RESEARCH ARTICLE / ARAŞTIRMA

DOI: 10.4274/mjima.galenos.2025.24222.6
Mediterr J Infect Microb Antimicrob 2025;14:24222.6
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2025.24222.6

Predictive Value of Procalcitonin and Lymphocyte Count for Secondary Infection Risk in Patients Hospitalized with Influenza Pneumonia

İnfluenza Pnömonisi Nedeniyle Hastaneye Yatırılan Hastalarda Prokalsitonin ve Lenfosit Sayımının Sekonder Enfeksiyon Riski İçin Öngörücü Değeri

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Abstract

Introduction: The primary complications of influenza are secondary infections, particularly pneumonia, which contribute to increased morbidity and mortality. Currently, no reliable methods exist to differentiate secondary infections occurring alongside influenza. This study aimed to evaluate the role of procalcitonin (PCT) and lymphocyte count in predicting mortality and diagnosing secondary infections in patients hospitalized with influenza pneumonia.

Materials and Methods: Patients with confirmed influenza and radiological evidence of lung infiltration on chest X-ray or computed tomography were included. Medical records were reviewed retrospectively. Patients were classified into two groups: those with influenza alone and those with influenza and a secondary infection. The highest PCT level and the lowest lymphocyte count recorded during hospitalization were analyzed for their association with secondary infection risk and mortality.

Results: Among 66 patients, 30 (45%) were treated in the intensive care unit (ICU), while 36 (55%) received care in the general ward. Secondary infections were identified in 29 patients (43.9%). Although ICU admission rates did not differ between groups, mortality was 38.4% in patients with secondary infections and 3% in those with influenza alone. During the 5-day influenza treatment period, C-reactive protein and PCT levels showed no significant differences between groups. The highest median PCT levels in discharged and deceased patients were 1.63 and 9.8 µg/L, respectively (p=0.005). The mean lowest lymphocyte count in discharged and deceased patients were 300 cells/mL and 100 cells/mL, respectively (p=0.008). Among patients with a lowest lymphocyte count below 200 cells/mL, the secondary infection rate was 73% compared to 35.3% (p=0.031) in those with a count above 200 cells/mL. Additionally, mortality was 46% vs. 9.8% (p=0.001), and hospital stay was longer at 20 (13-40) days vs. 15 (9-19) days (p=0.047), respectively.

Conclusion: Patients hospitalized with influenza frequently develop secondary infections, which are linked to higher mortality. A lymphocyte count below 200 cells/mL is associated with an risk of secondary infection, prolonged hospitalization, and higher mortality. Although elevated PCT levels were also linked to an increased risk of secondary infections and mortality, this association was not statistically significant.

Keywords: Influenza, secondary infection, lymphopenia, procalcitonin, pneumonia, mortality

Cite this article as: İnci SS, Tekin E, Ilgın C, Karakurt S. Predictive value of procalcitonin and lymphocyte count for secondary infection risk in patients hospitalized with influenza pneumonia. Mediterr J Infect Microb Antimicrob. 2025;14:24222.6.

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Received/Geliş Tarihi: 09.06.2024 **Accepted/Kabul Tarihi:** 28.01.2025

Epub: 04.02.2025
Published: 18.03.2025

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Öz

Giriş: İnfluenzanın başlıca komplikasyonları, mortalite ve morbiditede artışa neden olan sekonder enfeksiyonlar, özellikle de pnömonidir. Mevcut yöntemler influenzaya eşlik eden sekonder enfeksiyonları güvenilir bir şekilde ayırt edememektedir. Bu çalışmada, influenza pnömonisi nedeniyle hastaneye yatırılan hastalarda prokalsitonin (PCT) ve lenfosit değerlerinin mortalite ve sekonder enfeksiyon tanısı üzerindeki etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmaya influenza polimeraz zincir reaksiyonu testi pozitif olan ve akciğer grafisinde veya bilgisayarlı tomografisinde akciğer infiltrasyonu bulguları olan hastalar dahil edildi. Hastaların tıbbi kayıtları retrospektif olarak incelendi. Hastalar iki gruba ayrıldı: sadece influenza enfeksiyonu olanlar ve influenza ile birlikte sekonder enfeksiyonu olanlar. Hastanede yatış sırasında ölçülen en yüksek PCT düzeyi ve en düşük lenfosit sayısı sekonder enfeksiyon ve mortalite riski açısından araştırıldı.

Bulgular: Çalışmaya dahil edilen 66 hastanın 30'u (%45) yoğun bakım ünitesinde (YBÜ), 36'sı (%55) serviste tedavi edildi. Toplamda 29 hastada (%43,9) eşlik eden sekonder enfeksiyon gelişti. YBÜ'ye yatış oranı gruplar arasında farklılık göstermemekle birlikte, ölüm oranı influenzaya sekonder enfeksiyonun eşlik ettiği hastalarda %38,4, sadece influenza enfeksiyonu olan hastalarda ise %3'tü. İnfluenza tedavisinin 5 günü boyunca, C-reaktif protein ve PCT düzeylerinin takibi gruplar arasında önemli farklılıklar göstermedi. Taburcu edilen ve ölen hastalarda en yüksek medyan PCT konsantrasyonları sırasıyla 1,63 ve 9,8 µg/L idi (p=0,005). Taburcu edilen ve ölen hastalarda ortalama en düşük lenfosit seviyeleri sırasıyla 300 hücre/mL ve 100 hücre/mL idi (p=0,008). Yatış sırasında ölçülen en düşük lenfosit sayısı 200 hücre/mL'nin altında olan hastalarda, en düşük lenfosit sayısı 200 hücre/mL'nin üzerinde olan hastalara kıyasla, sekonder enfeksiyon oranı sırasıyla %73'e karşı %35,3 (p=0,031), ölüm oranı %46'ya karşı %9,8 (p=0,001) ve hastanede kalış süresi 20 (13-40) güne karşı 15 (9-19) gündü (p=0,047).

Sonuç: İnfluenza nedeniyle hastaneye yatırılan hastalarda sıklıkla daha yüksek ölüm ile ilişkili olan sekonder enfeksiyonlar gelişir.
Lenfosit sayısının <200 hücre/mL olması sekonder enfeksiyon gelişme riski, uzamış hastanede kalış süresi ve yüksek mortalite ile ilişkilidir. Artmış PCT konsantrasyonu istatistiksel anlamlı olmamakla birlikte, sekonder enfeksiyon ve mortalite riskinde artışa yol açmaktadır.

Anahtar Kelimeler: Grip, sekonder enfeksiyon, lenfopeni, prokalsitonin, pnömoni, ölüm oranı

Introduction

Influenza viruses, which primarily circulate during winter, have historically caused pandemics approximately every decade. Secondary infections, particularly pneumonia[1,2], are the most common complications of influenza and are associated with increased morbidity and mortality[3,4]. Since influenza strains responsible for pandemics generally cause self-limiting illnesses, the accurate diagnosis and treatment of concurrent bacterial infections are essential to reducing mortality and morbidity. During the 2009 H1N1 influenza outbreak, the incidence of secondary infections among intensive care unit (ICU)-admitted influenza patients was reported to be 18-34%, significantly contributing to increased mortality[5,6].

Currently, no reliable method exists to differentiate viral from bacterial lower respiratory tract infections in patients with influenza. The 2019 American Thoracic Society-Infectious Diseases Society of America Guidelines recommend empirical antibiotic therapy for patients with influenza pneumonia[7]. However, ruling out secondary infections could help reduce unnecessary antibiotic use, lower healthcare costs, minimize adverse effects, and prevent the emergence of multidrug-resistant infections.

In infection management, procalcitonin (PCT) is not recommended for initiating antibiotic therapy but is advised for guiding antibiotic discontinuation[8]. However, data on the role of PCT in predicting secondary infections in H1N1 patients are limited, and findings remain inconsistent[9-12].

Lymphopenia frequently occurs in viral infections, and leukocytosis with relative lymphopenia has been widely used for diagnosing influenza A H1N1 in emergency settings[13-16]. Prolonged lymphopenia has been linked to respiratory failure and increased mortality in patients with influenza pneumonia[17]. However, its role in diagnosing secondary infections in influenza patients remains uncertain.

This study aimed to assess the impact of PCT and lymphocyte levels on diagnosing secondary infections and predicting mortality in patients hospitalized with influenza pneumonia.

Materials and Methods

This study was approved by the Marmara University Ethics Committee (approval number: 09.2020.969, dated: 02.10.2020). Due to the retrospective, observational, cross-sectional design of the study, written informed consent was not obtained from the patients. The study included patients who were monitored in the ICU or inpatient ward following a diagnosis of influenza pneumonia between October 2018 and January 2020. Influenza pneumonia was diagnosed based on a positive influenza quantitative reverse transcription polymerase chain reaction test from a nasal swab, along with evidence of lung infiltration on chest X-ray or computed tomography. Patients younger than 18 years were excluded.

Patient medical records were reviewed retrospectively using hospital information management systems and patient files. Data collected included demographic characteristics, comorbidities, coexisting viral infections, empirical antibiotic

and antiviral treatment (dose and duration), daily C-reactive protein (CRP), PCT, leukocyte (white blood cell) count for the first 5 days, highest PCT and lowest lymphocyte levels recorded during hospitalization, length of stay in the inpatient ward, ICU severity scores [Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment], use of mechanical ventilation (invasive and non-invasive), vasopressor therapy, ICU and total hospitalization duration, and in-hospital mortality.

A total lymphocyte counts of <1000 cells/mL (<1x10^9/L) in adults is defined as lymphopenia[18]. In our laboratory, the reference range for PCT is 0-0.5 µg/L, while the normal range for CRP is 0-5 mg/L.

Patients were categorized into two groups: those with influenza infection only and those with influenza accompanied by a secondary infection. Bacteremia was diagnosed in patients with infection symptoms based on bacterial growth in aerobic and anaerobic cultures from two sets of blood samples collected from separate venous sites. Cases of contamination and colonization were excluded by assessing clinical findings consistent with bacteremia and elevated inflammatory markers. However, the infection source was not recorded for patients diagnosed with bacteremia. Patients with secondary infections were further classified into two groups: those with concurrent infection (developing a secondary infection within 72 hours of influenza diagnosis) and those who developed secondary infection after completing influenza treatment (occurring between 5 days and 1 month of continued hospitalization). No patients developed secondary infection between the third and fifth days of treatment. All groups were compared based on recorded data, including secondary infectious agents and antibiotic use. The highest PCT level and lowest lymphocyte count during hospitalization were analyzed for their association with secondary infection risk and mortality. Additionally, the relationship between secondary infection development and mortality was examined based on the presence and duration of lymphopenia. Patients were classified into three groups: those without lymphopenia, those with lymphopenia lasting ≤5 days, and those with lymphopenia lasting >5 days.

Statistical Analysis

Statistical analysis was conducted using Number Cruncher Statistical System (NCSS) 2007 Statistical Software (Utah, USA) and Stata version 15.1, year 2017 (StataCorp 4905, Texas, USA). The independent t-test was used to compare descriptive statistical measures (mean, standard deviation, median, and interquartile range) and normally distributed binary variables. The Mann-Whitney U test was applied for comparing binary groups of non-normally distributed variables, while the Kruskal-Wallis test was used for comparisons involving three groups of non-normally distributed variables. Qualitative data were analyzed using the chi-squared test and Fisher's exact test. A p-value of <0.05 was considered statistically significant.

Results

General Characteristics of Patients

A total of 66 patients diagnosed with influenza pneumonia and hospitalized between October 2018 and January 2020 were included in the study. Of these, 54 patients presented to the emergency department due to influenza, while 12 were diagnosed during hospitalization for other conditions. Among the patients, 30 (45%) received treatment in the ICU, and 36 (55%) were treated in the inpatient clinic.

The mean age of the patients was 69 years (ranging from 51 to 76 years). Hypertension (53.3%) and diabetes mellitus (31.8%) were the most common comorbidities. Additionally, 50% of the patients had chronic respiratory diseases, including chronic obstructive pulmonary disease, restrictive lung disease, and lung malignancies (Table 1).

It was noted that 90% of patients received antibiotic therapy, with 50% starting antibiotics on the first day of hospitalization.

Relationship Between Influenza and Secondary Infection

A total of 29 patients (43.9%) developed a secondary infection. Among these, bacteremia was identified in 12 patients (41.3%),

Table 1. General characteristics of patients with an influenza diagnosis

Number of patients	**66**
Sex: Female[a]	39 (59.1%)
Age (years)[b]	69 (51-76)
Chronic disease[a]	65 (98.5%)
Hypertension	35 (53.1%)
Diabetes mellitus	21 (31.8%)
Ischemic heart disease, congestive heart failure	28 (42.4%)
Prior cerebrovascular event, dementia	8 (12.1%)
Chronic renal failure	8 (12.1%)
Immunosuppression	7 (10.6%)
Malignancy (solid organ)	14 (21.2%)
Malignancy (hematologic)	6 (9.1%)
Chronic obstructive pulmonary disease	15 (22.7%)
Other respiratory diseases	14 (21.2%)
Complainta	
Cough-phlegm	23 (42.5%)
Dyspnea	33 (61.1%)
Runny nose	5 (9.2%)
Fever	7 (12.9%)

[a]Values are presented as n (%), [b]values are presented as median (25-75%)

bacterial pneumonia in 19 patients (65.5%), and urinary tract infection in 15 patients (51.72%).

Across 57 secondary infections in 29 patients, 10 different infectious agents were detected. The most common pathogens were *Acinetobacter baumannii* (7 cases, 12.2%), *Klebsiella pneumoniae* (5 cases, 8.7%), *Escherichia coli* (4 cases, 7%), *Pseudomonas aeruginosa* (2 cases, 3.5%), other *Gram-negative bacteria* (4 cases, 7%), *Staphylococcus aureus* (6 cases, 10.5%), *Enterococcus* species (9 cases, 15.7%), *Corynebacterium* species (3 cases, 5.2%), *Candida albicans* (10 cases, 17.5%), and non-*albicans Candida* species (7 cases, 12.2%).

Secondary infections were observed in 12 out of 36 patients (33%) in the inpatient clinic and in 17 out of 30 patients (56%) in the ICU. Among ICU patients, the APACHE II score was significantly higher in those with secondary infection [median, 20 (17-26)] compared to those without [median, 15 (12-17), p=0.007].

Although ICU admission rates did not differ significantly between groups, mortality was higher in patients with secondary infections (10/29, 34.4%) compared to those without (2/37, 5.4%) (p=0.001). The median hospital stay was longer in patients with secondary infections [22 days (14-40)] than in those without [13 days (7-16)] (p=0.001) (Table 2).

No significant differences were observed in CRP, PCT, or WBC values at admission between patients with and without secondary infections (Table 3).

Association of PCT with Secondary Infection and Clinical Outcomes

During the 5-day course of influenza treatment, CRP and PCT levels showed no significant difference between groups (Figure 1).

Although the highest PCT levels recorded during hospitalization were higher in patients with secondary infections compared to those without (2.77 µg/L vs. 1.71 µg/L), the difference was not statistically significant. In patients with secondary infections, PCT levels stopped declining after day 3.

When patients were grouped based on PCT levels, there were no significant differences in mortality or length of hospitalization (Table 4). However, the mean highest PCT levels were 1.63 µg/L in discharged patients and 9.8 µg/L in deceased patients (p=0.005). The median highest PCT concentrations were significantly higher in ICU patients (6.05 µg/L) compared to those in the inpatient clinic (1.25 µg/L) (p = 0.001).

Table 2. The comparison of clinical characteristics between patients with influenza only and those with accompanying secondary infection

Patients followed up in the ICU (n=30)	**With secondary infection (n=17)**	**Without secondary infection (n=13)**	**p-value**
APACHE II score during ICU stay[b]	20 (17-26)	15 (12-17)	0.0073
SOFA score during ICU stay[b]	6 (3-10)	5 (3-7)	(0.05)
Length of ICU stay, day[b]	6 (4-10)	5 (4-5)	>0.05
Length of service hospitalization before ICU[b]	3 (1-5)	1 (0-2)	>0.05
Mechanical ventilation needed[a]	9 (60.0%)	6 (40.0%)	>0.05
Mechanical ventilation duration[b]	6 (2-10)	4 (2-4)	>0.05
Non-invasive mechanical ventilation needed[a]	5 (50.0%)	5 (50.0%)	>0.05
Vasopressor needed[a]	7 (58.33%)	5 (41.67%)	>0.05
Mortality[a]	10 (58.8%)	0 (0.0%)	(0.001)
Patients followed up in the service (n=36)	**With secondary infection (n=12)**	**Without secondary infection (n=24)**	**p-value**
H1N1 diagnosis location			
Admission to the emergency department caused by influenza[a]	6 (22.22%)	21 (77.28%)	(0.036)
Diagnosed with influenza during hospitalization[a]	6 (66.67%)	3 (33.3%)	
Need for non-invasive mechanical ventilator[a]	3 (33.33%)	6 (66.67%)	>0.05
Non-invasive mechanical ventilation duration[b]	10 (8-19)	3.5 (2-10)	>0.05
Length of Service Stay, days[b]	20 (14-40)	11 (6.5-14.5)	**0.0033**
Mortality[a]	**0 (0%)**	**2 (8.3%)**	**>0.05**

[a]Values are presented as n (%), [b]values are presented as median (25-75%)

Relationship Among Lymphopenia, Secondary Infection, and Clinical Outcomes

At the time of influenza diagnosis, 51 patients (77%) had a lymphocyte count of <1000 cells/mL. Among the patients, 6 (0.9%) did not experience lymphopenia during hospitalization, 16 (24%) had lymphopenia lasting ≤5 days, and 44 (66%) had lymphopenia lasting >5 days. No significant differences in mortality rates or secondary infection development were found between these groups.

The mean lowest lymphocyte count in discharged patients was 300 cells/mL, compared to 100 cells/mL in deceased patients (p=0.008). ICU patients had a mean lowest lymphocyte count of 200 cells/mL, while those in the inpatient clinic had a mean of 350 cells/mL (p=0.03).

Patients with the lowest lymphocyte count below 200 cells/mL during hospitalization had a significantly higher rate of secondary infection (73% vs. 35.3%, p=0.031), higher mortality rate (46% vs. 9.8%, p=0.001), and longer hospital stays [20 days (13-40) vs. 15 days (9-19), p=0.047)] compared to those with counts above 200 cells/mL (Table 4).

Table 3. Comparison of patients with influenza based on secondary infection groups

	Secondary infection			p-value
	None (n=37)	Concurrent (n=15)	After (n=14)	
The unit where H1N1 was diagnosed[a]				>0.05
Emergency room	33 (61.11%)	10 (18.51%)	11 (20.37%)	
Service	4 (33.33%)	5 (41.67%)	3 (25.0%)	
Empirical antibiotics[a]	34 (59.65%)	12 (21.05%)	11(19.3%)	>0.05
The unit where H1N1 treatment was administered[a]				
ICU	13 (43.33%)	6 (20%)	11 (36.66%)	>0.05
Service	24 (66.66%)	9 (25%)	3 (8.33%)	
The highest level of procalcitonin[b]	1.71 (0.17%-6.6%)	1.58 (0.21-2.95)	9 (1.23-23)	>0.05
The lowest lymphocyte count[b]	300 (200-500)	300 (100-500)	300 (100-400)	>0.05
At the time of diagnosis				
CRP (mg/L)[b]	112 (51-156)	51 (37-117)	79 (41-102)	>0.05
PCT (µg/l)[b]	0.2 (0.11-1.47)	0.14 (0.1-0.7)	0.18 (0.13-0.29)	>0.05
Leukocyte, (x103 mL)[b]	9.6 (7%-12.3%)	11.1 (7.5-16.4)	9.4 (6.2%-17.5%)	>0.05
The length of ICU stay days[b]	5 (4-5)	5 (5-12)	7 (4-10)	>0.05
The length of service stay days[b]	10 (6-14)	20 (14-38)	43.5 (19-68)	**0.0061**
The length of hospital stay days[b]	13 (7-16)	17 (14-32)	33 (18-68)	**0.0001**
Mortality[a]	**1 (0.02%)**	**4 (0.26%)**	**7 (50.0%)**	**0.0003**

[a]Values are presented as n (%), [b]values are presented as median (25-75%). CRP : C-reactive protein, PCT: Procalcitonin, ICU: Intensive care unit

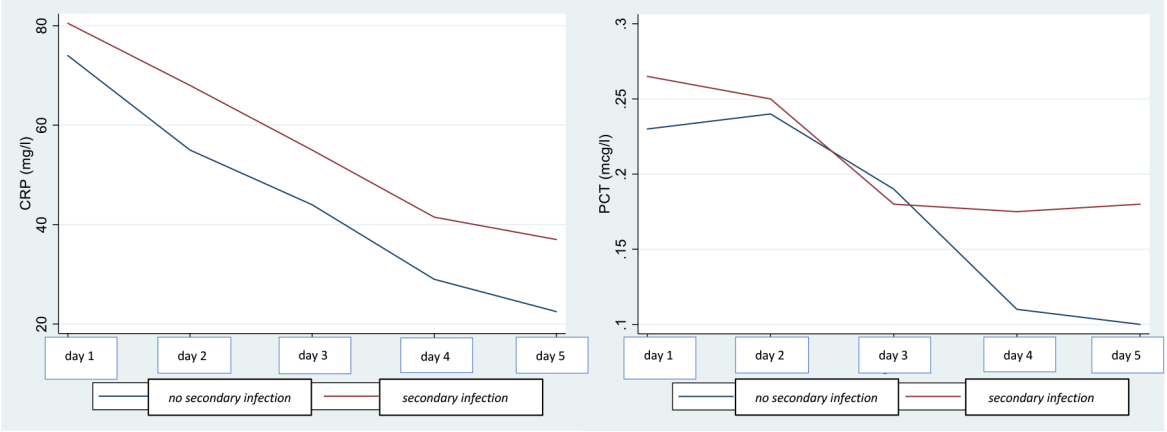


Figure 1. CRP and PCT levels during 5-day influenza treatment in patients with and without secondary infection
CRP: C-reactive protein, PCT: Procalcitonin

Table 4. The relationship between the highest PCT value and the lowest lymphocyte count with secondary infection, mortality, and length of hospitalization

	Groups according to highest PCT level				p-value	Groups according to lowest lymphocyte count		p-value
	0-0.5 µg/L (n=22)	0.5-2 µg/L (n = 11)	2-10 µg/L (n=16)	>10 µg/L (n=17)		<200 (n=15)	>200 (n=51)	
Secondary infection[a]	7 (31.8%)	5 (45.4%)	8 (50%)	9 (52.9%)	0.562	11 (73 %)	18 (%35)	0.031
Mortality	1 (4.5%)	1 (10%)	4 (26.6%)	6 (35.3%)	0.057	7 (46%)	5 (9.8)	0.001
The length of hospitalization[b]	15 (12-18)	14.5 (9-20)	16 (7.5-24.5)	17 (10-32)	0.965	20 (13-40)	15 (9-19)	0.047

[a]Values are presented as n (%), [b]values are presented as median (25-75%), PCT: Procalcitonin

Discussion

In this study, patients with influenza pneumonia and a lymphocyte count below 200 cells/mL had significantly higher rates of secondary infections, longer hospital stays and increased mortality. Although higher PCT levels tended to correlate with an increased frequency of secondary infections and mortality, the differences were not statistically significant.

The risk of secondary infection is higher in influenza pneumonia compared to other viral pneumonias, likely due to influenza A's ability to target alveolar macrophages via the PB1-F2 protein[19,20]. The pooled prevalence of influenza bacterial co-infection was 20.3% (95% confidence interval =16.0-25.4) in a meta-analysis including 63 articles; however, in our study, the rate was 43.9%[21].

The link between secondary infections and increased mortality remains controversial[5,6,10,22,23]. In our study, patients with secondary infections had significantly longer hospital stays and higher mortality rates (p<0.0001).

Lymphopenia is commonly seen in viral infections and is frequently used to help diagnose influenza A H1N1 in emergency settings[13-15]. Hage et al.[16] found that relative lymphopenia occurred in all patients with influenza A H1N1, with the lowest lymphocyte count typically reached by day 3.5.

The role of lymphopenia in the development of secondary infections in influenza remains unclear, although it has been associated with poor prognosis. In hospitalized influenza A H1N1 patients, a lymphocyte count <800 cells/mL at admission was identified as an independent risk factor for respiratory failure[24]. Cui et al.[25] found that persistent lymphopenia after 5 days was a risk factor for mortality, with ICU patients having a lymphocyte count of 580 cells/mL and non-ICU patients having 1065 cells/mL. In our study, ICU patients had a lymphocyte count of 200 cells/mL, while those in the inpatient clinic had 350 cells/mL. Similarly, Cui et al.[25] reported lymphocyte count of 580 cells/mL in deceased patients and 790 cells/mL in survivors. In our study, the lowest lymphocyte count in discharged and deceased patients were 300 cells/mL and 100 cells/mL, respectively. Although lymphopenia is not a definitive risk factor for mortality, most surviving patients (93.1%) showed improvement in lymphocyte count within approximately 5 days. Lymphopenia lasting longer than 5 days was observed in 70% of deceased patients and 6.8% of survivors[25]. In our study, no statistically significant differences in secondary infection or mortality were found between patients with no lymphopenia, lymphopenia lasting <5 days, or lymphopenia lasting >5 days.

In the study by Lalueza et al.[17], 59% of patients had lymphopenia (<1000 cells/mL) at hospitalization, with the rate increasing to 71.7% during the hospital stay. Lymphopenia (<500 cell/mL) at admission was linked to respiratory failure, while the lowest lymphocyte value (<300 cell/mL) was associated with both respiratory failure and poor prognosis[17]. In our study, no statistically significant correlation was found between secondary infection development and lymphocyte level at the time of diagnosis.

Consistent previous studies, we observed that increased mortality was associated with longer hospitalization in patients with a lymphocyte count <200 cells/mL during hospitalization. Additionally, the secondary infection rate was significantly higher in the group with a lymphocyte count <200 cells/mL.

In a meta-analysis of six studies examining the relationship between PCT and secondary infection, the area under the curve (AUC) value for PCT was 0.68 for detecting secondary infection, with a sensitivity of 84% and a specificity of 64%. The AUC value was 0.73 in the subgroup of ICU patients[26]. In our study, the PCT value at admission was not significantly predictive of secondary infection. The AUC value for mortality in our study was 0.61.

Another study emphasized that the course of PCT, rather than a single measurement, is important. It reported that high baseline

PCT levels decreased over time in both ICU patients with isolated influenza and those with secondary infection, with significantly lower PCT levels at 24, 48, and 120 hours in the isolated H1N1 group compared to the secondary infection group[27]. In our study, PCT values were high at baseline and decreased over time in both groups. When comparing PCT values at 0, 24, 48, 72, 96, and 120 hours, the rate of decline in PCT levels after 72 hours in the group with secondary infection tended to decrease, but no statistical significance was found. Additionally, the frequency of secondary infections was 31.8% in those with the highest PCT values below 0.5 and 53% in those with values over 10. Thus, a tendency for increased secondary infection frequency was observed with higher PCT values ($p>0.05$). Mortality was 4.5% in those with the highest PCT values below 0.5, 10% in those with values between 0.5 and 2, 26.5% in those with values between 2 and 10, and 35.5% in those with values above 10. As PCT values increased, mortality also tended to increase ($p=0.057$). The lack of statistical insignificance may be due to the small sample size.

Study Limitations

The primary limitation of our study is its retrospective, single-center design. Only patients with microbiologically confirmed secondary infections were included, while those with clinically suspected secondary infection were excluded. However, the lack of culture growth results could influence the findings. Additionally, the empirical antibiotic therapy administered to most patients might have impacted the results.

This, however, remains debatable, as some studies suggest that excluding patients receiving empirical antibiotic therapy does not alter the results[28]. While lymphopenia was considered, another limitation is that other potential causes of lymphopenia were not explored.

Conclusion

Patients hospitalized with influenza had high rates of secondary infections, which were linked to increased mortality. A lymphocyte count of <200 cells/mL was found to be an indicator of the risk for secondary infections, prolonged hospitalization, and higher mortality. Although higher PCT levels were associated with a tendency for increased secondary infections and mortality, this relationship was not statistically significant.

Ethics

Ethics Committee Approval: This study was approved by the Marmara University Ethics Committee (approval number: 09.2020.969, dated: 02.10.2020).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.K., Concept: S.K., Design: S.S.İ., Data Collection or Processing: E.T., Analysis or Interpretation: C.I., Literature Search: S.S.İ., Writing: S.S.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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