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COVID 19 AND NON-COVID PNEUMONIA: STATISTICAL ANALYSIS AND MORPHOLOGICAL CHARACTERISTICS ACCORDING TO SECTIONAL STUDIES (2020–2024)

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Relevance. COVID-19 remained a leading infectious disease shaping global and national mortality, including Ukraine in 2020–2024. By 2025, confirmed cases exceeded 5.5 million, with over 112,000 deaths (≈2,600 per 1 million). Mortality was highest among elderly patients, underscoring their vulnerability. Despite a decline in severe cases in 2025, morphological aspects of pulmonary injury remain crucial for differential diagnosis and prognostication.

Objective. To identify morphological features of pneumonia in deceased patients of different ages and sexes during COVID-19 and post-COVID periods (2020–2024), considering disease duration.

Materials and Methods. A retrospective cohort study analyzed 1,664 deaths from COVID-19 and complications in Odesa. Autopsies (n = 299) were performed using standard histological techniques per Ministry of Health of Ukraine regulations. Cases were stratified into five yearly groups (2020–2024) and subdivided into 10-year age intervals. Sex distribution and morphological features of pulmonary injury were assessed relative to hospitalization duration.

Results. Two mortality peaks occurred in 2021 and 2023. The highest number of deaths was in the 61–70 and 71–80 age groups (876 cases, >52 %). Pulmonary changes included bilateral multisegmental involvement, interstitial edema, microthrombosis of pulmonary arterial branches, and hyaline membrane formation in groups 1–3. In the post-COVID period, most cases showed bacterial pneumonia with septic complications, without confirmed SARS-CoV-2 infection.

Conclusions. COVID-19 is associated with a distinct complex of morphological lung changes determining severity and fatal risk. In the post-COVID period, mortality shifted toward bacterial pneumonia, emphasizing the need for standardized laboratory verification and morphological monitoring to ensure accurate differential diagnosis and optimize clinical management.

Keywords: COVID-19, pneumonia, autopsy, lung morphology, thrombosis.

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COVID-19 ТА НЕКОВІДНІ ПНЕВМОНІЇ: СТАТИСТИЧНИЙ АНАЛІЗ І МОРФОЛОГІЧНА ХАРАКТЕРИСТИКА ЗА ДАНИМИ СЕКЦІЙНИХ ДОСЛІДЖЕНЬ (2020–2024 РР.)

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Актуальність. COVID-19 у 2020–2024 рр. визначав структуру смертності в Україні та світі. Станом на 2025 рік зареєстровано понад 5,5 млн випадків і 112 тис. смертей (2600 на 1 млн населення), найбільше серед осіб 61–80 років. Проведено ретроспективне

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Стаття поширюється на умовах ліцензії

дослідження 1664 летальних випадків у м. Одеса, включно з 299 автопсіями. Виявлено два піки смертності (2021, 2023), морфологічні зміни легень характеризувалися двостороннім полісегментарним ураженням, інтерстиційним набряком, мікротромбозами та гіаліновими мембранами. У постковідний період превалювали бактеріальні пневмонії із септичними ускладненнями. Отримані дані підтверджують специфічний комплекс морфологічних змін при COVID-19, що визначає тяжкість перебігу та високий ризик летальних наслідків, і підкреслюють необхідність стандартизованої лабораторної верифікації та морфологічного контролю для коректної диференційної діагностики й оптимізації клінічної тактики.

Ключові слова: COVID-19, пневмонія, автопсія, морфологія легень, тромбоз

Introduction

Pneumonia remains one of the leading causes of mortality worldwide, in Europe, and in Ukraine, showing complex dynamics depending on its etiology – COVID-19, bacterial, and non-COVID viral forms. According to the World Health Organization, more than 2.5 million deaths from pneumonia are registered globally each year, accounting for about 15 % of all deaths from infectious diseases [1]. Community-acquired pneumonia (CAP) continues to represent a major cause of hospitalization and mortality among adults. In the United States, more than 1.4 million emergency department visits are attributed to CAP annually, and the 30-day mortality among hospitalized patients is approximately 6 % [2]. Mortality rates are particularly elevated in elderly individuals and those with chronic comorbidities, underscoring the persistent burden of the disease and the need for improved preventive and therapeutic strategies. COVID-19 between 2020 and 2024 significantly altered the structure of mortality from respiratory infections. In Ukraine, by 2025 the number of confirmed cases exceeded 5.5 million, while deaths surpassed 112,000, corresponding to approximately 2,600 deaths per 1 million population [3]. The highest number of deaths was recorded in the 61–80 age groups, which is consistent with European data indicating the particular vulnerability of elderly patients [4].

In the post-COVID period, there has been a rise in bacterial pneumonias, frequently complicated by sepsis. *Streptococcus pneumoniae* and *Staphylococcus aureus* remain the leading etiological agents, and their role in mortality has been confirmed by both Ukrainian and European studies [5]. At the same time, non-COVID viral pneumonias, particularly those associated with influenza and respiratory syncytial virus, show seasonal peaks in mortality. During 2022–2023, these overlapped with COVID-19 waves, complicating differential diagnosis [6].

Morphological studies continue to be a key tool for clarifying pathogenesis, predicting disease course, and guiding optimal clinical management in patients with pneumonias of different origins.

Objective of the study. To identify the morphological features of pneumonia in deceased patients of different ages and sexes during the COVID-19 and post-COVID periods (2020–2024), to analyze their dynamics according to year of study and duration of hospitalization, and to assess sex-related differences, the relative risk (RR) and odds ratios (OR) of fatal outcomes across age groups.

Materials and Methods

The study examined cases of death caused by COVID-19 registered at three medical institutions in Odesa: Municipal Clinical Hospital No. 1, Municipal Clinical Hospital No. 10, and Municipal Hospital No. 8, from 2020 to 2024. Informed consent for the processing of personal data was obtained from all patients upon admission to the hospital and is documented in their medical records. A retrospective cohort analysis was conducted using data from 1,664 deceased individuals recorded in these databases, as well as autopsy results from 299 deceased patients with severe COVID-19 who had been hospitalized and received oxygen therapy – primarily via oxygen concentrators.

All cases were classified into five groups according to the year of death: 2020, 2021, 2022, 2023, 2024 (hereinafter referred to as 0, 1, 2, 3, 4, respectively). Additionally, all cases were divided into age subgroups with 10-year intervals (Table 1). Within each annual and age subgroup, an analysis was performed on the sex distribution of fatal outcomes between male and female patients.

Descriptive statistics were applied, including calculation of means, standard deviations (SD), medians, and quartiles. Absolute numbers (n) were complemented by relative indicators (%). Comparisons between age groups were performed: differences between men and women were assessed using Pearson's χ^2 test; one-way analysis of variance (ANOVA) was used to compare mean values across years, while Fisher's exact test was applied in cases

Table 1

Number of deceased patients with pneumonia by age and sex, 2020–2024 abs. (n)

Groups	2020 abs. (n)			2021 abs. (n)			2022 abs. (n)			2023 abs. (n)			2024 abs. (n)			Total abs. (n)		
Sex Age (years)	Tot.	m.	f.	Tot.	m.	f.	Tot.	m.	f.	Tot.	m.	f.	Tot.	m.	f.	Tot.	m.	f.
21–30	**1**	–	1	**2**	1	1	**–**	–	–	**2**	1	1	**2**	1	1	**7**	3	4
31–40	**2**	2	–	**4**	2	2	**3**	2	1	**7**	3	4	**2**	1	1	**18**	10	8
41–50	**7**	4	3	**93**	38	55	**16**	8	8	**81**	43	38	**8**	6	2	**205**	99	106
51–60	**31**	17	14	**167**	84	83	**13**	6	7	**85**	43	42	**11**	7	4	**307**	157	150
61–70	**43**	24	19	**196**	96	100	**23**	9	14	**160**	77	83	**16**	9	7	**438**	215	223
71–80	**33**	18	15	**201**	93	108	**35**	19	16	**143**	101	42	**26**	16	10	**438**	247	191
≥81	**23**	10	13	**127**	59	68	**13**	3	10	**60**	30	30	**28**	10	18	**251**	112	139
Total abs. (n)	**140**	75	65	**790**	363	427	**103**	47	56	**538**	298	240	**93**	50	43	**1664**	833	831

of small sample sizes. Risk assessment was conducted by calculating RR and OR of death in men compared with women for each age group. For RR and OR, 95 % confidence intervals (CI) were reported. Mortality trends across years were evaluated using linear regression analysis. The relationship between age and mortality was assessed using Pearson's correlation coefficient (r). Statistical significance was defined at $p < 0.05$. All calculations were performed according to the methodology described by Antomonov [7], using standard statistical analysis software packages (SPSS v.26.0, R v.4.3.0).

For morphological examination, autopsy material in all groups was collected from the most affected areas of lung parenchyma, specifically: the most consolidated regions saturated with exudate – most often fragments from the lower lobes of both lungs – pulmonary vessels with thrombosis, and areas containing small bronchi with intraluminal exudate.

The specimens were embedded in paraffin blocks. Histological sections were stained using standard techniques. Sampling was performed in accordance with the requirements of the Order of the Ministry of Health of Ukraine dated March 28, 2020, No. 722 "Standards of Medical Care: Coronavirus Disease (COVID-19)" [8].

Morphological examination was conducted using standard methodologies applied in pathology departments of the corresponding specialization, according to the Order of the Ministry of Health of Ukraine dated September 6, 2021, No. 1877 "On the Approval of the Procedure for Performing Pathological Autopsies" [9]. The study was conducted in compliance with the principles of the Ethical Code of the World Medical Association (Declaration of Helsinki).

Research results and their discussion

The study showed that in group 0, the number of deaths reported by Municipal Clinical Hospital No. 1, Municipal Clinical Hospital No. 10, and Municipal Hospital No. 8 in Odesa totaled 140, of which 65 were women (46.42 %) and 75 were men (53.58 %). Among these, only 3 patients were under the age of 40(2.14 %), while the number of deaths in the 51–80 age groups reached 107, accounting for 76.42 %, with a predominance in the 61–70 age group – 43 cases (30.71 %). Autopsy was performed in 30.47 % of the deceased in this group. Comparison between subgroups revealed that the χ^2 test did not demonstrate statistically significant differences between sexes ($p>0.05$). RR for males in the 51–70 age groups was approximately 1.2–1.3, with 95 % confidence intervals including unity. Trend analysis demonstrated that linear regression confirmed an increase in the number of deaths with advancing age ($r = 0.82$, $p < 0.001$).

In group 1, the number of deaths increased 5.6 times compared to the previous group, totaling 790 cases. Of these, 363 were men (45.94 %) and 427 were women (54.05 %). There were 6 deceased individuals under the age of 40(0.76 %). The largest share of deaths occurred in the 71–80 age subgroup, with 201 cases (25.44 %). Autopsies were performed in only 14.16 % of cases. In this group, the χ^2 test revealed a statistically significant difference in the 41–50 age subgroup ($p < 0.05$), where females accounted for 59.1 % of deaths. OR for male mortality in the 51–60 age subgroup was 1.3(95 % CI 1.05–1.62). Trend analysis demonstrated that linear regression also confirmed an increase in the number of deaths with advancing age ($r = 0.85$, $p < 0.001$).

In group 2, the number of registered deaths sharply declined to 103. The sex distribution among the deceased mirrored that of group 1: 47 men (45.64 %) and 56 women (54.36 %). The highest mortality was observed in the 71–80 age subgroup, with 35 deaths (33.98 %), including 19 men. Autopsies were performed in 24.32 % of cases. Comparison between subgroups demonstrated that the χ^2 test revealed a statistically significant sex difference in the 81+ year subgroup ($p < 0.05$). OR for male mortality in the 61–70 age subgroup was 1.5(95 % CI 1.02–2.21), indicating a significantly higher risk. Trend analysis showed that the correlation between age and the number of deaths remained strong, with linear regression confirming this association ($r = 0.84$, $p < 0.001$).

In group 3, the total number of deaths from pneumonia and its complications was 538. Of these, 298 were men (55.39 %) and 240 were women (44.61 %). The number of deaths in the 61–70 and 71–80 age subgroups was almost double that of adjacent age groups – 160 and 143 respectively. Specifically, the highest number of deaths occurred in the 61–70 subgroup, where 77(48.12 %) were men and 83(51.88 %) were women. Meanwhile, the number of deaths in the 71–80 age subgroup remained consistent with other groups; however, here the male mortality rate reached 101 cases, accounting for 70.63 % of that subgroup. Autopsies were performed in 15.63 % of cases. In this group, comparison between subgroups indicated a tendency toward a higher proportion of male deaths in the 71–80 age subgroup; however, the differences were not statistically significant ($p>0.05$). Risk assessment showed that RR for male mortality in the 61–70 age subgroup was 1.2(95 % CI 0.95–1.52). Linear regression analysis confirmed a consistent age-related increase in the number of deaths ($r = 0.81$, $p < 0.001$).

Group 4 included 93 fatal cases of pneumonias of various etiologies. In this group, 57 autopsies were performed, representing 61.29 % of the total – significantly exceeding the autopsy rates in other groups. Among the deceased, 50 patients (53.76 %) were male and 43(46.23 %) female. There were 4 deceased patients under the age of 40(4.30 %), while the highest number of deaths occurred in the 71–80 age subgroup – 28 cases (40.89 %). Notably, in this group, the average duration of hospitalization for nearly half the patients was 5 days, with the shortest being 45 minutes and the longest 19 days. In this group, the χ^2 test revealed a statistically significant difference in the 81+ year subgroup ($p < 0.05$). OR for male mortality relative to females in the 61–70 age subgroup was 1.3(95 % CI 0.95–1.78). The correlation between age and the number of deaths remained strong, with linear regression confirming this association ($r = 0.83$, $p < 0.001$).

Analysis of the data on deceased patients with COVID-19 revealed two peaks in the number of fatal cases, occurring in 2021 (group 1) and 2023 (group 3) (Fig. 1). Age-related indicators in these groups follow similar trends: the highest number of deaths was recorded

in the 61–70 and 71–80 age subgroups (Fig. 2). The sex distribution of deceased patients varied. In group 1, women predominated among the deceased, whereas in group 3, the majority were men. In the remaining groups, the difference between sexes was minimal.

The number of deaths among individuals aged 21–30 and 31–40 remained consistently low across all years. Throughout the entire study period, the main burden of mortality fell on the elderly and senile age groups, specifically: 61–70 years: 438 cases (26.3 %); 71–80 years: 438 cases (26.3 %); 81 and older: 251 cases (15.1 %). The highest number of elderly deaths occurred in 2021, with 524 deaths among individuals aged 61 and older, accounting for 66.3 % of all fatalities that year. One-way analysis of variance (ANOVA) revealed statistically significant differences in the mean number of cases across years ($p < 0.001$). The greatest burden was observed in 2021(790 cases), whereas in 2022 and 2024 the number of cases was markedly lower (103 and 93, respectively). These findings indicate sharp fluctuations in dynamics, most likely associated with external factors such as pandemic waves or changes in reporting systems.

Analysis of autopsy results revealed certain patterns in the development of morphological lung changes among the deceased, depending on the etiology and the time interval from disease onset to death. Identical changes were observed in groups 0, 1, 2, and 3; therefore, the description of these alterations was summarized collectively.

According to the pathological anatomy department data, the duration of hospital stay for patients in these groups who died from pneumonia and its complications ranged from 1 day to 1 month, most commonly between 10 and 17 days.

In most cases, bilateral polysegmental lung involvement was observed, affecting the middle and lower lobes of the right lung and the lower lobe of the left lung, with pathological foci predominantly located subpleurally (Fig. 3).

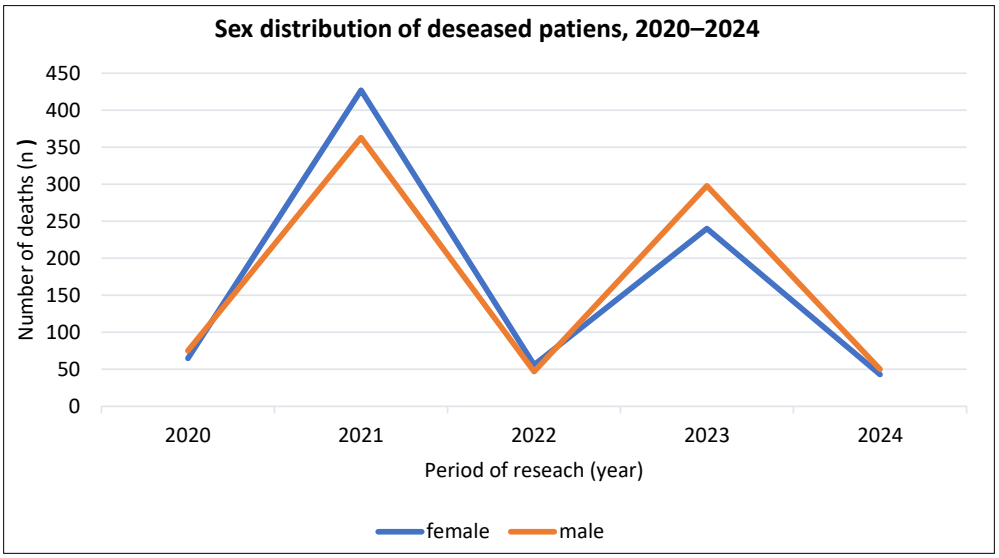


Fig. 1. Sex distribution of deceased patients, 2020–2024

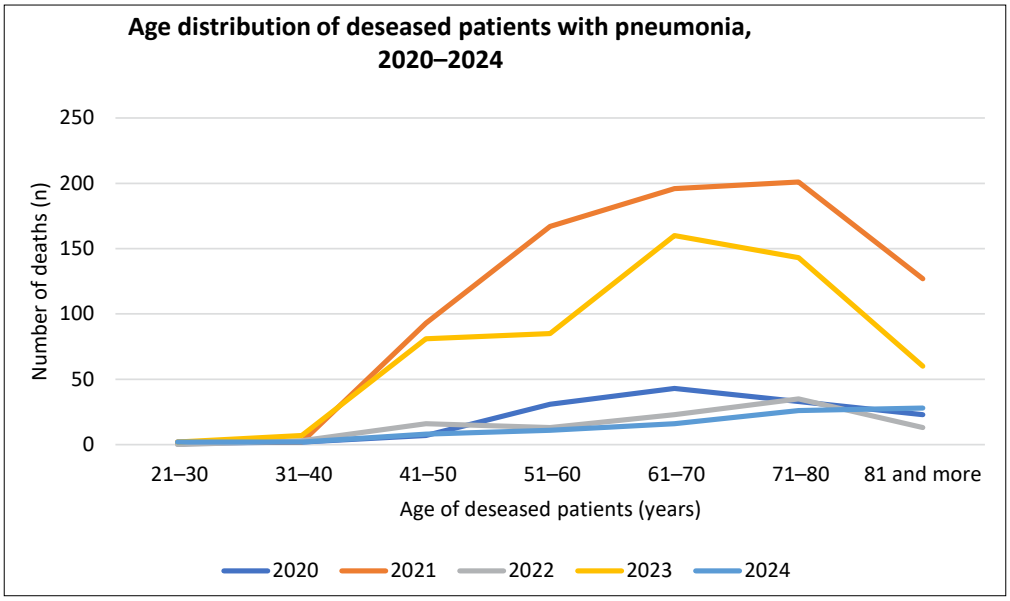


Fig. 2. Age distribution of deceased patients, 2020–2024

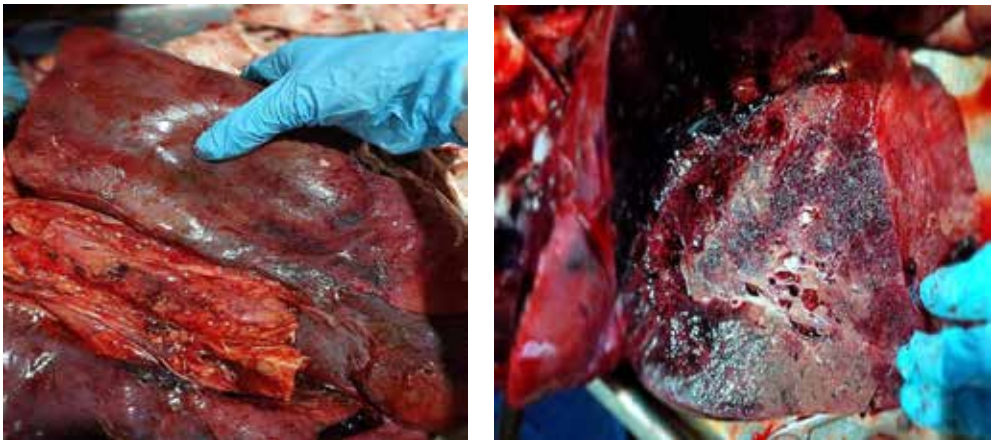


Fig. 3. Lungs of a patient with confirmed COVID-19, multiple areas of consolidation with a tendency to coalesce, without free exudate

In cases where the primary cause of death was cardiopulmonary failure, pronounced interstitial edema with a hemorrhagic component was observed, along with the formation of multiple thrombi in the small branches of the pulmonary artery (Figures 4, 5). These changes were noted during periods ranging from 5–7 days up to 2 weeks. In the early stages, desquamation of the bronchial and alveolar epithelium was observed. Additionally, perivascular and peribronchial lymphocytic infiltration developed, accompanied by a small number of polymorphonuclear leukocytes, macrophages, and erythrocytes.

Such morphological changes identified in the lung tissue of patients with COVID-19 exhibit a number of characteristic features. The constellation of these changes and their severity indicate that they are characteristic of this infection. In particular, the literature describes interstitial inflammation, diffuse alveolar damage, hyaline membrane formation, and microvascular thrombosis, which together form a typical morphological complex specific to coronavirus infection [10–12]. The Ukrainian autopsy experience provides valuable confirmation of the morphological hallmarks of severe COVID-19 lung injury. Matskevych et al. reported bilateral multisegmental involvement with pronounced interstitial edema, widespread microthrombosis, and the formation of hyaline membranes, all of which were strongly associated with fatal outcomes [13]. These findings emphasize the prognostic importance of morphological verification, particularly in cases where clinical and radiological data remain inconclusive. The study underscores that histopathological examination not only clarifies differential diagnoses but also contributes to risk stratification and therapeutic decision-making in critically ill patients.

Similar findings were reported in the multicenter prospective HISTOCOVID study ($n = 169$), where most patients with fatal COVID-19 demonstrated diffuse alveolar damage with the formation of hyaline membranes and microthrombosis of small vessels [14]. This confirms that the combination of interstitial edema and thrombosis represents a characteristic morphological complex of COVID-19, distinguishing it from classical bacterial pneumonias. Moreover, the authors noted certain morphological differences in the development of diffuse alveolar damage in COVID-19 compared with other viral pneumonias. Vascular injury in COVID-19-related lung pathology was observed more frequently than in conventional acute respiratory distress syndrome and influenza.

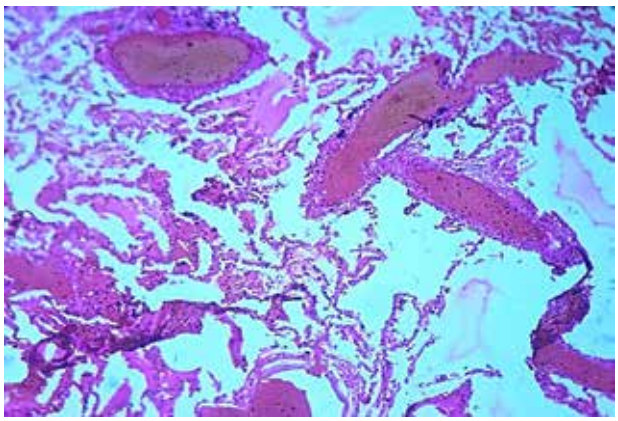


Fig. 4. Multiple thromboses of small branches of the pulmonary artery in the lungs of a patient with pneumonia associated with COVID-19. Hematoxylin and eosin staining. ×200

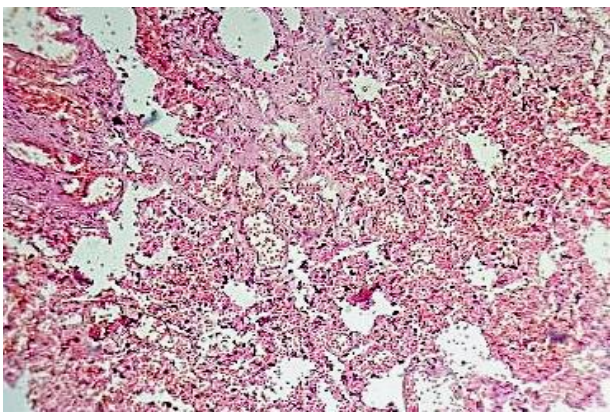


Fig. 5. Pronounced interstitial edema with numerous erythrocytes in the lungs of a patient with pneumonia associated with COVID-19. Hematoxylin and eosin staining. ×200

Our findings regarding the morphological changes in the lungs in COVID-19 are consistent with current evidence on the role of the cytokine storm in the pathogenesis of severe complications. In particular, Rasputniak et al. [15] emphasize that excessive production of pro-inflammatory cytokines, such as interleukin-1, interleukin-6, tumor necrosis factor-α, and VEGF, contributes to the development of systemic inflammation, endothelial dysfunction, and microvascular thrombosis, which explains the morphological features observed in our study.

Correlation of clinical records with autopsy findings revealed that in 20 % of cases the primary cause of death was multiple organ failure. In such cases, several characteristic pulmonary morphological features were observed. These included marked interstitial hemorrhagic edema of both lungs, multiple thromboses of pulmonary arterial branches, formation of hyaline membranes along the alveolar surfaces, and fibrosis of the lung parenchyma. These changes were typically identified within 2–3 weeks from disease onset (Fig. 6).

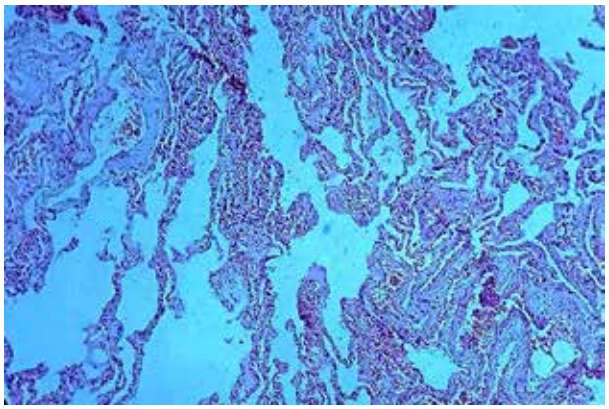


Fig. 6. Dilation of some alveoli, presence of hemorrhagic exudate, and hyaline-like deposits. Hematoxylin-eosin staining. ×200

Our analysis demonstrates that COVID-19 is associated with a distinct spectrum of morphological lung alterations, including bilateral multisegmental involvement, interstitial edema, microthrombosis of pulmonary arterial branches, and hyaline membrane formation. These changes define the severity of the disease course and explain the high risk of fatal outcomes. Importantly, such morphological features have also been confirmed in radiological observations, where ground-glass opacities and consolidations reflect the underlying alveolar damage and microvascular pathology [4; 16]. In the post-COVID period, the predominance of bacterial pneumonias with septic complications indicates a shift in the etiological structure of mortality, reinforcing the necessity of standardized laboratory verification and continuous morphological monitoring to ensure accurate differential diagnosis and guide clinical management.

Our results are consistent with the data of Yakovenko et al. [11], who reported a typical morphological complex of changes associated with multiple organ failure developing within 2–3 weeks of COVID-19. This complex includes hemorrhagic edema, thrombosis, formation of hyaline membranes, and progression of fibrosis.

It is believed that the pathogenesis of vascular manifestations is largely driven by the direct action of the viral agent via ACE2 receptors, which provokes significant platelet activation followed by fibrin thrombus formation [12]. These lesions are systemic because these receptors are not only located on vascular endothelial cells but also on the surface of type 2 alveolocytes, nerve cells and glial cells, and the intestines, leading to corresponding symptomatology.

In all examined cases of groups 0–3, thrombosis development was noted, especially in the small branches. The formation of multiple vascular thrombi has been confirmed by other researchers [17–19]. The authors mention immune mechanisms contributing to coagulopathy and thrombosis, endothelial injury, and thromboembolic complications, which can persist [17, 18]. It can be assumed that such a morphological pattern may lead to irreversible changes and the development of terminal conditions.

Analysis of autopsy data from patients in group 4 showed a morphological picture differing from that observed in the previous groups. Macroscopically, significant consolidations of the lung parenchyma developed with a tendency to involve a larger volume of the lung lobes: the lower and/or middle lobes of the right lung and the lower lobe of the left lung. Consolidation foci had gray or red coloration and were located both peripherally and in the perihilar region. Microscopically, hyperemia, edema, and fibrin exudation with a significant content of neutrophilic leukocytes in the alveolar spaces were observed, accompanied by varying amounts of erythrocytes and macrophages in different clinical cases.

The bronchial walls exhibited varying degrees of inflammatory process intensity, including hyperemia, edema, focal necrotic changes, and epithelial desquamation into the bronchial lumen.

The causes of death in this group were more often septic complications and multiple organ failure. Unfortunately, the infectious agent causing these clinical cases was not identified. Only 3 clinical cases had confirmed coronavirus disease. It cannot be excluded that the described morphological changes in the lungs of deceased patients in group 4 are mostly uncharacteristic of coronavirus disease and caused by other pathogens.

Several authors indicate pronounced immunosuppression leading to the proliferation of bacterial infections – most commonly Klebsiella pneumoniae, Pseudomonas spp., Escherichia coli, and Staphylococcus spp. Such immunosuppression contributes to the rapid deterioration of patients' conditions, resulting in bacterial pneumonia and sepsis. In some cases, secondary infection develops with generalization of the process and progression to septic states and multiple organ failure, which ultimately become the cause of death [13; 17].

Microscopically, characteristic features such as hyperemia, edema, and fibrin exudation into the alveolar spaces, along with varying amounts of polymorphonuclear leukocytes, erythrocytes, and macrophages, are indicative of bacterial pneumonias in different clinical cases. This is an important finding that pathomorphologists use for the differential diagnosis of bacterial versus viral lung lesions.

These aspects highlight the necessity of developing standards for mandatory bacteriological and virological confirmation of clinical cases of death due to pneumonia of any etiology.

Conclusions

1. The key predictor of mortality is age: the highest number of deaths occurred in the 61–70 and 71–80 year groups, confirming the particular vulnerability of elderly patients.

2. Mortality dynamics during the study period showed two peak years–2021 and 2023–which correspond to pandemic waves and reflect the influence of external factors on fatality rates.

3. Sex differences were variable: in 2021, women predominated among the deceased, whereas in 2023 men predominated; in other years, differences between sexes were not statistically significant.

4. Statistical analysis (Pearson's χ^2, ANOVA, Fisher's exact test) confirmed significant differences in certain age groups (41–50 and 81+ years), while in most groups differences did not reach statistical significance.

5. Risk assessment (RR and OR) demonstrated that in middle-aged groups (51–70 years) male mortality risk was somewhat higher, whereas in the oldest group (81+) women predominated.

6. Morphological changes in the lungs in COVID-19 were characterized by bilateral multisegmental involvement, interstitial edema, microthrombosis, and formation of hyaline membranes. In the post-COVID period, features of bacterial pneumonia with septic complications predominated.

7. The results confirm the need for differentiated preventive and therapeutic strategies for different age and sex groups, as well as the importance of morphological verification for differential diagnosis of viral and bacterial pneumonias.

Conflict of interest. The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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