



## ORIGINAL ARTICLE

# VITAMIN D STATUS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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## ABSTRACT

**Background:** Skeletal morbidities are a common initial presentation and outcome in acute lymphoblastic leukemia(ALL). Vitamin D plays a vital role in the physiological regulation of calcium and phosphate transport and bone mineralization. Also high (25(OH)) level and high vitamin d intake at the time of diagnosis and initiation of anticancer treatment were associated with improved outcome.

**Methods:** Twenty five ALL patients admitted to hematology and oncology unit, children hospital Zagazig University in one-year .vitamin D (25 (OH)) level was assessed in all patients at diagnosis. Patients were classified into deficient vitamin D (0-20)ng/ml , insufficient vitamin D (20-30)ng/ml and sufficient vitamin D (30-50)ng/ml. Statistical analysis was done to determine relation between different groups and ALL patients characteristics. **Results:** Vitamin D deficient in 24% of patients, vitamin D insufficient in 48% of patients, and vitamin D sufficient in 28% of patients. There was high statistical difference between different groups regarding bone pain and sex. **Conclusions:** A non-sufficient level in childhood all (deficiency and insufficiency) is common in childhood ALL and this is related to bone pain as initial clinical presentation. Vitamin D is related to presentation and prognosis of ALL in children.

**Key words:** Acute lymphoblastic leukemia; Vitamin D, Bone pain

## INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood. It accounts for 25 % of all pediatrics cancer. Skeletal morbidities are very common with ALL initially and during treatment [1].

Vitamin D plays an important role in regulation of calcium and phosphate transport and bone mineralization. It was considered that vitamin D deficiency involved in development of rickets in

children and osteomalacia in adults [2]. Several studies showed that vitamin D has a role in decreasing the risk of cancer. High 25(OH) D and high vitamin D intake at the time of diagnosis and initiation of anticancer treatment were associated with improved outcome and good prognosis [3].The most reliable way to determine Vitamin D status is by measuring serum 25-hydroxyvitamin D (25(OH)D) [4].

The aim of this study was to assess vitamin D status in pediatric patients with ALL and to identify risk factors for vitamin D deficiency.

### METHODS

Our study was a cross sectional study which included all newly diagnosed acute lymphoblastic leukemia patients admitting to hematology and oncology unit, children's hospital, Zagazig University in one year.

Inclusion criteria were newly diagnosed acute lymphoblastic leukemia patients age (1-18) years old and both sexes

Exclusion criteria were acute lymphoblastic leukemia on therapy, patients with other malignancies and relapse ALL

Consent was obtained from relatives of patients and Approval for performing the study was obtained from pediatric Department, Faculty of Medicine, and Zagazig University after Institutional Review Board of Zagazig University (IRB-ZU) approval.

All subjects in the study were subjected to Full medical history and Full physical examinations.

They were also subjected to Laboratory investigations including

-Complete blood count (CBC) by (systmex KX-21) with examination of leishman stained peripheral smears , serum electrolytes.

-patients were evaluated for calcium(Ca),phosphorus(Ph) and alkalinephosphatase(ALP)

- Serum vitamin D (25(OH)) level assessment after end of consolidation therapy using an enzyme-linked immunosorbent (ELISA) technique.

Serum [25(OH) D] levels of 20 to 30 ng/ml defined Vitamin D insufficiency, and a level of <20 ng/ml defined vitamin D deficiency, while levels >30 ng/ml defined normal vitamin D level (sufficient) [5].

- Bone marrow aspiratiation with examination of Leishman stained films was

done and examined for morphology and immunophenotype.

The patients were divided to 3 groups:

Group (1) included patients with vitamin D deficiency.

Group (2) included patients with vitamin D insufficiency.

Group (3) included patients with vitamin D sufficient.

### Statistical analysis:

Relation between vitamin D status and patients characteristics was statistically analyzed by computer using Statistical Package of Social Services version 22 (SPSS), as showing in Table (3). Suitable statistical tests of significance were used after checked for normality.

Continuous quantative variables e.g age were expressed as the mean  $\pm$  SD & median (range). Comparison of several groups median was done by Kruskal Wallis test.

Categorical qualitative variables were expressed as absolute ferquencies (number)& relative frequencies (percentage) and comparison between several groups median was done by chi square test.

The results were considered statistically significant when the significant probability was less than 0.05 ( $P < 0.05$ ). P-value  $< 0.001$  was considered highly statistically significant (HS), and P-value  $\geq 0.05$  was considered statistically insignificant (NS).

### RESULTS

Table (1) shows that the mean age of the studied group is  $8.08 \pm 3.79$  years old, with a range from 3 to 15 years old. About 2/3 of the studied group (64.0%) are male. About 2/3 of them diagnosed as common ALL (68%).mean of peripheral blast cells was  $66.33 \pm 20.97$  while mean of bone marrow blast cells was  $83.8 \pm 18.48$ . the mean of WBCs was  $27.9 \pm 115.13$  and mean of hemoglobin was  $9.17 \pm 1.06$  . forty four percent of the patients Suffered from bone

pain at diagnosis .Regarding bone minerals mean of calcium was  $9.47 \pm 0.609$  ,mean of phosphorus was  $4.17 \pm 0.41$  and mean of alkaline phosphatase was  $110 \pm 16.8$ .

Table (2) shows that the mean of serum vitamin D (25(OH)) level among the studied group is  $25.17 \pm 6.9$  ng/ml, with a range from (13-35). About %24 of the patients were deficient in vitamin D. %28 of the patients were of insufficient level and (48.0%) were sufficient in vitamin D.

Table (3) shows that mean Age in patients with vitamin D deficiency  $7.6 \pm 2.7$  years .84% are males. 67% of them suffered from common ALL. All patients with a deficient level of vitamin d suffered from bone pain.

It was a high statistical significance in patients groups regarding bone pain. P value=0.005.

In patients with vitamin D Insufficiency mean age were  $8.8 \pm 4.3$  years. 58 % of them was Male and 42% was female .Common ALL immunophenotype was in 67% and T ALL immunophenotype was in 33%. 33% of insufficient vitamin D level patients suffered from bone pain.

Patients with vitamin D sufficiency mean age was  $7.1 \pm 3.8$  years. 57% of them were Male and 43 % were female. Common ALL immunophenotype was in %71 of patients and T-ALL immunophenotype was in %29 of patients of patients of patients. Only 14% of them suffered from bone pain.

**Table 1.** Characteristics of all studied patients.

ITEM	Studied patients (N=25)	
	No.	%
<b>Sex</b>		
Male	16	64.0
Female	9	36.0
<b>Age (years)</b>		
Mean $\pm$ SD	$8.08 \pm 3.79$	
Median (Range)	9(3-15)	
<b>Immunophenotype</b>		
Common ALL	17	%68
T ALL	8	%32
<b>Lab</b>		
Blast cells%		
Mean	$66.33 \pm 20.97$	
range	70(25-98)	
Bone marrow blast %		
Mean	$83.8 \pm 18.48$	
range	90(25-98)	
WBCs $\times 10^9/l$		
Mean	$27.9 \pm 115.13$	
range	3.2 ( 1.3-580)	
Hemoglobin g/dl		
Mean	$9.17 \pm 1.06$	
range	9( 6.5-11)	
<b>Clinical presentation</b>		

Bone pain	11	%44
<b>Bone minerals</b>		
Calcium mg/dl		
Mean	9.47±0.609	
range	9.5(8.16-10.70)	
Phosphorus mg/dl		
Mean	4.17±0.41	
range	4.2(3-5)	
Alkaline phosphatase U/L		
Mean	110±16.8	
range	108 (70-141)	

**Table 2.** Vitamin D level and status among the studied ALL patients.

Item	Studied patients (N=25)	
	No	%
<b>Vitamin D level ng/ml</b>		
Mean ± SD	25.17±6.9	
Median (Range)	26(13-35)	
<b>Vitamin D status ng/ml</b>		
Deficiency (0-20)	6	24
Insufficiency (20-30)	12	48
Sufficiency (30-50)	7	28

**Table 3.** relation between vitamin D status and patient characteristics in our study

Item	Group (1) (N=6)		Group (2) (N=12)		Group (3) (N=7)		p-value
	N	%	N	%	N	%	
<b>Age</b>							
Mean	7.6±2.7		8.8±4.3		7.1±3.8		0.604 #
range	(5-10)		(3-15)		(3-14)		
<b>Sex</b>							
Male	5	%83	7	%58	4	%57	0.526*
female	1	%16	5	%41	3	%42	
<b>IPT</b>							
Common ALL	4	%67	8	%67	5	%71	0.974*
T ALL	2	%33	4	%33	2	%29	
<b>lab</b>							
Blast%							0.518#
Mean	63.33 ± 19.66		62± 26.62		72.86 ±22.15		
range	30-90		98.00		30-90		
Bm blast%							

Mean range	86.17 ± 7.22 80-97	78.17± 28.27 98.00	87.86 ±19.09 45-98	0.293#
Wbc X10 <sup>9</sup> /l				
Mean range	2.98 ± 1.73 1.3-6	4.87± 3.13 2.20- 12.20	3.26± 0 .99 1.5-4.3	0.354#
Hb g/dl				
Mean range	9.43± 1.098 8-11	9.16 ± 1.28 6.50 - 11.00	8.99 ±0.63 8.2-10	0.727#
<b>Clinical presentation</b>				
Bone pain	6 %100	4 %33	1 %14	0.005**
<b>Bone minerals</b>				
Ca mg/dl				
Mean Range	9.5 ±0 .39 8.9- 10	9.47±0.603 8.16-10.30	9.46 ±0 .83 8.19-10.7	0.991#
Ph mg/dl				
Mean range	4.3±0 .4 4-5	4.115±0.503 3-5	4.17 ±15.67 4-4.4.5	0.840#
Alp U/L				
Mean range	117.33 ±13.23 101-140	104.58±18.298 70-126	113±0.142 97-141	0.438#

\*chi square #kruskal wallis \*\*significant p-value

## DISCUSSION

Bone disease has been reported previously in association with ALL in children and adults. But no clear mechanism has been identified. One possibility is direct involvement of bone by disease. In addition the effects of chemotherapy on gastrointestinal and renal handling of nutrients may cause alterations in mineral homeostasis that eventually lead to abnormal turnover of bone mineral [6]. Therefore, our aim of work is to assess vitamin D status in pediatric patients with ALL and to identify risk factors for vitamin D deficiency.

Regarding immunophenotyping results in this work it was found that about 2/3 of studied group diagnosed as common ALL (68%).and (32%) of them are of T-ALL. In most studies that discussed ALL immunophenotype it was reported that common ALL is the most predominant immunophenotype in childhood ALL. In study by Zhai et al, C-ALL phenotype

present 72% of the patients and T-ALL presented 7% of patients [7] and in Veerman et al., C-ALL was in 52 % of patients [8]. No one of patients in our study has B-ALL immunophenotype .This may be explained by low number of studied ALL patients in our study compared to other studies.

In this work bone pain was presented in (44%) of patients. Clinical findings in our study match that in most studies .Study carried out by Sinigaglia concluded that (34.4%) of ALL patients had bone pain [9]. Musculoskeletal pain was present in 36% of patients at the time of diagnosis in the study performed by Halton [10].

In the current work we biochemically evaluated status of bone in children with ALL through measuring of ( calcium,phosphorus and ALP ).The mean serum Ca levels at diagnosis was 9.47.±0.6 mg/dl. This value correlates with that of [9] who reported that mean of Ca at diagnosis 9.48 mg/dl.

In the present study, we assessed vitamin D status in ALL pediatric patients. The current study revealed that the mean of vitamin D level at diagnosis among the studied group is  $25.17 \pm 6.9$  ng/ml. while Demisory et al. who reported that the mean of vitamin D level at diagnosis among the studied group is  $19.03 \pm 10.98$  ng/ml [11]. Possible explanations for this variation are differences in reference data and methods of vitamin D assessment [12]. Poorer levels of vitamin D were related to the season of evaluation and they decrease with increase of age as stated in different studies [13-15]. According to vitamin D status at diagnosis of ALL among our ALL patients, 24% of children with ALL were deficient in vitamin D level, 48% Insufficient and 28% Sufficienct. This is consistent with the study done by Helou et al who reported that 71% of leukemic children were in abnormal level of vitamin D at diagnosis [16]. It was noticed that there was association between vitamin D statuses and gender with study which revealed also that younger ages were associated with vitamin d deficiency [13], however in our work it was no statistical significance gender and age and vitamin d deficiency. in the present study, there was no significant difference between age, sex and vitamin D levels at diagnosis. Our findings are compatible with Simmons et al' [14] and Choudhary et al.[17] findings that reported there was not enough evidence to suggest treatment type or gender were associated with low serum 25(OH) D levels.

### CONCLUSION

More than half of children diagnosed with ALL are with Non-sufficient levels (deficiency and insufficiency) of vitamin D .Vitamin D status is related to bone pain in ALL.

#### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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