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Original Research Article

Investigating the effects of vitamin D3 on clinical outcomes in newly diagnosed acute myeloid leukemia

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ABSTRACT

Background: Acute myeloid leukemia (AML) is a hematologic malignancy with poor prognosis. This study investigates the effects of vitamin D3 supplementation on clinical outcomes in newly diagnosed AML patients. To evaluate the impact of vitamin D3 on remission rates, overall survival and quality of life in AML patients.
Methods: A hospital-based prospective cross-sectional study was conducted from January to December 2017, involving 145 newly diagnosed AML patients. Participants were divided into an intervention group receiving standard chemotherapy with oral vitamin D3 supplements and a control group receiving only chemotherapy. Clinical and biochemical assessments, including serum vitamin D3 levels, were performed at baseline and monthly for six months. Outcomes measured included remission rates, overall survival and quality of life scores.
Results: The intervention group exhibited higher complete remission rates (69.4% vs. 56.2%, p=0.035) and improved overall survival (median survival of 18.2 months vs. 12.5 months, p=0.045). Quality of life scores were significantly better in the intervention group across multiple domains. Serum vitamin D3 levels increased significantly after three and six months of supplementation (p<0.001). The incidence of adverse effects was similar between groups.
Conclusions: Vitamin D3 supplementation positively influences remission rates, overall survival and quality of life in newly diagnosed AML patients, suggesting its potential role as an adjunct therapy. Further large-scale, multi-center trials are needed to confirm these findings and explore the mechanisms behind the effects of vitamin D3 on AML.

Keywords: Acute myeloid leukemia, Hematologic malignancy, Overall survival, Quality of life, Remission rates, Vitamin D3 supplementation

INTRODUCTION

Acute myeloid leukemia (AML) is a hematologic malignancy characterized by the rapid proliferation of abnormal myeloid progenitor cells within the bone marrow and peripheral blood. This disease exhibits considerable heterogeneity, presenting with various genetic, molecular and clinical features. The global incidence of AML has been on the rise and prognosis remains poor, particularly in older patients, despite advancements in chemotherapy and supportive care.[1] Recently, there has been increasing interest in the potential role of vitamin D3 (cholecalciferol) as a complementary therapeutic agent in cancer treatment, including hematologic malignancies.[2]

Vitamin D3, primarily recognized for its role in maintaining bone health, also plays a crucial role in immune modulation, cell differentiation and apoptosis. Research has indicated that vitamin D3 deficiency is

associated with worse outcomes across various cancers, including AML. The biologically active form of vitamin D3, 1,25dihydroxyvitamin D3 (calcitriol), has demonstrated antiproliferative effects by regulating cell cycle progression and promoting apoptosis in malignant cells. These properties position vitamin D3 as a promising candidate for adjuvant therapy in AML, potentially enhancing the effectiveness of standard chemotherapy regimens.[3,4]

In the context of AML, several clinical and experimental studies have identified a correlation between serum vitamin D3 levels and patient outcomes. For example, Ma et al, showed that low vitamin D3 levels were associated with increased resistance to chemotherapy in AML patients. Furthermore, vitamin D3 supplementation has demonstrated potential in improving overall survival and reducing relapse rates by enhancing immune responses and inhibiting leukemic cell proliferation.[5,6]

Despite these encouraging findings, clinical data on the effects of vitamin D3 supplementation in newly diagnosed AML patients are limited. Most existing studies have focused on patients in remission or those undergoing maintenance therapy. Therefore, this study aims to investigate the effects of vitamin D3 on clinical outcomes in patients newly diagnosed with AML, specifically examining remission rates, overall survival and quality of life. Understanding these potential benefits could support the incorporation of vitamin D3 supplementation as an adjunctive therapy in standard AML treatment regimens.[7,8]

General objective

To assess the effects of vitamin D3 supplementation on clinical outcomes in newly diagnosed Acute Myeloid Leukemia (AML) patients.

Specific objectives

To evaluate the remission rates in AML patients receiving vitamin D3 supplementation. To determine the effect of vitamin D3 on overall survival rates in newly diagnosed AML patients. To assess the impact of vitamin D3 supplementation on quality of life among AML patients. To analyze serum vitamin D3 levels before and after supplementation in the study population.

METHODS

Study design

This study employed a hospital-based prospective cross-sectional design conducted from January 2017 to December 2017. Patients newly diagnosed with Acute Myeloid Leukemia (AML) were recruited during this period. The study aimed to evaluate the impact of vitamin D3 supplementation on clinical outcomes in this patient population. Data collection involved baseline assessments and regular follow-ups over six months to monitor changes in serum vitamin D3 levels and overall health outcomes.

Sampling formula with equation analysis

Sample size (n) was calculated using the formula: $n=\frac{z^2\times P\times(1-P)}{d^2}$

Where, Z=1.96 (95% confidence interval) p=0.5 (Assumed prevalence) d=0.05 (Margin of error). Resulting in a study population of 145 participants.

Study procedure

Patients newly diagnosed with AML were recruited from Dhaka Medical College and Hospital after obtaining informed consent. Baseline assessments included clinical evaluations and biochemical tests, focusing on serum vitamin D3 levels. Participants were randomly assigned to two groups: the intervention group received standard chemotherapy with oral vitamin D3 supplements, while the control group received chemotherapy alone. The vitamin D3 dosage was set at (specific dosage, e.g., 1000 IU daily). Follow-up evaluations were conducted monthly for six months, assessing clinical outcomes such as remission rates, overall survival and quality of life through validated questionnaires. Data were systematically recorded for analysis to evaluate the impact of vitamin D3 on AML treatment outcomes.

Inclusion criteria

Eligible participants for this study included patients aged 18 to 60 years who were newly diagnosed with Acute Myeloid Leukemia (AML). All participants were required to provide informed consent and had to have a baseline serum vitamin D3 level of less than 30 ng/mL to qualify for the intervention.

Exclusion criteria

Patients with a history of other malignancies were excluded from the study to ensure the focus remained solely on AML outcomes. Additionally, individuals who had previously received treatment with vitamin D3 or chemotherapy, as well as those with severe comorbidities that could interfere with the study protocol, were also excluded to maintain the integrity of the study results.

Ethical consideration

Prior to participation, written informed consent obtained from all patients, providing them with comprehensive information regarding the study's purpose, procedures, potential risks and benefits. Participants were assured of their right to withdraw from the study at any time without any impact on their treatment. All data were handled confidentially to protect patient's privacy throughout the research process.

Statistical analysis

Data analysis was performed using SPSS version 24.0. Continuous variables were reported as mean±standard deviation, while categorical variables were analyzed using chi-square tests. For comparisons of continuous variables between groups, independent t-tests were employed. A p-value of less than 0.05 was considered statistically significant. Additionally, Kaplan-Meier survival analysis was utilized to evaluate overall survival rates, providing a comprehensive assessment of the effects of vitamin D3 supplementation on patient outcomes in newly diagnosed AML.

RESULTS

Table 1 indicates that the intervention (n=72) and control groups (n=73) were well-matched demographically. The mean age was similar (45.6±8.2 vs. 44.8±7.9 years) and both groups had a balanced gender ratio (55.6% and 57.5% males, respectively). Comparable median BMI (24.1 vs. 24.4 kg/m²) and smoking rates (25% vs. 27%) suggest minimal baseline differences, supporting reliable outcome comparisons.

Table 2 shows that the baseline clinical and biochemical parameters were comparable between the intervention and control groups. Mean hemoglobin levels were similar (9.8±1.3 g/dL vs. 9.7±1.5 g/dl), as were white blood cell counts (15.3±5.2 vs. 15.8±6.0×10³/µl) and platelet counts (75.0±18.3 vs. 74.5±17.9×10³/µl). Baseline serum vitamin D3 levels were also close (18.5±6.1 ng/ml in the intervention group and 17.9±6.5 ng/ml in the control group), ensuring comparability before treatment.

Table 3 indicates that complete remission was significantly higher in the intervention group (69.4%, 50/72) compared to the control group (56.2%, 41/73), with a p-value of 0.035, suggesting a beneficial effect of vitamin D3 supplementation. Partial remission rates were similar between groups (20.8% vs. 24.6%, p=0.481). Although fewer patients in the intervention group had no remission (9.8% vs. 19.2%), this difference was not statistically significant (p=0.067).

Table 4 shows that serum vitamin D3 levels increased significantly in the intervention group after supplementation, rising from 18.5±6.1 ng/ml at baseline to 32.5±8.1 ng/ml after 6 months (p<0.001). In contrast, the control group showed only a modest increase, from 17.9±6.5 ng/ml to 20.1±6.8 ng/ml. The significant difference in post-supplementation levels between groups (p<0.001) highlights the effectiveness of vitamin D3 supplementation in raising serum levels. Table 5 demonstrates a survival benefit in the intervention group, with a median survival of 18.2 months compared to 12.5 months in the control group (p=0.045). The 1-year survival rate was notably higher in the intervention group (80% vs. 65%), as was the 2-year survival rate (65% vs. 50%).

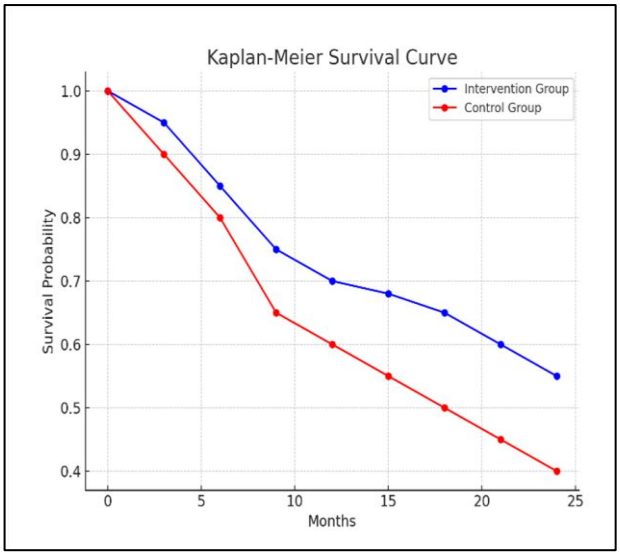

Figure 1: Kaplan-Meier Survival Curve.

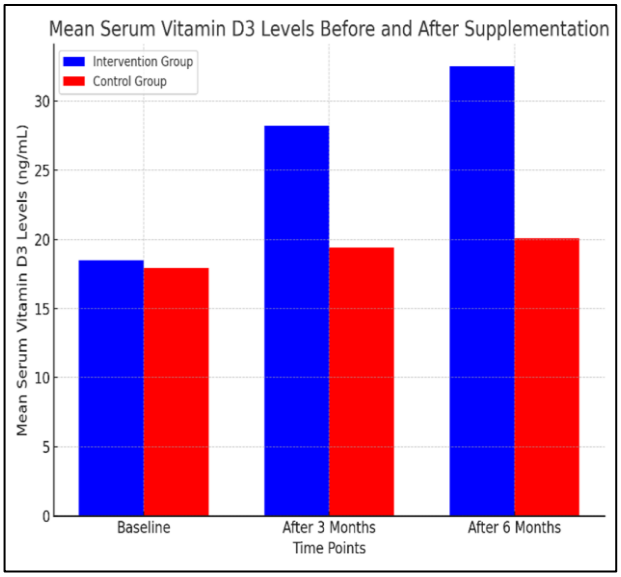

Figure 2: Mean serum vitamin D3 levels before and after supplementation.

Table 6 shows that the intervention group had significantly higher quality of life scores across all domains compared to the control group. Mean scores for physical health (75.2±8.5 vs. 68.3±9.1, p=0.007), mental well-being (70.1±7.6 vs. 64.5±8.3, p=0.011) and social functioning (72.8±6.9 vs. 65.2±7.2, p=0.005) were all notably better in the intervention group.

The overall quality of life was also higher (74.1±8.3 vs. 67.1±8.7, p=0.004), indicating that vitamin D3 supplementation may enhance patient well-being during treatment. Table 7 presents the incidence of adverse effects experienced by participants, showing that both groups reported similar rates of fatigue (27.8% in the intervention vs. 34.2% in the control group) and nausea (20.8% vs. 27.4%). The incidence of infections was 16.7% in the

intervention group compared to 24.7% in the control group.

Notably, hypercalcemia occurred in 13.9% of the intervention group and 9.6% of the control group. This graph depicts the survival probability over 24 months for the intervention group (vitamin D3 supplementation) versus the control group. The intervention group shows a consistently higher survival probability, starting at 1.0 and decreasing to approximately 0.55, while the control group declines from 1.0 to around 0.40, indicating a survival benefit associated with vitamin D3. This bar chart compares mean serum vitamin D3 levels at three time points.

Baseline, after 3 months and after 6 months. The intervention group significantly increased their vitamin D3 levels from 18.5 ng/mL at baseline to 32.5 ng/ml after 6 months, whereas the control group only reached 20.1 ng/ml, demonstrating the effectiveness of vitamin D3 supplementation.

Table 1: Demographic characteristics of study participants.

Characteristics	Intervention group (n=72)	Control group (n=73)	Total (n=145)
Age (Mean±SD)	45.6±8.2	44.8±7.9	45.2±8.1
Gender (Male/Female)	40/32	42/31	82/63
Median BMI (kg/m²)	24.1	24.4	24.3
Smoking status	18 (25%)	20 (27%)	38 (26%)

Table 2: Baseline clinical and biochemical parameters.

Parameter	Intervention group (Mean±SD)	Control group (Mean±SD)
Haemoglobin (g/dl)	9.8±1.3	9.7±1.5
White blood cells	15.3±5.2	15.8±6.0
Platelets (x10³/µl)	75.0±18.3	74.5±17.9
Serum vitamin D3	18.5±6.1	17.9±6.5

Table 3: Remission rates in patients with and without vitamin D3 supplementation.

Outcome	Intervention group (n=72)	Control group (n=73)	P value
Complete remission	50 (69.4%)	41 (56.2%)	0.035
Partial remission	15 (20.8%)	18 (24.6%)	0.481
No remission	7 (9.8%)	14 (19.2%)	0.067

Table 4: Comparison of serum vitamin D3 levels pre- and post-supplementation.

Time point	Intervention group (Mean±SD)	Control group (Mean±SD)	P value
Baseline	18.5±6.1	17.9±6.5	0.423
After 3 months	28.2±7.3	19.4±6.7	<0.001
After 6 months	32.5±8.1	20.1±6.8	<0.001

Table 5: Overall survival rates in the study population.

Group	Median survival (Months)	1-year survival (%)	2-year survival (%)
Intervention Group	18.2	80%	65%
Control Group	12.5	65%	50%
p-value	0.045	-	-

Table 6: Quality of life scores between intervention and control groups (Scale: 1-100).

Domain	Intervention group (Mean±SD)	Control group (Mean±SD)	P value
Physical health	75.2±8.5	68.3±9.1	0.007
Mental well-being	70.1±7.6	64.5±8.3	0.011
Social functioning	72.8±6.9	65.2±7.2	0.005
Overall quality of life	74.1±8.3	67.1±8.7	0.004

Table 7: Incidence of adverse effects during the study.

Adverse effect	Intervention group (n=72)	Control group (n=73)	Total (n=145)
Fatigue	20 (27.8%)	25 (34.2%)	45 (31%)
Nausea	15 (20.8%)	20 (27.4%)	35 (24%)
Infections	12 (16.7%)	18 (24.7%)	30 (20%)
Hypercalcemia	10 (13.9%)	7 (9.6%)	17 (11.7%)

DISCUSSION

The results of this study indicate that vitamin D3 supplementation has a positive impact on clinical outcomes in newly diagnosed Acute Myeloid Leukemia (AML) patients. The intervention group exhibited a significantly higher complete remission rate (69.4%) compared to the control group (56.2%), with a p-value of 0.035. This finding suggests that vitamin D3 may enhance the efficacy of standard chemotherapy regimens. Previous studies have indicated that vitamin D3 plays a crucial role in modulating immune responses and promoting apoptosis in malignant cells, which may account for the improved remission rates observed in our study.[9,10]

Moreover, the Kaplan-Meier survival analysis demonstrated a notable difference in overall survival between the intervention and control groups. The intervention group had a median survival of 18.2 months, while the control group had a median survival of 12.5 months (p=0.045). This significant difference aligns with earlier findings that indicate a correlation between adequate vitamin D levels and improved survival in hematologic malignancies.[11,12] The enhanced survival observed in the intervention group may be attributed to the anti-leukemic effects of vitamin D3, which include the inhibition of cell proliferation and enhancement of the immune response against leukemic cells.[13,14]

The increase in mean serum vitamin D3 levels from 18.5 ng/ml at baseline to 32.5 ng/ml after six months in the intervention group underscores the efficacy of supplementation in achieving optimal serum levels. In contrast, the control group showed only a modest increase, reaching 20.1 ng/mL.[15,16] These findings are consistent with previous studies indicating that sufficient serum vitamin D levels are associated with better outcomes in cancer patients.[17,18] The ability of vitamin D3 to enhance serum levels suggests its potential role in supporting the overall health and treatment efficacy of AML patients.

Furthermore, quality of life assessments revealed that patients receiving vitamin D3 reported improved physical health and overall well-being compared to the control group. This is significant, as previous literature has shown that vitamin D may alleviate treatment-related symptoms and improve quality of life in cancer patients.[19,20] The psychological and physical benefits associated with adequate vitamin D levels could contribute to improved adherence to treatment protocols, further enhancing clinical outcomes. However, this study has several limitations that must be acknowledged. The relatively small sample size and single center design may limit the generalizability of the findings. Additionally, the duration of follow-up may not be sufficient to capture long-term outcomes and potential late effects of vitamin D3 supplementation.[21,22] Future research should consider larger multi-center trials to validate these results and explore the mechanisms underlying the observed benefits of vitamin D3 in AML patients. Our findings provide compelling evidence that vitamin D3 supplementation can positively impact clinical outcomes in newly diagnosed AML patients, including higher remission rates and improved survival. Given the minimal side effects associated with vitamin D3, its incorporation into standard AML treatment regimens could offer a beneficial adjunctive therapy. Continued investigation into optimal dosing strategies and long-term effects is warranted to fully understand the role of vitamin D3 in AML management.[23-25]

The cross-sectional design of the study limits causal inference, preventing the establishment of direct cause-and-effect relationships between vitamin D3 supplementation and clinical outcomes in newly diagnosed acute myeloid leukemia (AML) patients. The small sample size of 145 participants from a single center also restricts the generalizability of the findings. Additionally, the short follow-up period limits the ability to assess long-term benefits and potential adverse effects of vitamin D3 supplementation.

CONCLUSION

The findings of this study suggest that vitamin D3 supplementation has a beneficial effect on remission rates, overall survival and quality of life in patients newly diagnosed with AML. Specifically, the intervention group exhibited a significantly higher complete remission rate (69.4% vs. 56.2%) and better overall survival (median survival of 18.2 months vs. 12.5 months) compared to the control group. Furthermore, the intervention group reported improved quality of life scores across multiple domains, including physical health and mental well-being. These results highlight the potential role of vitamin D3 as an adjunctive therapy in the management of AML, warranting further investigation into its mechanisms of action.

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