

Low circulatory cholesterol, high density lipoproteins-cholesterol, low density lipoproteins-cholesterol levels at intensive care unit admission: An underexplored predictor of mortality in critically ill patients

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ABSTRACT

Objective: This study evaluated the relationship between serum cholesterol, HDL-C, and LDL-C at ICU admission and mortality among critically ill patients.

Materials and Methods: A prospective observational study took place at the Department of Pathology, Quaid-e-Azam Medical College, from September 2023 to August 2024. Critically ill patients aged 18 years or older were included, with lipid profiles measured within 24 hours of ICU admission. Serum total cholesterol, HDL-C, LDL-C, inflammatory markers, and clinical parameters were analyzed. Statistical analysis was made between survivors and non-survivors using t-tests, chi-square tests, and correlation analyses. Correlations between lipid parameters (TC, HDL-C, LDL-C) and illness-severity/inflammatory markers (SOFA score and CRP) were examined using Spearman's rank correlation.

Results: Among 100 critically ill patients, survivors had significantly higher serum total cholesterol (129 ± 32.8 mg/dL vs. 83 ± 29.5 mg/dL), HDL-C (22.8 ± 3.28 mg/dL vs. 14.8 ± 2.79 mg/dL), and LDL-C (73.0 ± 17.37 mg/dL vs. 40.8 ± 19.2 mg/dL) than non-survivors ($p < 0.001$). Early mortality (≤ 7 days) was linked to lower serum lipid levels than late mortality (> 7 days). Elevated serum CRP, higher SOFA scores, and prolonged ICU stays further correlated with poor outcomes.

Conclusion: At ICU admission, low cholesterol, HDL-C, and LDL-C levels are strongly linked with increased mortality. Lipid profiling should be integrated into ICU risk stratification models to optimize patient management and improve outcomes.

Keywords: Critical illness, Cholesterol, HDL-C, LDL-C, ICU mortality.

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INTRODUCTION

Critically ill patients often experience significant metabolic disruptions that affect lipid balance, with cholesterol and its subtypes, HDL-C and LDL-C, playing vital roles in immune response, inflammation regulation, and cellular stability [1]. While a lower level of serum cholesterol is traditionally linked with a decreased risk of cardiovascular disease [2], recent studies in critical illness show that lipid concentrations are profoundly depressed, typically total cholesterol 76.57 ± 29.39 mg/dL, HDL-C 18.56 ± 8.9 mg/dL,

and LDL-C 32.1 ± 11.7 mg/dL, and such reductions are associated with poorer clinical outcomes, including higher mortality rates [3,4]. These challenges to the conventional view of cholesterol as solely a cardiovascular risk factor underscore its broader physiological importance. Body mass index (BMI) is also relevant, as adiposity influences baseline lipid concentrations and the host response in critical illness [5]. Systemic inflammation, stress-related metabolic shifts, and impaired liver function are key drivers of lipid changes in critically ill patients [6]. Conditions such as sepsis, acute respiratory distress syndrome (ARDS), and multi-organ failure, which are prevalent in intensive care units (ICUs), are often marked by significant drops in serum total cholesterol, HDL-C, and LDL-C [7]. These declines are primarily due to cytokine-mediated suppression of cholesterol production and increased lipid utilization by

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immune cells [8]. HDL-C is particularly important for regulating inflammation and aiding in pathogen removal, while LDL-C supports innate immunity by neutralizing bacterial toxins [9]. As a result, reduced serum lipid levels during acute illness may weaken the immune response, contributing to worse patient outcomes [10].

A recent meta-analysis highlighted that lower serum lipid levels at ICU admission have a strong association with increased mortality rates in patients with sepsis and other critical illnesses [11]. However, most research has focused on Western populations, with limited data from resource-constrained regions like Pakistan. Given differences in genetics, diet, and healthcare access, the effects of lipid changes on critically ill patients in Pakistan remain poorly understood. Local studies indicate that sepsis accounts for 40-50% of ICU admissions in major hospitals across the country, with mortality rates in Pakistani ICUs being notably higher than in developed nations [12,13]. This disparity emphasizes the need to evaluate prognostic markers, such as serum lipid levels, within the local context.

Similarly, increasing awareness of lipid abnormalities in critical illness, their inclusion in ICU risk assessment models remains limited. Traditional scoring systems, such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE II), focus mainly on physiological and laboratory measures but do not consider lipid profiles [14]. Given the strong association between cholesterol levels and mortality, integrating serum lipid measurements into ICU prognostic tools could improve risk evaluation and support targeted treatments [15]. The study aims to address the research deficiency by evaluating the relationship between serum lipid levels and mortality in severely ill patients in Pakistan. This research explores these connections to enhance risk stratification, inform clinical practices, and investigate the potential for lipid-focused therapies in ICU settings.

MATERIAL AND METHODS

This was a prospective observational study conducted at the Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur, from September 2023 to August 2024. The study's objective was to investigate the relationship between circulatory levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) at the time of ICU admission and death in severely ill patients.

This study enrolled 100 critically ill patients admitted to the ICU at Bahawal Victoria Hospital throughout the study period. The sample size for this study was determined using the standard formula for proportions, considering a 95% confidence interval ($Z = 1.96$), an estimated prevalence of low cholesterol among ICU patients of 30% ($p = 0.30$) based on previous studies [3], and a margin of error of 5% ($E = 0.05$). Using the formula $n = Z^2 \cdot p \cdot (1-p) / E^2$, the calculated sample size was 93.7. To ensure adequate statistical power and account for potential data variability, the sample size was rounded up to 100.

The inclusion criteria were as follows:

1. Patients age ≥ 18 years
2. Patients admitted in the ICU with critical conditions requiring intensive monitoring and care.
3. Patients for whom lipid profiles were estimated within the 1st 24 hours of ICU admission.

Exclusion criteria included:

1. Those Patients who are on lipid-lowering therapy (e.g., statins) in the preceding six months.
2. Individuals with known chronic liver disease or nephrotic syndrome, as these conditions significantly alter lipid metabolism.
3. Patients discharged or deceased within 24 hours of ICU admission without complete lipid profile data.

Upon admission to the ICU, demographic data, clinical history, and laboratory parameters were recorded for each patient. Venous blood

samples (serum) were collected from all eligible patients within 24 hours of their admission to the ICU. Lipid concentrations of total cholesterol, HDL-C, LDL-C, and albumin levels were estimated by using enzymatic colorimetric methods on a fully automated analyzer (Cobas c303, Roche Diagnostics) in the pathology laboratory of Quaid-e-Azam Medical College.

Other clinical and biochemical tests, like inflammatory markers (C-reactive protein [CRP] and procalcitonin) and organ function tests (renal and hepatic panels), were also collected. ICU grading systems, which include the APACHE II and SOFA, were used to grade the severity of illness.

Before applying statistical tests, the normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were analyzed using independent t-tests, while non-normally distributed variables were compared using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test or Fisher's exact test as appropriate. Survival status was compared with lipid levels and other categorical variables. Additionally, early mortality (≤ 7 days) and late mortality (> 7 days) were analyzed using the appropriate statistical tests based on data distribution. To assess the relationship between serum lipid levels and clinical parameters such as SOFA score and inflammatory markers (e.g., CRP), Pearson's correlation coefficient (r) was calculated for normally distributed variables, while Spearman's rank correlation was used for non-normally distributed data. Continuous variables were presented as mean $\pm$ standard deviation (SD) for normally distributed data or median (interquartile range) for non-normally distributed data, and categorical variables were reported as n (%). All statistical analyses were performed using SPSS version 25, and a p -value < 0.05 was considered statistically significant.

The study was done after receiving ethical approval from the Institutional Review Board (IRB) no: QAMC-2538-2023 dated 17 August 2023 of Quaid-e-Azam Medical College. The

patients were enrolled in the study after taking written informed consent from patients or their parents. Patient secrecy was maintained by anonymizing data and restricting access to authorized personnel only.

RESULTS

This study analyzed serum lipid profiles and their association with mortality among critically ill patients admitted to the intensive care unit (ICU). A total of 100 patients were included, and their lipid levels were measured within the first 24 hours of admission. The study population had diverse critical conditions, with sepsis being the most common diagnosis, followed by acute respiratory distress syndrome (ARDS), multiorgan failure, and trauma. The distribution of diagnoses is presented in Table-I.

The predominance of sepsis and ARDS underscores the inflammatory and metabolic challenges faced by critically ill patients. The high prevalence of these conditions highlights the importance of understanding lipid metabolism in this population (Table-I). Serum lipid levels were significantly lower in non-survivors compared to survivors. Mean (SD) total cholesterol, HDL-C, and LDL-C were significantly lower in non-survivors than in survivors ($p < 0.001$, independent t-test). The detailed lipid profile comparison is presented in Table-II.

Non-survivors exhibited significantly lower total cholesterol, HDL-C, and LDL-C levels than survivors (Table-II). This suggests that lower levels of these parameters may be associated with a higher mortality risk in critically ill patients. Serum albumin was also lower in non-survivors (3.2 ± 1.2 vs 3.8 ± 0.6 g/dL; $p < 0.001$), consistent with greater illness severity. By contrast, BMI was modestly lower in non-survivors but not statistically significant ($p = 0.08$), and sex distribution did not differ ($p = 0.27$).

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The inflammatory marker C-reactive protein was significantly higher in non-survivors compared to survivors (Mean (SD): 25.0 (8.0) mg/L vs. 12.0 (5.0) mg/L, $p < 0.001$, independent t-test), further supporting the hypothesis that lower lipid levels may be associated with a heightened inflammatory response.

Among non-survivors, patients who died early (≤ 7 days) had significantly lower lipid levels than those who died later (> 7 days). The comparison of lipid levels between early and late mortality groups is summarized in Table-III.

Patients who died early had significantly lower total cholesterol, HDL-C, and LDL-C levels compared to those who died later (Table-III). This finding reinforces the role of lipid levels as a potential marker of disease severity and rapid deterioration in critically ill patients.

Lipid Levels and Disease Severity: A significant negative correlation was observed between lipid levels and disease severity, as assessed by the SOFA score. Non-survivors had significantly higher SOFA scores than survivors (Mean (SD): 12.0 (3.0) vs. 6.0 (2.0), $p < 0.001$, Pearson correlation analysis). Moreover, a longer ICU stay was associated with lower lipid levels (Pearson's correlation coefficient $r = -0.52$, $p < 0.001$), suggesting that reduced serum lipid levels may predict prolonged critical illness.

Additionally, non-survivors had a longer ICU stay than survivors (Mean (SD): 12.0 (4.0) days vs. 8.0 (3.0) days, $p < 0.001$, independent t-test). Similarly, the total hospital stay was significantly prolonged in non-survivors (Mean (SD): 15.0 (5.0) days vs. 10.0 (4.0) days, $p < 0.001$, independent t-test). These findings suggest that patients with lower lipid levels tend to have prolonged critical illness trajectories.

A strong inverse correlation was observed between lipid levels and mortality, as well as disease severity markers. Total cholesterol showed a significant negative correlation with the SOFA score ($r = -0.68$, $p < 0.001$) and ICU length of stay ($r = -0.52$, $p < 0.001$). Similarly, LDL-C was negatively correlated with the SOFA score ($r = -0.61$, $p < 0.001$). Additionally, HDL-C demonstrated a strong inverse correlation with CRP levels ($r = -0.57$, $p < 0.001$). These findings highlight the prognostic significance of lipid levels in critically ill patients, highlighting their potential role in predicting clinical outcomes. These data collectively highlight the prognostic value of total cholesterol, HDL-C, and LDL-C levels in critically ill patients. The observed differences in serum lipid profiles between survivors, non-survivors, and patients with early and late mortality provide compelling evidence for their role as biomarkers in critical illness. These results also highlight the need for further research to explore whether therapeutic interventions targeting lipid levels could improve outcomes in this vulnerable population.

Table-I: Distribution of Diagnoses in the Study Population (n=100).

Diagnosis	Number of Patients, n (%)
Sepsis	45 (45.0)
ARDS	25 (25.0)
Multiorgan Failure	15 (15.0)
Trauma	10 (10.0)
Others	5 (5.0)
• Postpartum hemorrhage	1
• Disseminated Intravascular Coagulation	2
• Road Traffic Accident	1
• Gunshot	1

Table-II: Lipid profiles in survivors and non-survivors (n=100).

Parameter	Survivors, Mean (SD) N=60	Non-Survivors, Mean (SD) N=40	p-value
Age	45.2 (14.8)	50.1 (23.7)	0.002
Gender			0.27
• Male	36	28	
• Female	24	12	
BMI	26.2 (4.9)	24.7 (4.6)	0.08
Serum Albumin (g/dL)	3.8 (0.6)	3.2 (1.2)	<0.001
Total Cholesterol (mg/dL)	129.0 (32.8)	83.0 (29.5)	<0.001
HDL-C (mg/dL)	22.8 (3.3)	14.8 (2.8)	<0.001
LDL-C (mg/dL)	73.0 (17.4)	40.8 (19.2)	<0.001

Table-III: Total cholesterol, HDL-C, and LDL-C levels and estimated time of mortality.

Parameter	Early Death (≤7 Days), Mean (SD)	Late Death (>7 Days), Mean (SD)	p-value
Total Cholesterol (mg/dL)	64.2 (10.5)	96.3 (8.8)	<0.001
HDL-C (mg/dL)	12.1 (1.1)	16.2 (1.8)	<0.001
LDL-C (mg/dL)	27.7 (6.8)	53.0 (7.1)	<0.01

DISCUSSION

This study investigated the relationship between serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), and mortality in critically ill patients admitted to the intensive care unit (ICU). The findings demonstrated that non-survivors had markedly lower levels of total cholesterol (83 ± 29.5 mg/dL vs. 129 ± 32.8 mg/dL, $p < 0.001$), HDL-C (14.8 ± 2.79 mg/dL vs. 22.8 ± 3.28 mg/dL, $p < 0.001$), and LDL-C (40.8 ± 19.2 mg/dL vs. 73.0 ± 17.37 mg/dL, $p < 0.001$) compared to survivors. These relationships were quantified using independent *t*-tests, and correlation analyses further validated the findings. Specifically, total cholesterol was strongly inversely correlated with SOFA score ($r = -0.68$, $p < 0.001$), LDL-C with SOFA score ($r = -0.61$, $p < 0.001$), and HDL-C with CRP levels ($r = -0.57$, $p < 0.001$). These correlations suggest that lower serum lipid levels are significantly associated with increased disease severity, systemic inflammation, and adverse clinical outcomes. These results highlight the prognostic significance of lipid metabolism in critically ill patients.

The findings are consistent with a meta-analysis of 70 studies, which found that critically ill patients with reduced serum total cholesterol, HDL-C, and LDL-C levels had significantly higher mortality rates³. Similarly, a large-scale observational study in sepsis patients reported

that low LDL-C (<70 mg/dL) was related to a 41% increased chance of in-hospital mortality [7]. This underscores the paradoxical role of LDL-C in critical illness, where its depletion weakens immune function despite its known association with cardiovascular risk. A study using the TriNetX global database identified a U-shaped relationship between LDL-C and all-cause mortality, with both extremely low (<50 mg/dL) and high (≥ 130 mg/dL) LDL-C levels linked to higher mortality risk [4]. Our findings align with this, as non-survivors exhibited significantly lower LDL-C levels than survivors, suggesting that excessive lipid depletion in severely diseased patients may have harmful effects.

While our study found a strong inverse correlation between serum lipid levels and mortality, this was quantitatively demonstrated through correlation analyses. Total cholesterol showed a strong negative correlation with SOFA scores ($r = -0.68$, $p < 0.001$), LDL-C with SOFA ($r = -0.61$, $p < 0.001$), and HDL-C with CRP ($r = -0.57$, $p < 0.001$). These statistical findings confirm that as lipid levels decrease, clinical severity and systemic inflammation increase. These support growing concerns in the literature about optimal lipid thresholds in critically ill patients. Some studies have argued for LDL-C reduction in chronic cardiovascular contexts [16], but during acute illness, this may compromise host defenses. LDL-C binds

endotoxins and HDL-C exerts anti-inflammatory effects, and their depletion, as reflected in our correlation data, may exacerbate disease progression [7,17]. These results strengthen the call for individualized lipid management during critical illness, especially in ICU patients.

From a clinical perspective, our results suggest that serum lipid measurements, especially within the first 24 hours of ICU admission, could be incorporated into existing risk stratification tools such as SOFA or APACHE II. The predictive power of lipid values, particularly their correlation with SOFA scores and CRP, supports their use as adjunctive biomarkers. Interventional possibilities have been proposed in recent trials, including enteral lipid therapy, albumin-bound lipid emulsions, or HDL mimetics, which are under investigation as immune-supportive strategies in sepsis and ARDS [9,13].

Notably, our study found that patients with early mortality (≤ 7 days) had significantly lower serum cholesterol levels than those with late mortality (> 7 days). Specifically, patients who died early had lower total cholesterol (64.2 ± 10.5 mg/dL), HDL-C (12.1 ± 1.1 mg/dL), and LDL-C (27.7 ± 6.8 mg/dL), all with $p < 0.001$. This pattern mirrors findings from a prospective cohort of septic patients, where total cholesterol levels < 100 mg/dL at ICU admission predicted rapid clinical deterioration [18]. This suggests that early lipid depletion could serve as an indicator for disease severity, prompting the need for timely interventions to prevent a rapid decline. However, whether lipid supplementation strategies, such as enteral lipid therapy or albumin-bound lipid infusion, could mitigate this risk remains an area for future investigation [19]. Baseline nutritional indices were not extreme in our cohort. Mean BMI was 26.2 ± 4.9 kg/m² in survivors versus 24.7 ± 4.6 kg/m² in non-survivors ($p = 0.08$), and admission serum albumin averaged 3.8 ± 0.6 g/dL versus 3.2 ± 1.2 g/dL ($p < 0.001$). These values lie largely within normal to mildly reduced ranges and are therefore unlikely to account for the strong association we observed between lower circulating cholesterol fractions and mortality.

Prior ICU literature shows that mortality risk concentrates at BMI extremes, particularly underweight, while overweight/mild obesity frequently exhibits neutral or lower adjusted mortality risk [20], and that the prognostic signal of albumin is most pronounced with marked hypoalbuminemia (< 30 g/L [< 3.0 g/dL]), with albumin at admission offering limited discrimination compared with SOFA/ APACHE severity scores [21]. In this context, residual confounding from BMI or albumin is unlikely to explain our findings, which align with meta-analytic evidence that reduced total cholesterol, HDL-C, and LDL-C at ICU admission track with higher mortality in critical illness [3].

Regionally, our study is one of the few to provide data from Pakistan, a lower-middle-income country where ICU mortality remains high and sepsis is the leading cause of admission. In Pakistan, ICU mortality rates remain significantly higher than in developed countries, with sepsis accounting for 40-50% of ICU admissions [12,13]. Previous research has primarily focused on Western and East Asian populations, where genetic and environmental factors may influence lipid metabolism [3,4]. Given the paucity of data from South Asia, our findings offer valuable insights into local patterns of lipid metabolism and its prognostic relevance. These findings should stimulate further research into lipid-based interventions that are both cost-effective and scalable in resource-limited settings.

The strengths of our study include its prospective design, early standardized lipid assessment, and robust statistical analysis that accounted for correlations with multiple clinical parameters. However, several limitations must be acknowledged. This was a single-center study, and the sample size ($n=100$) may limit generalizability. Lipid levels were only measured at ICU admission; serial measurements could provide a dynamic view of lipid fluctuations during illness. Additionally, despite excluding patients with chronic liver disease and prior statin use, unmeasured confounders such as nutritional deficiencies or undiagnosed dyslipidemia may have influenced baseline lipid levels.

One of the significant observations from this study is the younger age distribution of LA-positive individuals which was significantly lower than that of LA-negative individuals). This finding aligns with study from Pakistan by Anwar M *et al* which retrospectively analyzed the past seven years of data for Lupus shows a higher prevalence in younger populations presenting with thrombotic strokes or recurrent pregnancy loss with mean age of 28 years [16].

In terms of gender distribution, LA positivity was more frequently observed in females (11 cases) compared to males (2 cases); however chi-square test revealed no statistical significance. These findings align with the observations reported by Dabit JY *et al.*, who also found no significant association between gender and Lupus anticoagulant positivity. Their study demonstrated a wide variation in the male-to-female ratio, ranging from 1:1 to 10:1, further supporting the lack of consistent gender-based predisposition in such cases [4]. However, the slight female predominance remains noteworthy, as it may point to broader autoimmune and hormonal influences, as suggested in other autoimmune conditions[17]. The combined analysis of aCL IgG and anti- β 2GPI IgG positivity revealed that out of 89 double-positive samples, 13 were also positive for Lupus anticoagulant, indicating a potential additive effect of concurrent antibody positivity. Although this trend suggests a possible association, the lack of statistical significance may be attributed to the limited sample size and the relatively weak p-values, warranting further investigation in larger cohorts.

CONCLUSION

This study demonstrates clear, statistically supported evidence that lower levels of total serum cholesterol, HDL-C, and LDL-C at ICU admission are significantly associated with increased mortality in critically ill patients. Because standard lipid assays are inexpensive and widely accessible, these measurements may serve as useful early indicators of patient risk. Future multicenter research should examine lipid changes over time, assess

whether adding lipids to existing risk scores improves prediction, and explore therapies aimed at restoring protective lipoprotein function.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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AUTHORS CONTRIBUTION

Sara Reza: Conceptualization, literature review, write-up, final approval, accountable for all aspects of publication.

Hafiz Muhammad Salman Yousaf: Data collection and data analysis, final approval, accountable for all aspects of publication.

Saira Saleem: Data collection, proofreading, and final editing of manuscript, final approval, accountable for all aspects of publication.

REFERENCES

1. Feingold KR. Introduction to Lipids and Lipoproteins. [Updated 2024 Jan 14]. In: Feingold KR, Anawalt B, Blackman MR, *et al.*, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK305896/>
2. Jung E, Kong SY, Ro YS, Ryu HH, Shin SD. Serum cholesterol levels and risk of cardiovascular death: A systematic review and a dose-response meta-analysis of prospective cohort studies. *Int J Environ Res Public Health*. 2022; 19(14): 8272. DOI: <https://doi.org/10.3390/ijerph19148272>
3. Taylor R, Zhang C, George D, Kotecha S, Abdelghaffar M, Forster T, *et al.* Low circulatory levels of total cholesterol, HDL-C, and LDL-C are associated with death of patients with sepsis and critical illness: systematic review, meta-analysis, and perspective of observational studies. *eBioMedicine*. 2024; 100: 104981. DOI: <https://doi.org/10.1016/j.ebiom.2024.104981>
4. Scudeler TL, Costa LMA, Nunes RAB, Schneidewind RO, Brito TM, Pereira DCG, *et al.* Association between low-density lipoprotein cholesterol levels and all-cause mortality in patients with coronary artery disease: a real-world analysis using data from an international network. *Sci Rep*. 2024; 14: 29201. DOI: <https://doi.org/10.1038/s41598-024-80578-w>
5. Shahraz J, Joukar F, Sheida F, Yeganeh S, Maroufizadeh S, Baghaee M, *et al.* Associations between body mass index (BMI) and dyslipidemia: results from the PERSIAN Guilan Cohort Study (PGCS). *Obes Sci Pract*. 2025; 11(1): e70055. DOI: <https://doi.org/10.1002/osp4.70055>
6. Guo J, Chen S, Zhang Y, Liu J, Jiang L, Hu L, *et al.* Cholesterol metabolism: physiological

- regulation and diseases. *MedComm* (2020). 2024; 5(2): e476. DOI: <https://doi.org/10.1002/mco2.476>
7. Feng Q, Wei WQ, Chaugai S, Leon BGC, Mosley JD, Leon DAC, *et al.* Association between low-density lipoprotein cholesterol levels and risk for sepsis among patients admitted to the hospital with infection. *JAMA Netw Open*. 2019; 2(1): e187223. DOI: <https://doi.org/10.1001/jamanetworkopen.2018.7223>
8. Denimal D. Antioxidant and anti-inflammatory functions of high-density lipoprotein in type 1 and type 2 diabetes. *antioxidants*. 2024; 13(1): 57. DOI: <https://doi.org/10.3390/antiox13010057>
9. Johannesen CDL, Langsted A, Mortensen MB, Nordestgaard BG. Association between low-density lipoprotein cholesterol and all-cause and cause-specific mortality in Denmark: prospective cohort study. *BMJ*. 2020; 371: m4266. DOI: <https://doi.org/10.1136/bmj.m4266>
10. Peng K, Li X, Wang Z, Li M, Yang Y. Association of low-density lipoprotein cholesterol levels with the risk of mortality and cardiovascular events: a meta-analysis of cohort studies with 1,232,694 participants. *Medicine* (Baltimore). 2022; 101(48): e32003. DOI: <https://doi.org/10.1097/md.00000000000032003>
11. Luo F, CRDS study investigators. Post-treatment level of LDL-C and all-cause mortality in patients with atherosclerotic cardiovascular disease: evidence from a real-world setting. *Eur J Prev Cardiol*. 2023; 30(12): 1207–15. DOI: <https://doi.org/10.1093/eurjpc/zwad354>
12. Raza HA, Hashmi AP, Khakwani MM, Ali MH, Jamil B. Review of sepsis in Pakistan: how far have we come? *IJID Regions*. 2024; 10:108-113. DOI: <https://doi.org/10.1016/j.ijregi.2023.12.002>
13. Aziz PA, Nasir Z, Shahzad G, Mahmood A, Pathan S, Raja RA. ICU burden in a tertiary care hospital in Pakistan: a descriptive analysis. *Anaesth Pain Intensive Care* 2018; 22(4): 431-7. Available from: <https://www.apicareonline.com/index.php/APIC/article/view/1022/1709>
14. Moreno R, Rhodes A, Piquilloud L, Hernandez G, Takala J, Gershengorn H, *et al.* The sequential organ failure assessment (SOFA) score: Has the time come for an update? *Crit Care*. 2023; 27: 15. DOI: <https://doi.org/10.1186/s13054-022-04290-9>
15. Mumtaz H, Ejaz MK, Tayyab M, Vohra LI, Sapkota S, Hasan M, *et al.* APACHE scoring as an indicator of mortality rate in ICU patients: a cohort study. *Ann Med Surg (Lond)*. 2023; 85(3): 416-21. DOI: <https://doi.org/10.1097/ms9.00000000000000264>
16. Mahajan K, Nagendra L, Dhall A, Dutta D. Impact of early initiation of ezetimibe in patients with acute coronary syndrome: A systematic review and meta-analysis. *Eur J Intern Med*. 2024; 124: 99-107. DOI: <https://doi.org/10.1016/j.ejim.2024.02.004>
17. Sridevi C, Malani S, Chaudhary PH, Nalawade DD, Shokeen A. Evaluation of lipid profile management in coronary artery disease patients on statin therapy: A single-centre, retrospective, observational study. *Cureus*. 2024; 16(10): e71942. DOI: <https://doi.org/10.7759/cureus.71942>
18. Liu SH, Liang HY, Li HY, Ding XF, Sun TW, Wang J. Effect of low high-density lipoprotein levels on mortality of septic patients: a systematic review and meta-analysis of cohort studies. *World J Emerg Med*. 2020; 11(2): 109-116. DOI: <https://doi.org/10.5847/wjcm.i.1920-8642.20.20.008>
19. Zhang S, Lu Z, Wu Z, Xie J, Yang Y, Qiu H. Determination of a “specific population who could benefit from rosuvastatin”: a secondary analysis of a randomized controlled trial to uncover the novel value of rosuvastatin for the precise treatment of ARDS. *Front Med (Lausanne)*. 2020; 7: 598621. DOI: <https://doi.org/10.3389/fmed.2020.598621>
20. Pepper DJ, Sun J, Welsh J, Cui X, Suffredini AF, Eichacker PQ. Increased body mass index and adjusted mortality in ICU patients with sepsis or septic shock: A systematic review and meta-analysis. *Crit Care*. 2016; 20(1): 181. DOI: <https://doi.org/10.1186/s13054-016-1360-z>
21. Yu YT, Liu J, Hu B, Wang RL, Yang XH, Shang XL, *et al.* Expert consensus on the use of human serum albumin in critically ill patients. *Chin Med J (Engl)*. 2021; 134(14): 1639–54. DOI: <https://doi.org/10.1097/CM9.0000000000001661>