



Effect of Chemotherapy on Lipid Parameters in Acute Myeloid Leukemia: A Prospective Observational Study.

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Abstract

Background:

Altered lipid metabolism has been increasingly linked to cancer pathophysiology, including acute myeloid leukemia (AML). Chemotherapy may influence lipid homeostasis, yet data from Indian populations remain limited. This research sought to assess the impact of induction chemotherapy on serum lipid parameters in AML patients.

Methodology:

In cooperation with the Department of Medicine (Clinical Hematology Unit), the Department of Biochemistry carried out a prospective observational study at PGIMS, Rohtak, from September 2017 to September 2019. Forty participants were enrolled—20 newly diagnosed AML cases and 20 sex- and age-matched healthy controls. Lipid parameters, including TG, LDL-C, VLDL-C, HDL-C, and TC, were measured before and after induction chemotherapy in cases and once in controls. ANOVA and the Student's t-test were used for statistical analysis, and $p < 0.05$ was deemed significant.

Results:

Before chemotherapy, AML patients showed significantly lower TC, LDL-C, and HDL-C levels, and higher TG and VLDL-C levels compared to controls ($p < 0.01$). Following chemotherapy, TC and HDL-C levels increased, while TG and VLDL-C decreased significantly ($p < 0.01$), indicating partial normalization of lipid parameters. LDL-C changes were not statistically significant between pre- and post-chemotherapy values.

Conclusion:

Hypocholesterolaemia and hypertriglyceridemia are common in AML patients before chemotherapy, possibly due to increased lipid utilization by leukemic cells. Chemotherapy tends to restore lipid parameters toward normal levels, reflecting metabolic recovery and disease control.

Recommendation:

Routine lipid profiling should be incorporated in AML management to monitor treatment-related metabolic alterations. To confirm the prognostic significance of cholesterol parameters and investigate the therapeutic applications of lipid-modulating medications like statins, larger multicentric studies are advised.

Keywords: Acute myeloid leukemia, chemotherapy, lipid profile, triglycerides, cholesterol, hypocholesterolemia, prospective study

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Introduction

Clonal proliferation and the accumulation of immature myeloid precursors in peripheral blood and bone marrow are characteristics of acute myeloid leukemia (AML), a malignant condition of the hematopoietic stem cells. This uncontrolled expansion of blasts suppresses normal hematopoietic activity, resulting in anemia,

thrombocytopenia, and neutropenia, which clinically present as pallor, bleeding tendencies, and recurrent infections. The most prevalent kind of adult acute leukemia is AML, which accounts for nearly four-fifths of all cases, with an annual incidence of around 3–4 per 100,000 population. The disease predominantly affects older individuals, though it may occur in younger adults



as well, and is reported slightly more often in males. The WHO classification categorizes AML based on cytogenetic and molecular features, highlighting its biological diversity and prognostic variability. Despite improvements in diagnostic methods and chemotherapy protocols, AML remains a challenging malignancy, with a considerable proportion of patients experiencing relapse after achieving remission.

In recent years, the metabolic adaptations of cancer cells have gained significant attention. Altered metabolism is now recognized as a hallmark of malignancy, supporting uncontrolled growth and survival under stressful conditions. Among these pathways, lipid metabolism plays a central role in cancer progression. Lipids serve as critical components for membrane biosynthesis, energy storage, and intracellular signaling. Leukemic cells, in particular, show enhanced cholesterol uptake and synthesis to meet their high metabolic demands. Studies have reported a decline in serum cholesterol and lipoprotein levels in AML patients, which is thought to result from increased lipid consumption by the proliferating leukemic cells. Such changes are not merely metabolic consequences but may also influence disease behavior and treatment outcomes, as lipid availability can affect membrane dynamics, drug transport, and apoptotic signaling.

Chemotherapy—the cornerstone of AML treatment—can also alter systemic metabolism, including lipid profiles. The typical induction protocol, sometimes known as "7 + 3," consists of three days of an anthracycline, like daunorubicin, and seven days of cytarabine. While this protocol induces remission in many patients, its effects extend beyond the hematologic system. Cytotoxic agents may modify hepatic function, oxidative balance, and lipid biosynthesis pathways, leading to fluctuations in serum lipid levels during and after therapy. Previous studies have documented that TC, LDL-C, and HDL-C levels are often reduced, whereas triglyceride concentrations tend to rise in patients with hematologic malignancies. Banker and colleagues suggested that AML cells depend heavily on cholesterol for survival, and that inhibiting cholesterol synthesis with agents such as statins could enhance the effectiveness of chemotherapy. These observations point toward a close relationship between lipid metabolism, disease activity, and treatment response in AML.

Although several international studies have explored lipid alterations in leukemia, information from the Indian population remains limited. Genetic background, dietary habits, and environmental influences may cause variations in lipid metabolism and treatment response among Indian patients compared to those in Western populations. Therefore, understanding these biochemical patterns in local settings is of both clinical and academic importance.

The study aimed to assess how chemotherapy influences these lipid parameters and whether post-treatment normalization reflects metabolic recovery and disease remission. The findings may contribute to a better understanding of metabolic changes in AML and help evaluate the potential role of lipid profiling in patient monitoring and prognosis.

Methods

Study Design and Setting

This hospital-based **prospective observational study** was conducted from September 2017 to September 2019, in the Department of Medicine (Clinical Hematology Unit) and the Department of Biochemistry at Pt. B.D. Sharma PGIMS, Rohtak, collaborated to perform a prospective observational study.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki after obtaining approval from the Institutional Ethics Committee.

Participants

A total of 40 participants were enrolled: 20 consecutive newly diagnosed adult AML cases (age ≥ 18 years) and 20 healthy sex- and age-matched controls (no known hematologic malignancy or lipid-lowering therapy) selected from hospital staff or volunteers.

Inclusion Criteria

- Newly diagnosed AML confirmed by bone marrow examination or flow cytometry ($\geq 20\%$ blast cells).
- Age ≥ 14 years.
- Patients receiving standard induction chemotherapy (cytarabine + daunorubicin).

Exclusion Criteria

- Patients with diabetes mellitus, thyroid disorders, liver or renal disease, or those on lipid-lowering medications.

Bias Section

To minimize selection bias, consecutive eligible patients were enrolled during the study period. Measurement bias was reduced by using standardized laboratory techniques for lipid profile estimation. Data analysis was performed using predefined statistical methods to limit analytical bias.

Data collection

At baseline (prior to the start of induction chemotherapy for cases), fasting blood samples were drawn from both cases and controls for the estimation of serum lipid parameters: TG, LDL-C, VLDL-C, HDL-C, and TC, and if available, ApoB and ApoA-I. Baseline demographic and clinical data (age, sex, BMI, AML subtype, cytogenetics/ELN risk category) were recorded for cases. Cases underwent standard induction chemotherapy for AML as per institutional protocol (e.g., 7+3 regimen or equivalent). On completion of induction (day 28–30 or at bone marrow response assessment), a repeat fasting lipid profile was drawn in the cases. Controls were not subjected to a second draw.

Statistical analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean $\pm$ standard deviation. Pre- and post-chemotherapy lipid parameters were compared using a paired t-test. A p-value <0.05 was considered statistically significant.

Results

Participant Flow

During the study period, a total of 27 newly diagnosed patients with suspected Acute Myeloid Leukemia (AML) were assessed for eligibility. Of these, 5 patients were excluded: 2 did not meet the inclusion criteria, 1 had pre-existing dyslipidemia, and 2 declined to participate. The remaining 22 patients fulfilled eligibility criteria and were enrolled in the study.

Among the enrolled patients, 2 were excluded from the final analysis due to loss to follow-up after initiation of chemotherapy. Therefore, 20 AML patients completed both baseline and post-induction chemotherapy lipid profile assessments and were included in the final analysis. For the control group, 23 healthy individuals were screened. Three individuals were excluded (two did not meet age-matching criteria, and one declined consent). Finally, 20 healthy age- and sex-matched controls were included in the study.

Thus, the final analysis comprised 40 participants: 20 AML patients and 20 healthy controls.

1. Demographic Characteristics

Twenty AML patients and twenty healthy controls made up the study's total of 40 participants. Among the AML group, 8 were females (40%), and 12 were males (60%), with a mean age of 36.9 ± 15.3 years (range: 14–61 years). The control group had a comparable age and sex distribution ($p > 0.05$), ensuring appropriate matching between cases and controls.

2. Changes in Serum Lipid Parameters

At baseline (Group I, before chemotherapy), AML patients showed significant alterations in serum lipid levels when compared to healthy controls (Group III). TC, LDL-C, and HDL-C were notably reduced, whereas triglycerides and VLDL-C were elevated.

Following induction chemotherapy (Group II), there was a significant improvement in lipid profile, particularly a rise in HDL-C and a reduction in TG and VLDL-C ($p < 0.01$).

This suggests that chemotherapy partially reverses the dyslipidemia associated with active AML.

Figure 1: Comparison of Mean Lipid Parameters Before and After Chemotherapy in AML Patients

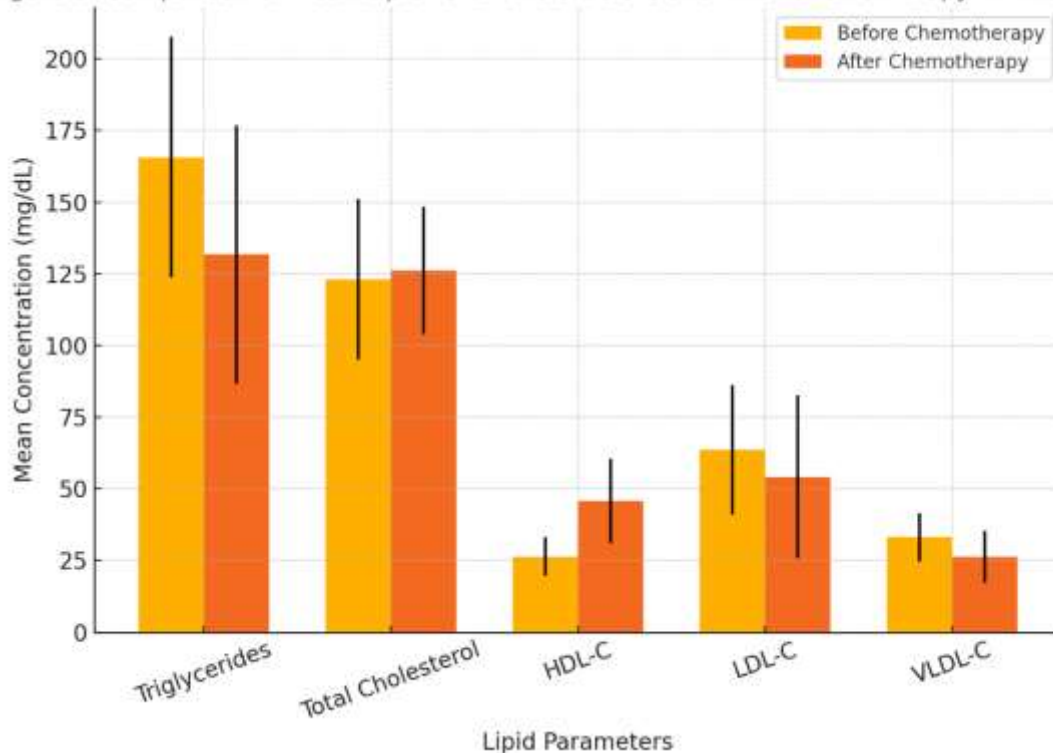


Table 1. Comparison of lipid profile among AML patients and controls

Lipid Parameter (mg/dL)	Group I – Before Chemotherapy (Mean ± SD)	Group II – After Chemotherapy (Mean ± SD)	Group III – Controls (Mean ± SD)	ANOVA <i>p</i> -value
Triglycerides	165.65 ± 41.96	131.75 ± 45.02	96.30 ± 17.07	<0.001
Total Cholesterol	123.05 ± 27.96	126.25 ± 22.17	156.85 ± 10.93	<0.001
HDL-C	26.35 ± 6.79	45.75 ± 14.81	41.25 ± 4.74	<0.001
LDL-C	63.55 ± 22.57	54.15 ± 28.45	86.35 ± 11.84	<0.001
VLDL-C	33.14 ± 8.43	26.35 ± 9.00	19.25 ± 3.44	<0.001

Discussion

The present study examined changes in lipid profile among patients with AML before and after induction chemotherapy. Prior to treatment, AML patients showed significantly increased TG and VLDL-C and decreased TC, HDL-C, and LDL-C values compared to healthy controls. Following chemotherapy, HDL-C levels increased, whereas triglycerides and VLDL-C decreased significantly. These changes suggest that the altered lipid metabolism observed in active AML is at least partially reversible after successful chemotherapy. The improvement in lipid parameters likely corresponds to

disease remission and restoration of normal metabolic activity.

The pattern of lipid abnormalities observed in this study agrees with several earlier reports. Musolino et al. [6] found low serum cholesterol and HDL-C and elevated TG levels in leukemia and lymphoma patients, while Zyada et al [5]. demonstrated that hypocholesterolemia correlates with the degree of blast cell proliferation. Both studies attributed these changes to enhanced LDL receptor expression in malignant cells, leading to accelerated cholesterol uptake. Banker and colleagues further reported that leukemic cells increase both cholesterol synthesis and import to sustain growth and resist chemotherapy. The partial normalization of lipid

parameters following treatment in our patients supports this mechanism, indicating that lipid derangements are disease-driven rather than inherent metabolic defects.

Several mechanisms may explain the lipid alterations seen in AML. Leukemic cells are metabolically active and utilize cholesterol for membrane assembly, intracellular signaling, and steroid biosynthesis, resulting in depletion of circulating cholesterol. In addition, hepatic synthesis of lipoproteins may be impaired due to leukemic infiltration or systemic inflammation. Elevated cytokines such as IL-6 and TNF- α suppress hepatic apolipoprotein production and promote lipolysis, increasing triglyceride turnover. After induction chemotherapy, as leukemic burden and inflammatory activity decline, hepatic function and lipid metabolism begin to normalize, leading to restoration of cholesterol and HDL-C levels and reduction in triglycerides.

Cholesterol is vital for cell membrane organization and the formation of lipid rafts, which are platforms for receptor-mediated signaling. Leukemic cells frequently upregulate enzymes in the mevalonate pathway—particularly HMG-CoA reductase—to enhance cholesterol biosynthesis. This adaptation supports cell proliferation and protects malignant cells from chemotherapy-induced apoptosis. Experimental studies have demonstrated that inhibition of this pathway can make AML cells more sensitive to cytarabine and anthracyclines. Luo et al. and Zhao et al. [10] reported that blocking cholesterol synthesis promoted apoptosis in AML cells, while Huang et al. found that adding statins to chemotherapy increased cytotoxicity. These findings emphasize that cholesterol metabolism is not merely a bystander effect but an active participant in leukemic survival and resistance mechanisms.

The findings of this investigation indicate that lipid profile assessment may have clinical value beyond routine biochemical evaluation. Hypcholesterolemia could serve as a biochemical indicator of active disease, while normalization of lipid levels may reflect treatment response. Since AML cells appear dependent on cholesterol for proliferation, targeting cholesterol metabolism may enhance chemotherapy effectiveness. Banker et al. hypothesized that cholesterol-dependent AML subtypes might respond differently to therapy, and that statins or other lipid-lowering agents could improve remission rates. Recent clinical observations also link specific lipidomic patterns with relapse risk and poor outcomes, indicating that metabolic monitoring might help in identifying high-risk patients.

Although the present study offers valuable insight, certain limitations must be recognized. The sample size was modest, which restricts the generalization of results. Long-term follow-up was not performed to correlate lipid

normalization with relapse-free survival or overall survival. Factors such as nutritional status, dietary intake, and baseline metabolic disorders could also influence lipid levels, but were not assessed in this study. Future research should include larger, multicentric cohorts with longitudinal follow-up to determine whether lipid profile changes can reliably predict remission or relapse. Integration of lipidomics and molecular genetics may further clarify how metabolic alterations interact with specific genetic mutations in AML. Additionally, clinical trials evaluating statin-based metabolic therapy in conjunction with chemotherapy are warranted to explore its potential role in improving outcomes.

In summary, this study demonstrates that AML is associated with marked disturbances in lipid metabolism, characterized by hypocholesterolemia and hypertriglyceridemia before chemotherapy. Following treatment, lipid parameters showed significant improvement, likely due to a reduction in tumor burden and recovery of hepatic lipoprotein synthesis. These findings highlight the close relationship between lipid metabolism and leukemic activity. Monitoring lipid profiles could provide useful, inexpensive adjunctive information for evaluating treatment response. Furthermore, targeting cholesterol biosynthesis through agents like statins may represent a promising adjunct to standard chemotherapy regimens. Continued exploration of metabolic pathways in AML could lead to the development of metabolically guided therapeutic strategies that complement existing treatment modalities and potentially improve patient prognosis.

Generalizability

The findings of this study may be generalized to similar tertiary care hospital settings involving newly diagnosed AML patients receiving standard induction chemotherapy. However, extrapolation to other malignancies or different treatment regimens should be done cautiously.

Conclusion

In this prospective observational study, patients with acute myeloid leukemia demonstrated significant alterations in serum lipid parameters before initiation of chemotherapy, characterized by reduced TC, LDL-C, and HDL-C, along with elevated triglycerides and VLDL-C. Following induction therapy, partial normalization of lipid levels was observed, suggesting a metabolic response paralleling hematologic remission. These findings indicate that lipid dysregulation in AML is disease-related and may reflect leukemic cell proliferation and metabolic activity.



Limitations of the Study

The study was conducted in a single center with a relatively small sample size. Long-term lipid profile changes were not assessed. Additionally, potential confounding factors such as dietary habits and baseline metabolic status were not fully controlled.

Recommendation

Routine assessment of lipid profiles in AML could provide a simple biochemical marker for treatment response and disease monitoring. Moreover, targeting cholesterol metabolism through pharmacologic interventions, such as statins, may enhance the efficacy of standard chemotherapy regimens. Larger prospective studies are warranted to validate these findings and to explore the therapeutic potential of integrating lipid-modulating agents in AML management.

List of Abbreviations

AML – Acute Myeloid Leukemia

HDL – High-Density Lipoprotein

LDL – Low-Density Lipoprotein

TG – Triglycerides

TC – Total Cholesterol

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The authors declare that no specific funding was received for this study from any public, commercial, or not-for-profit funding agencies.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

Neeraj Yadav: Conceptualization, study design, data collection, biochemical analysis, manuscript drafting.

Islam Khan: Data analysis, interpretation of results, manuscript review.

Aditi Singh: Study supervision, critical revision of manuscript.

Sarita Choudhary: Study coordination, final manuscript editing, correspondence, and overall oversight.

All authors read and approved the final manuscript.

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