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# Lipid alterations in relation to inflammation and outcome in patients with community-acquired bacterial acute lower respiratory tract infections: A case-control study

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## Abstract

# Background

Acute infection is associated with alterations in lipid metabolism. We investigated admission lipid profiles in patients hospitalized with acute bacterial lower respiratory tract infections (LRTIs) and their associations with inflammatory biomarkers and outcome.

# Methods

A single-center prospective observational case-control study was conducted at the University Hospital of Patras, Greece, between December 2025 and July 2026, including 233 patients with acute bacterial LRTIs and 100 hospitalized controls frequency-matched for age, sex, and major comorbidities. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured within the first 24 hours of admission. Associations with inflammatory biomarkers and survival status were assessed. Multivariable logistic regression analysis included SOFA, neutrophil-to-lymphocyte ratio (NLR), HDL-C, LDL-C, CRP, and TG.

# Results

Patients with LRTIs had higher TG concentrations than controls (126.4 ± 105.3 vs. 98.8 ± 64.2 mg/dL, p = 0.032). HDL-C concentrations were lower, with a borderline between-group difference (34.7 ± 22.5 vs. 41.0 ± 16.3 mg/dL, p = 0.050), whereas TC and LDL-C did not differ significantly. In-hospital mortality in the LRTI group was 24.4% (57/233). Non-survivors had lower HDL-C concentrations than survivors (26.4 ± 17.1 vs. 39.0 ± 22.5 mg/dL, p = 0.001). TC, LDL-C, and TG did not differ significantly by survival status. HDL-C was inversely correlated with C-reactive protein (r = − 0.343, p < 0.001) and lactate (r = − 0.207, p = 0.042). In the multivariable model, only SOFA was significantly associated with in-hospital mortality whereas HDL-C and TG showed inverse associations with mortality, but neither reached statistical significance.

# Conclusions

Acute bacterial LRTIs were associated with higher TG concentrations and a borderline reduction in HDL-C compared to hospitalized controls. Lower admission HDL-C levels were associated with mortality in unadjusted comparisons.

## Introduction

Infection and systemic inflammation are associated with profound and dynamic alterations in lipid metabolism, resulting in changes in the circulating concentrations, composition, and functional

properties of plasma lipids and lipoproteins. Increasing evidence suggests that lipoproteins extend beyond their classical role in lipid transport and metabolism and may participate in host defense as components of the innate immune response. [1, 2]

High-density lipoprotein (HDL) has attracted particular interest because of its anti-inflammatory, antioxidant, immunomodulatory, and endothelial-protective properties. [3] In addition, circulating lipoproteins can bind and neutralize bacterial products, including lipopolysaccharide (LPS) derived from Gram-negative bacteria and lipoteichoic acid from Gram-positive bacteria. [4–9] During acute inflammation, cytokine- and endotoxin-mediated signaling may alter hepatic lipid synthesis, lipoprotein remodeling, and lipid clearance, resulting in substantial changes in circulating lipid concentrations. [5]

Although infection-associated alterations in lipid metabolism have been described in sepsis [3] and other systemic inflammatory conditions, the clinical significance of routine lipid measurements in patients with acute LRTIs remains incompletely understood. Particularly, it remains uncertain whether lipid parameters are associated with inflammatory biomarkers and whether their alterations may help clinicians identify patients at increased risk of adverse outcomes.

The aim of our study was to investigate plasma concentrations of TC, TG, HDL-C, and LDL-C in patients hospitalized with acute bacterial LRTIs and to compare these parameters with those of matched hospitalized controls. We additionally investigated the associations between lipid parameters, inflammatory biomarkers, and in-hospital mortality.

We hypothesized that acute LRTI would be associated with alterations in the circulating lipid profile and that specific lipid parameters, particularly HDL-C, would be associated with disease severity and adverse clinical outcome.

## Patients and methods

We conducted a prospective single-center case-control study involving patients diagnosed with acute bacterial lower respiratory tract infections (LRTIs) and a control group. A total of 233 patients who were admitted at the General University Hospital of Patras, Greece, were enrolled between December 2025 and July 2026. Exclusion criteria were: (1) pregnancy, (2) age under 18 years, (3) severe medical conditions such as malignancy, acquired immunodeficiency syndrome (AIDS), liver cirrhosis or any other acute hepatopathy, (4) current use of lipid-lowering therapy and a known history of hereditary liver disease.

Additionally, 100 individuals who were admitted to the hospital at the same time for any other reason except infection were enrolled as a control group. Controls were frequency-matched to the LRTI group according to age, sex, and major comorbidities, including hypertension, diabetes mellitus, and autoimmune diseases. Matching was performed at the group level rather than on an individual patient-to-patient basis. The control group was selected independently of lipid measurements and clinical outcomes to ensure comparability between the two study populations.

The clinical outcome was in hospital mortality. Survivors were patients discharged alive, and non-survivors were patients who died from any cause during hospitalization.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of the General University Hospital of Patras (75/9-2-2021). Given the prospective nature of the study and the use of routinely collected laboratory data, the requirement for individual informed consent was waived by the Ethics Committee.

### Laboratory analysis

Diagnosis of bacterial lower respiratory tract infection was based on clinical symptoms, including fever, cough, purulent sputum and dyspnea, combined with laboratory and/or radiological findings, in accordance with WHO guidelines. All patients on admission had negative results when testing for influenza viruses, respiratory syncytial virus (RSV), and SARS-CoV-2.

Patient records were reviewed to retrieve admission laboratory results and information on comorbidities and concomitant medications. Blood samples were obtained within the first 24 hours of admission, irrespective of fasting status. Samples were centrifuged for 10 minutes and analyzed within three hours.

### Lipid profile determination

A lipid panel comprising TC, HDL-C, LDL-C, and TG was measured within the first 24 hours of admission using a Roche/Hitachi Cobas c501 automated analyzer. Patients with LRTIs received antibiotic treatment according to relevant international and local hospital guidelines. Associations of lipid parameters with WBC, NLR, CRP, lactate, and ferritin were evaluated.

### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 25. Continuous variables were assessed for distributional characteristics and are presented as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables are presented as frequencies and percentages. Comparisons between independent groups were performed using the Mann–Whitney U test for continuous variables and the appropriate test for categorical variables. Associations between continuous variables were assessed using Pearson's or Spearman's correlation coefficient, according to data distribution.

Binary logistic regression was performed among patients with bacterial LRTIs to evaluate factors associated with in-hospital mortality. The dependent variable was in-hospital mortality. SOFA, NLR, HDL-C, LDL-C, CRP, and TG were entered simultaneously into the multivariable model. Results are presented as regression coefficients (B), standard errors (SE), adjusted odds ratios (OR), and 95% confidence intervals (95% CI). All tests were two-sided, and $p < 0.05$ was considered statistically significant.

## Results

**Baseline characteristics**

Among the 233 patients with lower respiratory tract infections (LRTIs), the mean age was 75.5 ± 15.2 years; 60.6% were men and 39.4% were women. The mean SOFA score on admission was 4.5 ± 2.7, and 65 patients (27.9%) met the criteria for sepsis. During hospitalization, 57 patients (24.4%) in the LRTI group died, while 176 (75.6%) survived. In the control group, 5 patients (5.0%) died during hospitalization.

**Lipid profile at hospital admission**

Patients with LRTIs had higher TG plasma concentrations than controls (p = 0.032). HDL-C concentrations were lower, with a borderline between-group difference (p = 0.050). TC and LDL-C did not differ significantly between groups. Results are presented in Table 1 and Figure 1.

**Table 1. Plasma lipid profile at hospital admission in patients with lower respiratory tract infections and control patients**

| Parameter (mg / dL) | Infected patients | Control patients | P value |
|---|---|---|---|
| Total cholesterol ( TC ) | 131.4 ± 42.0 | 149.3 ± 62.0 | 0.198 |
| Triglycerides ( TG ) | 126.4 ± 105.3 | 98.8 ± 64.2 | 0.032* |
| HDL cholesterol ( HDL ) | 34.7 ± 22.5 | 41.0 ± 16.3 | 0.050 |
| LDL cholesterol ( LDL ) | 81.3 ± 38.4 | 88.5 ± 47.8 | 0.652 |

*Values are presented as mean ± standard deviation (SD). *p < 0.05. The HDL-C comparison (p = 0.050) is described as borderline.*

**Figure 1**. Distribution of admission lipid concentrations in patients with bacterial LRTIs and hospitalized controls. Boxes represent the interquartile range, with the median shown as a horizontal line. Concentrations are expressed in mg/dL.

**Admission plasma lipid concentrations according to outcome**

Within the infection group, non-survivors had statistically significant lower HDL cholesterol (HDL-C) levels at admission than survivors. No statistically significant differences in total cholesterol (TC), triglyceride (TG), or LDL cholesterol (LDL-C) levels were observed between survivors and non-survivors. The results are summarized in **Table 2.**

**Table 2. Plasma lipid levels at hospital admission according to in-hospital survival in patients with acute lower respiratory tract infections**

| Parameter (mg / dL) | Survivors | Non- survivors | P value |
|---|---|---|---|
| Total cholesterol ( TC ) | 137.0 ± 44.4 | 125.3 ± 50.1 | 0.102 |
| Triglycerides ( TG ) | 126.9 ± 112.8 | 108.7 ± 52.8 | 0.375 |
| HDL cholesterol ( HDL -C) | 39.0 ± 22.5 | 26.4 ± 17.1 | **0.001** |
| LDL cholesterol ( LDL ) | 83.5 ± 40.5 | 79.0 ± 39.0 | 0.581 |

*Values are presented as mean ± standard deviation (SD). Statistical significance was defined as P* < 0.05.

**Correlations between plasma lipid parameters and inflammatory and metabolic biomarkers in the LRTI group**

Among patients with LRTIs, lactate was inversely correlated with TC (r = −0.305, p = 0.002), HDL-C (r = −0.207, p = 0.042), and LDL-C (r = −0.236, p = 0.021). Ferritin was positively correlated with LDL-C (r = 0.232, p = 0.030) and TG (r = 0.508, p < 0.001). CRP was inversely correlated with TC (r = −0.214, p = 0.026) and HDL-C (r = −0.343, p < 0.001), and positively correlated with TG (r = 0.211, p = 0.029). No statistically significant correlations were observed between WBC or NLR and any lipid parameter. Results are presented in Table 3.

**Table 3: Correlations Between Lipid Parameters and Inflammatory Biomarkers in the LRTI group**

| Biomarker | TC | HDL -C | LDL -C | TG |
|---|---|---|---|---|
| WBC | r=0.042, p=0.648 | r=-0.017, p=0.854 | r=0.023, p=0.799 | r=0.023, p=0.798 |
| NLR | r=0.006, p=0.947 | r=-0.056, p=0.538 | r=-0.025, p=0.784 | r=0.061, p=0.505 |
| Lactate | r=-0.305, **p=0.002** | r=-0.207, **p=0.042** | r=-0.236, **p=0.021** | r=0.014, p=0.892 |
| Ferritin | r=0.069, p=0.522 | r=-0.160, p=0.133 | r=0.232, **p=0.030** | r=0.508, **p<0.001** |
| CRP | r = −0.214, **p = 0.026** | r = −0.343, **p < 0.001** | r = −0.117, p = 0.231 | r = 0.211, **p = 0.029** |

**Multivariable logistic regression analysis of in-hospital mortality**

In multivariable logistic regression (n=202) including HDL-C, LDL-C, triglycerides, SOFA score, CRP, and NLR, only SOFA score was significantly associated with in-hospital mortality. Each one-point increase in SOFA score was associated with 24.1% higher odds of death (adjusted OR 1.241, 95% CI 1.057–1.457; p = 0.008). HDL-C and triglycerides showed inverse associations with mortality, but neither reached statistical significance (adjusted OR 0.971, 95% CI 0.941–1.001; p = 0.061, and adjusted OR 0.993, 95% CI 0.986–1.000; p = 0.051, respectively). LDL-C, CRP, and NLR were also not significantly associated with mortality in the adjusted model (all p > 0.05). (Table 4).

**Table 4**. Multivariable logistic regression analysis of factors associated with in-hospital mortality among patients with LRTIs

| Variable | B | SE | Adjusted OR | 95% CI | p value |
|---|---|---|---|---|---|
| HDL-C (mg/dL) | −0.029 | 0.016 | 0.971 | 0.941–1.001 | 0.061 |
| LDL-C (mg/dL) | 0.007 | 0.005 | 1.007 | 0.997–1.017 | 0.146 |
| TG (mg/dL) | −0.007 | 0.004 | 0.993 | 0.986–1.000 | 0.051 |
| **SOFA score** | **0.216** | **0.082** | **1.241** | **1.057–1.457** | **0.008** |
| CRP | 0.027 | 0.024 | 1.027 | 0.980–1.077 | 0.263 |
| NLR | 0.006 | 0.010 | 1.006 | 0.987–1.025 | 0.561 |
| Constant | −1.096 | 0.860 | 0.334 | — | 0.203 |

## Discussion

We investigated the plasma lipid parameters in patients with acute bacterial LRTIs on hospital admission and their associations with inflammatory biomarkers and hospital outcome. Compared to hospitalized controls, patients with LRTIs had higher TG plasma concentrations and lower HDL-C concentrations, with the latter difference being borderline. Plasma TC and LDL-C concentrations did not differ significantly between the group of respiratory infected patients and the matched control no-infected patients. Among patients with LRTIs, HDL-C was lower in non-survivors in unadjusted comparisons; However, the inverse association between HDL-C and in-hospital mortality did not reach statistical significance after

adjustment for SOFA score and the other included covariates (adjusted OR 0.971, 95% CI 0.941–1.001; p = 0.061).

In our cohort, the LRTI group of patients had higher triglyceride concentrations and lower HDL-C, with a borderline difference for HDL-C, whereas TC and LDL-C did not differ significantly from controls. This pattern is consistent with the concept of infection-associated dyslipidemia, in which inflammatory activation is accompanied by reduced HDL-C and increased triglyceride-rich lipoproteins. Previous studies have similarly reported alterations in circulating lipoproteins during acute bacterial infection and sepsis. Grion et al. demonstrated that HDL-C concentrations on hospital admission were associated with the subsequent development of severe sepsis, supporting a potential role of HDL in the host response to infection. [8] Viral respiratory infections have also been associated with distinct sputum lipid profiles, although these findings are not directly comparable with circulating lipid measurements [6]

The alterations in lipid metabolism observed during acute infection are biologically plausible and are increasingly recognized as part of the host response to infection. During the acute-phase response, inflammatory cytokines and endotoxin-mediated signaling modify hepatic lipid synthesis, lipoprotein composition, and lipid clearance. Consequently, circulating lipid concentrations may change substantially during systemic inflammation. Lipoproteins are not merely transport particles but also participate in innate immunity by binding and neutralizing bacterial products, including lipopolysaccharide and lipoteichoic acid. [9]

Several correlations were observed between lipid parameters and CRP, lactate, and ferritin. Kumari et al. also examined associations between lipid parameters and inflammatory markers in patients with COVID-19. [10] Differences in infection type and study population should be considered when comparing those findings with our bacterial LRTI cohort.

The most clinically relevant finding of our study was the significantly lower HDL-C concentration among non-survivors than survivors in the lower respiratory tract infection group. HDL-C also showed inverse associations with mortality, in multivariable logistic regression, although this did not reach statistical significance (p = 0.061).In contrast, TC, LDL-C, and TG concentrations did not differ significantly between survivors and non-survivors. The lower HDL-C concentrations observed among non-survivors are consistent with previous evidence linking low HDL-C to adverse outcomes in severe infection. In a prospective study of patients with severe sepsis, Chien et al. reported lower HDL-C concentrations among patients who subsequently died and identified an HDL-C concentration below 20 mg/dL on the first day of severe sepsis as an independent predictor of mortality [11]. More recently, a systematic review and meta-analysis including 24 observational studies and 2,542 critically ill patients found that non-survivors had significantly lower HDL-C concentrations at ICU admission than survivors, with a pooled mean difference of approximately − 7 mg/dL. [12] Our findings therefore add further support to the association between low plasma HDL-C concentrations and adverse outcomes during acute infectious illness, specifically in the subcategory of patients hospitalized with lower respiratory tract infections. Several mechanisms may explain this association. HDL participates in the neutralization and

clearance of bacterial lipids, particularly LPS, and possesses anti-inflammatory, antioxidant, and endothelial-protective properties. Consequently, a low HDL-C concentration may reflect not only reduced circulating cholesterol content but also a broader transformation of HDL into a dysfunctional acute-phase lipoprotein.[9]

The triglyceride findings deserve consideration as well. Although triglycerides were significantly higher in infected patients than in control group, they did not differ significantly between survivors and non-survivors. This suggests that the increase in TG may be more closely related to the acute inflammatory/metabolic response to infection than to short-term mortality itself. This finding deserves further investigation, although it is supported by a meta-analysis of critically ill patients with sepsis, which found an association between mortality and lower TC, HDL-C, and LDL-C, but not in admission triglyceride concentrations. [13]. Therefore, although hypertriglyceridemia may accompany acute infection, it does not establish a protective effect of triglycerides.

This study has several strengths. First, lipid measurements were obtained during the first 24 hours of hospitalization, providing information at an early stage of the infectious episode. Second, the study enrolled a control group matched for age, sex, and comorbidities, allowing comparison of lipid profiles between patients with lower respiratory tract infections and patients hospitalized for other causes. Third, the study evaluated lipid parameters in relation to several inflammatory biomarkers and to clinical outcomes.

Several limitations should nevertheless be acknowledged. First, this was a single-center observational study, which limits the generalizability of the findings. Second, the observational design does not permit causal inference. Third, lipid concentrations were measured at a single time point, preventing assessment of longitudinal changes during infection and recovery. Fourth, although patients receiving lipid-lowering therapy were excluded, residual confounding by nutritional status, liver function, metabolic disease, or other unmeasured factors cannot be excluded. Fifth, blood samples were collected irrespective of fasting status, which may have affected TG concentrations. Sixth, age was not included in the multivariable model, leaving possible residual confounding. The correlation analyses were exploratory and involved multiple comparisons, so their findings should be interpreted cautiously.

In conclusion, acute bacterial LRTIs were associated with higher plasma TG concentrations and a borderline reduction in HDL-C compared with hospitalized controls without infection. Among patients with LRTIs, HDL-C concentrations were significantly lower in non-survivors and inversely correlated with CRP and lactate. However, the association between HDL-C and in-hospital mortality did not reach statistical significance after adjustment for SOFA score and the other included covariates. Prospective multicenter studies incorporating serial lipid measurements and established clinical severity scores are warranted to determine whether lipid parameters provide incremental prognostic information in patients with acute respiratory infections.

## Declarations

**Funding**: This research received no external funding.

**Institutional Review Board Statement:** This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board: Scientific, Research, and Ethics Committee of Patras University Hospital (Ref. No. 75/9-02-2021).

**Informed Consent Statement**: Informed consent was obtained from all subjects involved in this study.

**Data Availability Statement**: The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Conflicts of Interest**: The authors declare that they have no conflicts of interest.

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# Figures

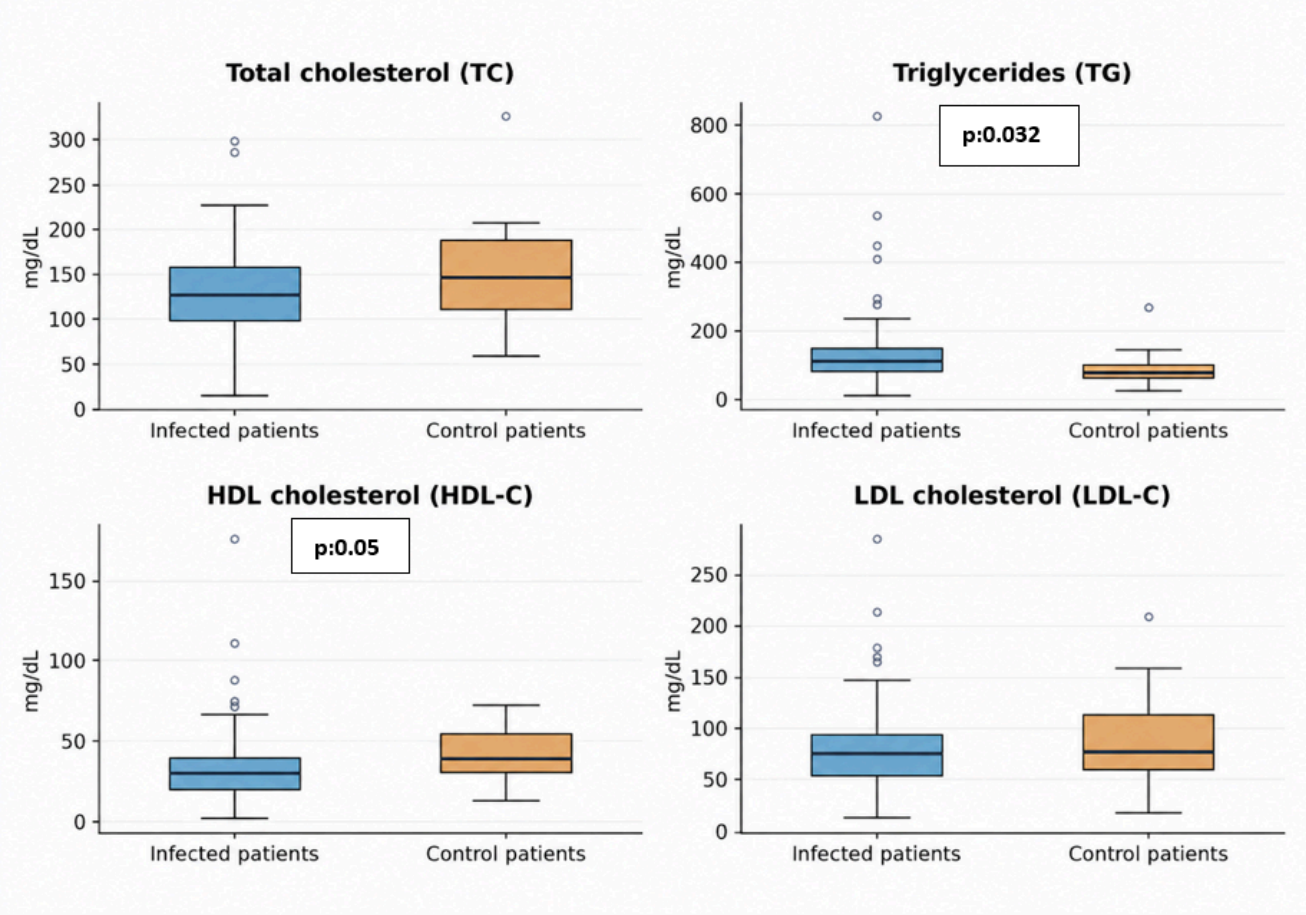



**Figure 1**

Distribution of admission lipid concentrations in patients with bacterial LRTIs and hospitalized controls. Boxes represent the interquartile range, with the median shown as a horizontal line. Concentrations are expressed in mg/dL.