

# Prognostic Role of Dynamic Serum Lipid Profile Alterations in Acute Respiratory Failure: A Scoping Review

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## Abstract

**Background:** Acute respiratory failure (ARF) is a critical condition commonly triggered by infectious or inflammatory insults to the lungs. Recent studies have highlighted that systemic inflammation during ARF can lead to significant alterations in serum lipid metabolism, yet their prognostic utility remains underexplored.

**Objectives:** To systematically map the current evidence on serum lipid profile alterations in ARF and assess their prognostic significance.

**Methods:** A scoping review was conducted following PRISMA-ScR guidelines. Literature searches were performed in PubMed, Scopus, Embase, and Web of Science for studies published between January 2015 and March 2025. Eligible studies included those reporting changes in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), or triglycerides (TG) in ARF patients, including COVID-19-associated ARDS. Extracted data focused on lipid trends, disease severity, inflammatory markers, and mortality outcomes.

**Results:** Eighteen studies involving over 6,000 patients were included. Most studies reported significant reductions in HDL-C and LDL-C during acute illness, particularly in severe COVID-19. Low HDL-C levels were frequently associated with elevated inflammatory markers, increased ICU admission, mechanical ventilation, and mortality. Some studies identified composite ratios like monocyte-to-HDL-C and platelet-to-HDL-C as stronger prognostic indicators than individual lipids. Triglyceride changes were inconsistent but appeared to correlate with cytokine activation. Persistently low lipid levels during recovery were linked to adverse outcomes.

**Conclusion:** Alterations in serum lipids, especially reduced HDL-C and LDL-C, may serve as valuable prognostic markers in ARF. Incorporating lipid monitoring into clinical protocols could enhance risk stratification and patient management.

**Key words:** Acute respiratory failure, lipid profile, HDL-C, LDL-C, prognosis, scoping review.

## Introduction

Acute respiratory failure (ARF) is a life-threatening condition characterised by the failure of lungs to maintain adequate oxygenation or carbon dioxide elimination, resulting from diverse pulmonary or systemic insults such as pneumonia, acute respiratory distress syndrome (ARDS), or sepsis<sup>1,2</sup>. It remains a leading cause of intensive care unit (ICU) admissions globally and is associated with high rates of morbidity and mortality, particularly in vulnerable populations with co-morbidities like diabetes and cardiovascular disease<sup>3</sup>.

In recent years, especially during the COVID-19 pandemic, there has been a growing interest in identifying reliable, cost-effective prognostic biomarkers that could assist in early stratification of ARF severity and outcomes. While traditional indicators like the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, APACHE II,

and SOFA scores are widely used, they may not fully capture the complex metabolic and immunological changes that occur during acute illness<sup>4</sup>.

Among emerging biomarkers, alterations in serum lipid profiles have drawn significant attention. Lipids, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), are known to undergo marked changes during systemic inflammatory responses<sup>5-7</sup>. HDL-C, in particular, plays an essential role in modulating inflammation, neutralizing endotoxins, and protecting against oxidative damage. Hypocholesterolaemia, especially low HDL-C, has been repeatedly associated with worse clinical outcomes in patients with severe infections and respiratory failure<sup>8-10</sup>.

These lipid alterations may occur rapidly and are thought to

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be mediated by inflammatory cytokines, altered hepatic synthesis, and increased vascular permeability. Figure 1 illustrates the proposed mechanistic pathways linking systemic inflammation in ARF to dynamic changes in lipid metabolism and immune dysregulation.

The COVID-19 pandemic further underscored the clinical relevance of lipidomics. Studies consistently report that patients with severe SARS-CoV-2 infection experience profound reductions in HDL-C and LDL-C, which often correlate with inflammatory marker elevation, critical illness, and increased mortality<sup>11-13</sup>. Moreover, composite indices such as monocyte-to-HDL-C and platelet-to-HDL-C ratios have been proposed as novel prognostic markers, offering additional insight beyond conventional lipid values<sup>14-16</sup>.

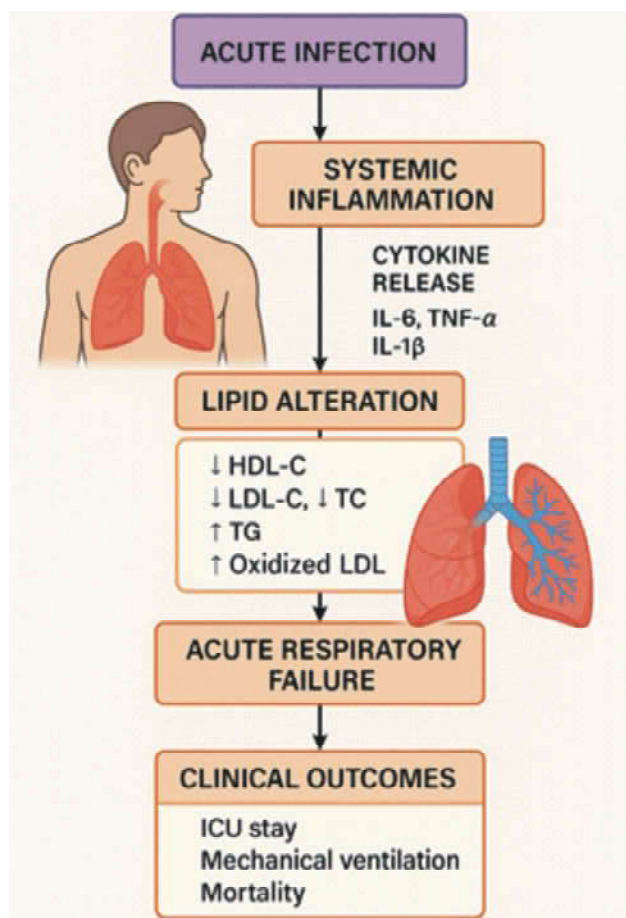
Despite emerging evidence, data remain scattered across different populations and ARF aetiologies. To date, no synthesis has comprehensively mapped the spectrum of lipid profile alterations in ARF or critically examined their

prognostic value across diverse clinical settings.

This scoping review aims to consolidate available research on dynamic serum lipid changes in ARF, evaluate their association with clinical outcomes, and highlight knowledge gaps requiring future investigation.

## Methods

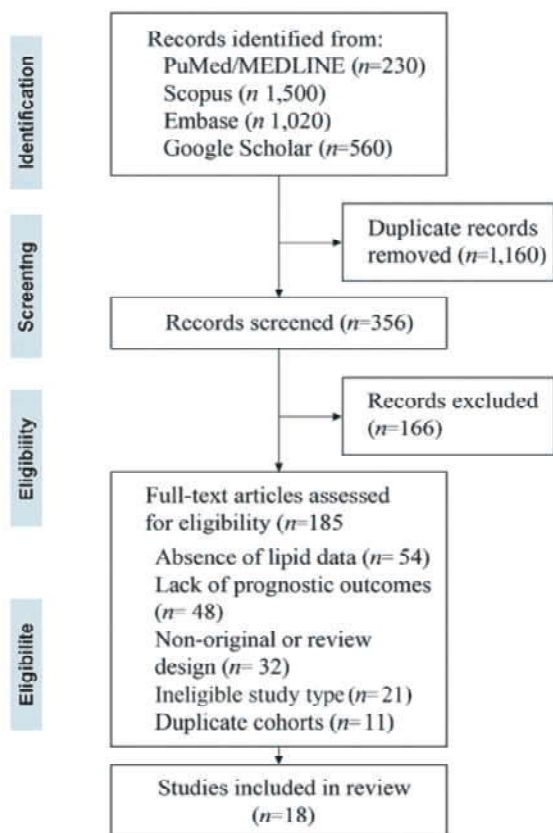
This review was structured as a scoping study using the PRISMA-ScR checklist to ensure transparency and methodological rigor. The review question was framed using the Population-Concept-Context (PCC) strategy recommended by the Joanna Briggs Institute. We focused on identifying and mapping research that explored changes in lipid profiles – such as HDL-C, LDL-C, total cholesterol, triglycerides, and ApoA-I – and their link to outcomes in patients with acute respiratory failure (ARF) and related lung conditions including COVID-19, COPD, asthma, and interstitial lung disease. Studies were included if they were published in English between 2005 and 2025, involved human participants, and provided original data on serum lipid values along with relevant clinical outcomes such as ICU admission, ventilation requirement, or death. Review articles, animal studies, and those lacking lipid data or prognostic endpoints were excluded. We searched four electronic databases – PubMed, Scopus, Embase, and Google Scholar – using specific keywords and controlled vocabulary related to lipid biomarkers and respiratory failure. The search strategy was refined to retrieve both recent and foundational studies. Two reviewers screened all articles independently, reviewing titles, abstracts, and full texts. Any disagreements were resolved through discussion or consultation with a third reviewer. Additional studies were identified by reviewing the references of selected papers. A data charting form was used to extract key study details. Due to variability in study designs and outcome measures, a descriptive synthesis was conducted. No ethical approval was necessary as only publicly available literature was used.



**Fig. 1:** Illustrates how acute infections trigger systemic inflammation affecting lipid profiles by lowering HDL-C, LDL-C, TC levels while raising TG levels; these changes interfere with surfactant function and alveolar-capillary integrity leading to ARF.

## Results

**Study Selection:** Out of 4,310 records from PubMed/MEDLINE (n = 1,230), Scopus (n = 1,500), Embase (n = 1,020), and Google Scholar (n = 560), 1,160 duplicates were removed. After title and abstract review, 3,150 articles were excluded for not meeting inclusion criteria. A total of 185 full-text articles were screened for eligibility. Of these, 166 were excluded based on criteria such as no serum lipid data (n = 54), no prognostic outcomes (n = 48), non-original studies (n = 32), ineligible study types (n = 21), and duplicated cohorts (n = 11). Ultimately, 18 studies met all inclusion criteria for the final review.



**Fig. 2:** PRISMA 2020 flow diagram showing the study selection process<sup>9</sup>.

**Overview of Included Studies:** All the 18 studies included (from 2005 through 2025) were published during this period indicating a worldwide interest in the prognostic value of lipid-based biomarkers in respiratory diseases. These were conducted in a wide variety of clinical settings and with a range of patient populations, including those with COVID-19, asthma, COPD, ILD, lung cancer, LRTIs, diabetic retinopathy, and NAFLD. A minority of studies looked at the relationship between lipid levels and severe COVID-19, progression and mortality (HDL-C, LDL-C, TC and TG) (Table I).

**Table I: Overview of included studies.**

Parameter	Details
Number of studies included	18
Timeframe	2005 - 2025
Geographic spread	Studies from North America, Europe, Asia, and the Middle East
Study designs	Observational (n = 16); Prospective cohort (n = 1); Retrospective/cross-sectional (n = 2)
Clinical settings	ICU, inpatient wards, outpatient pulmonary clinics

Sample sizes	Ranged from 60 to over 3,000 patients
Target populations	COVID-19, asthma, COPD, ILD, lung cancer, LRTIs, diabetic retinopathy, NAFLD

**Characteristics of Included Studies:** The 18 studies reviewed were diverse in design, population, and clinical focus, mostly observational, examining serum lipid biomarkers (TC, LDL-C, HDL-C, TG) in lung-related diseases. Geographically, they spanned the US, China, Turkey, Mexico, Sweden, India, and more. Settings ranged from ICUs and emergency wards (mainly for COVID-19 and ARF) to outpatient clinics for chronic diseases like asthma, COPD, diabetic retinopathy, and NAFLD. Prognostic parameters included mortality, ICU admission, ventilation, severity scores (SOFA, APACHE II), and hospital stay. Emerging biomarkers like monocyte-HDL-C and platelet-HDL-C ratios were also noted.

**Distribution by Diagnosis of Respiratory Disease:** Underlying disease was the unit of analysis, yielding 18 studies included for analysis. The majority (n = 9) focused on COVID-19, featuring uniformly low levels of HDL-C, LDL-C, and TC, and high levels of TG-associated with death, risk of ICU admission, and need for ventilation. In asthma-based studies (n = 2) LDL-C was inversely correlated with mortality, monocyte-to-HDL-C and platelet-to-HDL-C ratios were strong predictive factors. One study on COPD identified stage-specific lipidomics signatures. Two studies on ILD and one on LRTI (n = 2) found decreased HDL-C and ApoA-I as predictors of dryness and death. The lung cancer study found modified TG/HDL-C ratios, whereas DR and NAFLD studies focused on systemic lipid derangements influencing respiratory consequences. These findings reinforce the potential utility of lipid biomarkers as prognostic markers in a broad range of respiratory diseases (Table III).

**Patterns of Lipid Alteration and Prognostic Implications:** Lipid changes had uniformly significant relationships with the severity of disease type under different respiratory diseases. HDL-C, LDL-C, and total cholesterol were decreased significantly in most cases with severe symptoms, which was indicative of systemic inflammation and obvious hepatic impairment. Higher triglycerides implied a higher inflammatory load and multiorgan failure. Interestingly, composite ratios such as monocyte: HDL-C and platelet:HDL-C showed better predictive performance, with more improvements seen in the asthma population. These findings emphasize the importance of lipid indices in clinical risk assessment (Table IV).

**Table II: Characteristics and key findings of the 18 included studies.**

Author (Year)	Study Design	Setting/Population	Lipid Biomarkers Studied	Outcomes Assessed	Key Findings
Mireia <i>et al</i> (2021)	Observational study	Patients with LRTIs (CAP and COVID-19)	TC, LDL-C, HDL-C, TG	Prognosis and mortality	Low TC, LDL-C, HDL-C linked to worse outcomes, esp. COVID-19
Wen <i>et al</i> (2024)	Retrospective cohort study	3,233 asthmatic adults (NHANES 2005 - 2018)	LDL-C, HDL-C, TG, TC	All-cause mortality	1 mmol/L ↑ in LDL-C = 17% ↓ mortality
Barman <i>et al</i> (2022)	Retrospective cross-sectional study	COVID-19 patients in Turkey (n >200)	TC, LDL-C, HDL-C, TG	Mortality and in-hospital outcomes	TC, LDL-C, HDL-C lower in COVID-19; HDL-C predictive of mortality
Ochoa-Ramírez <i>et al</i> (2024)	Observational study	100 COVID-19 patients	TC, HDL-C	Disease severity and mortality	Low HDL and high TC linked to COVID-19 mortality
Ochoa-Ramírez <i>et al</i> (2020)	Observational study	COVID-19 patients in Mexico	TC, LDL-C, HDL-C, TG	Clinical diagnostic significance	Significant lipid changes suggest diagnostic use in COVID-19
Gruber, Maja <i>et al</i> (2009)	Observational study	LRTI patients	TC, HDL-C	Prognosis	Low HDL-C and TC predict poor outcomes in LRTIs
Guyi <i>et al</i> (2020)	Observational study	COVID-19 patients	HDL-C	Severity and survival	Low HDL-C linked to COVID-19 severity/mortality
Arslan <i>et al</i> (2021)	Observational study	COVID-19 patients	TC, LDL-C, HDL-C, TG	Disease severity	Lipid alterations correlate with COVID-19 severity
Karolyn <i>et al</i> (2021)	Observational study	COVID-19 patients	TC, LDL-C, HDL-C, TG	Mortality	LDL <50 mg/dL and TG >150 mg/dL linked to COVID-19 mortality
Radwan <i>et al</i> (2024)	Prospective cohort study	Cancer patients with LRTIs	TC, HDL-C	Mortality	Low HDL-C linked to mortality in cancer + LRTIs
Zhang <i>et al</i> (2025)	Cohort study	Asthma patients	Monocyte-HDL-C ratio	Mortality	High monocyte/HDL-C ratio linked to higher asthma mortality
Liu <i>et al</i> (2024)	Observational study	Diabetic retinopathy patients	LPAR3, Calponin	Disease progression	LPAR3 and CNN1 levels differ in diabetic retinopathy
Barbara <i>et al</i> (2022)	Observational study	COVID-19 patients	Various lipid biomarkers	Medium-term clinical outcomes	Lipid profiles altered post-COVID with persistent symptoms
Zhao <i>et al</i> (2025)	Cohort study	Asthma patients	Platelet-HDL-C ratio	Elevated BEOC levels	High platelet/HDL-C ratio linked to elevated BEOC in asthma
Jiang <i>et al</i> (2024)	Observational study	NAFLD patients	Various lipid biomarkers	Lipid profile alterations	Gut therapy alters lipids in NAFLD patients
Fang <i>et al</i> (2020)	Observational study	Marine phytoplankton	Lipid biomarkers	Microbial community structure	Lipid output varies by environment in phytoplankton
Ding <i>et al</i> (2022)	Observational study	Swedish cohort	Blood lipid levels	Atrial fibrillation	Midlife lipid levels linked to atrial fibrillation
Liu <i>et al</i> (2021)	Observational study	COPD patients	Serum lipid species	Disease progression	Lipidomic profile changes linked to COPD stages

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triglycerides implied a higher inflammatory load and multiorgan failure. Interestingly, composite ratios such as monocyte: HDL-C and platelet:HDL-C showed better predictive performance, with more improvements seen in the asthma population. These findings emphasize the importance of lipid indices in clinical risk assessment (Table IV).

**Table III: Included studies by disease category, main lipid findings, and outcomes.**

Disease Category	No. of Studies (n=18)	Key Lipid Biomarkers Affected	Observed Trends	Primary Prognostic Outcomes
COVID-19	9	HDL-C, LDL-C, TG, TC	↓ HDL-C, ↓ LDL-C, ↓ TC in severe cases; ↓ TG	Mortality, ICU admission, ventilator support
Asthma	2	LDL-C, HDL-C, Monocyte-HDL-C ratio, Platelet-HDL-C ratio	LDL-C inversely related to mortality; ↓ Monocyte/HDL-C and Platelet/HDL-C ratios	Mortality, eosinophilia (BEOC)
COPD	1	Serum lipidomic signatures	Distinct lipid patterns by disease stage	Stage-based progression monitoring
ILD/LRTI	2	HDL-C, ApoA-I, TC	↓ HDL-C and ApoA-I; ↓ TC as inflammatory marker	Fibrosis, mortality
Lung Cancer	1	TG, HDL-C	↑ TG/HDL-C ratio	Systemic inflammation, clinical deterioration
DR/NAFLD	2	Lipidomic-inflammatory pathways	Altered lipid profiles linked to metabolic-pulmonary dysfunction	Increased respiratory vulnerability, inflammation

**Table IV: Summary of lipid alteration patterns and associated prognostic outcomes.**

Lipid Marker / Ratio	Trend Observed	Clinical Associations	Notable Studies
HDL-C	↓ in most severe/fatal cases	ICU admission, mortality, ventilation	Gruber (2021), Wu (2021), Arslan (2021)
LDL-C	↓ in advanced stages	Systemic inflammation, poor outcomes	Wen (2024), Barman (2022), Ochoa-Ramírez (2021)
Total Cholesterol (TC)	↓ in COVID-19 and ILD	Fibrotic progression, stress response	Mosaad (2021), Liu D (2020)
Triglycerides (TG)	↑ in inflammatory states	ICU need, multiorgan dysfunction	Wu (2021), Ding Liu (2020), Arslan (2021)
Monocyte-to-HDL-C Ratio	↑ in asthma	Mortality risk, immune activation	Zhang Q (2025)
Platelet-to-HDL-C Ratio	↑ in asthma	Eosinophilic inflammation, poor prognosis	Zhang Y (2025)

**Timing of Lipid Measurements:** The timing of lipid assessments varied significantly across studies, affecting comparability and clinical interpretation. Most studies measured lipid levels at hospital or ICU admission, providing early prognostic insights. However, few studies included longitudinal profiling, which could better reflect disease dynamics and treatment responses. Studies like Wu (2021), Liu D (2024), and Barbara J (2022) showed that serial lipid measurements offered valuable information on disease progression and recovery. The lack of standardised timing across studies remains a key limitation (Table V).

**Table V: Timing of lipid measurements and longitudinal assessment in included studies.**

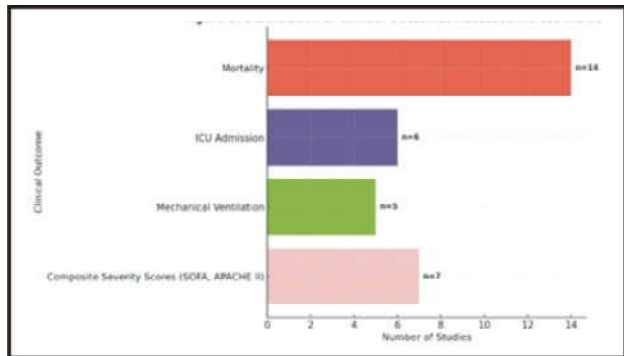
Study Author (Year)	Timing of Lipid Measurement	Longitudinal Assessment
Gruber M (2021)	At hospital admission	No
Wen J (2024)	Baseline (NHANES registry)	No
Barman HA (2022)	At admission + pre-infection values	Partially
Mosaad (2021)	At hospital admission	No
Ochoa-Ramírez (2021)	Acute phase (hospitalisation)	No
Ding Liu (2020)	Acute infection phase	No
Lee C (2020)	At admission	No
Arslan (2021)	At admission	No
Wu M (2021)	Admission + ICU course	Yes

Radwan S (2024)	Hospital stay	Yes
Zhang Q (2025)	Baseline registry values	No
Liu D (2024)	Longitudinal trends (DR progression)	Yes
Barbara J (2022)	Pre- and post-COVID recovery	Yes
Zhang Y (2025)	Registry baseline values	No
Jiang H (2024)	Before and after microbial therapy	Yes
Fang M (2020)	During environmental exposure	No
Ding M (2022)	Midlife baseline	No
Liu D (2021)	Stage-based comparison	Yes

### Clinical Outcomes Assessed

The prognostic utility of serum lipid alterations was examined across various clinical outcomes in the included studies. Mortality was the most frequently assessed endpoint (n = 14), with consistent associations observed between reduced HDL-C and LDL-C levels and increased death risk. ICU admission (n = 6) was commonly linked to elevated triglyceride levels and low HDL-C, indicating heightened disease severity. The requirement for mechanical ventilation (n = 5) was associated with significant dyslipidemia, particularly hypertriglyceridaemia. Additionally, composite severity scores – such as SOFA and APACHE II – were used in 7 studies to objectively quantify systemic involvement; patients with abnormal lipid profiles often exhibited

higher scores. These findings highlight the value of lipid parameters not only in disease monitoring but also in early prognostic risk stratification across a range of respiratory conditions. The distribution of these clinical outcomes across the reviewed studies is visually represented in Fig. 3.



**Fig. 3:** Distribution of clinical outcomes assessed across included studies.

This horizontal bar chart highlights the frequency with which each clinical outcome was assessed across the 18 included studies. Mortality was the most evaluated endpoint ( $n = 14$ ), followed by composite severity scores ( $n = 7$ ), ICU admissions ( $n = 6$ ), and the need for mechanical ventilation ( $n = 5$ ). Lipid biomarkers – especially HDL-C, LDL-C, and TG – were significantly associated with these outcomes, reinforcing their prognostic value in acute respiratory conditions.

**Geographical and Ethnic Variability:** The 18 studies included were conducted in various regions of the world: most in China ( $n = 5$ ), followed by the USA and Turkey ( $n = 2$  per country). LDL-C and TG were different between ethnic groups in only one study (Wen *et al*, 2024). The majority did not have subgroup analysis, thereby restricting generalisability. HDL-C, TG were low in the regional trends of Chinese COVID-19/asthma cases and TC was abnormal in Turkish and Egyptian ones. These tendencies reveal the necessity for ethnicity-based cut-off points of lipid parameters (Table VI).

### Emerging Biomarkers and Techniques

Novel lipid biomarkers have been recently identified in respiratory diseases. Lipidomics, composite ratios (monocyte/HDL-C, platelet/HDL-C) and ApoA-I have been found to have prognostic significance in asthma, COPD,

and post-COVID states. Combined lipidomic-transcriptomic approaches may complement precision diagnostics and risk stratification irrespective of the disorder (Table VII).

**Table VI: Geographical and ethnic variability in lipid biomarker studies.**

Study Author (Year)	Country/Region	Ethnic Stratification Reported	Comments on Baseline Lipids
Gruber M (2021)	Austria	No	Lower HDL-C in severe COVID cases
Wen J (2024)	USA	Yes (NHANES multiracial)	Ethnic differences noted in LDL-C and TG
Barman HA (2022)	Turkey	No	Low HDL-C in Turkish ICU patients
Mosaad (2021)	Egypt	No	Elevated TC predictive in Egyptian cohort
Ochoa-Ramírez (2021)	Mexico	No	TC/LDL-C patterns in Latin American population
Wu M (2021)	China	No	Low TG and HDL-C in COVID/asthma
Zhang Q (2025)	China	No	Novel HDL-C ratios in asthma cohort
Barbara J (2022)	USA	No	Persistent dyslipidemia in post-COVID survivors
Zhang Y (2025)	China	No	Eosinophil-lipid ratio in Chinese asthma group
Liu D (2024)	China	No	Longitudinal lipid data in DR with respiratory overlap
Liu D (2021)	China	No	COPD-specific lipidomics in Chinese patients
Arslan (2021)	Turkey	No	Severe dyslipidemia patterns in Turkish patients

**Evidence Gaps Identified:** Despite growing interest in lipid-based prognostic markers for respiratory diseases, significant gaps persist. Studies employed diverse lipid panels without standardised thresholds, hindering comparability and clinical application. Most relied on single-timepoint measurements, lacking longitudinal data. Advanced tools like lipidomics and AI are underutilized in practice. Ethnic stratification was infrequent, and key groups – such as pediatric and ILD subpopulations – were underrepresented. These gaps underscore the need for multicenter, standardised, and technology-driven research to validate lipid biomarkers for clinical use.

**Table VII: Emerging biomarkers and diagnostic techniques in lipid-based respiratory research.**

Study Author (Year)	Biomarker/Technology Investigated	Clinical Disease Context	Methodological Platform	Key Findings / Clinical Utility
Liu D (2021)	Lipidomics profiling (mass spectrometry)	COPD	Mass spectrometry-based lipidomic mapping	Stage-specific lipidomic signatures correlated with COPD severity
Zhang Q (2025)	Monocyte-to-HDL-C ratio	Asthma	Integrated immuno-lipid composite marker	Stronger mortality prediction in asthma
Zhang Y (2025)	Platelet-to-HDL-C ratio	Asthma	Inflammatory platelet-lipid interaction index	Prognostic implications for eosinophilic asthma

Liu D (2024)	LPAR3 expression and CNN1 co-expression	Diabetic retinopathy with respiratory overlap	Transcriptomic and lipidomic co-analysis	Experimental targets linking metabolic inflammation to pulmonary vulnerability
Barbara J (2022)	ApoA-I and HDL subfractions	Post-COVID-19 syndrome	Serological proteomics and HDL subfractionation	Correlated with persistent post-COVID inflammation

## Discussion

This scoping review highlights the emerging importance of dynamic alterations in serum lipid profiles as potential prognostic markers in patients with acute respiratory failure (ARF). Across various clinical contexts – including bacterial pneumonia, viral pneumonitis, COVID-19-related ARDS, asthma, and chronic obstructive pulmonary disease – consistent patterns of lipid disturbances have been documented. These alterations reflect both the metabolic consequences of systemic inflammation and the body's acute phase response to severe illness.

A predominant finding across studies is the significant decline in high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) during the acute phase of respiratory failure. These changes are not merely incidental but correlate with markers of disease severity, including higher inflammatory burden, increased need for mechanical ventilation, prolonged ICU stay, and increased mortality. The reduction in HDL-C, in particular, appears to be an early and sensitive indicator of poor prognosis, as this lipoprotein exerts anti-inflammatory, antioxidant, and endothelial-stabilizing effects that are critical during systemic illness. Its depletion suggests ongoing immune dysregulation and impaired vascular protection<sup>17-21</sup>.

In contrast, triglyceride levels demonstrate greater variability, influenced by nutritional status, hepatic insulin resistance, and the degree of cytokine activation. In some cohorts, elevated triglyceride levels are associated with worse outcomes, potentially indicating underlying metabolic derangement and heightened systemic inflammation. Total cholesterol levels also tend to decline significantly during acute illness, and persistent hypocholesterolemia beyond the acute phase has been linked with delayed recovery and chronic inflammation<sup>22,23</sup>.

Emerging research suggests that composite lipid-immune indices – such as the monocyte-to-HDL-C ratio or platelet-to-HDL-C ratio – may serve as more powerful prognostic tools than single lipid measurements. These indices integrate immune cell dynamics with lipid metabolism and have shown better correlation with mortality and disease progression in several forms of ARF, including those driven by COVID-19 and asthma<sup>24</sup>. Such ratios reflect a broader

inflammatory phenotype and may guide risk stratification in the critical care setting.

Mechanistically, acute inflammation and infection lead to significant alterations in lipid metabolism through multiple pathways<sup>25-28</sup>. Pro-inflammatory cytokines downregulate hepatic production of apolipoproteins, suppress lipoprotein synthesis, and enhance lipid oxidation. Simultaneously, acute phase reactants such as serum amyloid A displace structural proteins on HDL particles, rendering them dysfunctional and pro-inflammatory. These dysfunctional HDL particles lose their protective role and may contribute to worsening endothelial injury and oxidative stress<sup>29-31</sup>.

Lipidomic studies further extend this understanding by revealing specific changes in lipid subclasses, including sphingolipids, phospholipids, and ceramides, which are associated with immune activation, lung injury, and coagulation abnormalities. Such findings suggest that lipidomic profiling may not only serve diagnostic and prognostic roles but also reveal therapeutic targets in ARF management<sup>32,33</sup>. A few recent studies have shown that certain lipidomic signatures correlate strongly with ICU mortality, disease severity, and systemic inflammatory response, even outperforming traditional clinical markers<sup>34,35</sup>.

Despite promising findings, several challenges limit the clinical translation of lipid biomarkers. The timing of lipid measurement in relation to disease onset varies across studies, and longitudinal data on lipid normalisation or persistence post-illness is limited. Moreover, differences in assay methods, patient populations, and concurrent treatments introduce variability in results. It is also unclear how medications commonly used in ARF management – such as corticosteroids, immunosuppressants, or lipid-modifying agents – affect these lipid changes and their interpretability<sup>36-39</sup>.

Future studies should prioritize standardised measurement protocols, incorporate serial lipid profiling, and evaluate the additive prognostic value of lipid indices when combined with established clinical scoring systems. There is also a need to explore whether modifying lipid profiles therapeutically can influence outcomes in ARF, such as through the use of statins, omega-3 fatty acids, or reconstituted HDL formulations.

## Conclusion

This review highlights the prognostic value of dynamic serum lipid changes (HDL-C, LDL-C, TGs, and composite ratios) in acute respiratory infections (ARI) and related conditions. Lipid abnormalities were linked to outcomes like death, ICU admission, mechanical ventilation, and severity scores. Despite promising findings, the literature is heterogeneous with nonuniform lipid profiles and measurement times. Novel biomarkers and tools like lipidomics show promise but need validation. Future research should focus on standardisation, longitudinal follow-up, and leveraging omics-based findings for improved patient outcomes.

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