be challenging because the clinical signs of pneumonia are often overshadowed by manifestations of congestive heart failure, such as dyspnoea, tachycardia, tachypnoea and crackles on lung auscultation. Similarities in the radiological picture of pneumonia and CHF create difficulties in differentiating between these two conditions, and one of the tools used is repeated chest X-rays after diuretic administration (6).

Oxidative stress (OS) activation is one of the main pathogenic pathways leading to inflammation in the course of bacterial infections. Reactive oxygen species (ROS) and OS play a central role in the aetiology of cell dysfunction and tissue damage in patients with CAP. ROS also modulate a number of cell signalling pathways, which result in the release of inflammatory mediators (7). At the same time, it is well known that an important role in the pathogenesis of CHF belongs to the activation of OS markers. Various ROS have been reported to be involved not only in inducing changes in cardiac contractile activity but are also considered to be mediators of myocardial cell injury (8, 9). Studies showed the damage produced by the oxidative status and the protective role of antioxidants on the cardiovascular system (10).

In this study, we aimed to analyse clinical, radiological and laboratory data, OS parameters inclusively, in patients with CAP and CHF. Also, we hypothesised that CAP in patients with CHF contributes to elevation of pro-oxidative markers and a decrease of antioxidative markers.

Materials and methods

We conducted a prospective cohort study in the Department of Internal Medicine, Clinical Synthesis Discipline, Holy Trinity Municipal Hospital, Chisinau, Republic of Moldova, between October 2020 and October 2022. This study included 210 patients, divided into two groups according to the presence of CHF: group 1 – 105 patients – with CAP and CHF (study group) and group 2 – 105 patients – with CAP and without CHF (control group).

The clinical diagnosis of CAP was established according to the clinical and paraclinical criteria stipulated in international guidelines: the presence of infectious impregnation syndrome, signs of respiratory failure and radiological confirmation of pulmonary infiltrate. The diagnosis of CHF was assumed based on typical signs and symptoms: dyspnoea, fatigue, tachypnoea, oedema and pulmonary rales. Confirmation of the diagnosis was possible in patients with elevated natriuretic peptides and structural or functional alteration of the heart present on echocardiography.

The inclusion criteria in this study were: patients with CAP and the mandatory presence of clinical and paraclinical features for pneumonia (acute onset, physical pulmonary condensation syndrome and new radiological pulmonary infiltrate), criteria for CHF (oedema, dyspnoea, cough, wet rales in the lower areas of the lungs, infiltrates on the chest X-rays and decreased exercise tolerance), previously established CHF (according to the outpatient card and hospital records), age of patients older than 50 years, patients' ability to communicate well with the researcher and the ability to understand and comply with the study requirements.

The following parameters of the pro-oxidative status were examined: ischaemia-modified albumin, advanced glycation end products (AGE-verperlin-like and AGE-pentosidine-like), advanced oxidation protein products (AOPP) and malonic dialdehyde (MDA). Antioxidative markers that were determined in the serum of the patients were total antioxidant activity (AAT) (with Cupric Reducing Antioxidant Capacity (CUPRAC) and 2,2'-Azinobis-3-Ethylbenzthiazolin-6-Sulfonic Acid (ABTS) methods), superoxide dismutase (SOD) and catalase.

The obtained data were statistically processed using IBM SPSS Statistics 26.0 (IBM) and Microsoft Office Excel 2010. All results are presented as $M \pm m$, where M is the sample mean and m is the error of the mean. The following methods were used for statistical data processing: Fisher test (or Fisher–Irwin test and exact χ^2 test) for non-parametric data and One-Way ANOVA test ('analysis of variance') for parametric data.

Results

The age of the patients in the study group was between 50 years and 92 years, and the mean age was 70.6 ± 8.89 Interval of

Confidence (CI 95% [68.8–72.3]) years. The proportion of women in group 1 was higher than that of men: 57 (54.3%; 95% CI [44.8–64.1]) and 48 (45.7%; 95% CI [35.9–55.2]), respectively. In group 2, there were more men than women: 54 (51.4%; CI 95% [42.3–61.0]) and 51 (48.6%; CI 95% [39.0–57.7]), respectively. There were no significant differences between groups ($\chi^2 = 0.686$; $df = 1$; $P = 0.407$). In both groups, the majority of patients lived in urban areas: 85 (81.0%) and 93 (88.6%), respectively, with no statistical difference between the groups ($\chi^2 = 2.360$; $df = 1$; $P = 0.125$). The hospital length was significantly longer in group 1 compared to group 2: 11.96 ± 3.76 days versus 10.82 ± 2.93 days, respectively, ($F = 6.020$; $P = 0.015$).

Arterial hypertension was the most common comorbidity in group 1: 103 (98.0%) patients, compared to 84 (80.1%) patients in group 2. Atrial fibrillation was present only in group 1 – 54 (51.4%; 95% CI [42.2–61.0]) patients. Type 2 diabetes mellitus was revealed in 41 (39.0%; 95% CI [29.9–48.4]) patients in group 1 versus 25 (23.8%; CI 95% [15.8–32.4]) patients in group 2, $P = 0.017$. Cerebrovascular disease was present in 47 (44.8%; 95% CI [35.5–54.3]) patients in group 1 and in 25 (23.8%; 95% CI [16.0–32.3]) patients in group 2, $P = 0.001$. Chronic kidney disease occurred more frequently in group 1 compared to group 2: 21 (20.0%; 95% CI [12.6–27.4]) patients and 6 (5.7%; 95% CI [1.9–10.8]) patients, respectively, $P = 0.002$ (Table 1). In CAP and CHF group, dyslipidaemia was present in 20 (19.0%; 95% CI [12.3–26.7]) patients and chronic liver disease in 13 (12.4%; 95% CI [6.3–18.7]) patients, with no statistical difference between the groups.

According to the clinical symptoms, dyspnoea was present at the onset of the disease in most patients from group 1: 98 (93.3%; CI 95% [87.6–98.0]) patients, compared to group 2: 73 (69.5%; CI 95% [60.5–78.1]) patients, and the difference being statistically significant ($\chi^2 = 19.681$; $df = 1$; $P < 0.0001$). Cough was another symptom present at the onset of the disease: dry cough was present in 41 (39.0%; CI 95% [29.7–48.5]) patients in group 1 and in 58 (55.2%; CI 95% [45.2–65.3]) patients in group 2. Productive cough was experienced by 26 (24.8%;

95% CI [17.0–32.8]) patients in the CHF group and 36 (34.3%; 95% CI [24.6–43.7]) patients in group 2.

Physical examination of the chest revealed that 21 (20.0%; CI 95% [12.3–28.4]) patients from the group with CAP and CHF presented local increase of vocal fremitus on lung palpation, compared to 22 (21.0%; CI 95% [13.0–28.7]) patients without CHF, ($\chi^2 = 0.029$; $df = 1$; $P = 0.864$). Localised dullness on percussion was determined in 13 (12.4%; 95% CI [6.5–18.8]) patients from group 1 versus 8 (7.6%; 95% CI [2.8–13.0]) patients from group 2, ($\chi^2 = 1.323$; $df = 1$; $P = 0.250$). Local decreased vesicular murmur presented 74 (70.5%; CI 95% [60.6–78.6]) patients in group 1 versus 55 (52.4%; CI 95% [42.9–61.2]) patients ($\chi^2 = 7.255$; $df = 1$; $P = 0.007$). Unilateral crackles were determined on lung auscultation in 27 (25.7%; 95% CI [17.9–35.2]) patients from group 1, compared to group 2 – 29 (27.6%; 95% CI [19.6–37.4]) patients, and bilateral crackles – in 41 (39.0%; 95% CI [30.6–48.6]) patients from group 1 versus 20 (19.0%; 95% CI [12.0–26.7]) patients from group 2, ($\chi^2 = 11.183$; $df = 2$; $P = 0.004$).

Radiological examination was performed in all patients included in this study. Thus, the presence of the alveolar pattern was determined in 38 (36.2%; 95% CI [27.3–45.1]) patients from group 1, and the interstitial pattern was observed in 67 (63.8%; 95% CI [54.9–72.7]) patients, without significant differences between the groups. Analysing the extent of pulmonary involvement in patients with CAP and CHF, we determined that bilateral consolidation was more frequent – 63 (60.0%; 95% CI [50.5–69.1]) patients, followed by polysegmental extension – in 27 (25.7%; 95% CI [17.7–34.3]) patients, segmental (1–2 segments) – in 10 (9.5%; 95% CI [4.3–15.5]) patients and lobar – in 5 (4.8%; CI 95% [1.0–9.3]) patients, also without significant differences between the groups. The presence of pleural effusion on admission was significantly higher in patients from group 1 compared to those from group 2: 41 (39.0%; 95% CI [30.6–49.5]) patients and 14 (13.3%; CI 95% [7.3–20.0]) patients, respectively ($\chi^2 = 17.958$; $df = 1$; $P < 0.0001$).

Table 1. Concomitant diseases in patients with CAP and CHF.

	Group 1 (n = 105)		Group 2 (n = 105)		P, df = 1
	Abs.	%	Abs.	%	
Dyslipidaemia	20	19.0	16	15.2	$\chi^2 = 0.536$; $P = 0.464$
Chronic liver disease	13	12.4	8	7.6	$\chi^2 = 1.323$; $P = 0.250$
Atrial fibrillation	54	51.4	0	0	$\chi^2 = 72.692$; $P < 0.0001$
Arterial hypertension	103	98.0	84	80.1	$\chi^2 = 19.552$; $P < 0.0001$
Chronic kidney disease	21	20.0	6	5.7	$\chi^2 = 9.563$; $P = 0.002$
Type 2 diabetes mellitus	41	39.0	25	23.8	$\chi^2 = 5.657$; $P = 0.017$
Cerebrovascular disease	47	44.8	25	23.8	$\chi^2 = 10.229$; $P = 0.001$

CAP, community-acquired pneumonia; CHF, chronic heart failure.

Regarding the values of OS markers (Table 2), we observed that patients in group 1 presented lower values of ischaemia-modified albumin compared to group 2: 229.77 ± 57.23 $\mu\text{M/L}$ and 236.60 ± 64.35 $\mu\text{M/L}$, respectively, without statistical significance. AGE-pentosidine-like values were higher in patients from group 1 (598.79 ± 251.68 $\mu\text{M/L}$) compared to group 2 (544.55 ± 197.20 $\mu\text{M/L}$), ($F = 3.021$; $P = 0.084$). AGE-verperlysin-like was also higher in group 1 compared to group 2: 449.14 ± 169.38 $\mu\text{M/L}$ versus 455.24 ± 160.66 $\mu\text{M/L}$, with no significant differences between groups.

Advanced oxidation protein products were less expressed in patients with CHF (95.21 ± 63.05 $\mu\text{M/L}$) compared to those without CHF (105.95 ± 55.21 $\mu\text{M/L}$). Additionally, MDA had a higher mean value in group 1 versus group 2: 17.46 ± 6.94 $\mu\text{M/L}$ and 16.07 ± 4.72 $\mu\text{M/L}$, respectively ($F = 2.869$; $P = 0.092$).

We also analysed the values of antioxidative markers. Thus, the total AAT with the CUPRAC method had higher values

in patients from group 1 (6.70 ± 4.62 $\mu\text{M/L}$), compared to those from group 2 (4.99 ± 4.29 $\mu\text{M/L}$). The differences were statistically significant in both groups ($F = 7.647$; $P = 0.006$) (Figure 1). Total AAT with the ABTS method was higher in patients with CHF: 132.22 ± 21.48 $\mu\text{M/L}$ compared to those without CHF: 128.23 ± 22.21 $\mu\text{M/L}$, with no statistical significance between the groups. SOD values were not significantly different between group 1 and group 2: 62.72 ± 13.37 u/c and 62.33 ± 16.47 u/c, respectively.

At the same time, catalase was determined in lower values in patients from group 1 (21.88 ± 10.01 $\mu\text{M/L}$), compared to group 2 (23.16 ± 11.54 $\mu\text{M/L}$), statistically insignificant.

Analysing the inflammatory response parameters, we observed that serum lactate dehydrogenase values were significantly higher in the CHF group compared to group 2: 232.65 ± 109.80 u/L and 192.40 ± 44.98 u/L, respectively, showing a statistically significant difference between both groups ($F = 12.076$; $P = 0.001$). There were no statistical

Table 2. Comparison of OS markers in patients with CAP and CHF.

Parameters	Group 1 (n = 105)		Group 2 (n = 105)		F	P
	Mean	SD $\pm$	Mean	SD $\pm$		
AIM ($\mu\text{M/L}$)	229.7775	57.23919	236.6077	64.35578	0.660	0.417
AGE-pentosidine-like ($\mu\text{M/L}$)	598.7908	251.68051	544.5575	197.20439	3.021	0.084
AGE-verperlysin-like ($\mu\text{M/L}$)	449.1497	169.38287	455.2475	160.66932	0.072	0.789
PPOA ($\mu\text{M/L}$)	95.2128	63.05108	105.9567	55.21101	1.726	0.190
Catalase ($\mu\text{M/L}$)	21.8819	10.01078	23.1646	11.54527	0.740	0.391
AAT with CUPRAC ($\mu\text{M/L}$)	6.7012	4.62461	4.9987	4.29101	7.647	0.006
AAT with ABTS ($\mu\text{M/L}$)	132.2233	21.48573	128.2355	22.21592	1.748	0.188
SOD (u/c)	62.7206	13.37431	62.3362	16.47029	0.034	0.853
MDA ($\mu\text{M/L}$)	17.4629	6.94660	16.0739	4.72922	2.869	0.092

AAT, antioxidant activity; AIM, Ischemia Modified Albumin; AGE, Advanced Glycation End Products; CAP, community-acquired pneumonia; CHF, chronic heart failure; MDA, malonic dialdehyde; OS, oxidative stress; PPOA, Advanced Oxidation Protein Products; SD, Standart Deviation; SOD, superoxide dismutase.

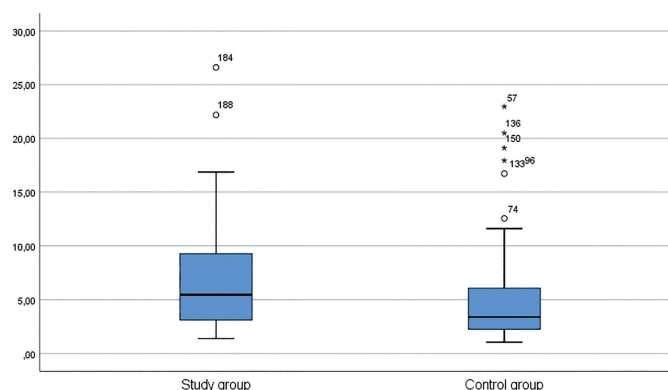


Figure 1. Total AAT with CUPRAC method in patients with CAP and CHF. AAT, antioxidant activity; CAP, community-acquired pneumonia; CHF, chronic heart failure.

differences regarding the number of white blood cells from the full blood count in group 1 compared to group 2: $10.36 \pm 7.13 \times 10^9/L$ and $10.52 \pm 5.58 \times 10^9/L$, respectively. The mean value of the erythrocyte sedimentation rate was significantly lower in group 1 compared to group 2: 21.17 ± 15.98 mm/h and 29.89 ± 19.47 mm/h ($F = 12.561$; $P < 0.0001$). C-reactive protein values were lower in group 1 (35.98 ± 58.10 mg/L) compared to group 2 (47.30 ± 70.04 mg/L), $P = 0.204$.

Positive final evolution of the disease presented 101 (96.2%; 95% CI [92.3–99.1]) patients from group 1, manifested by clinical, radiological and laboratory data improvement. In group 1, death occurred in 4 (3.8%; 95% CI [0.9–7.7]) patients with severe bilateral pneumonia and multiple comorbidities. At the same time, in group 2, all patients showed a positive clinical outcome ($\chi^2 = 4.078$; $df = 1$; $P = 0.043$).

Discussions

The diagnosis of CAP in patients with CHF remains a challenge in the clinical practice of both internists and cardiologists (11). Similar clinical manifestations of these two comorbidities, as well as a poor clinical picture of CAPs in elderly patients, can delay the correct diagnosis of CAP and the initiation of an appropriate treatment (12).

Analysing the presence and role of comorbidities in patients with CAP and CHF, we determined that arterial hypertension was the most common concomitant pathology, followed by atrial fibrillation, cerebrovascular disease, diabetes mellitus, chronic non-obstructive bronchitis, chronic anaemia, chronic kidney disease, dyslipidaemia, chronic liver disease and hypothyroidism. Similar results were obtained in a study conducted by Smeets et al. (4), who aimed to assess the most frequent comorbidities associated with heart failure and reported that arterial hypertension was the most common – 48% of cases, followed by ischaemic heart disease – 31% of cases and atrial fibrillation – 29% of cases.

Regarding the symptoms of CAP in patients with CHF, we found that dyspnoea was present at the onset of the disease in most of the patients: 98 (93.3%) patients, followed by dry cough – 41 (39.0%) patients and productive cough – 26 (24.8%) patients. Only 8 (7.6%) patients had chest pain at the onset of the disease. Similar data were obtained in a study conducted by Cha et al. (13), which aimed to determine clinical and laboratory data in hospitalised patients with CAP and CHF. The results of his study showed that the most common onset symptoms were: dyspnoea (90.5%), retrosternal pain (44.2%) and cough (38.8%).

In our study, radiological changes were represented by the alveolar pattern in 38 (36.2%) patients with CAP and CHF

and the interstitial pattern in 67 (63.8%) patients. Bilateral extension of the infiltrate was the most frequent – 63 (60.0%) patients, followed by polysegmental extension of the infiltrate – 27 (25.7%) patients, segmental (1–2 segments) – 10 (9.5%) patients and lobar – 5 patients (4.8%). According to Bobilev et al. (14), in a study that aimed to determine the clinical features of CAP in patients with CHF, the presence of alveolar-type infiltrate was determined in 60% of patients and interstitial-type infiltrate – in 32% of patients. In the same study, multi-lobe infiltrate was found in 52% of cases and lobar infiltrate in 48% of cases, which is in contradiction with the results obtained in this study.

Analysing the inflammatory response in patients with CAP and CHF, we determined that only serum lactate dehydrogenase values were significantly higher in the CAP and CHF groups (232.65 ± 109.80 u/L), and the other markers (white blood cell count, C-reactive protein and erythrocyte sedimentation rate) had similar mean values in both groups. Similar results were obtained in a study conducted by Erez et al. (15), that included a cohort of 158 patients with very high isolated LDH, admitted to the internal medicine department during a 3 year period. They aimed to analyse serum LDH as a distinguishing clinical biomarker and as a predictor of in-hospital outcome in admitted medical patients, and demonstrated that high serum LDH level at admission was a useful marker for pneumonia diagnosis, compared with the control group (24.6% vs. 10.1% respectively, $P = 0.0003$).

Subsequently, we analysed the values of pro-oxidative markers (ischaemia-modified albumin, advanced glycation end products, protein products of advanced oxidation, MDA) and antioxidative markers (total AAT with CUPRAC and ABTS methods, SOD, catalase). Thus, pro-oxidant activity, manifested by increased values of AGE-pentosidine-like, AGE-verperlysin-like and MDA, was more expressed in patients with CAP and CHF, compared to the control group. This can be explained through a more expressed association between pro-OS markers activation and cardiovascular events in patients with CAP, such as cardiac arrhythmias, systolic and diastolic dysfunction of the left ventricle and the development of chronic congestive heart failure (16).

The antioxidant defence system in patients with CAP and CHF in our study was determined by increased levels of total AAT with CUPRAC and ABTS methods. At the same time, catalase had lower values in the CHF group. The increased levels of antioxidative stress markers in our study can be explained by an imbalance between the increased formation of ROS and the elimination or neutralisation of ROS by an antioxidant system, and it can have direct implications in the evolution of CAP in patients with CHF. In contrast with our results, a study by Reshetar (17) demonstrated an excessive accumulation of

final lipid peroxidation products in combination with insufficient activation of antioxidant defence in patients with CAP. In our study, we demonstrated that in patients with CAP and CHF, antioxidant defence system is being simultaneously activated, with the increased values of total AAT with CUPRAC and ABTS methods.

In our study, most of the patients (96.2%) from the group with CAP and CHF showed a positive outcome by the end of antibacterial treatment, manifested by the improvement of clinical data, decline of inflammatory markers and radiological resolution of pneumonia. Similar data were obtained in a study that followed the course of CAPs in 7449 hospitalised patients (18). Peyrani et al. (19) showed that 77% of patients had a positive final outcome of pneumonia, and death occurred in 6% of cases.

Limitation

In this study, there were limitations in performing a broader panel of OS markers, including glutathione assessment, as well as inflammatory markers (such as serum procalcitonin levels). Also, there are possible confounding variables that may influence OS markers, such as presence of chronic conditions (metabolic syndrome, hypertension and diabetes mellitus), which are implied to dysregulate the human antioxidant system. Further studies may be needed to confirm findings in a broader population.

Conclusions

The radiological manifestations, represented by bilateral expansion of the pulmonary infiltrate and the presence of pleural effusion, in association with worsening dyspnoea at the onset of the disease, are characteristic for patients with CAP and CHF. The hypothesis of the study, which assumes that the coexistence of CAP and CHF results in an excessive accumulation of pro-oxidative reaction products, was not fully confirmed, the counterbalancing of OS being mainly achieved by increasing the total AAT with the CUPRAC method.

Author's contributions

(1) First author: Virginia Cascaval. (2) Corresponding author: Virginia Cascaval. (3) Coordinating author: Tatiana Dumitras.

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Institutional review board statement

This study was conducted according to the Declaration of Helsinki's guidelines and approved by the local Ethics Commission. The 'Nicolae Testemitanu' State University of Medicine and Pharmacy, Chisinau, Republic of Moldova – Ethics Committee approved the protocol on 4th December 2019, no. 18.

Informed consent statement

Informed consent was obtained from all subjects involved in this study.

Data availability statement

Data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of interest

The authors declare no conflict of interest.

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