Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Different outcomes in nosocomial pneumonia, focus on lymphocyte/monocyte ratio: a comparative analysis between patients from home and patients from nursing home

Aldo Pezzuto

pezzutoaldo@libero.it

Sapienza University of Rome

Erminio Carriero

Sapienza University of Rome

Teresa Palermo

Sapienza University of Rome

Daniel Piamonti

Sapienza University of Rome

Patrizio Pasquinelli

Sapienza University of Rome

Alessio Simoniello

Sapienza University of Rome

Elisa Desideri

Sapienza University of Rome

Massimo Ciccozzi

Università Campus Bio-Medico

Andrea Gallippi

Sapienza University of Rome

Elisabetta Carico

Sapienza University of Rome

Gerardo Salerno

Sapienza University of Rome

Giuseppe Tonini

Università Campus Bio-Medico

Alberto Ricci

Sapienza University of Rome

Article

Keywords: Nosocomial pneumonia, lymphocyte/monocyte ratio, respiratory failure, MDR, hospital length of stay, pneumonia resolution

Posted Date: September 4th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10540892/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

BACKGROUND: Nosocomial pneumonia is a critical condition in which patients contract a severe illness associated with hospitalization including patients treated with mechanical ventilation.

We compared inflammatory and clinical parameters, in patients coming from home and patients coming from nursing home.

METHODS:

In the pulmonology department of our hospital (Sant'Andrea, Sapienza University**)** a group of 102 patients were retrospectively analyzed. They had beenhospitalized due to respiratory failure and worsening symptoms developing nosocomial pneumonia, which is defined as pneumonia occurring 48 hours after hospital admission.

At the admission all patients underwent chest X-ray and haematological tests for cell blood count detection (CBC), high-sensitive C reactive protein (sCRP), procalcitonin. A lymphocyte-monocyte (ly/mo) ratio was also calculated as an indirect parameter. An arterial sampling for blood gas analysis was also drawn. A chest X-ray check was performed at the discharge.

A complete medical history was taken and clinical values were gathered including spirometry data,

The population was stratified in two groups according to their origin, whether from home or from nursing homes. The subgroups were compared with each other for all considered laboratory and clinical parameters. The procalcitonin along with PaO2/FiO2 and ly/mo ratio were detected at time 0(at the admission) and time 1(at the discharge).

RESULTS:

Patients coming from nursing home showed a higher percentage of multi-drug resistance (MDR) and a longer length of hospital stay. Going into depth, the percentage of multidrug resistant patients was significantly higher in the study group (coming from nursing homes) ($p<0.0001$). Significant differences were also found regarding the hospital length of stay ($p<0.04$) and the PaO2/FiO2 rate ($p<0.01$). The lymphocyte/monocyte ratio was found to be lower in nursing-home patients with a significant statistical value($p<0.03$).

No significant differences were found between groups, regarding age, body mass index (BMI) and C-reactive protein (CRP). At the discharge a higher percentage of pneumonia resolution was found in the control group ($p<0.03$). The difference in values between groups remained significant even at the follow-up examination upon discharge.

It was found a close correlation of lymphocyte/monocyte ratio with PaO2/FiO2 ratio and hospital length of stay.

In the multi-regression model lymphocyte/monocyte ratio is an independent factor affecting respiratory failure development.

CONCLUSION

In the group of patients from nursing homes a lower lymphocyte/monocyte ratio and PaO2/FiO2 ratio was found together with a longer hospital length of stay, suggesting a reduced immune response and increased exposure in the study group. The percentage of MDR was higher in the study group compared with patients from home. Lymphocyte/monocyte ratio is associated with respiratory failure development.

INTRODUCTION

Nosocomial pneumonia occurs typically 48 hours after hospital admission and it is characterized by different types of pathways and risk factors (1).

It is usually classified into Hospital-Acquired Pneumonia (HAP), defined as pneumonia developing 48 hours after admission without mechanical ventilation, and Ventilator-Associated Pneumonia (VAP), a subset of HAP occurring more than 48-72 hours after intubation for mechanical ventilation.

There are some factors, depending on host or therapy that affect nosocomial pneumonia development. Many general risk factors include intravenous injections, antibiotics, hospitalization for more than 2 days, malnutrition, old-age, sinusitis, endotracheal and nasogastric tubes, chronic diseases, patients who undergo dialysis (1,2).

Health-care associated pneumonia (HCAP) is a risk factor of developing multidrug-resistant pneumonia (MDR). The latter is influenced by some conditions such as**:** hospitalization for ≥2 days within the preceding 90 days, antibiotic use over previous 90 days, residence in a nursing home or extended care facility, home infusion therapy, chronic dialysis, home wound care.

Nosocomial pneumonia accounts for 15% of all nosocomial infections and affect up to 2% of hospitalized patients. Gram-negative bacteria, including Pseudomonas aeruginosa, Enterobacter, Acinetobacter, are involved in a high percentage of cases. Gram-positive account for about 30% of cases among which Staphylococcus aureus is prevalent (2).

The overall mortality depends on clinical setting, specific conditions and presence of comorbidities (3,4).

According to the literature, nosocomial pneumonia causes an increase in the length of hospital stay.

Pathophysiological mechanisms lead to the growth of virulent microorganisms, and bacterial colonization, especially in clinical care setting (5).

On the other side in community-acquired pneumonia the most common pathogens are S pneumoniae, M. Catharralis, H.Influenzae and L.pneumophila(6). The incidence of antibiotic resistance is variable**,**

mainly depending on the virulence of the pathogen and the excessive use of antibiotics empirically.

The aim of this study is to investigate potential prognostic variables, including lymphocyte/monocyte ratio and to find functional, clinical, laboratory differences between the group of hospitalized patients coming from home and those from nursing homes.

The main outcomes to be compared are hospital length of stay, lymphocyte/monocyte ratio, PaO2/FiO2 ratio, the percentage of pneumonia resolution, the percentage of multidrug resistances.

The study was approved by S.Andrea- Sapienza Ethic Committee.

METHODS

This is a mono-centre cohort study with retrospective analysis.

One hundred and two patients who were admitted to our Institution were retrospectively analyzed.

Cases were defined as people who acquired pneumonia 48 hours or more after admission. MDR was defined as a drug resistance to at least 3 classes of antibiotics, affecting and prolonging the length of hospital stay (7).

Inclusion criteria were : on objective examination of the chest the presence of rales or presence of dullness to percussion and any of the following: purulent sputum new onset or a change in characteristics of sputum; a pathogenic organism isolated from blood culture; a pathogen isolated from a specimen obtained by bronchial lavage aspiration, bronchial brushing or sputum; a chest radiographic examination showing new or progressive ground glass opacities, consolidations, cavities or pleural effusion**.**

Exclusion criteria included severe comorbidities that would prevent diagnostic or therapeutic procedures.

They were stratified and divided into group 1, the study group, of patients from nursing homes (48 patients) and group 2 as a control group (54) coming from home.

Clinical history data was collected focusing on risk factors such as poor nutrition encompassing intravenous alimentation or nasogastric nutritional supplementation, a history of smoking and comorbidities, such as chronic obstructive pulmonary disease (COPD), chronic conditions, cognitive impairment, diabetes mellitus, malignancy, previous recurrent infections, and information whether the patient is coming from a nursing home or from home.

Venous blood sampling was drawn for cell counts and indices of inflammation such as C reactive protein and lymphocyte/monocyte rate calculation. An arterial blood sampling was also drawn for arterial blood gas analysis.

PaO2/FiO2 and procalcitonin (PCT), ly/mo were detected at time 0(at the admission) and time 1 (at the discharge),

Additionally, radiological checks (chest X-ray) were performed at time 0 and time 1 in order to radiologically assess the outcome.

The length of hospital stay, pneumonia resolution at the discharge if partial or completewere recorded.

Statistical analysis

Descriptive statistics was employed to analyse the variables overall.

The analysis was carried out on the intention to treat population. Pneumonia resolution, the length of hospital stay, PaO2/FiO2 rate were the main outcomes. The other variables examined were ly/mo ratio, MDR.

All values were represented as median and interquartile range. The Spearman's correlation test was also calculated to establish specific relationships between variables.

The Mann-Whitney U test was used to compare not normally distributed continuous variables between groups, while the contingency table test was used to evaluate categorical variables. A value of $p<0.005$ was set as statistical significance value.

A multiple linear regression was performed in order to assess independent predictors of respiratory failure. All the variables studied were used as covariates.

The sample size was estimated based on the difference of the means: at least 36 patients for each group, with statistical power of 0.80 and a significance value $p <0.05$.

SPSS version 24 was used for the analysis.

RESULTS

The overall data show us the following findings:

In table 1

The median age was 71, 29% of patients were current smokers, COPD was roughly found in about 30% of patients, pack-years median value was 15. The presence of respiratory failure and pleural effusion was found in over 50% of cases.

The most frequent isolated bacteria were gram negative, among which Enterobacter cloacae (5%), Klebsiella pneumoniae (20%), Pseudomonas aeruginosa (17%), Acinetobacter baumani (30%).

The main comorbidities were diabetes (8%), hypertension (40%), alimentation disorders**,** dysphagia 10 %.

The main antibiotics used were piperacillin-tazobactam, meropenem/vabobactam , and ceftazidime/avibactam in MDR patients. Linezolid was used in methicillin-resistant S.aureus.

In table 2 we can observe the following data: inflammatory marker CRP was higher in group 1 (patients from nursing home) than in group 2 though without significant difference, whereas procalcitonin value was similar; moreover, the length of stay was longer in group 1 **-** 15 days vs 12 with significant statistical value($p<0.04$). Multiple bacterial infection was found in both groups, whilst the percentage of MDR was higher in group 1($p<0.0001$). No difference was found about BMI and severe comorbidities. The lymphocyte/monocyte ratio was lower in group 1($p<0.03$). The PaO2/FiO2 ratio was worse in group 1 than group 2 with a significant value($p<0.01$). No significant difference**s** were found regarding pack-years and COPD finding.

Eventually, the percentage of pneumonia resolution was higher in patients coming from home ($p<0.03$).

At the discharge checkup, the PaO_2/FiO_2 ratio had improved more significantly in the study group as well as ly/mo ratio, whereas procalcitonin improved in both groups but the difference was not significant. All patients underwent oxygen therapy owing to respiratory failure development.

Only 2% of patients were treated by mechanical ventilation.

Table 3 shows the correlation of lymphocyte/monocyte ratio with CRP ($p<0.04$) with PaO2/FiO2 ($p<0.02$), and with the length of stay ($p<0.04$).

In table 4 a multiple linear regression analysis highlights that ly/mo ratio is associated with respiratory failure development ($p<0.004$).

In figure 1 and 2 we can see pneumonia at the admission and after treatment in a patient who completely recovered.

A complete radiologic regression of consolidations was observed in patients who had a clinical improvement.

DISCUSSION

In the present study we compared patients from nursing home (study group)with patients from home.

It is a monocentric cohort study, with an estimated sample size based on difference of the means. The aim was to highlight differences in the development of multidrug-resistant infections, length of hospital stay laboratory and functional parameters. In addition, certain markers of immune-inflammatory response were evaluated, including lymphocyte-to-monocyte ratio.

The baseline clinical condition, level of consciousness, and BMI were comparable between the two groups.

Our results, highlighting a worse outcome in nursing home patients, are consistent with the literature. Indeed, living in a nursing home represents a risk factor for the development of nosocomial pneumonia; furthermore, it can contribute to the development of multidrug-resistant respiratory infections. Other general risk factors associated with the development of nosocomial pneumonia include age, sex, comorbidities, the presence or absence of chronic lung disease, a history of antibiotic treatment or bronchial aspiration roentgenographic bilateral pulmonary involvement, shock, respiratory failure (5,7).

Nosocomial pneumonia is an emerging issue, spreading greatly in health-care settings. It is the leading cause of death from any nosocomial infection in critically ill patients, despite improvements in supportive therapy, prevention strategies, and advanced antimicrobial therapy (8,9).

In the current study the main risk factors were represented by comorbidities and previous nursing home hospitalization. The main comorbidities were diabetes, hypertension, COPD. Our findings showed a longer length of stay in subjects coming from nursing home compared to patients coming from home, suggesting more severe impairment and a more difficult-to-achieve immune-inflammatory response in the study group. Both sputum and bronchoscopy were performed to collect organic sample for microbiological examination (BALF).

According to the scientific literature, endoscopic procedures are the gold standard for identifying pathogens, just as other procedures are essential for optimal patient monitoring. Bronchoscopy is the main invasive test for collecting secretion whenever sputum is not enough to identify bacteria (10).

Chest X-rays and chest CT scans are the imaging techniques that should be used in conjunction with laboratory tests for patients follow up.

In the present study there is a higher percentage of patients who had a complete resolution of pneumonia at radiological check in patients coming from home compared to patients from nursing home. A higher percentage of multidrug resistant subjects is also found in the group coming from nursing home and the main bacteria isolated were enteric gram negatives and staphylococcus aureus in accordance with the literature (7-9).

In MDR patients, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Acinetobacter baumanii complex are the predominant species favoured by healthcare-associated pneumonia requiring specific antibiotics (9,11). Acinetobacter is a gram negative with intrinsic antibiotic resistance (12). In the present study Staphylococci were the most commonly isolated Gram-positive pathogens, while the main Gram-negative pathogens were Pseudomonas, Klebsiella pneumoniae, and Acinetobacter baumanii.

Upon the discharge, patients in the control group had a better improvement of parameters such as PaO2/FiO2 and ly/mo ratio compared to the study group.

Among the parameters that were studied, lymphocyte/monocyte ratio is determined as a marker of the immune-inflammatory response, and it is closely linked with PaO2/FiO2 rate. The latter is associated with respiratory failure development. So far, the ly/mo ratio was deeply studied in Covid-19 patients and

it was found that a low level was associated with severe SARS-Cov2 infection and progression of the same(13).It has also been studied in cancer where a low value is associated with a more aggressive form of the disease (14).

We think that oxidative stress exposure along with conditions associated with immune system depression could favour nosocomial pneumonia with a worse outcome (15)

Regarding treatments during hospitalization, new generations of antibiotics have been used, based on the antibiotic susceptibility test, such as the association meropenem/vabobactam and third generation cephalosporins ceftazidime/avibactam. Both drugs inhibit the activity of a number of beta-lactamases produced by Gram-negative bacteria in carbapenase-producing enterobacteria (16,17). Other combinations of antibiotics that have been used include piperacillin/tazobactam along with aminoglycoside or fluoroquinolone. Those drugs have an excellent activity against P aeruginosa, and should be used for serious nosocomial infections (18-20).

LIMITATIONS OF THE STUDY

The study is a retrospective monocentric cohort study, it needs further studies and investigations.

However it is indicative of some specific variables that are associated with the outcomes.

CONCLUSION

Patients from nursing homes were generally more exposed and at greater risk of multidrug-resistant infections.

A higher rate of MDR was observed in patients coming from nursing home along with a longer length of stay, and worse respiratory failure.

In addition, a higher percentage of pneumonia resolution at the discharge was found in control group.

Lymphocyte/monocyte ratio is an easy, inexpensive, and reproducible parameter of immuno-inflammatory state. It is closely correlated with length of stay and with PaO2/FiO2. It is also associated with respiratory failure development.

Abbreviations

ly/mo ratio
lymphocyte/monocyte
PCT
procalcitonin
CRP
C reactive protein

MDR
multi-drug resistance

Declarations

ACKNOWLEDGEMENTS

A full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

P.D, P.A, R.A, B.V, P.P, P.T contributed to the study design, data analysis and interpretation;

S.G, S.A, C.E contributed to the laboratory analysis and to the writing of the manuscript;

S.G, C.M contributed to the statistical analysis;

C.E, G.A contributed to the recruitment of the subjects;

FUNDING INFORMATION

This study was not supported by any foundation.

CONSENT

Each patient has completed the informed consent form.

ETHICS STATEMENT

The study protocol conforms to the principles of the Declaration of Helsinki and has been approved by the medical ethics committee of Sapienza Sant'Andrea university (Protocol No. 656)

DATA AVAIBILITY DECLARATION

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT TO PUBLISH DECLARATION

Not applicable

References

1. Sikora, A., Zahra, F. & Nosocomial, I. Apr 27. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32644738. (2023).

2. Lynch, J. P. 3 rd. Hospital-acquired pneumonia: risk factors, microbiology, and treatment. Chest. ;119(2 Suppl):373S-384S. (2001). 10.1378/chest.119.2_suppl.373s. PMID: 11171773.
3. Ait Hssain, A. et al. Incidence, risk factors and outcomes of nosocomial infection in adult patients supported by extracorporeal membrane oxygenation: a systematic review and meta-analysis. *Crit. Care*. **28** (1), 158. 10.1186/s13054-024-04946-8. (2024). PMID: 38730424; PMCID: PMC11088079.
4. Coston, T. D. et al. Severity of inhalation injury and risk of nosocomial pneumonia: a retrospective cohort study. Chest. Jul 2:S0012-3692(24)04572-0. (2024). 10.1016/j.chest.2024.06.3770. Epub ahead of print. PMID: 38964672.
5. Cunnion, K. M. et al. Risk factors for nosocomial pneumonia: comparing adult critical-care populations. Am J Respir Crit Care Med. ;153(1):158 – 62. (1996). 10.1164/ajrccm.153.1.8542110. PMID: 854211.
6. Vaughn, V. M., Dickson, R. P., Horowitz, J. K. & Flanders, S. A. Community-Acquired Pneumonia: A Review. *JAMA* **332** (15), 1282–1295. 10.1001/jama.2024.14796 (2024).
7. Magiorakos, A. P. et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin. Microbiol. Infect.* **18** (3), 268–281. 10.1111/j.1469-0691.2011.03570.x.0 (2012).
8. Tacconelli, E. et al. European Society of Clinical Microbiology. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect. ;20 Suppl 1:1–55. (2014). 10.1111/1469-0691.12427. PMID: 24329732.
9. Lynch, J. P. 3 rd. Hospital-acquired pneumonia: risk factors, microbiology, and treatment. Chest. ;119(2 Suppl):373S-384S. (2001). 10.1378/chest.119.2_suppl.373s. PMID: 11171773.
10. Herer, B. et al. Diagnosis of nosocomial pneumonia in medical ward: repeatability of the protected specimen brush. *Eur. Respir J.* **18** (1), 157–163 (2001).
11. Torres, A. et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator associated pneumonia. Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator associated pneumonia (VAP) of the European Respiratory Society, European Society of intensive care Medicine, European Society of Clinical Microbiology and infrctious diseases. *Eur. Respir J.* ; **50**(3) (2017).
12. Maragakis, L. L., Tucker, M. G., Miller, R. G., Carroll, K. C. & Perl, T. M. Incidence and prevalence of multidrug-resistant Acinetobacter using targeted active surveillance cultures. *JAMA* **299**, 2513–2514 (2008).
13. Xing, Y. et al. Analysis of factors for disease progression in 61 patients with COVID-19 in Xiaogan, Hubei, China. *Eur. Rev. Med. Pharmacol. Sci.* **24** (23), 12490–12499 (2020).
14. Szabó, V. et al. The Lymphocyte-to-Monocyte Ratio (LMR) as a Novel Biomarker for Cervical Cancer Risk Stratification in Conization Patients. *J. Clin. Med.* **14** (17), 6057. 10.3390/jcm14176057 (2025).
15. Pezzuto, A. et al. Oxidative stress in smokers with and without COPD: what variables are associated? *Minerva Med.* **116** (5), 369–374 (2025).

16. Mills, J. P. & Marchaim, D. Multidrug-Resistant Gram-Negative Bacteria: Infection Prevention and Control Update. Infect Dis Clin North Am. ;35(4):969–994. doi: 10.1016/j.idc.2021.08.001. PMID: 34752228. (2021).
17. Almyroudi, M. P. et al. Novel Antibiotics for Gram-Negative Nosocomial Pneumonia. *Antibiot. (Basel)*. **13** (7), 629. 10.3390/antibiotics13070629. (2024). PMID: 39061311; PMCID: PMC11273951.
18. Plata-Menchaca, E. P. & Ferrer, R. Current treatment of nosocomial pneumonia and ventilator-associated pneumonia. *Rev. Esp. Quimioter*. **35** (Suppl 3(Suppl 3), 25–29. 10.37201/req/s03.06.2022. (2022). Epub 2022 Oct 24. PMID: 36285853; PMCID: PMC9717466.
19. Assefa, M. Multi-drug resistant gram-negative bacterial pneumonia: aetiology, risk factors, and drug resistance patterns. *Pneumonia (Nathan)*. **14** (1), 4. 10.1186/s41479-022-00096-z (2022).
20. Xu, E., Pérez-Torres, D., Fragkou, P. C., Zahar, J. R. & Koulenti, D. Nosocomial Pneumonia in the Era of Multidrug-Resistance: Updates in Diagnosis and Management. *Microorganisms* **9** (3), 534. 10.3390/microorganisms9030534 (2021).

Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures



Figure 1

Chest X-ray showing a consolidation of the left lower lobe



Figure 2

Chest X-ray at 1 month check showing a resolution of the consolidation

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- tablesspringer.docx