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THE EFFECT OF GLUCOCORTICOIDS ON BONE PROFILE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA AT ADAM MALIK HOSPITAL

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ABSTRACT
Glucocorticoids are essential in treating acute lymphoblastic leukemia (ALL) but may disrupt bone metabolism, affecting calcium, magnesium, phosphate, and alkaline phosphatase levels. This cross-sectional study enrolled 30 children ⩽18 years with ALL at Adam Malik Hospital, Medan, during April–May 2025 using consecutive sampling. All had received at least one week of glucocorticoid therapy and had complete bone profile data. Data were obtained from medical records and laboratory tests. Associations were analyzed using Spearman's correlation, Mann-Whitney test, and multiple linear regression. Most patients were male (53.3%) and classified as high-risk (60%), with 60% receiving dexamethasone for a median of 7 weeks. Calcium, phosphate, and alkaline phosphatase levels were generally within the normal range, but 50% of patients developed hypermagnesemia. Magnesium levels were significantly associated with the type of glucocorticoid (p=0.010), treatment duration (p=0.014), and age at diagnosis (p=0.006). No significant associations were found between glucocorticoid duration and calcium, phosphate, or alkaline phosphatase levels. Magnesium levels are influenced by glucocorticoid type, treatment duration, and age at diagnosis. Further studies with larger samples and additional biomarkers are needed to comprehensively understand the effects of glucocorticoids on the bone profile of children.

Keywords: acute lymphoblastic leukemia; bone profile; glucocorticoid; magnesium

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INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a hematologic malignancy characterized by the abnormal proliferation of immature lymphoid cells arrested at an early stage of differentiation. These cells can infiltrate the bone marrow, peripheral blood, and extramedullary sites. ALL is the most common type of leukemia in children, accounting for approximately 75–80% of all acute leukemia cases in the pediatric population (Kaplan, 2019; Malard & Mohty, 2020). Data from the National Comprehensive Cancer Network (NCCN, 2020) reported an annual incidence of 1.38–1.57 cases per 100,000 population in the United States, with around 1,500 deaths per year (Brown et al., 2020). The incidence of ALL among children in Asia is also relatively high, such as in Singapore, where it reaches 3.78 per 100,000 children (Brown et al., 2020). In Indonesia, a study reported an incidence rate of 4.32 per 100,000 children, with an estimated more than 3,400 new cases in 2018 (Garniasih et al., 2022). A report from Dr. Sardjito General Hospital even showed an increasing incidence in Yogyakarta Special Region and southern Central Java, from 1.9 per 100,000 in 1998 to 5.5 per 100,000 in 2009 (Wijayanti & Supriyadi, 2017).

Advances in therapy have significantly improved survival rates for ALL patients. One of the main components of treatment regimens is glucocorticoids, such as prednisone and dexamethasone, which exert a direct cytotoxic effect on lymphoblasts through apoptosis induction (Pourhassan et al., 2024; Hunger, 2016). Nevertheless, prolonged glucocorticoid use may cause serious adverse effects, including disturbances in bone metabolism (Pourhassan et al., 2024; Hua et al., 2023).

Glucocorticoid-induced bone metabolism disorders may include reduced bone mineral density, osteoporosis, fractures, and alterations in biochemical bone biomarkers such as calcium, magnesium, phosphate, and alkaline phosphatase (ALP) (Hua et al., 2023; Velentza et al., 2021). In children, this risk is particularly critical because treatment coincides with the phase of active bone growth. Therefore, bone profile biomarkers have the potential to serve as early indicators for detecting bone metabolism disturbances during therapy (Velentza et al., 2021). Based on this background, the present study aimed to analyze the relationship between glucocorticoid type and duration with bone profile parameters (calcium, magnesium, phosphate, ALP) in children with ALL at H. Adam Malik General Hospital, Medan.

METHOD

This cross-sectional study was conducted at the Pediatric Hemato-Oncology Inpatient Unit of Adam Malik General Hospital, Medan, from April to May 2025. Children aged ≤18 years with acute lymphoblastic leukemia (ALL) who had received at least one week of glucocorticoid therapy and had complete bone profile laboratory data (calcium, magnesium, phosphate, alkaline phosphatase) were included. Patients with bone metabolism disorders, chronic kidney disease, endocrine disorders, or incomplete medical records were excluded. A total of 30 patients were enrolled using consecutive sampling. Independent variables included type and duration of glucocorticoid therapy, age at diagnosis, sex, nutritional status, and ALL risk classification, while bone profile parameters served as the dependent variables. Data were collected from medical records and laboratory results. Statistical analysis was performed using SPSS. Normality was assessed with the Shapiro–Wilk test, group comparisons were made using the Mann–Whitney U test, and Spearman correlation was applied for numeric associations. Multivariate analysis was conducted using multiple linear regression, with $p<0.05$ considered statistically significant. The study was approved by the Ethics Committee of Universitas Sumatera Utara (approval number: 267/KEPK/USU/2025) and Adam Malik General Hospital, Medan (approval number: DP.04.03/D.XXVIII/2003/2025).

RESULT

A total of 30 patients met the study criteria, the majority of whom were male (53.3%) and classified as high-risk (60%). The most common nutritional status was normal (50%), as shown in Table 1.

Tabel 1.
Demographic and Clinical Characteristics of Patients

Variable	f	%
Sex		
Male	16	53,3
Female	14	46,7
Risk Group		
Standard	12	40,0
High	18	60,0
Nutritional Status		
Normal	15	50,0
Underweight	13	43,3
Overweight	2	6,7

The analysis of the relationship between glucocorticoid type and bone profile showed a significant difference in magnesium levels (p=0.010), while calcium, phosphate, and ALP did not show significant differences, as presented in Table 2.

Table 2.
Association Between Glucocorticoid Type and Bone Profile

Bone Profile	Prednisone	Deksametasone	p	Remark
Calcium (mg/dL)	9,0 ± 0,6	9,1 ± 0,6	0.719	NS
Magnesium (mg/dL)	2,22 (1,88–3,36)	1,94 (1,22–2,40)	0,010	Signifikan
Phosphate (mg/dL)	4,5 ± 0,8	4,1 ± 0,8	0.125	NS
ALP (U/L)	166,5 (88–212)	178 (78–440)	0.865	NS

Based on the analysis of the relationship between glucocorticoid duration and bone profile, among the four parameters analyzed, only magnesium levels were significantly associated with

glucocorticoid duration (p=0.014). Meanwhile, calcium, phosphate, and ALP levels showed no significant associations (p>0.05), as presented in Table 3.

Table 3.
Association Between Duration of Glucocorticoid Use and Bone Profile

Bone Profile	≤ 7 weeks Median (IQR)	> 7 weeks Median (IQR)	p-value
Calcium	9,1 (8,8–9,3)	9,0 (8,7–9,2)	0,346
Magnesium	2,5 (2,3–2,7)	2,8 (2,6–3,0)	0,014*
Phosphate	4,5 (4,1–4,8)	4,3 (4,0–4,7)	0,202
ALP	280 (250–305)	270 (240–300)	0,264

Table 4.
Multivariate Analysis of Factors Affecting Magnesium Levels

Dependent Variable	Independent Variable	p-value	95% CI
Calcium	Age	0,365	-0,741 – 0,283
	Age at diagnosis	0,437	-0,317 – 0,709
	Sex	0,350	-0,256 – 0,693
	Nutritional status	0,318	-0,213 – 0,628
	Steroid type	0,529	-0,714 – 0,377
	Steroid duration	0,460	-0,725 – -0,339
Magnesium	Age	0,005*	-0,125 – -0,611
	Age at diagnosis	0,002*	-0,647 – -0,159
	Sex	0,873	-0,208 – 0,243
	Nutritional status	0,937	-0,192 – 0,207
	Steroid type	0,338	-0,137 – 0,382
	Steroid duration	0,403	-0,357 – 0,149
Phosphate	Age	0,182	-0,234 – 1,159
	Age at diagnosis	0,191	-1,152 – 0,243
	Sex	0,706	-0,526 – 0,765
	Nutritional status	0,846	-0,626 – 0,517
	Steroid type	0,487	-0,489 – 0,995
	Steroid duration	0,637	-0,923 – 0,523
ALP	Age	0,399	-76,790 – 31,718
	Age at diagnosis	0,346	-29,081 – 79,570
	Sex	0,188	-83,254 – 17,317
	Nutritional status	0,554	-31,599 – 57,475
	Steroid type	0,636	-44,415 – 71,204
	Steroid duration	0,229	-90,036 – -22,656

The multivariate analysis showed that magnesium levels were significantly associated with age (p=0.005) and age at diagnosis (p=0.002). In contrast, other variables such as sex, nutritional status, steroid type, and duration of steroid use were not significantly associated with magnesium levels (p>0.05). No significant associations were found between independent variables and calcium, phosphate, or ALP levels, as presented in Table 4.

DISCUSSION

This study involved 30 pediatric patients with acute lymphoblastic leukemia (ALL), with a mean age of 7.3±4.7 years and a mean age at diagnosis of 6.8±4.7 years. Most patients were diagnosed during school age, consistent with reports from China and Indonesia showing higher incidence in children, particularly in the 0–4 year age group (Li et al., 2015; Supriyadi et al., 2011). Male predominance (53.3%) was observed, which aligns with other studies from Asia and other regions, where male-to-female ratios ranged from 1.49 to 1.88 (Li et al., 2015; Supriyadi et al., 2011). Nutritional status varied across the cohort, with half of the patients having normal nutrition, suggesting that ALL may occur independently of nutritional status.

Analysis of bone-related parameters showed that the mean values of calcium, magnesium, phosphate, and alkaline phosphatase (ALP) were within the normal range, except for magnesium, which was elevated in 50% of patients. This elevation may indicate early disturbances in mineral

metabolism during therapy. Similar findings were reported in Pakistan, where both calcium and magnesium were elevated in ALL patients (Afridi et al., 2018). In contrast, a Canadian study observed mild hypocalcemia and hypomagnesemia at baseline, with increases in magnesium and ALP only after therapy completion (Atkinson et al., 1989; Swaminathan, 2003; Cascella & Vaqar, 2025). Differences in study design, particularly timing of sample collection, may explain these discrepancies.

Glucocorticoid exposure is a well-known factor affecting mineral metabolism, through mechanisms such as magnesium retention and enhanced bone resorption, leading to increased serum magnesium. Therefore, magnesium levels could serve as an early marker of bone metabolism or renal function disturbances in children with ALL receiving glucocorticoids (Atkinson et al., 1989; Swaminathan, 2003; Cascella & Vaqar, 2025). Glucocorticoids act through both genomic and non-genomic pathways, and prolonged use (>6 weeks) is strongly associated with reduced bone mineral content and density (Inaba & Pui, 2010; Ahmed et al., 2002).

In this study, magnesium levels were the only bone parameter significantly affected, whereas calcium, phosphate, and ALP were not. This is consistent with reports from Canada, where long-term steroid use caused calcium loss, hypomagnesemia, and altered vitamin D metabolism (Halton et al., 1996), and with data from Jakarta showing hypocalcemia and vitamin D deficiency associated with chronic corticosteroid exposure (Santoso et al., 2010). The type of glucocorticoid may further influence toxicity. Dexamethasone, used by most patients in this cohort, is associated with higher risk of skeletal complications, including fractures and osteonecrosis, compared with prednisone, particularly in adolescents (Inaba & Pui, 2010; Bordbar et al., 2016; Ardissone et al., 2002; Ahmed et al., 2002).

Other chemotherapeutic agents, such as methotrexate, may aggravate bone loss by increasing bone resorption and calcium excretion (Kobza et al., 2021; Das et al., 2023). Corticosteroids additionally suppress calcium absorption, increase urinary calcium loss, reduce sex hormone levels, and inhibit vitamin D–dependent osteocalcin synthesis (Kobza et al., 2021; Soliman et al., 2022). Collectively, these mechanisms explain the multifactorial nature of bone changes in ALL.

Finally, magnesium levels were significantly associated with age at diagnosis, whereas calcium, phosphate, and ALP were not. Older children (>10 years) may have higher baseline BMD Z-scores but experience greater declines during intensive chemotherapy, likely due to impaired bone accrual (Inaba & Pui, 2010). Nutritional status showed no significant effect on bone parameters, although malnourished patients tended to have higher magnesium levels, while overweight patients had higher calcium, phosphate, and ALP. Prior studies indicate that malnutrition predisposes children to metabolic disturbances, including hypocalcemia, hypophosphatemia, vitamin D deficiency, and elevated ALP (Das et al., 2023). Additionally, steroid therapy can alter weight and glucose metabolism, predisposing patients to insulin resistance and long-term metabolic complications (Picáns-Leis et al., 2024).

CONCLUSION

This study showed that magnesium levels in children with acute lymphoblastic leukemia were significantly influenced by the type and duration of glucocorticoid administration as well as age at diagnosis. Patients receiving dexamethasone had higher magnesium levels compared with those receiving prednisone, and longer treatment duration tended to increase magnesium levels. In contrast, calcium, phosphate, and alkaline phosphatase levels were not significantly associated with either the type or duration of glucocorticoid use. These findings highlight the importance of monitoring mineral profiles, particularly magnesium, during glucocorticoid therapy to prevent bone metabolism complications. Prospective studies with larger sample sizes and additional biomarker evaluation are needed to strengthen these findings and to better understand the underlying mechanisms.

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