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CLINICAL PRESENTATION AND DIAGNOSIS OF PNEUMONIA IN IMMUNOCOMPROMISED

321.01 Internal Medicine (Pneumology)

Summary of the doctoral thesis in medical sciences

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Doctoral school in medical sciences.

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CONCEPTUAL LANDMARKS OF THE RESEARCH

The relevance and significance of the research study

Pneumonia is a significant clinical burden in immunocompromised individuals. It is a major cause of morbidity and mortality [1, 2].

Lung infections are among the most common types of infections in immunocompromised hosts [3, 4]. The diagnosis and therapeutic management of pneumonia in immunocompromised patients is challenging because of the continuing increase in both the number of immunocompromised people and their survival time, the high prevalence of lung disease and comorbidities in these patients, new treatments with immunosuppressive drugs, and advances in organ transplantation [4, 5]. These conditions lead to altered cell-mediated and/or humoral immunity and contribute to an increase in the number of immunocompromised individuals, thus increasing the incidence of opportunistic infections. The causes of severe immunosuppression are multiple. Treatments inducing immunosuppression (solid organ transplantation, bone marrow transplantation, systemic diseases) and antitumor chemotherapy cause alterations in the immune system and lead to decreased lymphocyte counts, suppression of the cellular immune response, decreased proinflammatory cytokines, impaired phagocytosis and chemotactic impairment. Malignant hematological diseases result in the proliferation of immature, non-functional leukocytes that compete with normal cells for medullary physiological niches. A number of diseases are characterized by disruption of cellular or humoral immune mechanisms, most commonly HIV/AIDS infection, less commonly congenital immunodeficiencies. Causes of secondary immunodeficiencies include metabolic disorders and chronic diseases - diabetes mellitus, liver cirrhosis, chronic renal failure - which reduce mitogen-induced lymphoproliferation, defective phagocytosis and reduced chemotacticity [3, 6, 7].

Pneumonia is a common complication in individuals with severe immunosuppression, with the highest incidence in HIV-infected patients - 50%, and in people with organ transplants it occurs in about 15% of cases [8]. The epidemiology and clinical manifestations of pulmonary infections are determined by the degree of immunosuppression (especially the presence of neutropenia) and may be different in immunocompromised HIV/AIDS-infected and HIV-negative immunocompromised patients. The course of pneumonia in immunocompromised individuals is unpredictable. Several factors can worsen the course, including the degree of immunosuppression, comorbidities, various etiological factors (such as opportunistic microorganisms), and particularly strains of nosocomial pathogens with increased virulence and a broad spectrum of antibiotic resistance [4]. Pneumonia in a compromised host often results in a complicated course, therapeutic failure, difficult

differential diagnosis, significant medical costs, delayed resolution, and persistence sequelae.

Currently, most international guidelines and national clinical protocols for community-acquired pneumonia in adults do not include immunocompromised patients. However, as the number of immunocompromised individuals increases, there is a growing need for improved management of lung infections and early diagnosis. Studies over past decade emphasize the crucial role of proper pneumonia case management and adherence to guidelines in influencing the course of the disease [9-11]. The diversity of causes of immunocompromise and the wide spectrum of infectious complications with atypical manifestations in immunocompromised hosts often lead to delayed diagnosis of pulmonary infections. In the Republic of Moldova, no studies have analyzed the specificities of clinical management of immunocompromised patients with pneumonia.

Aim of the study:

To study the clinical and paraclinical characteristics of pneumonia in immunocompromised patients and to develop recommendations to optimise management.

Objectives of research:

1. To study the etiological aspects of pneumonia in immunocompromised hosts.
2. To highlight the clinical and paraclinical features of pneumonia in immunodeficient hosts according to the cause of immunosuppression.
3. To evaluate the role of clinical scores in the management of pneumonia in immunocompromised patients in relation to disease severity.
4. To highlight the difficulties in case management of pneumonia in the immunocompromised host.
5. To develop practical recommendations for the management of pneumonia in immunocompromised patients according to the cause of immunosuppression.

Scientific research methodology

The research hypothesis and design were based on the objectives aimed of achieving the study's goal; the scientific research was conducted in the following stages: development of the research concept, selection of research methods, and definition of the study objectives. A descriptive and analytical cross-sectional observational study was performed on a representative sample of pneumonia patients. The patients were grouped into two subgroups based on their immune status. The research was conducted in the period 2018-2023, involving 192 pneumonia patients from Institute of Pulmonology "Chiril Draganiuc". The subjects in the study were

monitored during their hospitalization. Each subject was assigned an individual medical record containing general, clinical, imaging, microbiological and laboratory data collected upon admission and throughout their hospitalization. The highlight the etiological, clinical, paraclinical, and imaging features of pneumonia in immunocompromised patients, a cohort of 96 patients with community-acquired pneumonia was selected. These patients were evaluated according to the National Clinical Guidelines for Community-acquired pneumonia in Adults [12]. The analysis of the data was carried out using the functions and modules of Microsoft Office Excel, MedCalc and SPSS 22.

Novelty and originality of the research

The peculiarities of the presentation and clinical course of pneumonia in immunocompromised patients were explored, highlighting features that distinguish them from community-acquired pneumonia in immunocompetent patients. The etiological structure of pneumonia in immunocompromised patients was analyzed, considering the degree and cause of immunosuppression as well as microbial antibiotic resistance. It was demonstrated that pulmonary radiological changes resolve more slowly in immunocompromised patients with pneumonia and distribution of various opportunistic infections to this delayed resolution was identified.

Based on the study, several factors contributing to the delayed diagnosis of pneumonia in immunocompromised patients were identified, including delayed physician referral, a clinical presentation influenced by immunosuppression and underlying manifestations disease, and variable imaging findings. We assessed the applicability and relevance of clinical pneumonia severity scores in immunocompromised patients and established associations between prognostic factors and adverse outcome of pneumonia in this population.

Scientific problem solved in the thesis

The study highlighted key aspects of the clinical, etiological, and imaging features of pneumonia in immunocompromised individuals, leading to the development of a set of practical guidelines that may facilitate the early diagnosis of pneumonia in this population. Additionally, these principles can aid in identifying individuals at increased risk of unfavorable disease progression and delayed resolution of pulmonary radiological changes.

Theoretical significance and applicative value

The research results provide a theoretical framework concerning the clinical, etiological, and imaging aspects of pneumonia in immunocompromised individuals, which facilitated the development of practical recommendations for managing of pneumonia in this population. The data obtained offer theoretical support for

determining the scope and nature of care required for immunocompromised patients with pneumonia. This scientific work provides practical criteria for early diagnosis of pneumonia in immunosuppressed patients, emphasizing the need for widespread use of diagnostic methods, including microscopy, bacteriology, serology and molecular genetics. The data on the unique characteristics of the resolution of imaging changes, as obtained in the study, support the extension of radiological monitoring of pneumonia in immunocompromised patients beyong hospitalization.

Main scientific results submitted for thesis defense:

- The etiology of pneumonia in immunocompromised individuals is diverse. The most common bacterial pathogens identified were *E.coli, S.aureus, K. pneumoniae, P.aeruginosa, S.pneumoniae* and *S. haemolyticus,* with a high rate of antibiotic resistance. Fungal agents included *P. jirovecii, C. neoformans* and *Aspergillus spp.*, while viral pathogens such as SARS-CoV-2 and Cytomegalovirus were also identified. The broad spectrum of opportunistic infections necessitates the use of diagnostic methods: microscopic, bacteriological, serological and molecular genetic techniques, for early etiological diagnosis and timely treatment.
- The clinical features (insidious onset, dry cough, hypotension), imaging characteristics (bilateral radiological involvement, extension of lung lesions to two and more lung fields, interstitial-type opacities with diffuse distribution) and etiological factors (opportunistic pathogens) differentiate pneumonia in immunocompromised individuals from community-acquired pneumonia in immunocompetent individuals, potentially aiding in the early diagnosis of pneumonia in immunocompromised patients.
- Late presentation, clinical manifestations influenced by immunosuppression and underlying disease, and variable imaging findings are key factors contributing to the difficulty and delay in diagnosis, leading to a more severe course and higher mortality.
- Results evaluating the effectiveness of prognostic scores in pneumonia among immunocompromised patients highlight the SMRT-CO score as the more effective in assessing the risk of death and the need for invasive mechanical ventilation (IMV).

Implementation of scientific results

The results of the study are incorporated into undergraduate and postgraduate education at the Discipline of Pneumology and Allergology, in the Phthisiopulmonology department of the PI "Chiril Draganiuc", and the Pulmonology Department of the Hospital " Sf. Arh. Mihail". They are also used in the training process of medical staff within the Pulmonology and Allergology Discipline,

Department of Internal Medicine of the SUMPh "Nicolae Testemitanu". Additionally, two certificates of innovation and two implementation acts have been registered.

Approval of scientific results:

The thesis materials were presented and discussed at: 28th National Congress of the Romanian Society of Pneumology (Sinaia, 2024); Conference with international participation "Bronchoscopy and Thoracic Ultrasound in Pleuropulmonary Diseases" (Chisinau, 2019); Annual Scientific Conferences dedicated to the SUMPh "Nicolae Testemitanu" Days (Chisinau, 2019, 2020, 2022); National Conference with international participation "Romanian Pneumology from one side and the other side of the Prut" (online event, 2021); National Conference with international participation dedicated to the Medical Days of the Municipal Clinical Hospital "St. Ar. Mihail" (Chisinau, 2022); VIAREMO Respirology Society Conference (Chisinau, 2019).

Publications on the thesis topic. The scientific results obtained in this research have been published in 20 scientific works, including 9 articles (2 single-authors, 1 in SCOPUS-indexed journals), 2 textbooks (as co-author), 9 oral communication presentations.

Summary of the thesis' chapters. The thesis is presented on 121 pages, including: introduction, literature review (Chapter 1), research materials and methods (Chapter 2), presentation of own research results (Chapters 3-4), analysis and synthesis of the data obtained (Chapter 5), conclusions and practical recommendations. The paper cites 248 references; the iconographic material contains 48 tables, 11 figures and 1 appendix.

Keywords: pneumonia in immunocompromised hosts, opportunistic pathogens, prognostic scores.

THESIS CONTENT

1. PNEUMONIA IN IMMUNOCOMPROMISED PATIENTS - CLINICAL AND EVOLUTION ASPECTS

This chapter provides a synthesis of publications in the literature highlighting the key elements in the approach to pneumonia in immunocompromised patients. The etiological spectrum is discussed, including the most commonly implicated pathogens, clinical presentation and imaging features, and contemporary diagnostic approaches. Existing studies on the prognostic value of certain clinical and paraclinical parameters for predicting the course of these pneumonias are also reviewed. Additionally, the chapter explores the etiological aspects of pneumonia based on the underlying cause of immunosuppression. It further examines the value of applying prognostic scores in the evaluation of community-acquired pneumonia in immunocompromised patients.

2. CLINICAL DATA AND RESEARCH METHODS

2.1 Study design

The study group consisted of 192 patients with pneumonia, who were hospitalized between November 2018 and December 2023 at the Pneumology Department of "Chiril Draganiuc" Pneumology Institute.

Inclusion criteria for the immunocompromised group

1. Patients with compromised immune status (HIV infection, long-term systemic corticosteroid therapy, immunosuppressive treatments, post-chemotherapy, neoplasms, primary immunosuppression);
2. Patients with a confirmed diagnosis of pneumonia (clinic-imaging, biological confirmation);
3. Patients who have signed the informed consent;
4. Age over 18 years.

Inclusion criteria for the immunocompetent group:

1. Patients with a confirmed diagnosis of pneumonia (clinic-radiological, biological);
2. Patients who have signed the informed consent;
3. Age over 18 years.

Exclusion criteria:

1. Patients for whom it was not possible to complete questionnaires, physical examination, paraclinical investigations;
2. Patients in whom the diagnosis of pneumonia was invalidated as a result of investigations;
3. Patients who wished to withdraw from the study;
4. Patients with community-acquired pneumonia and significant comorbidities (diabetes mellitus, chronic renal failure);
5. Bacteriologically confirmed active pulmonary tuberculosis;
6. Patients who refused to participate in the study.

To highlight the clinic-paraclinical, etiological, imaging, and evolutionary features of pneumonia in immunocompromised patients, two study cohorts were established: the immunocompromised patient cohort (IP cohort), which included 96 immunocompromised individuals, and the immunocompetent patient cohort (CP cohort), which also included 96 patients. Diagnostic criteria were based on the guidelines for Community-acquired Pneumonia in Adults [12]. To examine clinical, paraclinical, and etiological characteristics based on the cause of immunosuppression, the IP cohort was further divided into two subgroups: pneumonia in immunocompromised and HIV-infected patients, and pneumonia in immunocompromised and non-

HIV-infected patients. To assess the risk factors for adverse outcomes in immunocompromised patients with pneumonia, the IP cohort was also divided into two groups: survivors (S), consisting of 81 cases, and deceased (D), consisting of 15 cases (patients who died during hospitalization), based on the criteria for defining adverse outcomes.

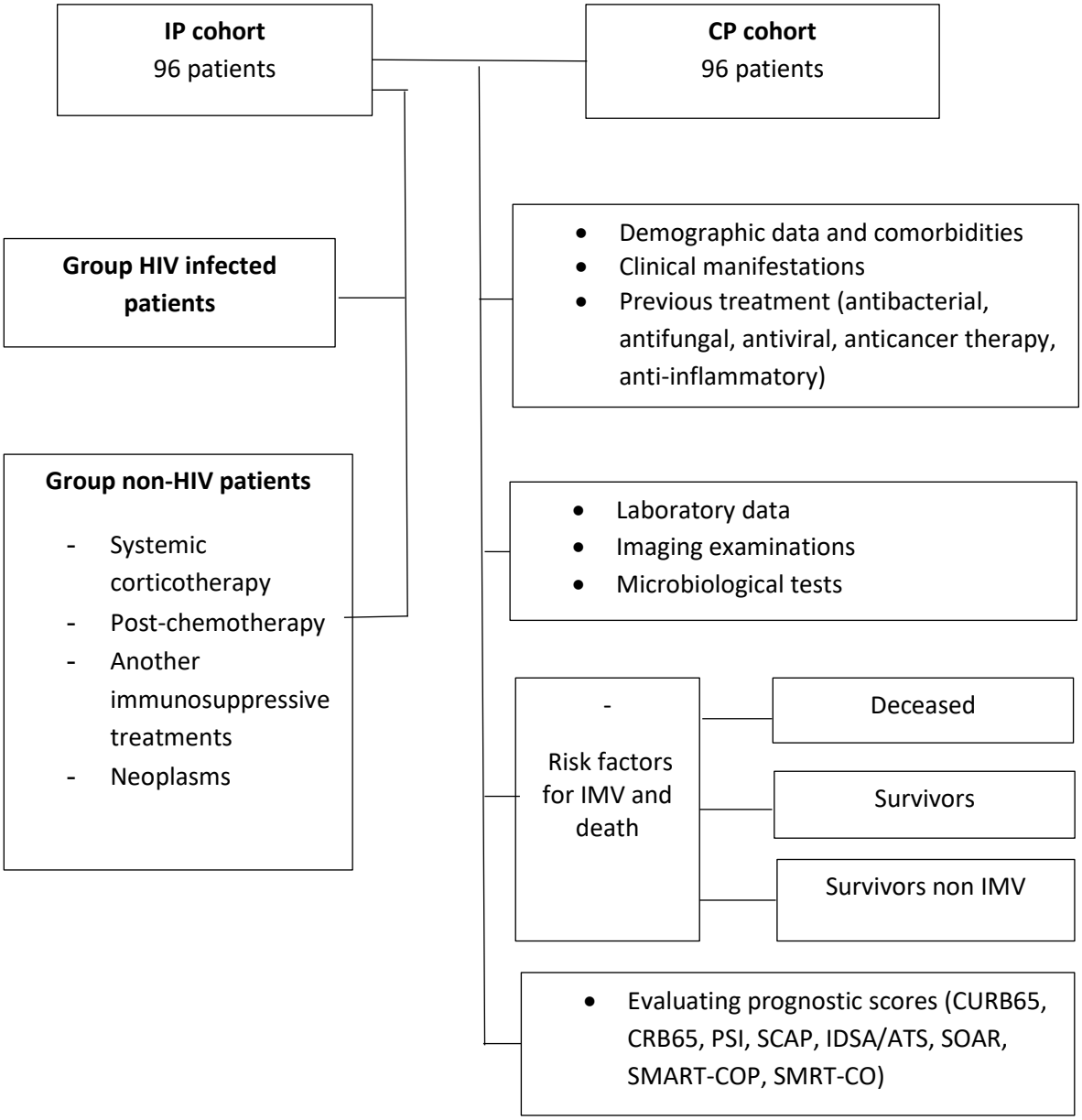

Figure 1. ***Study design***

2.2Methods of investigation

An individual medical record was created for each patient, containing general, clinical, imaging, microbiological, and laboratory data collected upon admission and during hospitalization, as well as details the treatment regimens administered.

Clinical data collection involved in-hospital assessment of symptoms, criteria for clinical stabilization [13], vital parameters (heart rate, blood pressure, respiratory rate, SpO2, t^{0}C), consciousness, and pulmonary physical signs, all of which were evaluated

daily. Paraclinical tests were performed based on the clinical indications for each patient and included: hemogram, chest X-ray, sputum AFB, sputum microbiology, blood culture, biochemical tests (creatinine, urea, glucose, prothrombin index, activated partial thromboplastin time, and fibrinogen), markers of systemic inflammation (C-reactive protein, procalcitonin, neutrophil/lymphocyte ratio), serum electrolytes. These indicators were assessed on admission and throughout the course of the study as clinically necessary. Peripheral blood oxygen saturation was monitored by pulse oximetry in all subjects. In cases with SpO2 ≤ 90%, arterial blood gases (PaO2, SaO2, PaCO2) and acid-base parameters (pH, HCO3) were assessed. HIV testing was conducted after prior counseling, with patient consent. Chest radiology and CT imaging were performed according to the radiologist's interpretation in the medical record. Radiological examinations were repeated daily for patients with severe pneumonia hospitalized in the ICU, and every 5-7 days for patients with moderate pneumonia hospitalized in the pneumology department, in accordance with the national clinical guidelines [12].

The etiological diagnosis of IP was made through microbiological examinations following specialized protocols (microscopy, cultures, molecular genetic methods, serological methods) to detect bacteria, fungi, and non-tuberculous mycobacteria in sputum and/or bronchoalveolar lavage, blood, and pleural fluid. Tests for parasitic infections and viruses were performed when clinically indicated. In most cases, confirmation of SARS-CoV-2 and influenza virus infections was made by real-time RT-PCR (Reverse Transcription Polymerase Chain Reaction) of nasopharyngeal secretions and blood. Additional investigations were carried out selectively based on medical indications, including bronchoscopy with transbronchial biopsy, followed by microbiological testing of biopsy samples, spinal puncture with cerebrospinal fluid analysis, and histological examination of tissue samples (biopsy, morphological material).

Prognostic assessment scores for pneumonia were calculated for all subjects in the IP and CP cohorts, including PSI [14], CURB-65 [15], CRB-65 [16], SCAP [17], IDSA/ATS [1], SOAR [18], SMART-COP [19] and SMRT-CO [19].

2.3 Methods of statistical analysis

The medical data of the subjects included in the study were encoded in individual data sheets and subsequently entered into an electronic table using Microsoft Office Excel. Statistical analysis was conducted using MedCalc and SPSS 22 programs, utilizing the respective functions and modules of these software tools. The analyzed variables were presented as percentages or as mean values with standard deviation. For the comparative analysis of the variables between the investigated groups, the following tests were used: the Chi-square ($\chi 2$) test for discrete variables (categorical, including dichotomous ones);

the student's t-test for comparing two groups by comparing means for normally distributed variables; and the Mann-Whitney U test for comparing more than two groups by globally comparing means for non-parametric variables. Predictive factors for the unfavorable progression of pneumonias were determined using the logistic regression model with the "step-by-step" method, when the dependent variable was dichotomous [20]. Results were expressed as odds ratio (OR) with the 95% confidence intervals (CI 95%). The accuracy of the generated models was verified by calculating the area under the curve (AUC - Area Under Curve). The evaluation of prognostic scores in immunocompromised patients with pneumonia included the calculation of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), with 95% confidence intervals for each risk class of the analyzed scores. The predictive accuracy and discriminatory power of prognostic scores was assessed by constructing ROC curves (Receiver Operating Characteristic) and calculating AUC.

3. CLINICAL-PARACLINICAL CHARACTERISTIC AND ETIOLOGICAL ASPECTS OF IMMUNOCOMPROMISED PNEUMONIA

3.1 Characteristic of pneumonia in immunocompromised hosts

A total of 192 patients, whose pneumonia was confirmed by imaging and laboratory data were included in the statistical analysis. Based on the criteria for immunocompromised status outlined above, 96 immunocompromised subjects were enrolled in the study, consisting of 60 (62,5%) females and 36 (37,5%) males, with an average age of 53,2±14 years (ranging from 25 to 82 years). The causes of immunosuppression were as follows: HIV infection, in 44 patients (45,8%), chemotherapy and/or antitumor radiotherapy in 23 patients (24%), daily corticosteroid treatment > 10 mg prednisolone in the last 3 months or with cumulative dose > 700 mg prednisolone in 21 patients (21,9%), anti-rheumatic treatment (DMARDs – disease-modifying antirheumatic drugs) in 5 patients (5,2%), myelosuppressive effect from other treatments (antiviral, cytostatic, biological) in 4 patients (4,1%), a smaller proportion were post-transplant patients (2/96,2%) and one patient with primary immunodeficiency (X-linked agammaglobulinemia). Among the 44 HIV infected patients, 42 (95,4%) had CD4 levels below 500 cells/µl, with 68,1% (30/44) having CD4 levels below 100 cells/µl. The diagnosis of HIV infection was confirmed as primary (at the stage of immune deficiency syndrome) in 59,1% of the cases (26/44). Every third patient in the IP group had at least one comorbidity, and two-thirds (66/96) of them had two or more comorbidities. The most common concomitant pathologies were cardiovascular diseases in 25,3% (24/96), neoplasms in 24% (23/96), tuberculous

sequelae (such as calcifications, fibrosis, and bronchiectasis) in 16.7% (16/96), and diabetes mellitus in 15,8 % (15/96). Smoking status was recorded in 16,7% of cases (16/96), while cachexia and obesity each accounted for 21,9% (21/96). The majority of cases of pneumonia in immunosuppressed patients had a severe course: 60,4% (53 diagnosed on the first day and 5 worsening during hospitalization), while 38,5% (37/96) had moderate and 1% (1/96) had mild severity. Death from severe pneumonia occurred in 25,6% (15/58) of cases. Immunocompromised patients generally required longer hospital stays. The median duration of hospitalization was 14 days (IQ 9-21). Fourteen patients were directly admitted to the ICU, with a median time to transfer to the ICU after admission of 2 days (range 1-8). Mechanical ventilation was needed in 16% of cases of pneumonia in immunocompromised patients, and the median duration of invasive ventilator support following to confirmation of pneumonia was 4 days (IQ 2-7). Analyzing the clinical presentation of pneumonia in immunocompromised hosts we found that the onset of the disease was acute in 61,5% (59/96) of patients. The most common symptoms were cough in 94,8% (91/96), with 52,1% (50/96) of cases presenting without sputum production, and dyspnea in 82,3% (79/96). Febrile syndrome was observed in 55,2% (53/96) of patients, with 13,5% (13/96) presenting with fever above 39˚C. Sweating was an important symptom in the clinical picture of immunocompromised pneumonia, reported in 39,6% (38/96) of cases. A smaller proportion of patients (38,5%, 37/96) had an insidious onset, with subfebrile temperatures (t˚ ≤ 38˚) in 31,3% (30/96) of cases. Productive cough was noted in 47,9% (46/96) of cases, with 18,8% (18/96) having mucous expectoration and in 15,6% (15/96) exhibiting mucopurulent expectoration. Hemoptysis was observed 13,5% (13/96) in immunosuppressed patients. In half of IP cohort subjects (43,6%, 41/96) the leukocyte count in peripheral blood was within the normal range (4-9*10^9/l). Severe leukocytosis (values >25*10^9/l) was recorded in a small number of cases (5,3%, 5/96), while leukopenia (<4*10^9/l) occurred in 16% (15/96). Deviations in the leukocyte formula were identified in 11% (11/96) of subjects. Among the most significant laboratory changes were lymphopenia (67%, 64/96), anemia (56%, 54/96), and elevated ESR (75%, 73/96). High LDH values (≥ 450 U/L) were recorded in 66,7% (54/96) of cases, and increased C-reactive protein (≥12 mg/l) was found in 62% (58/96) of cases. Elevated urea and creatinine were observed in 29,5% (28/96) of cases. Hyperglycemia was noted in 48,3% (41/96) of cases, with only 15 subjects having a prior diabetes before the onset of pneumonia. Liver dysfunction manifested as hypoproteinemia in 28,8% (17/59) of patients and hypoalbuminemia in 39,5% (23/64) of cases. Imaging findings revealed bilateral enlargement in 83,3% (80/96) of patients and multilobar involvement in 91,7% (88/96). Four or more lung fields were affected

in 65,6% (63/96) of subjects. Imaging characteristics were diverse, with high rates of diffuse interstitial opacities (79%, 76/96) and focal consolidations (66,7%, 64/96) observed. The most common complication was acute respiratory failure (65,6%, 63/96) of cases. Invasive mechanical ventilation was required in 15,6% of patients. Adult acute respiratory distress syndrome (ARDS) was recorded in 20,8% (20/96) of cases. Pleurisy was noted in 16 patients (16.7%), while pulmonary destruction and severe sepsis with abscess formation occurred in 11,5% (11/96) of cases.

3.2 Etiological aspects of pneumonia at immunocompromised

The etiology of pneumonia in immunocompromised subjects was confirmed in majority of cases (83,3%, 80/96). Microbiological examination was conducted on sputum specimens in 77% (75/96) of patients, and repeated sputum cultures were often necessary. In patients with dry cough or absence of cough, bronchial aspirates were collected and examined through via intubation tube or bronchoalveolar lavage (41%, 40/96). In complicated cases with pleurisy, pleural fluid cultures were also performed in 11,3% (11/96) of cases. Sputum cultures yielded positive results in 61 cases (63,5%; 95%CI: 54.2-72.9), while bronchial lavage cultures were positive in 10 cases (10,4%; 95%CI: 5.2-16.7). The most common findings in bacterial cultures were detected in 91% (65/71) of cases, with 28 cases showing bacterial infections in association with *Candida* species, rarely being informative for the etiology of pneumonia. Fungi were identified in 8,4% (6/71) of sputum specimens and nontuberculous mycobacteria were detected in 2 cases.

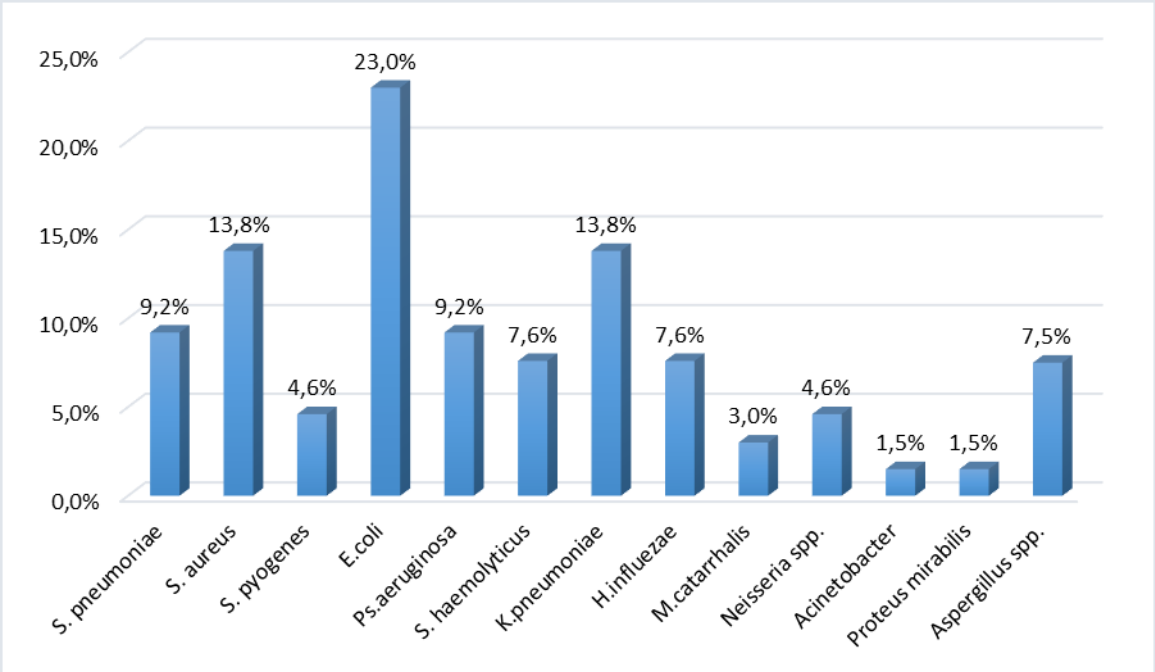

Figure 2. Germs identified in sputum/aspirate cultures in PI patients (N=71)

Among bacterial pathogens, the most commonly isolated *E.coli* (23%, 95CI:11,7-32,8), followed by *S. aureus* and *K. pneumoniae* (13,8%, 95CI:4,4-20,4), *S. haemoliticus* (7,6% (95CI:1,7-16,2) and *P. aeruginosa* (9,2%). *S.pneumoniae* was detected in four sputum cultures, and pneumococcal antigen was identified in two cases by rapid test. A smaller proportion of cases showed *H. influenzae* (7,6%) and *M. catarrhalis* (3%). *Acinetobacter*, *Proteus mirabilis* and *S.pyogenes* were isolated in one case each, from sputum specimens collected on the day of admission. In 54,9% (39/71) of cases *Candida spp.* was isolated and in six cases, fungi from the *Aspergillus spp.* genus were found (Figure 2). In the epidemiological context of the influenza season and COVID-19 pandemic, viral etiology was confirmed in 35 cases. *SARS-CoV-2* was identified in 31% (30/53, 95CI:17.7-35.4) of cases by PCR test and rapid antigen tests, with 30 out of 53 samples testing positive. Seasonal influenza was confirmed in three cases, and *Cytomegalovirus* was detected in two cases by histological examination. The most common fungal pathogen identified was *Pneumocystis jirovecii* (22,5%, 95CI:7.3-29.2), followed by *Cryptococcus neoformans* and *Aspergillus spp.* in 7,5% (95CI:2.1-11.5) of cases. *Pneumocystis jirovecii* was more frequently confirmed by sputum microscopy in 12 patients, but it was also detected by histological examination in five patients and by bronchoalveolar lavage one patient. In half of the patients, mixed etiologies of pneumonia were identified, with the most common combinations being between bacterial and fungal pathogens.

Clinical-evolutionary correlations

An important feature of the studied group was the late referral to medical care. The median duration from symptom onset to the first healthcare visit was 7.5 days (IQR 5-14), with 21 cases (21.9%) having been hospitalization at the district level prior to referral. Since delayed initiation of antibiotic therapy is known to be predictor of severity and mortality in pneumonia, we compared the median duration from symptoms onset to the start of antibacterial therapy in immunocompromised (IP) patients (7,5 days) with what of immunocompetent (CP) patients (5,4 days). The difference was statistically significant ($p<0,005$). In one-third of the analyzed cases, immunocompromised patients sought medical care more than 14 days after the onset of symptoms. The severity of the disease was associated with an increased length of hospitalization, with median stay of 15 days (IQR: 1-94), and stay in ICU of 8 days (IQR: 1-26). This was supported by a linear correlation between the length of hospitalization and disease severity, as indicated by the extension of pulmonary infiltrates ($r = 0,20$, $p<0,05$). Additionally, significant correlations were found between the length of stay and various clinical parameters, such as heart rate ($r = 0,32$, $p<0,05$), RNL ($r = 0,26$, $p<0,05$). A more aggressive course of pneumonia was observed in

patient with severe disease progression. This was confirmed by a direct linear relationship between the duration of ICU hospitalization, clinical parameters and some paraclinical markers: respiratory frequency ($r = 0,24$, $p<0,05$), neutrophil lymphocyte ratio (NLR) ($r = 0,32$, $p<0,05$), lactate dehydrogenase (LDH) level ($r = 0,42$, $p<0,05$) and extension of lung lesions ($r = 0,22$, $p<0,05$). In the same context, significant correlations were found between disease progression and imaging findings: interstitial lesions ($r = 0.46$, $p<0.05$), as well as the association of pulmonary consolidations with reticulations and ground-glass opacities ($r = 0,33$, $p<0,05$). A linear relationship between delayed resorption and fungal etiology in pneumonia among immunocompromised patients was demonstrated. The significant correlation was observed with *Pneumocystis jirovecii* ($r = 0,68$, $p<0,05$) and *Cryptococcus neoformans* ($r = 0,46$, $p<0,05$). Additionally, a significant correlation was noted between disease progression and NLR ($r =0,28$, $p<0,05$).

3.3. Particularities of pneumonias in immunocompromised hosts versus immunocompetent hosts

The clinical manifestations that distinguished the IP cohort included dyspnea, dry cough, hemoptysis, hypotension and low SaO2. These patients typically presented with insidious symptoms. In contrast, clinical signs more commonly associated with pneumonia, such as chest pain, productive cough, catarrhal symptoms and crackles, were observed more frequently in the CP cohort (Table 1). There were no significant differences in the blood count changes between the two cohorts. High levels of C-reactive protein (CRP>12 mg/l) were identified in both groups. However, a statistically significant difference was noted in the occurrence of anemia (defined as hemoglobin < 120 g/l and erythrocytes < $3*10^{12}$/l), which was more commonly observed in immunocompromised patients.

Significant differences between the IP and CP cohorts can be noted in imaging exams. In the IP group, the radiological presentation of lung lesions was mostly bilateral, with involvement of two ore more pulmonary fields. The middle and lower pulmonary areas were more frequently affected, with a diffuse distribution. The types of lesions most prevalent in the IP cohort were interstitial and mixed (alveolar and interstitial opacities). In contrast, in the CP cohort, the radiological expression was characterized by the classical consolidation with alveolar opacities and air bronchogram (Table 2).

Table 1. Clinical characteristics of IP and CP cohorts

	IP (N=96)		CP (N=96)		p
	n	%	n	%	
Acute onset	55	57,3	79	82,3	<0,001
Insidious onset	37	38,5	16	16,7	0,001
Dyspnea	96	100	67	69,7	<0,001
Chest pain	22	22,9	33	33,4	0,03
Cough	91	94,8	90	93,7	0,02
Expectoration	46	47,9	65	67,7	<0,001
Hemotysis	13	13,5	4	4,2	0,04
BP< 90/60 mm Hg	18	18,8	2	2,1	<0,001
SpO2 < 92%	33	34,4	20	20,8	0,008
Crackles	26	27,147	47	49	0,005

Comparative analysis revealed differences in the etiology of pneumonia in IP and CP cohorts. In the IP cohort, the etiology of pneumonia was confirmed in 83,3% of cases, whereas in the PC cohort, it was confirmed in only one-third of patients (31,2%). The spectrum of pathogenic microorganisms was diverse in the IP group. Among the most common pathogens identified in the sputum specimens of immunocompromised patients were fungi. *Pneumocystis jirovecii* was confirmed in 18,8% of cases, and *Cryptococcus neoformans* and *Aspergillus spp.* were detected in 6,3% cases.

Table 2. Radiological and laboratory characteristics of IP and CP cohorts

	IP N=96		CP N=96		p
	n	%	n	%	
Bilateral imaging impairment	80	83,3	46	47,9	<0,0001
Alveolar opacities	21	21,9	58	60,4	<0,0001
Interstitial opacities	34	34,5	13	13,5	<0,0001
Mixt opacities	41	42,7	25	26	<0,0001
Involvement of upper pulmonary fields	52	54,2	31	32,3	0,02
Involvement of the middle pulmonary fields	76	79,2	43	44,8	<0,0001
Involvement of the lower pulmonary fields	86	89,6	68	70,8	0,001
Extension of pulmonary lesions 1 lung field ≥ 2 lung fields	 21 75	 21,9 78,1	 64 32	 66,7 33,3	 <0,0001

Statistical differences were also noted in the case of bacterial etiology. In the IP cohort, the bacterial cause was identified in 41,7% of cases, while in the CP cohort, it was found in only 20,8% of cases. The most common bacteria identified were *K. pneumoniae*, *P.aeruginosa*, *E.coli* and *S.aureus*. An important feature was also the high

proportion of mixed infections (bacterial, fungal, viral), which occurred in 42,3% (42/80) of immunocompromised patients.

The independent associations with IP of variables that differentiated IP and CP cohorts were tested using a logistic regression model. As a result, six independent factors characterizing immunocompromised pneumonia were identified: insidious onset (OR 3.28, 95%CI 1.19-8.14), dry cough (OR 2,67, 95%CI 1,1-5,96), and, hypotension (OR 23,2 95%CI 1,56-347,1), bilateral radiological involvement (OR 3,12, 95%CI 1,1-8,14), extension of pulmonary lesions involving two and more pulmonary fields (OR 3,82, 95%CI 1,59-9,17), and the presence of interstitial opacities, which had a positive predictive role (OR 6,06, 95%CI 2,38-15,41) (Table 3).

Table 3. Logistical model for differentiating pneumonias to immunocompromised

	Coefficient	p	OR	95%CI
Dry cough	0,98	0,016	2,67	1,1-5,96
Arterial hypotension	3,14	0,02	23,2	1,56-347,1
Insidious onset	1,19	0,01	3,28	1,19-8,14
Bilateral radiological involvement	1,13	0,02	3,12	1,1-8,14
Extension of pulmonary lesions two and more pulmonary fields	1,34	0,003	3,82	1,59-9,17
Interstitial opacities	1,8	0,0001	6,06	2,38-15,41

4. EVOLUTIONARY ASPECTS OF PNEUMONIA IN IMMUNOCOMPROMISED

4.1 Estimation of applicability of prognostic scores in immunocompromised pneumonia

The mortality rate from immunocompromised pneumonias remains one of the highest among opportunistic infections in these patients. Limited studies have investigated the applicability of prognostic scores, both in terms of the need for IMV and the assessment of mortality risk. The prognostic scores selected in this study are validated for community-acquired pneumonia in immunocompetent patients. The analyzed prognostic tools include classic score such as CURB65, CRB65, and PSI, as well as the most recently implemented tools like IDSA/ATS, SCAP, SMART-COP, SMRT-CO, SOAR, CAP-PIRO and ADROP. The evaluation of their prognostic role involved an analysis of each score individually and a comparison between the scores.

Assessment of the application of prognostic scores to assess the need for invasive mechanical ventilation

A high rate of IMV was recorded in patients classified in the high-risk categories of the IDSA/ATS, SCAP, SMART-COP, SMRT-CO, SOAR, CURB65, CRB65 risk

scores. For IDSA/ATS and SMRT-CO, all patients who required IMV were classified in the high risk category for severe pneumonia. In contrast, for the CAP-PIRO score, over 60% of the patients who required IMV were included in the low and medium risk groups, while in the case of the ADROP score, 90% of patients requiring IMV were classified as low or medium risk. When applying the CURB65 score was applied to assess the need for invasive mechanical ventilation, the area under the curve ($AUC_{CURB65)}$ was 0,91. The critical value of the CURB-65 score, corresponding with optimal sensitivity and specificity, was found in risk class I (sensitivity 87,5%; specificity 79,49%). For the classes corresponding to severe pneumonia (CURB-65 >3), there was a significant reduction in sensitivity (43,75%). The CRB65 score demonstrated good discriminatory power in the case of estimating the need for IMV, with AUC_{CRB65} of 0,89. The threshold value obtained corresponded to the risk class I of the score. However, when considering the optimal threshold for severe pneumonia (CRB65 >3), sensitivity decreased significantly (6,25%) and the negative predictive values remained just above 80%. The PSI score exhibited good discriminatory power (AUC_{PSI} 0,84 in ROC analysis). The optimal sensitivity and specificity values were recorded at 87% and 66%, respectively, for class III of the score (threshold value). It is important to note that when the threshold value was raised from class III to classes IV and V (which correspond to severe pneumonia in the original validation studies), sensitivity decreased below 50%. For the score SMART-COP, the $AUC_{SMART-COP}$ was 0,89. The score with optimal sensitivity and specificity corresponded to risk class 2 with sensitivity 100%, specificity 65%, and NPV at 100%. This threshold value indicated an increased risk of severe pneumonia development. The AUC values for other recently implemented scores also demonstrated good discriminatory power: $AUC_{SMRT-CO}$ - 0,89 and AUC_{SOAR} – 0,81. Very good AUC values were obtained for the IDSA/ATS and CAP-PIRO scores, with $AUC_{IDSA/ATS}$ – 0,93 and $AUC_{CAP-PIRO}$ – 0,91, respectively. However, statistical superiority over the other scores analyzed was not demonstrated (Table 4). For CAP-PIRO, the threshold values were lower than those corresponding to severe pneumonia, and the severe progression classes, sensitivity values were reduced (37,5% and 6,25%). The SCAP score exhibited good discriminatory power (AUC_{SCAP} – 0,89) when assessing the need for the IMV. The obtained threshold value of the score corresponded to its moderate risk class (10-19 points), with sensitivity at 68,75% and specificity at 93,5%. Comparative analysis of these scores revealed that the SOAR score demonstrated statistically higher efficiency (Table 4). For classical scores (CURB65, CRB65, PSI), as well as for more recently implemented scores (SCAP, CAP-PIRO, SMART-COP, SMRT-CO, ADROP), no statistically significant differences were found. However, some clarification is

necessary. For scores corresponding to the high risk class of death, reduced sensitivity was observed for the prognosis of death PSI > IV – 50%, CURB65 > 3 – 50% and CRB65 > 2 – 64%. Similarly, for CAP-PIRO, SCAP, SMART-COP and SOAR, the sensitivity values for high-risk classes of severe pneumonia were extremely low (37,5%; 0%, 56,25% and 43,75%, respectively). However, scores with high specificity and sensitivity corresponded to the classes with medium or low risk. Only in the IDSA/ATS score demonstrated optimal sensitivity and specificity values corresponding to a high risk of severe pneumonia.

Evaluation of the application of the scores for the prognosis of death

A comparison of mortality rate within the risk groups of CURB65, CRB65, SCAP, SMART-COP, and SOAR revealed a progressive increase in mortality. However, in the low or medium risk classes of PSI, CURB65, SMART-COP, and CAP-PIRO, over 40% of all deaths were observed, with the ADROP score including 100% of deaths in these categories. Analysis of the mortality rate for the IDSA/ATS and SMRT-CO scores revealed that all cases of death were included in high-risk classes of severe pneumonia progression. For the CRB65 score, the high-risk class accounted for 80% (12/15) of the total deaths, with 3/15 cases (20%) classified in the medium risk group, a pattern also observed with the SOAR score. When assessing the prognosis of death, the CURB65 score demonstrated excellent discriminatory power (AUC_{CURB65} – 0,93). The threshold value corresponding to class 3 of the CURB65 score indicated a high risk of death, but with low sensitivity (46,67%) and NPV of 89,5%. The CRB65 score also showed excellent discriminatory power for predicting death (AUC_{CRB65} – 0,95). The threshold value of the CRB65 score corresponded to class 1 and when the threshold for severe pneumonia progression (CRB65>2) was applied, sensitivity decreased significantly (60%) and NPV is remained high (91,8%).

The assessment of the PSI score in predicting death demonstrated good discriminatory power (AUC_{PSI} – 0,84), with the threshold value corresponding to class III of the score, yielding a sensitivity of 93,3% and specificity of 66,%.However, when the threshold value was raised from class III to classes IV and V (which correspond to severe pneumonia in the original validation studies), the sensitivity of the score decreased to 46%. The AUC for the SMRT-CO score, when assessing the likelihood of death, was excellent ($AUC_{SMRT\text{-}CO}$ – 0,91). The optimal sensitivity and specificity values (100% and 66,6%, respectively) corresponded to the high risk class of the – SMRT-CO≥2 score. For the SMART-COP score, the $AUC_{SMART\text{-}COP}$ value was very good (0,92), but the threshold value corresponded to the middle severity class (class 3). Increasing the threshold value to class 5 resulted significant reduction in sensitivity to 60%. The SOAR score, in contrast, exhibited the lowest AUC_{SOAR} values, with low

sensitivity and specificity values (40%) in the classes corresponding to a severe course of pneumonia – 40%.

Table 4. AUC comparison of the analysed scores (p values are presented)

	CURB65	**CRB65**	**PSI**	**SCAP**	**CAP PIRO**	**IDSA/ ATS**	**SOAR**	**SMART-COP**	**SMRT-CO**	**ADROP**
CURB65		0,5	0,1	0,7	0,6	0,5	0,07	0,7	0,6	0,6
CRB65	*0,7*		0,3	0,6	0,8	0,3	0,2	0,9	0,9	0,9
PSI	***0,008***	***0,05***		0,1	0,1	0,06	0,6	0,3	0,3	0,4
SCAP	*0,4*	*0,4*	*0,2*		0,8	0,6	**0,0007**	0,5	0,5	0,1
CAPPIRO	*0,1*	*0,2*	*0,6*	*0,3*		0,7	**0,05**	0,6	0,6	0,4
IDSA/ATS	*0,9*	*0,7*	*0,07*	*0,6*	*0,2*		**0,04**	0,2	0,2	0,26
SOAR	***0,003***	***0,007***	*0,2*	***0,002***	***0,04***	***0,01***		0,1	0,1	0,07
SMART-COP	*0,7*	*0,6*	*0,1*	*0,8*	*0,2*	*0,7*	***0,006***		0,9	0,9
SMRT-CO	*0,6*	*0,5*	*0,1*	*0,8*	*0,2*	*0,6*	***0,005***	0,9		0,9
ADROP	*0,2*	*0,1*	*0,4*	*0,4*	*0,7*	*0,3*	***0,02***	0,9	0,5	

- Common numbers are p-values for AUC comparison obtained when applying scores to assess the probability of death occurring
- Numbers with Italic represent the p-values for the AUC comparison obtained when applying the scores to assess the need for applying the VMI

The discriminatory power of the CAP-PIRO score in predicting risk of death was good ($AUC_{CAP\text{-}PIRO}$ – 0,87). Optimal sensitivity and specificity values corresponded to the low-risk class of severe pneumonia. However, the CAP-PIRO score demonstrated inferior discriminatory power compared to the other scores analyzed (Table 4). Statistically significant differences were found when comparing $AUC_{CAP\text{-}PIRO}$ to AUC_{SOAR}. The discriminatory power for predicting death was superior in the CURB-65, CRB-65, SCAP, CAP-PIRO, and IDSA/ATS scores compared to SOAR. In contrast, the PSI score showed inferior discriminatory power when compared to CRB-65 and CURB-65. Notably, the threshold value with optimal sensitivity and specificity for the SMRT-CO score only corresponds to high risk classes for severe progression of pneumonia to immunocompromised patients.

4.2 Predicators of unfavorable evolution of pneumonias in immunocompromised patients

Predictors of the fatal course of pneumonia in immunocompromised hosts

To identify risk factors associated with fatal course of pneumonia, the PI cohort was divided into two groups: survivors (S) – 81 patients and deceased (D) – 15 patients. The variables that significantly differentiated the two groups were as follows: in the D group, patients who required ICU treatment were more prevalent, along with physical

signs of respiratory failure (mMRC IV dyspnea, respiratory rate > 30 b/min, SaO2 < 92%) and cardiovascular failure (blood pressure < 90/60 mm Hg). The majority patients in this group also required the application of invasive mechanical ventilation. Confusion/obnubilation, oliguria, and bronchial syndrome manifestations (e.g. bronchial rales), were more common among deceased subjects. Comparative analysis of laboratory parameters revealed that the deceased group had a higher frequency of inflammatory syndrome, evidenced by leukocytosis over $25*10^9$/l, an elevated neutrophil/lymphocyte ratio, as well as increased levels of urea and LDH. No significant differences were observed in imaging characteristics such as multilobar, bilateral, alveolar lesions, interstitial or mixed-type lesions, cavitary syndrome or pleurisy, between the two groups. All clinical, radiographic and laboratory variables that significantly differentiated the surviving and deceased groups were subsequently included in a logistic regression model.

Table 5. Risk factors for death in pneumonia

	Coefficient	**p**	**OR**	**95%CI**
Dypnea mMRC IV	2,54	0,01	12,7	1,8-90,9
Confusion	3,39	0,02	29,7	1,43-616,5
Oliguria	2,7	0,01	15,4	1,6-148,9
HIV infection	2,87	0,02	17,7	1,38-227
Coma	4,7	0,0003	119,7	8,84-1621
Leukocytosis > $25*10^9$/l	3,33	0,02	27,9	1,5-520,2
ARDS	3,39	0,02	29,7	1,43-616,5
IMV	5,43	0,0001	228	20-2597

Thus, the following variables with a prognostic significance for death were identified in immunocompromised patients with pneumonia: mMRC IV dyspnea, confusion, oliguria, HIV infection, coma, leukocytosis > $25*10^9$/l, ARDS, and the needed for IMV (Table 5). The AUC of the generated logistic model was 0,97 (95% CI 0,9-0,96), which demonstrating the high discriminatory efficiency for identifying potentially fatal cases. Among the variables included in the model coma, a duration of IMV ≥ 48 hours, and ARDS showed the highest prognostic power. The presence of any of these factors significantly increases the likelihood of death in the IP cohort.

GENERAL CONCLUSIONS

1. The etiology of pneumonia in immunocompromised patients is diverse. Among the most common pathogens identified in this study were bacterial agents, including *E. coli*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *S. pneumoniae* and *S. haemolyticus*; fungal agents such as *P. jirovecii, C.neoformans,* and *Aspergillus spp*. as well as viruses like SARS-CoV-2 and Cytomegalovirus.
2. The clinical presentation of pneumonia in immunocompromised patients differs from that of community-acquired pneumonia in immunocompetent individuals. It is characterized by low-grade fever, dry cough, progressive dyspnea, and hemoptysis. Symptoms have an insidious onset, often leading to a delayed diagnosis, which typically occurs at a stage when complications - such as acute respiratory failure, abscess formation, or sepsis – have already developed.
3. The resolution of pulmonary infiltrates in immunocompromised patients is slower compared to immunocompetent individuals. The diverse etiology, the presence of interstitial opacities (reticular, ground-glass), and the association with pulmonary consolidations on imaging examinations are important factors contributing to this delay.
4. Pneumonia in immunocompromised patients presents distinct clinical and imaging features compared to community-acquired pneumonia. These include an insidious onset, dry cough, and arterial hypotension, as well as radiological changes such as bilateral lung involvement, the extension of pulmonary lesions across two and more lung fields, and diffuse interstitial opacities. The presence of this clinical and imaging pattern may facilitate the early diagnosis of pneumonia in immunocompromised individuals.
5. The prognostic scores analyzed (CURB-65, CRB-65, PSI, SMART-COP, IDSA/ATS, SCAP, SOAR, CAP-PIRO, ADROP) underestimate the severity of pneumonia in immunocompromised patients and the likelihood of mortality. Among these, only the SMRT-CO score demonstrated the highest accuracy in assessing the need for invasive mechanical ventilation and the risk of death in patients with severe pneumonia.
6. Delayed medical presentation, a clinical picture influenced by immunosuppression, manifestations of the underlying disease, and varied imaging findings contribute to a challenging and delayed diagnosis, leading to severe disease progression and a high mortality rate.
7. The significant presence of opportunistic pathogens (*P.jirovecii*, *C.neoformans, Cytomegalovirus*) in the etiologic spectrum of pneumonia justifies the need for advanced diagnostic methods, such as microscopic, bacteriological, serological and

molecular-genetic techniques. The widespread application of these methods would facilitate early etiological diagnosis and the prompt initiation of treatment.

8. The diagnosis of pneumonia in immunocompromised individuals is often challenging. Given the varied clinical manifestations and atypical radiological findings, additional investigations such as high-resolution computed tomography and histological examination of lung tissue are often required for an accurate diagnosis.

PRACTICAL RECOMMENDATIONS

1. To enhance the diagnostic accuracy of microbiological tests in immunocompromised individuals, it is recommended to use a variety of diagnostic specimens, including spontaneous and/or induced sputum samples, as well as invasively collected bronchial specimens (bronchial aspirate, bronchoalveolar lavage).
2. The widespread implementation of fungal and opportunistic pathogen detection techniques in HIV-infected patients (including microscopy, cultures, serology, and molecular-genetic tests) is essential for accurate etiological identification and the selection of targeted treatment.
3. To assess the need for invasive mechanical ventilation and estimate mortality risk, the SMRT-CO prognostic score is recommended. In this context, the limited prognostic value of the CURB65 score in evaluating pneumonia severity in immunocompromised patients should be considered.
4. The use of high-resolution computed tomography of the chest, in addition to standard radiographic examinations, is essential for the accurate assessment of severe pneumonia extent, the characterization of imaging lesion types, and the detection of potential complications in immunocompromised patients.

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ADNOTARE

Scutaru Evghenia "Prezentarea clinică și diagnosticul pneumoniilor la imunocompromiși",
teză de doctor în științe medicale,
Chișinău, 2025

Structura tezei: teza este expusă pe 121 pagini text de bază ce include introducere, 5 capitole și concluzii. Lucrarea citează 245 surse bibliografice, fiind ilustrată prin 48 tabele, 11 figuri, 1 anexă. Rezultatele obținute sunt publicate în 20 lucrări științifice.

Cuvinte cheie: pneumonie la imunocompromiși, gazdă imunodeprimată, scoruri prognostice, factori prognostici.

Domeniul de studiu: 321.01 Boli interne (cu specificarea: Pulmonologie)

Scopul studiului: cercetarea particularităților clinice și paraclinice ale pneumoniilor la imunocompromiși și elaborarea recomandărilor pentru optimizarea managementului.

Obiectivele studiului: Studierea aspectelor etiologice ale pneumoniilor la imunocompromiși; Evidențierea particularităților clinice și paraclinice ale pneumoniilor la subiecții imunocompromiși, în funcție de cauza imunosupresiei; Evaluarea rolului scorurilor clinice în managementul pneumoniilor la imunocompromiși; Evidențierea dificultăților de management a cazului de pneumonie la gazda imunocompromisă; Elaborarea recomandărilor practice pentru managementul pneumoniilor la persoanele imunocompromise în funcție de cauza imunosupresiei.

Noutatea și originalitatea științifică: a fost evaluată aplicabilitatea și relevanța scorurilor clinice de severitate a pneumoniilor la persoanele cu statut imun compromis în condițiile serviciului medical din Republicii Moldova, a fost analizată structură etiologică a pneumoniilor la imunocompromiși în dependență de gradul și cauza imunosupresiei, au fost stabilite interrelații între factorii de prognostic și evoluția nefavorabilă a pneumoniilor la pacienții cu imunitate compromisă.

Problema științifică soluționată în teză: rezultatele studiului au permis elaborarea algoritmilor de conduită medicală. A fost evidențiat impactul spectrului de investigații accesibile la diferite etape de asistență medicală asupra managementului pneumoniei la imunocompromiși.

Semnificația teoretică și valoarea aplicativă a lucrării: evaluarea aspectelor clinico-evolutive ale PI a permis elaborarea recomandărilor practice privind managementul pneumoniei la persoanele cu imunosupresie.

Implimentarea rezultatelor științifice: Recomandările practice sunt utilizate în secția Ftiziopneumologie a IMSP IFP "Chiril Draganiuc", de asemenea în secția Pneumologie a IMSP SCM "Arhanghelul Mihail", și în procesul didactic de pregătire a cadrelor medicale la Disciplina pneumologie și alergologie, Departamentul Medicină Internă din IP USMF "Nicolae Testemițanu".

АННОТАЦИЯ

диссертации соискателя Скутару Евгения "Клиническая картина и диагностика пневмоний у лиц с иммунодефицитом", докторская диссертация по медицинским наукам, Кишинев, 2025

Структура диссертации: диссертация представлена на 121 страницах, включает введение, 5 глав и выводы. Библиография состоит из 245 источников. Материалы диссертации проиллюстрированы 48 таблицами, 11 рисунками и 1 приложения. По теме диссертации опубликованы 20 научных работы.

Ключевые слова: пневмонии у лиц с иммунодефицитом, иммуносупрессия, оценочные шкалы, прогностические факторы.

Область обучения: 321.01 Внутренние болезни (со спецификацией: пульмонология).

Цель исследования: исследование клинических и параклинических особенностей пневмоний у лиц с иммунодефицитом и разработка рекомендаций по оптимизации диагностики и лечения. **Задачи исследования:** Изучение этиологических аспектов пневмоний у больных с иммунодефицитом; Выявление клинических и параклинических особенностей пневмоний у лиц с иммунодефицитом в зависимости от причины иммунодефицита; Оценка роли клинических показателей в лечении пневмоний у лиц с иммунодефицитом; Выявление трудностей в ведении пневмониий у пациентов с иммунодефицитом; Разработка практических рекомендаций по лечению пневмоний у иммуносупрессивных пациентов в зависимости от причины иммунодефицита.

Научная новизна и оригинальность: была произведена оценка применимости и актуальности оценочных шкал тяжести пневмоний у больных с иммунодефицитом в условиях медицинской службы Республики Молдова, проанализирована этиологическая структура пневмоний у иммуносупрессивных пациентов в зависимости от тяжести и причины иммунодефицита, установлена взаимосвязь между некоторыми прогностическими факторами и неблагоприятным течением пневмоний у пациентов с ослабленным иммунитетом. Решенная научная проблема: результаты исследования позволили разработать алгоритмы тактики ведения пациентов с пневмониями в условиях иммунодефицита. Было отмечено влияние спектра исследований, доступных на разных этапах лечения, на ведение пневмоний у пациентов с ослабленным иммунитетом. **Теоретическая значимость и практическое применение:** оценка клинических и эволюционных аспектов ИП позволила разработать практические рекомендации по ведению пневмоний у лиц с иммунодефицитом.

SUMMARY

Scutaru Evghenia "Clinical presentation and diagnosis of pneumonia in immunocompromised",
PhD thesis in medicine,
Chisinau, 2025

Thesis structure: the thesis is written on 121 pages of main text including introduction, 5 chapters and conclusions. The manuscript cites 245 bibliographic references, and is illustrated by 48 tables, 11 figures. The thesis results are published in 20 scientific papers.

Keywords: pneumonia of immunocompromised, immunosuppressed host, prognostic scores, prognostic factors.

Domain of study: 321.01 Internal Medicine (Pulmonology)

Goal of the research: to investigate the clinical manifestations and paraclinical peculiarities of pneumonia in immunocompromised patients and to develop recommendations for optimizing management.

Objectives of research: To study the etiological aspects of pneumonia in immunocompromised hosts; Highlighting the clinical and paraclinical presentation of pneumonia of immunocompromised individuals, depending on the cause of immunosuppression; Determining the clinical and imaging aspects of pneumonia in immunosuppressed patients; Appreciate the usefulness of common prognostic scores applied in pneumonia in immunocompromised individuals. (5) Identification of the management difficulties in cases of pneumonia of the immunocompromised hosts. (6) Developing practical recommendations for the management of pneumonia in immunocompromised hosts based on the cause of immunosuppression.

Novelty and originality of research: for the first time in the Republic of Moldova, research on pneumonia in immunocompromised patients was conducted. The study evaluated the applicability and relevance of clinical severity scores in hospital conditions, analyzed the etiological structure of immunocompromised pneumonias based on the degree and cause of immunosuppression, and established the interrelations between prognostic factors and the unfavorable evolution of pneumonia in patients with compromised immunity.

Scientific problem addressed in the thesis: the results of the study have led to the development of diagnostic criteria and algorithms for pneumonia in immunocompromised hosts. The impact of the spectrum of investigations available at different healthcare stages on the management of pneumonia in immunocompromised individuals was emphasized.

SCUTARU Evghenia

CLINICAL PRESENTATION AND DIAGNOSIS OF PNEUMONIA IN IMMUNOCOMPROMISED

321.01 Internal Medicine (Pneumology)

Summary of the doctoral thesis in medical sciences

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