

DEXA Scan Finding In Iraqi Acromegaly Patients at National Diabetes Center

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Abstract: Background: Growth Hormone (GH) and Insulin-like Growth Factor (IGF-1) stimulate proliferation, differentiation and extracellular matrix production in osteoblastic cells. GH and IGF-1 also stimulate recruitment and bone resorption activity in osteoclastic cells. A chronic systemic GH and IGF-1 excess produces an increased bone turn over in acromegaly patients (pts). Osteoporosis, joint alterations and bone deformities have a great clinical relevance in acromegaly patients and favor mortality and morbidity. In the present study we evaluate the still unclear GH/IGF-1 activity on bone, Bone Mineral Density (BMD) and risk of osteoporotic Fractures, in relation to several Pt's variables in acromegaly patients. The present study examines 61 acromegaly patients with different age group and different variables and study their DEXA scan findings of them. **Objective of the study:** searching for DEXA scan findings in a group of acromegaly patients attending regularly the national center of diabetes at al-Yarmouk teaching hospital on a basis of scheduled appointments. **Patients and Methods:** this is a prospective cohort study of 61 patients attending the national center of diabetes at al-Yarmouk teaching hospital regularly on the basis of regular appointments from June 2016 to April 2017. **Results :** For the 61 patients, 41 Males(67.2%), 20 Females (32.8%) were chosen randomly and the age group between (24 – 68) years, 24 patients had osteopenia at spine Z-score, 5 patients shows osteoporosis, 23 patients had osteopenia at sine T-score. 19 patients had osteopenia at total hip Z-score, 7 patients had osteoporosis, 17 patients had osteopenia at total hip T-score. 3 patients had osteoporosis, 16 patients had osteopenia at intertrochanteric Z-score, 6 patients had osteoporosis, 18 patients had osteopenia at intertrochanteric T-score. In these patients the 10 years probability of fractures in different fracture type as follow: In Osteoporotic type with BMD the mean and SD was (3.73±0.57) %, range (2.12%-4.93%). In osteoporotic without BMD the mean and SD was (3.04±0.27)%, range was (2.10-3.64)%. In Hip fracture type with BMD the mean and SD was (0.55±0.57)%, and range was (0.01-1.9)%. In Hip fracture type without BMD the mean and SD was (0.27±0.18)%, their range was (0.10-0.80)%.

Keywords: BMD, SD, HIP FRACTURE.

INTRODUCTION

Growth Hormone (GH) and its peripheral mediator, Insulin-like Growth Factor-1 (IGF-1), play a significant role in the regulation of bone metabolism. The anabolic actions of GH on many organ systems, including bone, are well documented. During the pre-pubertal period GH stimulates longitudinal bone growth. During the adolescence and early adulthood it stimulates skeletal maturation till the achievement of peak bone mass. In adult age GH is important in the maintenance of bone mass through the regulation of bone turn-over. Serum GH levels decline with increasing age (GH secretion reduces by approximately 14% for each decade of adult life after puberty) and a dysfunctional GH axis may thus play a role in the pathogenesis of post-menopausal and senile osteoporosis. In fact, it has been hypothesized that the ageing process may be also due to a relative GH deficiency state (1). GH and its interactions with IGFs (insulin-like growth factors) and IGFBPs (insulin-like growth factors binding proteins) and locally produced IGFs and IGFBPs, acting in autocrine and paracrine ways, stimulate proliferation, differentiation and extracellular matrix production in osteoblastic like-cell lines and finally bone formation. GH also stimulates recruitment and bone resorption activity in osteoclastic like cells (2-4). While GH deficiency (GHD) has been shown to be involved

in determining bone loss and osteoporosis, the consequences of GH excess on bone are not clear. In fact, traditionally, acromegaly is considered as one cause of secondary osteoporosis; early studies showed hypercalciuria and negative calcium balance. However, bone mineral density (BMD) is not unequivocally reported to be decreased in acromegaly. Some studies showed normal or increased bone mass in patients with acromegaly because of the anabolic effects of GH on bone; although BMD measurements in the axial skeleton may be overestimated in patients with acromegaly because of the structural modifications of the spine occurring in these patients (5). Other studies showed that effect of GH on bone mass could be different in relation to sites investigated: GH excess has a different effect on the axial (70% trabecular bone) and appendicular skeleton (90% cortical bone) with unchanged or reduced vertebral density and increased forearm bone density (5-7). Reduction of bone mass in acromegaly, particularly in trabecular bone, could be also a consequence of many factors; one of the most important is hypogonadism. It is relatively common in patients with acromegaly because of tumor enlargement, associated hyperprolactinemia, surgery, radiation. Sex steroids deficiency leads to an increased rate of bone remodeling, shifting the balance toward bone resorption. It is possible that

trabecular bone, with its more intimate contact with the circulation, is influenced by sex steroids to a greater extent (2, 6, 8, 9). In the present study we evaluated the still unclear GH-IGF-1 activity on bone and risk of osteoporotic fractures, related to the gender, gonadal status, disease activity and BMD.

PATIENTS AND METHODS

This was a prospective cross sectional study carried out on 61 acromegaly patients were registered at the National Diabetes Center at Al-mustansyria college of medicine, selected on the basis of registered database of these patients in the National Diabetes Center and they were diagnosed on the base of elevated serum Growth hormone concentration and elevated concentration of Insulin like growth factor-1 and the presence of pituitary adenoma on MRI ,these patients were selected randomly on the bases of weekly visit over a periods of 8 months between July 2016 to April 2017 and sent for Dual Energy X-ray Absorptiometry scan at Al-Yarmouk Teaching Hospital. The following variables were known before recruitment in their medical records : Age, Gender ,Duration of Acromegaly , Age of Onset of Acromegaly , presence of Concomitant diseases , pituitary hypophysectomy were done or not, and to correlate with DEXA scan Variables which include T-score (means the number of standard deviation above or below the mean for the patients age, sex and ethnicity) , Z-score (means the number of standard deviation above or below the mean for a healthy 30-year –old adult of the same sex and ethnicity as the patient), BMD of spine , femur and Hip area , and 10 years probability of fractures. All subjects performed DEXA scan at

Al-Yarmouk teaching hospital , sites measured were the lumbar spine (L1-L4) ,the femoral neck , Intertrochanteric , and Total hip. BMD measured by DEXA was expressed as T-score and Z-score and the WHO consensus definitions were used for the diagnosis of osteoporosis (T-score < -2.5) and osteopenia (T-score between -2.5 and -1) . The results of DEXA scan were reported by multiple observers according to their scheduled duties in the DEXA scan department. Dual-energy X-ray absorptiometry (DXA, previously DEXA is a means of measuring bone mineral density (BMD). Two X-ray beams, with different energy levels, are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Dual-energy X-ray absorptiometry is the most widely used and most thoroughly studied bone density measurement technology. FRAX is a diagnostic tool used to evaluate the 10-year probability of bone fracture risk. It was developed by the World Health Organization Collaborating Centre for Metabolic Bone Diseases (1991-2010) at Sheffield University. FRAX integrates clinical risk factors and bone mineral density at the femoral neck to calculate the 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)

RESULTS

For the 61 patients , 41 Males(67.2%) ,20 Females (32.8%) acromegaly patients were chosen randomly on basis of weekly visit and the age group between (24 – 68) years and the mean and SD was (47.21±11.32) years .

Table 1: Baseline characteristics and clinical data of acromegaly Patients

		No	%
Age (years)	<30	6	9.8
	30---	10	16.4
	40---	14	23.0
	50---	21	34.4
	=>60	10	16.4
	Mean ±SD(Range)	47.21±11.32	(24-68)
Gender	Male	41	67.2
	Female	20	32.8
Age of Onset (years)	<30	15	24.6
	30---	28	45.9
	=>40	18	29.5
	Mean ±SD(Range)	34.82±8.33	(20-55)
Duration (years)	<5	8	13.1
	5---	14	23.0
	10---	16	26.2
	15---	13	21.3
	=>20	10	16.4
	Mean ±SD(Range)	12.52±6.84	(2-28)

Table 2: Baseline characteristics and clinical data of acromegaly Patients (continued)

		No	%
Concomitant Disease	Diabetes	10	16.4
	Hypertension	13	21.3
	DM & Hypertension	10	16.4
	No	28	45.9
Concomitant Disease; Diabetes	Yes	20	32.8
	No	41	67.2
Hypertension	Yes	23	37.7
	No	38	62.3
Others (AF, IHD, Thyrotoxicosis)	Yes	3	4.9
	No	58	95.1
Type of Adenoma	Macro-adenoma	46	75.4
	Micro-adenoma	15	24.6
Surgery (pituitary hypophysectomy)	Yes	21	34.4
	No	40	65.6

Table 1, 2, shows patients baseline characteristics and clinical data of the registered acromegaly patients which shows the followings:

61 registered acromegaly patients were selected 41 males (67.2%) , 20 females (32.8%) , age ranges between (24-68) (Mean \pm SD 47.21 \pm 11.32) years , their age of onset was (20-55) (Mean \pm SD 34.82 \pm 8.33) years , Acromegaly duration was between (2-28) (Mean \pm SD 12.52 \pm 6.84) years , 46 patients (75.4%) had pituitary Macro-adenoma, the rest (15 patients 24.6%) had Micro-adenoma , 21 patients (34.4 %) did pituitary hypophysectomy and 40 patients (65.6%) were not . The T-score at Femoral Neck region 14 males(34.1 %) and 2 Females (10%) show osteoporosis ; 3 Males (7.3%) and 2 (10 %) Females shows Osteopenia ; 24 males (58.5%) Males and 16 (80%) Females were normal, Z-score at femoral neck region shows 14 Males (34.1%) and 3 Females (15%) shows osteopenia , 27 Males (65.9%) and 17 females (85%) were normal, No statistical difference between Gender, Type of Adenoma, Hypophysectomy operations and BMD (P-value is insignificance) at this area. (Table 4, 5, 6)

At Inter-trochanteric area : The T-score shows 5 males (12.2%) and 1 Female (5%) osteoporotic , 12 males (29.3%) and 6 Females (30%) shows osteopenia , 24 males (58.5%) and 13 female (65%) were normal. The Z-score shows 3 males

(7.3%) only shows osteoporosis , 11 males (26.8%) and 5 females (25%) shows osteopenia , 27 males (65.9%) and 15 females (75%) were normal, , No statistical difference between Gender, Type of Adenoma, Hypophysectomy operations and BMD (P-value is insignificance) at this area. (Table 4, 5, 6)

At Total Hip : The T score shows 6 males (14.6%) and 1 females (5%) shows osteoporosis , 12 males (29.3%) and 5 females (25%) shows osteopenia , 23 males (56.1%) and 14 females (70%) were normal. The Z-score shows 15 males (36.6%) and 4 females (20%) shows osteopenia , 26 males (63.4%) and 16 females (80%) were normal, , No statistical difference between Gender, Type of Adenoma, Hypophysectomy operations and BMD (P-value is insignificance) at this area. (Table 4, 5, 6)

At spine (L1-L4) shows : The T-score shows 4 males (9.8%) and 1 females (5%) shows osteoporosis , 15 males (36.6%) and 8 females (40%) shows osteopenia , 22 males (53.7 %) and 11 females (55%) were normal. The Z-score in 16 males (39%) and 8 females (40%) shows osteopenia , 25 males (61%) and 12 females (60%) were normal, , No statistical difference between Gender, Type of Adenoma, Hypophysectomy operations and BMD (P-value is insignificance) at this area. (Table 4, 5, 6)

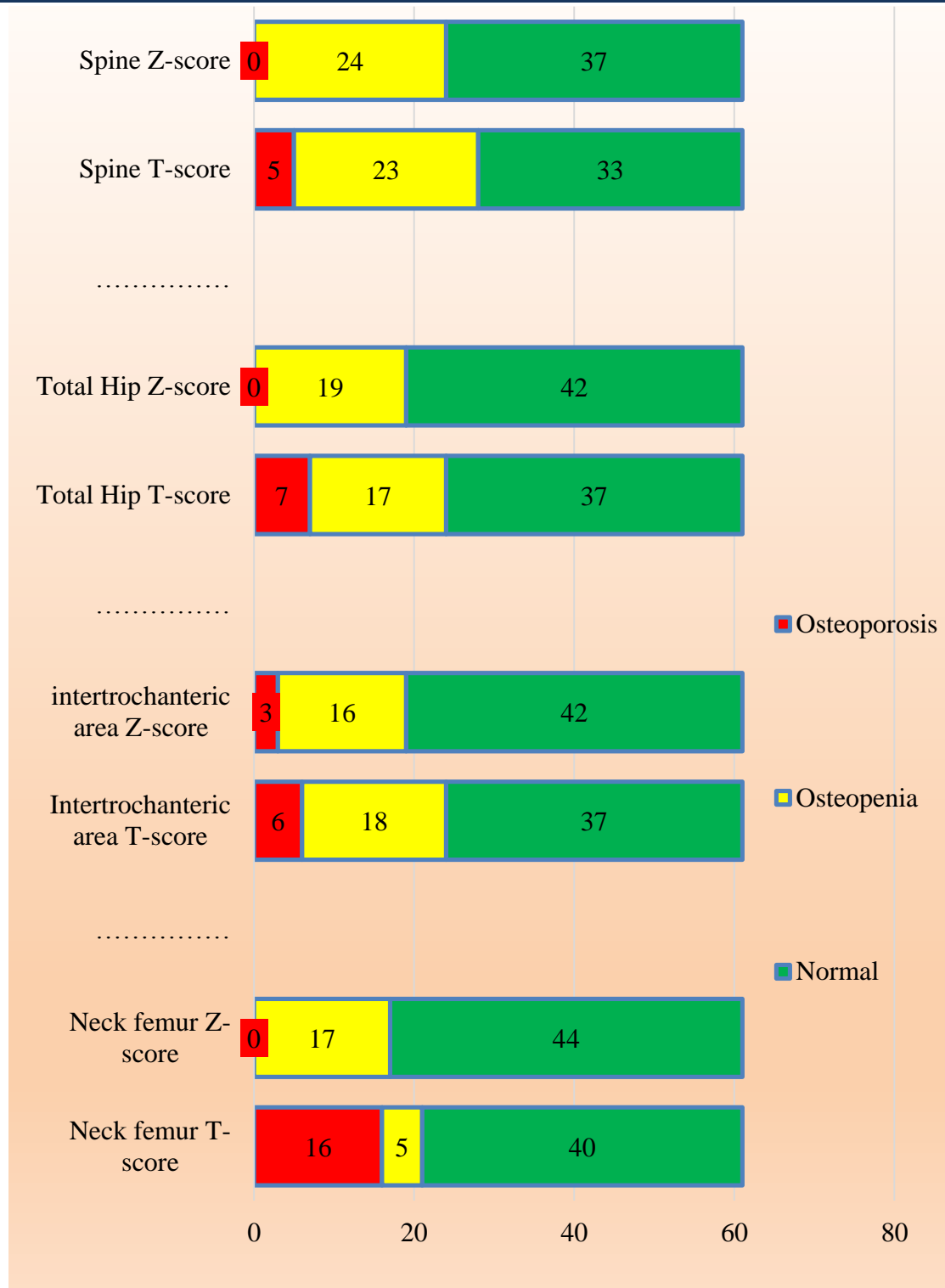


Figure 1: shows total number of patients which are osteoporosis , osteopenia on DEXA scan.

Table 4: The relation of gender and T , Z-scores of different areas

		Gender				P value
		Male		Female		
		No	%	No	%	
Neck femur						
T-score	Osteoporosis (> -2.5)	14	34.1	2	10.0	0.132
	Osteopenia (-1 -- -2.5)	3	7.3	2	10.0	
	Normal (<-1)	24	58.5	16	80.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.117
	Osteopenia (-1 -- -2.5)	14	34.1	3	15.0	
	Normal (<-1)	27	65.9	17	85.0	
Intertrochanteric area						
T-score	Osteoporosis (> -2.5)	5	12.2	1	5.0	0.669
	Osteopenia (-1 -- -2.5)	12	29.3	6	30.0	
	Normal (<-1)	24	58.5	13	65.0	
Z-score	Osteoporosis (> -2.5)	3	7.3	-	-	0.440
	Osteopenia (-1 -- -2.5)	11	26.8	5	25.0	
	Normal (<-1)	27	65.9	15	75.0	
Total Hip						
T-score	Osteoporosis (> -2.5)	6	14.6	1	5.0	0.449
	Osteopenia (-1 -- -2.5)	12	29.3	5	25.0	
	Normal (<-1)	23	56.1	14	70.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.189
	Osteopenia (-1 -- -2.5)	15	36.6	4	20.0	
	Normal (<-1)	26	63.4	16	80.0	
Spine						
T-score	Osteoporosis (> -2.5)	4	9.8	1	5.0	0.812
	Osteopenia (-1 -- -2.5)	15	36.6	8	40.0	
	Normal (<-1)	22	53.7	11	55.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.942
	Osteopenia (-1 -- -2.5)	16	39.0	8	40.0	
	Normal (<-1)	25	61.0	12	60.0	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table 5: shows the relation between Pituitary Surgery and T , Z-scores

		Surgery				P value
		Yes		No		
		No	%	No	%	
Neck femur						
T-score	Osteoporosis (> -2.5)	5	23.8	11	27.5	0.930
	Osteopenia (-1 -- -2.5)	2	9.5	3	7.5	
	Normal (<-1)	14	66.7	26	65.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.608
	Osteopenia (-1 -- -2.5)	5	23.8	12	30.0	
	Normal (<-1)	16	76.2	28	70.0	
Intertrochanteric area						
T-score	Osteoporosis (> -2.5)	2	9.5	4	10.0	0.990
	Osteopenia (-1 -- -2.5)	6	28.6	12	30.0	
	Normal (<-1)	13	61.9	24	60.0	
Z-score	Osteoporosis (> -2.5)	1	4.8	2	5.0	0.956
	Osteopenia (-1 -- -2.5)	6	28.6	10	25.0	
	Normal (<-1)	14	66.7	28	70.0	
Total Hip						

T-score	Osteoporosis (> -2.5)	2	9.5	5	12.5	0.942
	Osteopenia (-1 -- -2.5)	6	28.6	11	27.5	
	Normal (<-1)	13	61.9	24	60.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.789
	Osteopenia (-1 -- -2.5)	7	33.3	12	30.0	
	Normal (<-1)	14	66.7	28	70.0	
Spine						
T-score	Osteoporosis (> -2.5)	1	4.8	4	10.0	0.703
	Osteopenia (-1 -- -2.5)	9	42.9	14	35.0	
	Normal (<-1)	11	52.4	22	55.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.885
	Osteopenia (-1 -- -2.5)	8	38.1	16	40.0	
	Normal (<-1)	13	61.9	24	60.0	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table 6: the relation between Type of adenoma and T, Z-scores

		Type of Adenoma				P value
		Macro-adenoma		Micro-adenoma		
		No	%	No	%	
Neck femur						
T-score	Osteoporosis (> -2.5)	13	28.3	3	20.0	0.279
	Osteopenia (-1 -- -2.5)	5	10.9	-	-	
	Normal (<-1)	28	60.9	12	80.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.434
	Osteopenia (-1 -- -2.5)	14	30.4	3	20.0	
	Normal (<-1)	32	69.6	12	80.0	
Intertrochanteric area						
T-score	Osteoporosis (> -2.5)	5	10.9	1	6.7	0.203
	Osteopenia (-1 -- -2.5)	16	34.8	2	13.3	
	Normal (<-1)	25	54.3	12	80.0	
Z-score	Osteoporosis (> -2.5)	2	4.3	1	6.7	0.418
	Osteopenia (-1 -- -2.5)	14	30.4	2	13.3	
	Normal (<-1)	30	65.2	12	80.0	
Total Hip						
T-score	Osteoporosis (> -2.5)	6	13.0	1	6.7	0.208
	Osteopenia (-1 -- -2.5)	15	32.6	2	13.3	
	Normal (<-1)	25	54.3	12	80.0	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.666
	Osteopenia (-1 -- -2.5)	15	32.6	4	26.7	
	Normal (<-1)	31	67.4	11	73.3	
Spine						
T-score	Osteoporosis (> -2.5)	5	10.9	-	-	0.315
	Osteopenia (-1 -- -2.5)	18	39.1	5	33.3	
	Normal (<-1)	23	50.0	10	66.7	
Z-score	Osteoporosis (> -2.5)	-	-	-	-	0.077
	Osteopenia (-1 -- -2.5)	21	45.7	3	20.0	
	Normal (<-1)	25	54.3	12	80.0	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table 7: The 10 years probability of fractures in different fracture types, BMD in different areas, their mean, SD and range

The 10 years probability of fractures		
Osteoporotic With BMD	3.73±0.57	(2.12-4.93)
Osteoporotic No BMD	3.04±0.27	(2.10-3.64)
Hip With BMD	0.55±0.57	(0.01-1.900)
Hip No BMD	0.27±0.18	(0.10-0.80)
Neck femur BMD	0.89±0.12	(0.638-1.160)
Intertrochanteric area BMD	0.93±0.17	(0.643-1.500)
Total Hip BMD	0.91±0.13	(0.621-1.375)
Spine BMD	0.91±0.08	(0.637-1.090)

In these acromegaly patients the 10 years probability of fractures in different fracture type as follow:

In Osteoporotic type with BMD the mean and SD was (3.73±0.57) %, range (2.12%-4.93%).

In osteoporotic without BMD the mean and SD was (3.04±0.27)%, range was (2.10-3.64)%.

In Hip fracture type with BMD the mean and SD was (0.55±0.57)%, and range was (0.01-1.9)%.

In Hip fracture type without BMD the mean and SD was (0.27±0.18)%, their range was (0.10-0.80)%.

Table 8: the relation of gender with 10 years fractures probability

The 10 years probability of fractures	Gender		
	Male	Female	
	Mean ±SD (Range)	Mean ±SD (Range)	P value
Osteoporotic With BMD	3.85±0.65 (2.12-4.93)	3.48±0.22 (3.12-3.87)	0.016*
Osteoporotic No BMD	3.01±0.28 (2.10-3.63)	3.08±0.23 (2.73-3.64)	0.387
Hip With BMD	0.62±0.64 (0.01-1.90)	0.39±0.34 (0.02-1.20)	0.142
Hip No BMD	0.31±0.20 (0.10-0.80)	0.19±0.08 (0.10-0.36)	0.014*

*Significant difference between two independent means Students-t-test at 0.05 level.

Table 8 shows the relation between gender and 10 years probability of fractures shows statistically significance with osteoporotic fracture type with bone mineral density in relation to gender (P-value

of 0.016), and also there is statistically significance in hip fracture type without bone mineral density in relation to gender (P-value is 0.014), other types show no statistical significance related to gender.

Table 9: the relation between type of adenoma and 10 years fractures probability

The 10 years probability of fractures	Type of Adenoma		
	Macro-adenoma	Micro-adenoma	
	Mean ±SD (Range)	Mean ±SD (Range)	P value
Osteoporotic With BMD	3.75±0.60 (2.12-4.91)	3.67±0.48 (3.19-4.93)	0.613
Osteoporotic No BMD	3.03±0.28 (2.10-3.64)	3.05±0.23 (2.71-3.54)	0.811
Hip With BMD	0.58±0.56 (0.03-1.86)	0.45±0.61 (0.01-1.90)	0.434
Hip No BMD	0.26±0.17 (0.10-0.75)	0.31±0.21 (0.12-0.80)	0.354

*Significant difference between two independent means Students-t-test at 0.05 level.

Table 9 shows the relation between type of adenoma and 10 years probability of fractures

which shows no statistical difference with different types of fractures and type of adenoma.

Table 10: The relation between pituitary surgery and 10 years fractures probability

The 10 years probability of fractures	Surgery(Hypophysectomy)		
	Yes	No	
	Mean \pm SD (Range)	Mean \pm SD (Range)	P value
Osteoporotic With BMD	3.63 \pm 0.53 (3.02-4.93)	3.79 \pm 0.59 (2.12-4.91)	0.292
Osteoporotic No BMD	2.98 \pm 0.20 (2.71-3.54)	3.07 \pm 0.29 (2.10-3.64)	0.215
Hip With BMD	0.47 \pm 0.56 (0.01-1.90)	0.59 \pm 0.58 (0.02-1.86)	0.455
Hip No BMD	0.25 \pm 0.19 (0.10-0.80)	0.28 \pm 0.17 (0.10-0.75)	0.517

*Significant difference between two independent means Students-t-test at 0.05 level.

Table 10 shows the relation between hypophysectomy and 10 years probability of fractures revealed no statistical significance in relation to bone mineral density.

DISCUSSION

A different kinds of bone changes can be found in patients with acromegaly, but these changes are not usually associated with osteoporosis. GH and IGF1 increments in acromegaly had bone formation capability more than bone resorption, and osteopenia or osteoporosis that be found is caused by concomitant hypogonadism which was not dealt with in this study. The data showed that the effects of GH and IGF-1 on bone mineral metabolism and on risk of osteoporosis and osteoporotic fractures in patients with acromegaly, are complex and not yet clearly define. Our study, showed No significant difference statistically between women and men in DEXA scan parameters include those related to gender, type of adenoma, and hypophysectomy operation. There is numerical significance in number of patients that had decrease BMD but statistically not significance. There is statistically significance in relation of gender and 10 years probability of fractures in osteoporotic fracture type (with BMD) and Total hip (without BMD), while there is no statistically significance in relation of 10-years probability of fractures with both the type of adenoma and pituitary surgery. *G. Padova, et al.*, revealed that there was not any significant correlation between fractures and activity of disease or gonadal status, and also no significant difference between men and women in prevalence of vertebral fractures; it states that men often had multiple and more severe fractures than in women (maybe for a different sex steroids-modulated sensitivity of tissues {including bone} to the GH action). *Scillitani, et al.*, showed increased BMD at femoral level related to serum IGF-1 levels in patients with active disease (10). In our study we use the variables that was discussed in patient and method subject above, and did not use variables like disease activity, serum calcium, gonadal

function, serum parathyroid hormone, serum phosphate and correlate these variables with BMD. Vertebral fractures do not correlate with BMD, they may be found in patients who had normal or minimally decreased BMD (3, 11). In many forms of secondary osteoporosis, BMD is not a perfect predictor of future fracture risk as it is in post-menopausal osteoporosis. For that reason, the radiological approach is necessary for an accurate detection of vertebral fractures (12). DEXA scan may not reflect the bone health status, it is only one determinant of bone fractures and it was not sufficient for identifying patients at risk for fracture. BMD measurements at the different sites may be strongly influenced by the structural modifications of these site (like bone deformities, osteoarthritis or joint rigidity). Osteoporotic fractures developed in acromegaly patients may be correlated with an insufficient quality of bone that is one of the most important determinant of bone health.

LIMITATION

This study is limited by small number, did not include the relation of gonadal function, nutritional status of the patients.

CONCLUSION

- 1 . No relation between acromegaly and BMD abnormality in relation to gender, type of adenoma, and pituitary surgery.
- 2 . acromegaly is a risk factor for osteoporotic fractures, especially in men, that were considered at low risk of osteoporosis.

RECOMMENDATION

- 1-Acromegaly patients should be send for DXA scan to determine BMD and fracture risk.
- 2-it is necessary to perform a DXA of the spine at the time of diagnosis and during follow up visits.

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Source of support: Nil; **Conflict of interest:** Nil.

Cite this article as:

El Razaq Ahmed, Y.A., Kadum, E.A. and Rahmah, A.M. "DEXA Scan Finding In Iraqi Acromegaly Patients at National Diabetes Center." *Sarcouncil journal of Medical sciences* 3.2 (2024): pp 01-09.