Original Research Article

Evaluation of Bone Mass Density in Children and Adolescents with Acute Lymphoblastic Leukemia

Abstract

Background: Leukemia is a group of blood cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These blood cells are not fully developed and are called blasts or leukemia cells.

Aim of work: The aim of our study was to evaluate bone density by DXA scan in children and adolescents with Acute Lymphoblastic leukemia at diagnosis and after 6 m of treatment with chemotherapy.

Subject and methods: The study was conducted in Pediatric Department Hematology and Oncology Unit of Tanta University and Tanta Cancer Center, From November 2020 to November 2022.

Study subjects: Evaluation of Bone Mass Density in Children and Adolescents with Acute Lymphoblastic Leukemia, **Study design:** observational cross sectional. This study included 25 children were diagnosed with Acute Lymphoblastic Leukemia (the same 25 Patients were examined at diagnosis and after 6 months of treatment with chemotherapy)

Results: The mean age of this study children was 7.92+ 3.59 years in group I and 8.42+ 3.59 years in group II. The two groups were matched as regards weight, Height, and BMI.

In the present study Bone Mass Density was significantly lower in the leukemia children after 6 months treatment of chemotherapy (0.53±0.11), compared to leukemia children at time of diagnosis (0.59±0.11) ($P<0.05$). Also, bone mineral content and Z score were significantly lower in group II patients (20.5±7.82 and 1.120±0.37, respectively), compared to group I (23.13±9.18 and 2.25±0.45, respectively).

Conclusion: Bone Mass Density, bone mineral content and Z score are significantly lowered after chemotherapy of ALL patients. Since a reduced BMD predisposes to osteopenia and osteoporosis, the use of DXA scanning to evaluate and monitor BMD in children with ALL may be useful to identify those patients at risk for developing osteopenia, osteoporosis, and pathological fractures.

Keywords: Bone mineral density, Dual-energy X-ray absorptiometry and Acute lymphoblastic leukemia

Introduction

Leukemia is a group of blood cancers that usually start in the bone marrow and lead to large numbers of abnormal blood cells. These blood cells are not fully developed and are called embryonic or white blood cells. [1]

Damage to the bone marrow, by replacing normal bone marrow cells with a higher number of immature white blood cells, leads to a lack of blood platelets, which are important in blood clotting, and cells red blood cells leading to anemia. Diagnosis is usually made by blood tests or bone marrow aspiration.[2]

Factors that can increase your risk of developing certain types of leukemia, including previous cancer treatment, genetic disorders, exposure to certain chemicals, smoking, and a family history of leukemia bridge. [3]

Leukemia symptoms vary, depending on the type of leukemia. Common leukemia signs and symptoms including fever or chills, persistent fatigue, weakness, frequent or severe infections, losing weight swollen lymph nodes, enlarged liver or spleen, easy bleeding or bruising, recurrent nosebleeds,petechiae, excessive sweating, especially at night, bone pain or tenderness, skeletal abnormalities are commonly seen in children and adolescents with leukemia.[4]

Bone growth in length is not altered at leukemia diagnosis, as absolute height in children with leukemia is not different from healthy children However, bone density at leukemia diagnosis is altered prior to initiating chemotherapy.

At diagnosis, serum markers of bone formation, including osteocalcin, the carboxyl-terminal property of type I collagen, and bone-specific alkaline phosphatase, were low. Several studies have shown abnormally low levels of 1,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin D3, hypercalciuria, low parathyroid hormone, and low to normal levels of calcium, magnesium, and phosphate.[5]

During Acute lymphoblastic leukemia treatment, bone formation and resorption markers are increased resulting in a decrease in total body Bone mass density (mean -0.68, SD 1.26) within the first six months of treatment.

Lower Bone mass density at diagnosis is associated with higher prevalence of subsequent bony fractures during Acute lymphoblastic leukemia therapy, low lumbar spine Bone mass density at diagnosis and during treatment should be used to identify Acute lymphoblastic leukemia patients at significant risk for bony fractures and osteoporosis [6]. Poor nutrition, low vitamin D, and poor muscle mass contribute to the development or worsening of bone pathology during therapy that may result in osteoporosis, fracture, and Osteo necrosis. Endocrine abnormalities further contribute to the bone morbidity Bone mass density is measured by Dual-energy X-ray absorptiometry (DXA).

Aim of the Work

The aim of this work is to evaluate bone density by DXA scan in children and adolescent with Acute Lymphoblastic leukemia at diagnosis and after 6 months of treatment with chemotherapy

Patients and Methods

Study area setting: The study was conducted in Pediatric Department Hematology and Oncology Unit of Tanta University and Tanta Cancer Center, From November 2020 to November 2022.

Study subjects: Evaluation of Bone Mass Density in Children and Adolescents with Acute Lymphoblastic Leukemia

Study design: observational cross sectional.

This study included 25 children were diagnosed with Acute Lymphoblastic Leukemia (the same 25 Patients were examined at diagnosis and after 6 months of treatment with chemotherapy)

Individuals enrolled in this study are divided to:

- **Group (I):** 25 Children and Adolescents with Acute Lymphoblastic Leukemia at time of diagnosis
- **Group (II):**25 Children and Adolescents with Acute Lymphoblastic Leukemia after 6 months of treatment with chemotherapy **(1)**.
- **Inclusion criteria:**

Children and adolescents diagnosed as acute lymphoblastic leukemia, aged 2-18 years (Inaba and Pui, 2021). Blast cells in bone marrow aspiration were>20%.

Exclusion criteria:

I- Other types of malignancy.

II- Acute Lymphoblastic Leukemia with hyper leukocytosis

Methods:

All children in this study were subjected to the following:

1- History taking

History of age of onset, symptoms, signs, medical history and family history

2- Thorough clinical examination

3-Laboratory investigations: Routine investigation:

1-Complete blood count

2- Renal function tests

3- Liver function tests

4- Bone marrow aspiration.

5-Calcium panel: ionized calcium

6-Phosphorous

7-Magnesiunm

8- Alkaline phosphatase.

Specific investigation

1-Parathermone hormone

2-DXA scan (Madix90 IMD Generators S.R.L 2016) at diagnosis and 6 Months later after starting chemotherapy

Privacy of all data was guaranteed as follows:

- Every patient had a code number. The name and the address was kept in a special file.
- The results of the study was used only for scientific purpose and wasn't used for any other purposes.

Informed consent:

Informed consent was obtained from all patients after full explanation of benefits and risks of the study.

Risks on the participants in this study and how to manage:

<u>The risks to Participants and measures used to minimize these risks:</u>

No risks documented but unexpected risks that may occur during the course of the research will be cleared to the participants and ethical committee on time.

The adequate provision to maintain privacy of participants and confidentiality of data are as follows:

A special file was created to mark the patient code numbers in it.

- A code number has been placed for each patient, a code for the name and address

- The patient's name has been hidden when using the search.

- The results of the research were used for the scientific purpose only.

Statistical evaluation

Statistical presentation and evaluation of the prevailing look at become conducted, the usage of the mean, general deviation a look at through SPSS V.22.

1 - Student t-test:

For normally distributed quantitative variables, to compare between two studied groups.

2 - Mann Whitney test:

For abnormally distributed quantitative variables, to compare between two studied groups.

3 - F-test (ANOVA)

For normally distributed quantitative variables, to compare between more than two groups.

4 - Pearson coefficient

To correlate between two normally distributed quantitative variables.

Results

As regards Bone Mass Density, Bone Mineral content and Z score were significantly lower in the patient Group (II) compared to Group (I), ($P<0.05$).

Z score (Lumbar spine) Group (I) was in normal range (>-1) How ever in some patients BMD was mild decreased but still in normal range. Z score (Lumbar spine) Group (II) (56%) was in normal range (>-1), (40%) was osteopenia (-1 to-2) and (4%) was Osteonecrosis (<-2).

Table (4) and Figures (4) show that:

According to Total leucocyte count were significantly lower in the patient Groups (II) compared to Group (I), ($P<0.05$).

There was no significant difference between 2 groups in this Variable (Hemoglobin, Platelet, Hematocrit, mean corpuscular volume, Mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and Red cell distribution width - coefficient of variation) P>0.05)

Table (5) and Figures (6, 7) show that:

There were no significant differences in Calcium, ionized calcium, parathyroid hormone and Magnesium among the studied groups (P>0.05). However, Phosphorus and Alkaline phosphatase were significantly lower in the patient Groups (II) compared to Group (I), (P>0.05).

Table (1) Comparison between the two groups as regards BMD,BMC andZ score.

Variable (mean± SD)	group (I) (n=25)	group (II) (n=25)	*P*-Value
BMD	0.59±0.11	0.53±0.11	0.001*
BMC	23.13±9.18	20.5±7.82	0.001*
Z score	2.25±0.45	1.120±0.37	0.001*

BMD : Bone Mass Density, BMC Bone Mineral content, *: Statistically significant at $p \leq 0.05$

Table (1) and Figures (1,2) show that:

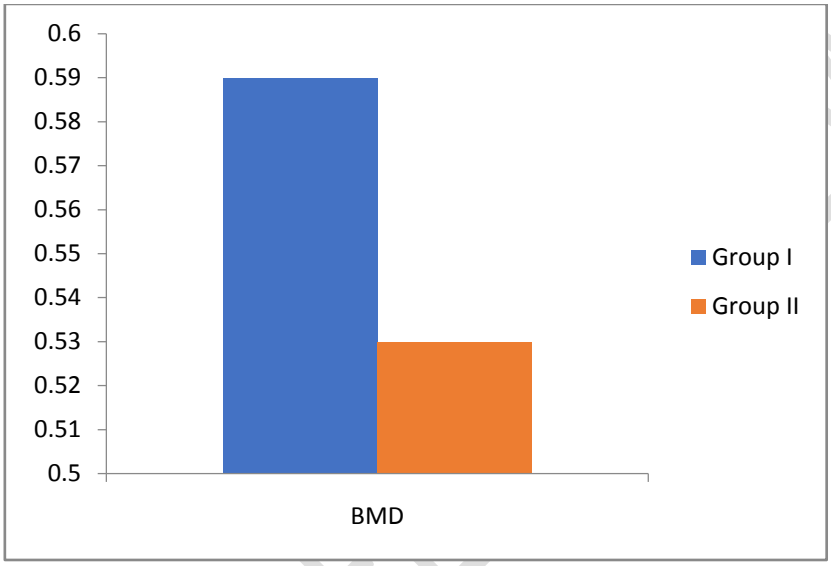


Figure (1):Comparison between of BMD among the studied groups .

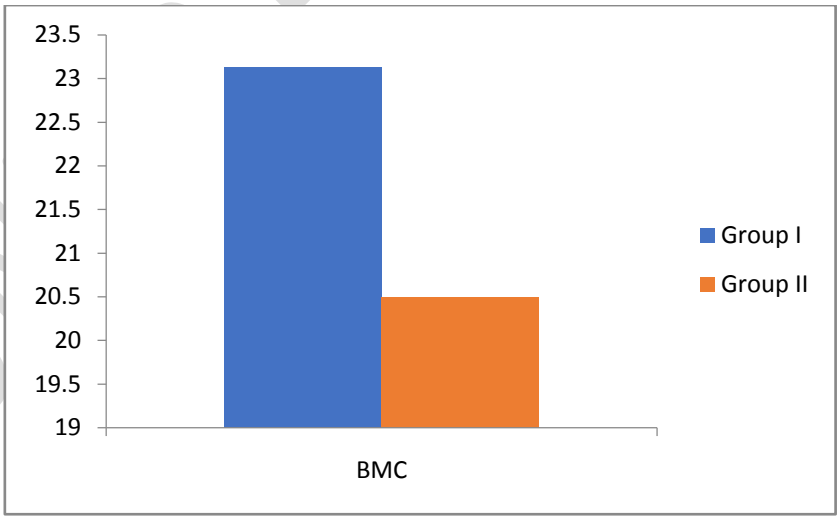


Figure (2):Comparison between of BMC among the studied groups .

Table (2): Comparison between the two groups as regards Z score (Lumbar spine)

Table (2) and Figures (3) show that:

Z score (Lumbar spine)	group (I) (n=25)	group (II) (n=25)
Normal (>-1)	25(100%)	14(56%)
Osteopenia(-1 to-2)	0	10(40%)
Osteonecrosis(<-2)	0	1(4%)

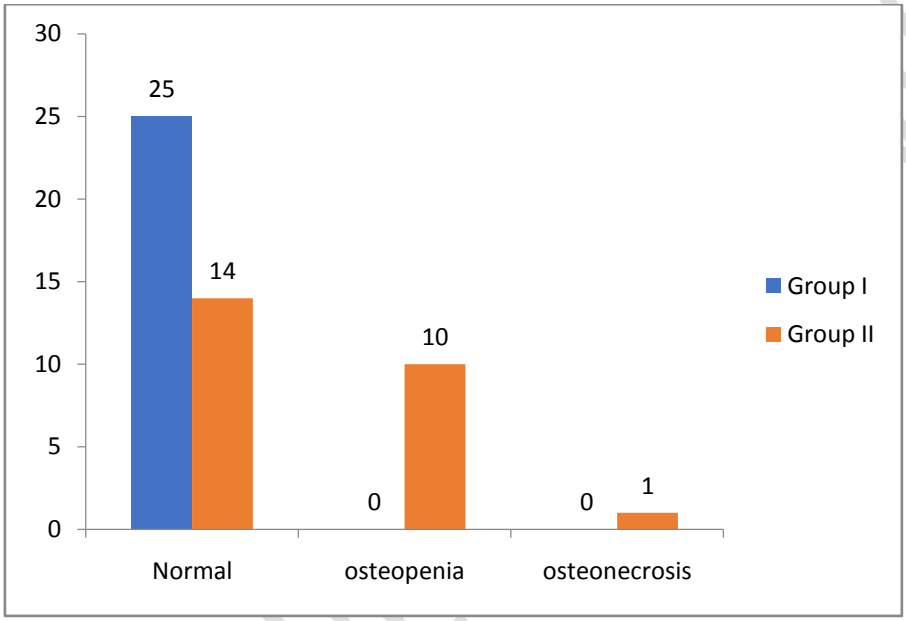


Figure (3): Comparison between the two groups as regards Z score (Lumbar spine)

Table (3) Comparison between the two groups as regards Total leucocyte count, Hemoglobin, Platelet, Hematocrit, MCV, MCH, MCHC and RDW-CV

Variable (mean± SD)	group (I) (n=25)	group (II) (n=25)	*P*-Value
Total leucocyte count	82.25±85.2	2.1120±0.676	0.001*
Hemoglobin	12.6±17.9	9.0880±0.635	0.311
Platelet	81.64±3.7	84.080±23.677	0.802
Hematocrit	37.04±2.09	37.32±2.154	0.699
MCV	81.12±4.35	81.12±4.76	0.948
MCH	26.76±2.02	26.96±2.15	0.743
MCHC	28.56±4.184	28.36±3.87	0.327
RDW-CV	12.59±1.00	12.75±0.94	0.573

MCHC: mean corpuscular hemoglobin concentration
MCH: Mean corpuscular hemoglobin
MCV: mean corpuscular volume
RDW-CV: Red cell distribution width - coefficient of variation
*: Statistically significant at $p \leq 0.05$

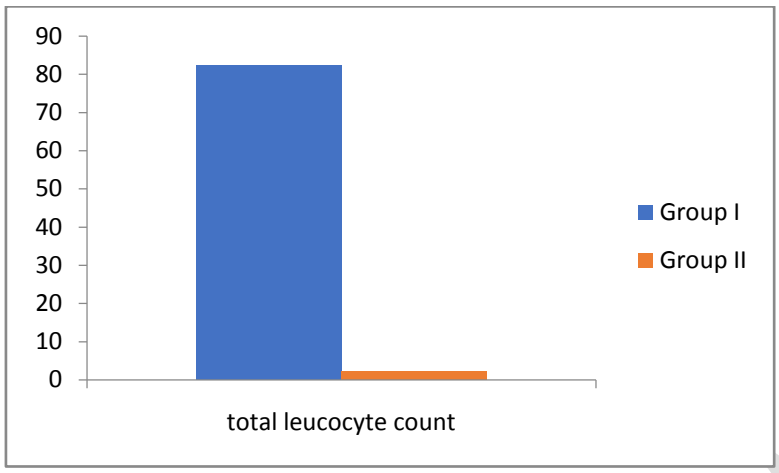


Figure (4) Comparison between the two groups as regards Total leucocyte count, Hemoglobin, Platelet, Hematocrit, MCV, MCH, MCHC and RDW-CV

Table (4) Comparison between both groups as regards the Alkaline phosphatase

Variable (mean± SD)	group (I) (n=25)	group (II) (n=25)	P-Value
Alkaline phosphatese	161.52±3.66	107.88±11.59	.001*

*: Statistically significant at p ≤ 0.05

There were significant differences Alkaline phosphatase among the studied groups (P<0.05).

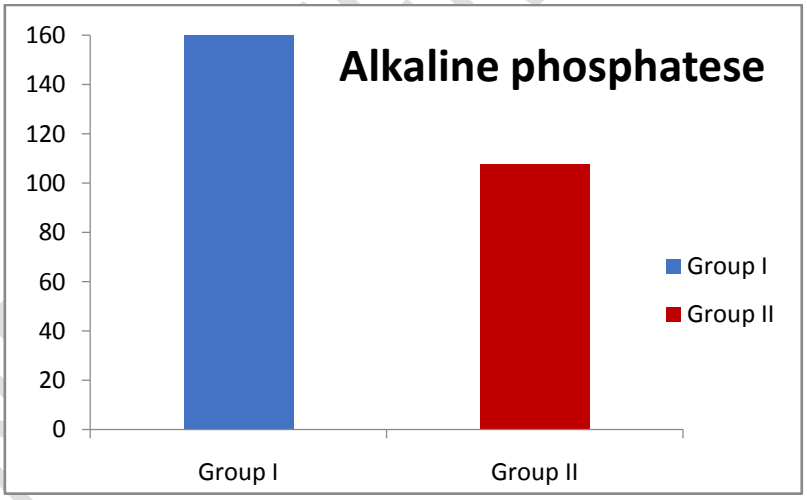


Figure (5) Comparison between both groups as regards the Alkaline phosphatese

Table (5): Comparison between both groups as regards the Calcium, Ionized calcium, para thyroid hormone, Magnesium, Phosphorus and Alkaline phosphatese

Variable (mean± SD)	group (I) (n=25)	group (II) (n=25)	P-Value
Calcium	9.2840±0.853	9.5080±0.46	.197
Ionized calcium	5.0560±0.227	5.0720±0.117	.760
para thyroid hormone	22.60±2.90	23.2000±2.23	.260
Magnesium	1.9960±0.14	1.96±0.124	.332
Phosphorus	4.980±59.11	2.5600±0.177	0.001*
Alkaline Phosphtase	161.52±3.66	107.88±11.59	0.001*

*: Statistically significant at $p \leq 0.05$

*Significant at $p<0.05$.
SD: standard deviation.

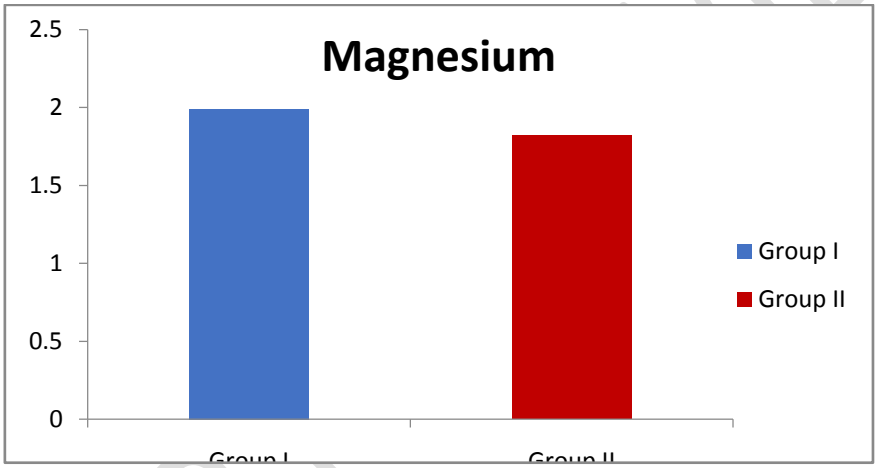


Figure (6) comparison between both groups according to Magnesium

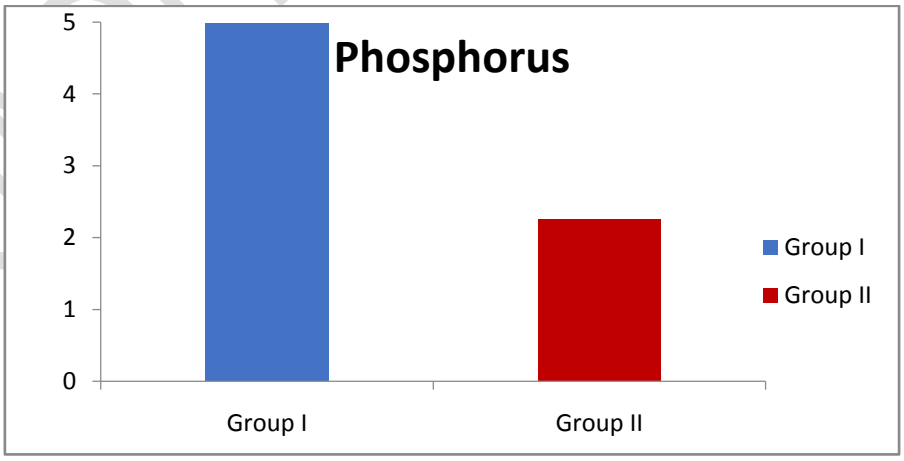
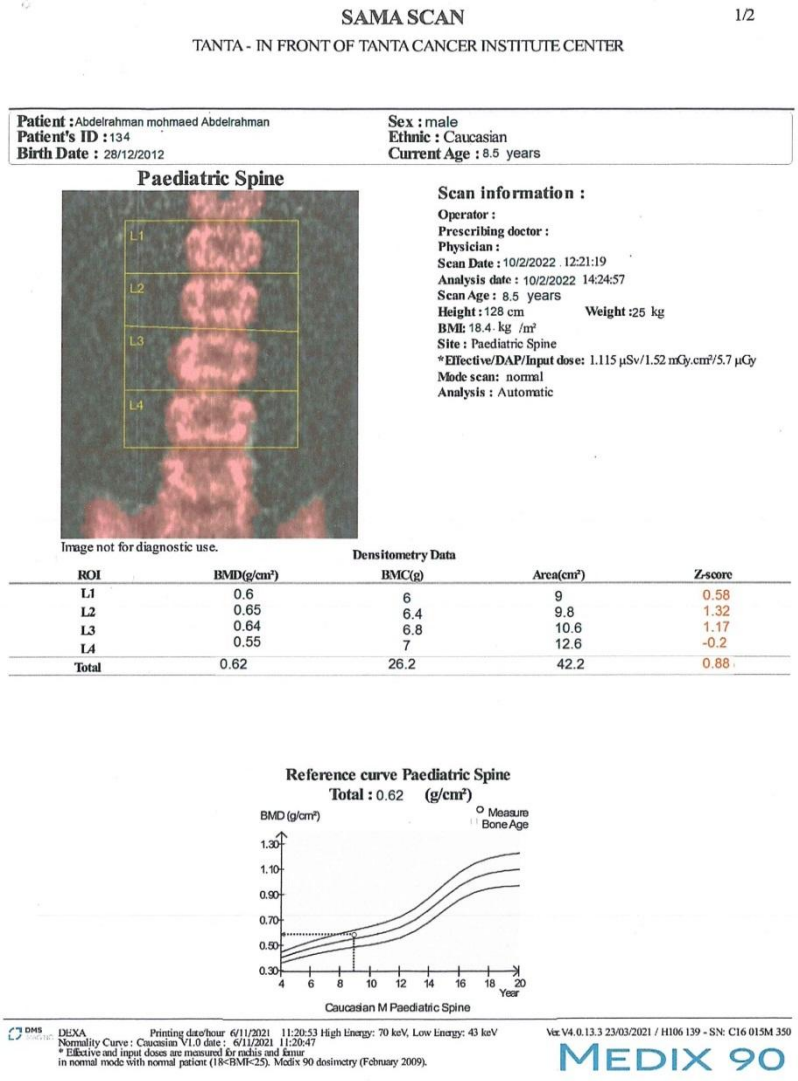


Figure (7) comparison between both groups according to Phosphorus

Cases

Normal cases Z score >-1

Case 1



SAMA SCAN 1/2

TANTA - IN FRONT OF TANTA CANCER INSTITUTE CENTER

Patient : Abdelrahman mohmaed Abdelrahman
Patient's ID : 134
Birth Date : 28/12/2012
Sex : male
Ethnic : Caucasian
Current Age : 8.5 years

Paediatric Spine

Image not for diagnostic use.

Scan information :
Operator :
Prescribing doctor :
Physician :
Scan Date : 10/2/2022 12:21:19
Analysis date : 10/2/2022 14:24:57
Scan Age : 8.5 years
Height : 128 cm **Weight :**25 kg
BMI: 18.4 kg /m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.6	6	9	0.58
L2	0.65	6.4	9.8	1.32
L3	0.64	6.8	10.6	1.17
L4	0.55	7	12.6	-0.2
Total	0.62	26.2	42.2	0.88

Reference curve Paediatric Spine
Total : 0.62 (g/cm²)

Caucasian M Paediatric Spine

DEXA Printing date/hour 6/11/2021 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 6/11/2021 11:20:47
* Effective and input doses are measured for rachis and femur in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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MEDIX 90

Picture 1 : SAMA scan at time of diagnosis (Z score >-1)

SAMA SCAN

TANTA - IN FRONT OF TANTA CANCER INSTITUTE CENTER

Patient : Abdelrahman mohmaed Abdelrahman
Patient's ID : 134
Birth Date : 28/12/2012

Sex : male
Ethnic : Caucasian
Current Age : 9y

Paediatric Spine

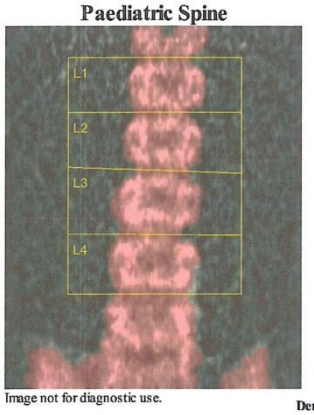


Image not for diagnostic use.

Scan information :

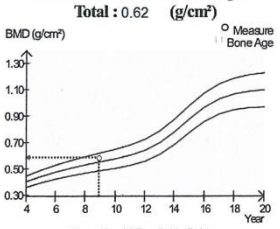
Operator :
Prescribing doctor :
Physician :
Scan Date : 9/8/2022 12:21:19
Analysis date : 9/8/2022 14:24:57
Scan Age : 9 years
Height : 129 cm **Weight :** 26 kg
BMI: 18.4 kg /m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.56	5	9	0.4
L2	0.53	5.33	9.8	-0.6
L3	0.5	5.4	10.6	0.9
L4	0.47	5.9	12.6	-1.3
Total	0.51	21.7	42.2	0.7

Reference curve Paediatric Spine

Total : 0.62 **(g/cm²)**



Caucasian M Paediatric Spine

DMS DEXA Printing date/hour 6/11/2021 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 6/11/2021 11:20:47
* Effective and input doses are measured for radius and femur
in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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MEDIX 90

Picture 2 : SAMA scan after 6 months of treatment with chemotherapy (Z score >-1)

Case of osteopenia Z score (-1 to -2)

Case 1

SAMA SCAN 1/2

TANTA - IN FRONT OF TANTA CANCER INSTITUTE CENTER

Patient : Heba Mohamed Ahmed
Patient's ID : 6567
Birth Date : 14/2/2009

Sex : Female
Ethnic : Caucasian
Current Age : 12.5 Years

Paediatric Spine

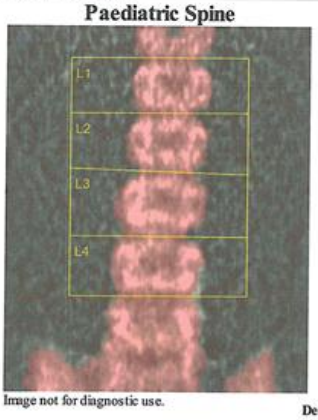


Image not for diagnostic use.

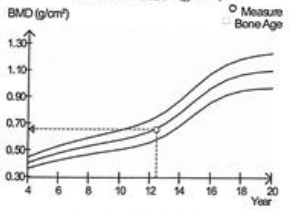
Scan information :

Operator :
Prescribing doctor :
Physician :
Scan Date : 10/2/2022 12:21:19
Analysis date : 10/2/2022 14:24:57
Scan Age : 12.5 Years
Height : 150 cm **Weight :** 51 kg
BMI: 22.6 kg/m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.73	7	9.5	-1.0
L2	0.68	7.5	11.01	-.58
L3	0.65	7.8	11.97	-.87
L4	0.65	10.5	16.1	-.87
Total	0.67	32.8	48.6	-.6

Reference curve Paediatric Spine
Total : 0.67 (g/cm²)



Caucasian M Paediatric Spine

DEXA Printing date/hour 10/2/2022 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 10/2/2022 11:20:47
* Effective and input doses are measured for rachis and femur in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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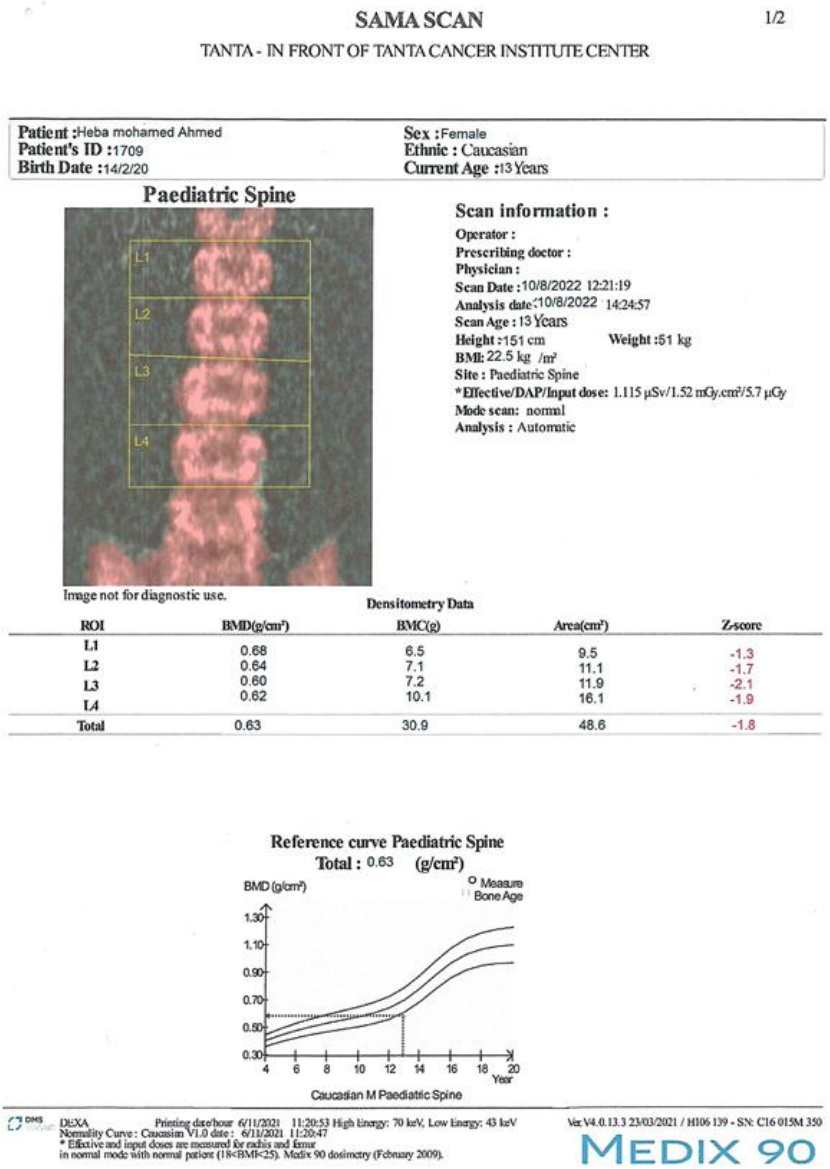
Picture 3 : SAMA scan at time of diagnosis Z score (-1 to -2)



SAMA SCAN 1/2

TANTA - IN FRONT OF TANTA CANCER INSTITUTE CENTER

Patient : Heba mohamed Ahmed
Patient's ID : 1709
Birth Date : 14/2/20
Sex : Female
Ethnic : Caucasian
Current Age : 13 Years

Paediatric Spine

Image not for diagnostic use.

Scan information :

Operator :
Prescribing doctor :
Physician :
Scan Date : 10/8/2022 12:21:19
Analysis date: 10/8/2022 14:24:57
Scan Age : 13 Years
Height : 151 cm **Weight :** 51 kg
BMI: 22.5 kg /m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.68	6.5	9.5	-1.3
L2	0.64	7.1	11.1	-1.7
L3	0.60	7.2	11.9	-2.1
L4	0.62	10.1	16.1	-1.9
Total	0.63	30.9	48.6	-1.8

Reference curve Paediatric Spine
Total : 0.63 (g/cm²)

Caucasian M Paediatric Spine

DEXA Printing date/hour 6/11/2021 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 6/11/2021 11:20:47
* Effective and input doses are measured for radius and femur in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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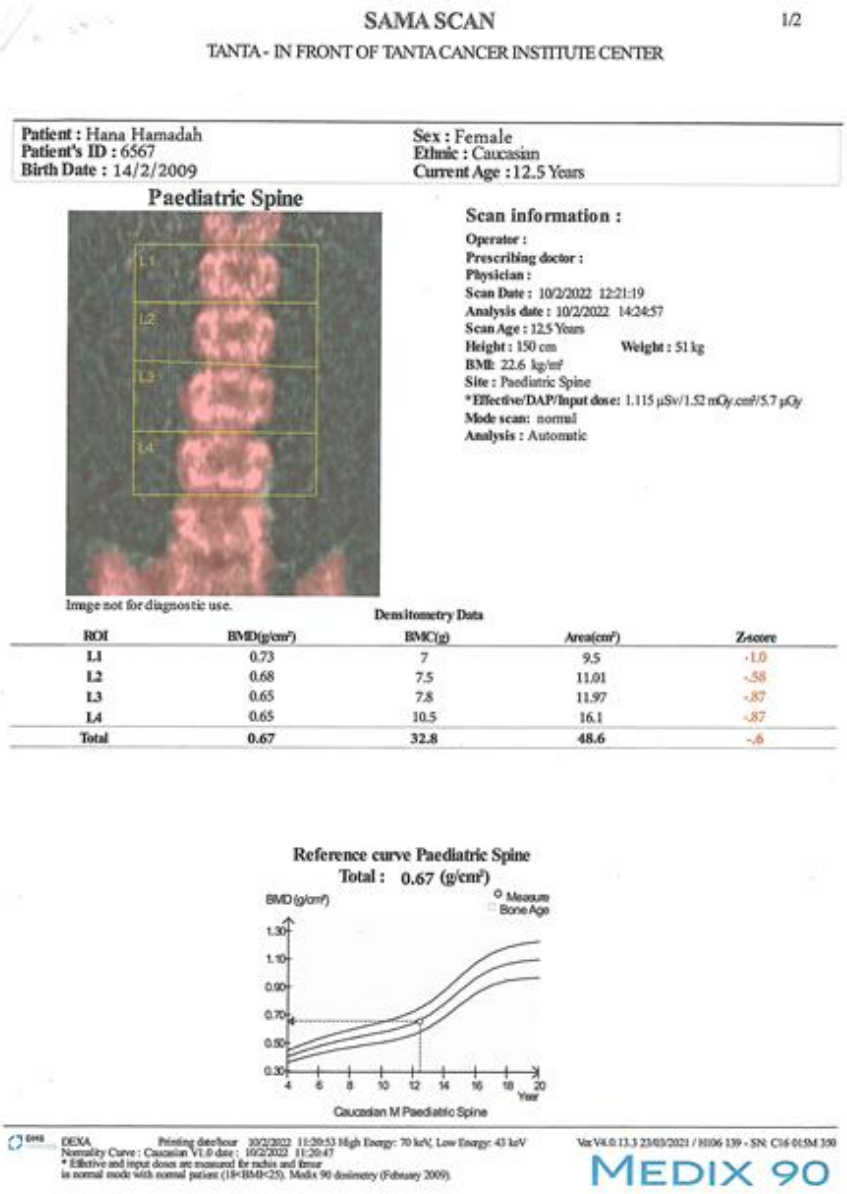
Picture 4 : SAMA scan after 6 months of treatment with chemotherapy Z score (-1 to -2)

Case of osteonecrosis Z score <-2

Case 1



SAMA SCAN 1/2

TANTA - IN FRONT OF TANTA CANCER INSTITUTE CENTER

Patient : Hana Hamadah
Patient's ID : 6567
Birth Date : 14/2/2009

Sex : Female
Ethnie : Caucasian
Current Age : 12.5 Years

Paediatric Spine

Image not for diagnostic use.

Scan information :

Operator :
Prescribing doctor :
Physician :
Scan Date : 10/2/2022 12:21:19
Analysis date : 10/2/2022 14:24:57
Scan Age : 12.5 Years
Height : 150 cm **Weight :** 51 kg
BMI: 22.6 kg/m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.73	7	9.5	-1.0
L2	0.68	7.5	11.01	-.58
L3	0.65	7.8	11.97	-.87
L4	0.65	10.5	16.1	-.87
Total	**0.67**	**32.8**	**48.6**	**-.6**

Reference curve Paediatric Spine
Total : 0.67 (g/cm²)

Caucasian M Paediatric Spine

DEXA Printing date/hour 10/2/2022 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 10/2/2022 11:20:47
* Effective and input doses are measured for rachis and femur
in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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MEDIX 90

Picture 5 : SAMA scan at time of diagnosis (Z score <-2)

Patient : Hana Hamadah Nasar
Patient's ID : 6567
Birth Date : 14/2/2009

Sex : Female
Ethnic : Caucasian
Current Age :13 Years

Paediatric Spine

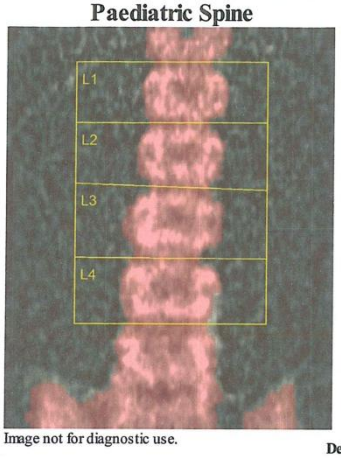


Image not for diagnostic use.

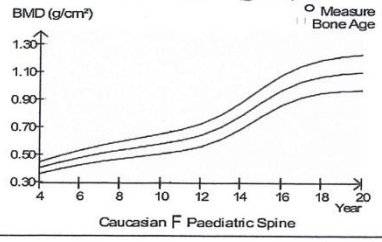
Scan information :

Operator :
Prescribing doctor :
Physician :
Scan Date : 9/8/2022 12:21:19
Analysis date : 9/8/2022 14:24:57
Scan Age :13 Years
Height : 152 cm **Weight :** 52 kg
BMI: 22.5 kg/m²
Site : Paediatric Spine
***Effective/DAP/Input dose:** 1.115 µSv/1.52 mGy.cm²/5.7 µGy
Mode scan: normal
Analysis : Automatic

Densitometry Data

ROI	BMD(g/cm²)	BMC(g)	Area(cm²)	Z-score
L1	0.58	5.56	9.5	-2
L2	0.56	6.2	11.01	-2.7
L3	0.57	6.9	11.97	-2.6
L4	0.57	9.3	16.1	-2.5
Total	0.57	28.2	48.6	-2.5

Reference curve Paediatric Spine
Total : 0.57 (g/cm²)



Caucasian F Paediatric Spine

DMS
DEXA Printing date/hour 10/2/2022 11:20:53 High Energy: 70 keV, Low Energy: 43 keV
Normality Curve : Caucasian V1.0 date : 10/2/2022 11:20:47
* Effective and input doses are measured for rachis and femur
in normal mode with normal patient (18<BMI<25). Medix 90 dosimetry (February 2009).

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MEDIX 90

Picture 6 : SAMA scan after 6 months of treatment with chemotherapy (Z score <-2)

Discussion

Acute lymphoblastic leukemia (ALL) is the most common cancer among pediatric and adolescent patients, and it accounts for major cancer-related deaths in childhood[7].

Despite advances in management, the backbone of therapy remains multi-agent chemotherapy with vincristine, corticosteroids and an anthracycline with allogeneic stem cell transplantation for eligible candidates[8]

Administration of chemotherapeutic agents destroys bone formation. Among current regimens of chemotherapy against ALL, osteotoxic drugs such as glucocorticoids, methotrexate, L-asparaginase, daunorubicin, and vincristine, as well as irradiation treatment, are predominant risk factors that equally cause deficient BMD[9]

Despite direct leukemic effects and exposure to multiple osteotoxic treatment regimens, which altogether induce demineralization, the most rapid skeletal development occurs during childhood and adolescence. Skeletal recovery after therapy completion in children with ALL is crucial, while bone metabolic status continues to change significantly in this age group. Survivors begin to recover lost bone mass after ALL therapy, while those who do not reach their optimal bone mineral acquisition experience critical bone loss 2 years following therapy cessation[10].

The current study was included 25 children and adolescents; 25 children and Adolescents with Acute Lymphoblastic Leukemia at time of diagnosis (Group I) and 25 children with leukemia after 6 months treatment of chemotherapy (Group II). The mean age of this study children was 7.92 $\pm$ 3.59 years in group I and 8.42+ 3.59 years in group II. The two groups were matched as regards weight, height and BMI.

In the present study Bone Mass Density was significantly lower in the leukemia children after 6 months treatment of chemotherapy (0.53±0.11), compared to leukemia children at time of diagnosis (0.59±0.11) ($P<0.05$).

In agreement with the present study Boot et al. reported that at diagnosis, 3 of 14 (21%) children with ALL had a low lumbar spine BMD. Markers of bone turnover were reduced. Total body BMD decreased during the first year of treatment, suggesting a negative effect of chemotherapy or other factors like decreased physical activity on cortical bone[11].

In contrast, Cox et al. stated that there were no significant changes between patients received chemotherapy and the control group in BMD at the end of treatment. While BMD declined in both the intervention and the control group, rates of decline did not differ between groups (P = 0.56)[12].

In the current study, bone mineral content and Z score were significantly lower in group II patients (20.5±7.82 and 2.1120±0.676, respectively), compared to group I (23.13±9.18 and 82.25±85.2, respectively). Z score (Lumbar spine) of all group I children and Adolescents with ALL at time of diagnosis was in normal range (>-1). While 56% of group II children had normal Z score (Lumbar spine) range, 40% had Osteopenia (-1 to-2) and 4% had osteonecrosis (< -2).

In concordance with the current study, Inaba and colleagues detected that the median BMD Z-score in 363 ALL patients was 0.06 at diagnosis, declined to −1.08 at week 120, but partly recovered to −0.72 after 2 years off therapy [13].

In concordance with this study, Aricò et al. reported that among ALL children received chemothrapy Overall, 15 of the 1421 patients developed symptomatic ON (1.1%)[14].

Dolu and colleagues in their study stated that a total of 18.66% (14 patients) of patients were osteoporotic (z score <-2 SD), 22.67% (17 patients) were osteopenic (z-score between -2 and -1 SD) and 58.67% (44 patients) presented normal z-scores (>-1 SD)[15].

Also, supporting to this study, Athanassiadou and colleagues data demonstrate that bone metabolism in children with ALL during consolidation therapy is disturbed, resulting in a reduced BMD and z-score with respect to healthy controls[16].

In this study children with leukemia after 6 months of treatment of chemotherapy had significantly lower Total leucocyte count (2.1120 ± 0.676), compared to children and adolescents with Acute Lymphoblastic Leukemia at time of diagnosis (82.25±85.2).

There was no significant difference between the 2 groups included in this study, regarding hemoglobin, platelet, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and red cell distribution width - coefficient of variation.

There was no significant difference according to Serum Glutamic Pyruvic Transaminase, serum glutamic-oxaloacetic in the patient Groups (II): Children with leukemia after 6 months treatment of chemotherapy compared to Group (I): Children with leukemia at time of diagnosis (P>0.05). However, AL-JUMAILI and coworkers in their study detected significantly higher AST and ALT levels among ALL children receiving chemotherapy[17].

Creatinine is commonly used as a measure of kidney function. The diagnosis of renal failure is often suspected when serum creatinine is greater than the upper limit of the normal interval. The higher values are noticed in leukemia [18]. This can explain the high creatinine values both at diagnosis and after 6 months of treatment.

In the present study the mean alkaline phosphatase level in children with leukemia after 6 months of treatment of chemotherapy was significantly lower (107.88±11.59), compared to Children with leukemia at time of diagnosis (161.52±3.66). Also, Phosphorus was significantly lower in the patient Groups (II) compared to Group (I) (P>0.05). However, there were no significant differences in calcium, ionized calcium, parathyroid hormone and magnesium among the studied groups (P>0.05).

Crofton et al. studied bone turnover and growth during and after continuing chemotherapy in children with acute lymphoblastic leukemia. It was found that the second year of continuing chemotherapy in children with ALL was associated with reduced bone ALP, which suggests

impaired osteoblast development and reduced mineralization of bone. After completion of treatment, bone ALP was restored to normal **(Crofton et al. 2000).**

Similarly, Asadi et al had studied 20 patients aged 8 + 2.4 years. Average serum calcium levels were 9 mg/dl before chemotherapy and 9.4 mg/dl after chemotherapy. Differences of phosphorous and alkaline phosphatase were not significant. Sixty five percent of patients had hypercalciuria before chemotherapy, but it has decreased subsequently. It seems that disturbances of mineral and especially calcium metabolism are common in ALL patients. Chemotherapy have not been found to have considerable effect on calcium mineral levels rather it appears that induction chemotherapy control the disease process with reduction of hypercalcemia[19].

Moreover, in Turkey's survey, levels of ALP, phosphorus, calcium, magnesium, 25-hydroxy vitamin-D and IGF-1 were assessed at the end of treatment in children (n=70) whose IGF 1 and 25-hydroxyvitamin D were reported lower than control group (p=0.033) (Gunes et al. 2010) Compared with our study included 25 children with ALL, the amounts of Ca, P, PTH and ALP were in normal range.

In contrast, Halton et al. reported that among ALL patients, normal plasma magnesium and ionic calcium were observed at diagnosis, but by 6 months on therapy, 84% of children had become hypomagnesemic[20].

According to this study results, there was significant correlation between BMD with age, BMC, and SGOT (P = 0.001). Also, There was significant correlation between Z score with all Variable and age, BMC, sex and BMD (P = 0.001).

Ghasemi et al. reported contradicting results with the present study where there was no significant difference in BMD after chemotherapy between the sexes among ALL patients[21].

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