RESEARCH ARTICLE

Evaluation of IL17A, FGF21 and CXC12 in Post-menopause Iraqi Sample with Osteoporosis and Osteopenia

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ABSTRACT

Osteoporosis (OP) is a systemic skeletal disorder that is characterized by reduced bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. The most frequent osteoporotic fractures are fractures of the hip, wrist, and spine. The exact causes of OP are still unknown; several factors contribute to the disorder.

Subjects and Methods: This study consists of patient groups, this group (Group A) was composed of 80 postmenopausal women with OP and osteopenia and the patient group was subdivided into two group; First group (GroupA1) was composed of 50 postmenopausal women with OP and the second group (Group A2) composed of (30) Postmenopausal Women with osteopenia. In addition, to control group (20), 5 mL of venous blood sample were collected from each patient and healthy control in the population study, and the blood sample was transferred to a clean gel tube, left at room temperature for at least 30 minutes for clotting, then centrifuged for 5–10 minutes at 3000 rpm. Then, separated and divided into aliquots to obtain the serum, then its kept frozen at -20°C until analysis. The obtained serum was used to measure IL17A, FGF21, CXC12, calcium, and alkaline Phosphatase (ALP). Measurement of IL17A, FGF21 and CXC12 levels were performed by ELISA. The total calcium and serum ALK were measured by spectrophotometric-based method.

Results: Serum levels of IL17A, FGF21 and CXC12 are significantly increased in Group A and subgroup (A1 and A2). Serum levels of total calcium and ALP are non-significant in Group A and sub group patients. Significant negative correlation between serum levels of IL17A and T score, FGF21 and T score, CXC12 and T score, IL 17A and Z score, IL17A and Calcium.

Conclusions: Serum levels of IL17A, FGF21 and CXC12 is significantly increased in Group A and subgroup patients. Serum levels of total calcium and ALP are non-significant in Group A and sub group patients. Significant negative correlation exists between serum levels of IL17A and T score, FGF21 and T score, CXC12 and T score in Groups A and A1.

Keyword: CXC12, FGF21, IL17A, Osteoporosis.

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INTRODUCTION

Osteoporosis (OP) is a systemic skeletal disorder that is characterized by reduced bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. The most frequent osteoporotic fractures are hip, wrist and spine fractures.[1] According to World Health Organization (WHO), osteoporosis is defined by bone mineral density at the hip or lumbar spine that is less than or equal to 2.5 standard deviations (SD) below the mean BMD of a young-adult reference population by measuring dual-energy X-ray absorptiometry (DEXA).[2] In Iraq, the prevalence of osteoporosis, osteopenia, and normal bone for spinal bone were 33.3, 48.0, and 18.7%; while for hip bone it was 60.0, 30.7, and 9.3%, respectively.[3] Interleukin 17 (IL-17) is a pro-inflammatory cytokine. The gene IL-17 is localized at the short arm of chromosome 6 in position 6p12, coding the 155-length protein product of amino acids. Interleukin 17A was the first cytokine of the IL-17 family to be discovered.[4] Its family includes six major isoforms: IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F. Six of these isoforms interact with the five receptors (IL-17RA-E).[5] IL-17, produced by Th17 cells, stimulate the production of macrophage colony-stimulating factor M-CSF and Receptor activator of nuclear factor Kappa-B ligand (RANK-L) in osteoblasts and mesenchymal stem cells. These factors enhance the formation of bone-resorbing osteoclasts from monocyte/macrophage precursors. IL-17 accelerates the osteogenic differentiation of mesenchymal stem cells

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and hampers adipogenic differentiation. Th17 cells are also RANKL-expressing T cells that support osteoclastogenesis.[6] Fibroblast growth factors (FGF) is defined as a hormone that binds to FGFR (Fibroblast growth factor receptors) with the help of β –klotho. FGF's perform a lot of autocrine/paracrine cell signaling mechanisms. FGF21 is expressed primarily in metabolic tissues in liver under physiological conditions, and other site include pancreas, white adipose tissue.[7] Chemokine 12 (CXCL12) is a chemokine; a small signaling protein secreted by cells that dictate migration and activation of other cells. Chemokines are differentiated from other cytokines by their size and structure. They are small, approximately 8–10 kDa, and form specific 3D configurations based on highly conserved cysteine residues, which categorize them into four. subfamilies: CXC, CC, CX3C, and its acts as a local paracrine signaling factor and long-distance chemokine to assist in mobilizing and targeting immune response and reparative cells to areas of injury and inflammation.[8]

SUBJECTS, MATERIAL AND METHODS

The study was conducted over 4 months from mars till June 2021 at Rheumatology and Rehabilitation Consultation Unit, Medical city, Baghdad Teaching Hospital. This study consists of patient groups composed of 80 Postmenopausal Women with osteoporosis and osteopenia and the patient group subdivided into two groups, first group composed of 50 Postmenopausal Women with osteoporosis and the second group composed of 30 Postmenopausal Women with osteopenia. In addition, to control group 20 as Healthy women without osteoporosis or osteopenia. The age of the subject is equal or more than 45 years. Disease female will be diagnosed as Osteoporosis and Osteopenia according to WHO. The selection and diagnosis of the patient will be doning under the supervision of a rheumatologist physician in Baghadad Medical City. This study protocol was approved by the local ethical committee of the College of Pharmacy, Baghdad University. Five-mL of venous blood sample were collected from each patient and healthy persons (control) in the population study. And the blood sample was transferred to a clean gel tube, left at room temperature for at least 30 minutes for clotting, then centrifuged for 5–10 minutes at 3000 rpm then, separated and divided into aliquots to obtain the serum, then kept frozen at -20°C until analysis.

The obtained serum was used to measure IL17A, FGF21, CXC12, calcium, and alkaline phosphatase (ALP). Measurement of IL17A, FGF21 and CXC12 levels were performed by Enzyme-Linked Immune Sorbent Assay (ELISA),[9-11] using commercially available human Kits provided by Cusabio (China). The principle of this technique is based on a quantitative Sandwich-Assay using two specific and high affinity antibodies. The plate of microtiter has been pre-coated with an antibody specific to the substance to measure. The results were expressed as nanogram per liter for both IL17A and CXC12 levels, while serum FGF21 level were expressed as pg/mL. The total calcium and serum ALP were measured by spectrophotometric based method using kits provided by BEACON (India).[12,13] The principle of this method is based on the formation of the colored complex. The values were expressed in mg/dL for serum total calcium and U/L for ALK.

Statistical Analysis

The results were analyzed by Statistical calculations made using the statistical package for the social sciences (SPSS) (version 20.0) program (SPSS Inc., Chicago, Illinois, USA) and Minitab version 18 software. T-test and ANOVA one way (were used to examine the difference in the mean of parameters evaluated between the studied groups). The correlation coefficient (r) was used to test the correlation between two variables. The results of the analysis with a p-value < 0.05 were considered significant and $p < 0.01$ highly significant. Statistical analysis and Graphs plotted were conducted by Microsoft Office Excel 2016 software.

RESULTS

Baseline Demographic and Clinical Characteristics

The clinical characteristic and baseline demographic of the study groups and the biochemical parameters of the patient groups and control as shown in Table 1. The study groups include Group A(Patients); include 70 post-menopause women with osteoporosis and osteopenia, and this group also subdivided into two groups; 40 post-menopause women with osteoporosis (Group A1) and 30 post-menopause women with osteopenia (Group A2). Group B (Control); include 20 post-menopause women as healthy control. The data is expressed as (mean ± SD) values of demographic parameters for patient groups. Table 1 showed non-significant difference ($p > 0.05$) in age and Years of menopause between Group A (57.57 ± 6.68,9.10 ± 5.89; respectively) compared to Healthy control (57.15 ± 5.47,7.35 ± 4.83; respectively). While The results of the study showed significant difference ($p < 0.05$) in BMI, WC, T score and Z score between Group A (31.82 ± 5.52,98.3 ± 11.9, -2.61 ± 0.89, -1.807 ± 0.516; respectively) compared to Healthy control (34.92 ± 5.2,104.85 ± 9.13, -0.316 ± 0.368, 0.905 ± 0.436; respectively) as shown in Table 1. The present study also showed a non-significant difference ($p > 0.05$) in age and Years of menopause in Group A1 (58.05 ± 6.47, 9.18 ± 5.57; respectively) and Group A2 (56.93 ± 7.01, 9.00 ± 6.38; respectively) compared to healthy control (Group B) (57.15 ± 5.47, 7.35 ± 4.83; respectively). At the same time, the mean value of BMI for GroupA1 was significantly higher than control (30.91 ± 6.08,34.92 ± 5.2; respectively). While the mean value of BMI was non-significant between Group A2 than healthy control (33.04 ± 4.48,34.92 ± 5.2; respectively) as shown in table 1. The results of the study also showed significant difference ($p < 0.05$) in WC, T score and Z score in Group A1 (97.6 ± 13.1, -3.245 ± 0.604, -1.835 ± 0.6; respectively) and Group A2 (99.2 ± 10.3, -1.77 ± 0.376, -0.547 ± 0.641; respectively) compared to Healthy control (104.85 ± 9.13, -0.316 ± 0.368,0.905 ± 0.436; respectively) as shown in Table 1.

Biochemical Parameters

Table 2 compares the biochemical parameters of the patients and control and the result expressed as mean ± SD.

Table 1: Demographic and clinical characteristics of Women Enrolled in the study

Data	*Group A (Post-menopause with osteoporosis and osteopenia) N = (70)*	*Group B (Healthy control) N = (20)*	*p-value*
Age (years)	57.57 ± 6.68	57.15 ± 5.47	0.775
BMI (kg/m^2)	31.82 ± 5.52*	34.92 ± 5.2	0.027
Years of menopause	9.10 ± 5.89	7.35 ± 4.83	0.183
WC (cm)	98.3 ± 11.9*	104.85 ± 9.13	0.012
T score	-2.61 ± 0.89*	-0.316 ± 0.368	<0.0001
Z score	-1.807 ± 0.516*	0.905 ± 0.436	<0.0001
Data	*Group A1 (Post-menopause with osteoporosis) N = (40)*	*Group B (Healthy control) N = (20)*	*p-value*
Age (years)	58.05 ± 6.47	57.15 ± 5.47	0.575
BMI (kg/m^2)	30.91 ± 6.08	34.92 ± 5.2	0.011
Years of menopause	9.18 ± 5.57	7.35 ± 4.83	0.197
WC (cm)	97.6 ± 13.1	104.85 ± 9.13	0.016
T score	-3.245 ± 0.604	-0.316 ± 0.368	<0.0001
Z score	-1.835 ± 0.6	0.905 ± 0.436	<0.0001
Data	*Group A2 (Post-menopause with osteopenia) N = (30)*	*Group B (Healthy control) N = (20)*	*p-value*
Age (years)	56.93 ± 7.01	57.15 ± 5.47	0.903
BMI (kg/m^2)	33.04 ± 4.48	34.92 ± 5.2	0.193
Years of menopause	9.00 ± 6.38	7.35 ± 4.83	0.304
WC (cm)	99.2 ± 10.3	104.85 ± 9.13	0.048
T score	-1.770 ± 0.376	-0.316 ± 0.368	<0.0001
Z score	-0.547 ± 0.641	0.905 ± 0.436	<0.0001

p-value < 0.05 considered significant
p-value < 0.01 considered high significant

Post menopause women with both osteoporosis and osteopenia (group A) had significantly higher mean serum IL17, FGF21 and CXC12 levels compared to healthy control ($p < 0.0001$), respectively (Table 2). In contrast, the serum levels of total calcium and ALK were insignificant when ($p > 0.05$) compared to healthy control, respectively. IL17A, FGF21 and CXC12 levels were significantly higher in both Group A1 ($p < 0.0001$) and Group A2 ($p < 0.0001$) than control, respectively. The mean value of serum total calcium for Group A1 was lower than control but non-significant ($p > 0.05$), while in Group A2, serum level of total calcium was higher than control but also still non-significant ($p > 0.05$). The mean value of serum ALP for GroupA1 was lower than control but non-significant ($p > 0.05$), while in GroupA2, serum level of ALK was also lower than control but also still non-significant ($p > 0.05$).

Correlations Studies

The correlation between the entire group and sub group patients has been tested by Pearson's correlation coefficient (r). The variable was considered statistically significant, at $p < 0.05$ and highly statistically significant at $p < 0.01$.

Correlation of Studied Variable in Sub groups of Study Population

Table 3 shows the correlation of the entire Group A. The present study is found significant positive correlations between the values of the age and years of menopause ($r = 0.825$, $p = 0.0001$), age and Z score ($r = 0.263$, $p = 0.028$), BMI and WC ($r = 0.325$, $p = 0.006$) in Group A. Also, there was significant positive correlations between serum levels of FGF21 and CXC12 ($r = 0.401$, $p = 0.001$) of Group A. In addition, there were significant negative correlation between serum levels of IL17A and T score ($r = -0.403$, $p = 0.001$), FGF21 and T score ($r = -0.495$, $p = 0.0001$), CXC12 and T score ($r = -0.441$, $p = 0.0001$), IL 17A and Z score ($r = -0.344$, $P = 0.004$), IL17A and Calcium ($r = -0.285$, $p = 0.017$). Table 4 show the correlation of Group A1. There were significant positive correlations between the values of age and years of menopause ($r = 0.806$, $p = 0.0001$), age and Z Score ($r = 0.499$, $p = 0.001$), T and Z score ($r = 0.382$, $p = 0.015$). Also, there was significant negative correlations between serum levels of IL17A and T score ($r = -0.313$, $p = 0.049$), serum levels of FGF21 and T score ($r = -0.386$, $p = 0.014$), serum levels of CXC12 and T score ($r = -0.374$, $p = 0.018$), of entire studied Group A1. Table 5 show the correlation of Group A2, the present study found significant positive correlations between the values of the age and years of menopause ($r = 0.85$, $p = 0.0001$), serum levels of FGF21 and CXC12 ($r = 0.513$, $p = 0.004$). Also, there was significant negative correlations between WC and T Score ($r = -0.399$, $p = 0.029$), serum levels of FGF21 and years of menopause ($r = -0.366$, $p = 0.047$), of Group A1.

Table 2: Mean ± SD for biochemical parameters of the patients and control

Data	*Group A (Post-menopause with osteoporosis and osteopenia) N = (70)*	*Group B (Healthy control) N = (20)*	*p-value*
Serum IL-17A (ng/L)	251 ± 115*	57.9 ± 28.8	<0.001
Serum FGF21 (pg\mL)	540 ± 285*	97.1 ± 54.7	<0.001
Serum CXC12 (ng\L)	436 ± 277*	179.6 ± 64.2	<0.001
Serum calcium (mg/dL)	9.11 ± 0.805	9.055 ± 0.701	0.760
Serum alkaline phosphatase (U/L)	54.8 ± 11.0	57.7 ± 12.1	0.342
Data	*Group A1 (Post-menopause with osteoporosis) N = (40)*	*Group B (Healthy control) N = (20)*	*p-value*
Serum IL-17A (ng/L)	280 ± 135*	57.9 ± 28.8	<0.0001
Serum FGF21 (pg\mL)	639 ± 334*	97.1 ± 54.7	<0.0001
Serum CXC12 (ng/L)	517 ± 339*	179.6 ± 64.2	<0.0001
Serum Calcium (mg/dL)	8.98 ± 0.693	9.055 ± 0.701	p = 0.698
Serum Alkaline Phosphatase (U/L)	56.6 ± 11.0	57.7 ± 12.1	p = 0.719
Data	*Group A2 (Post-menopause with osteopenia) N = (30)*	*Group B (Healthy control) N = (20)*	*p-value*
Serum IL-17A (ng/L)	212.3 ± 66.1*	57.9 ± 28.8	<0.0001
Serum FGF21(pg\mL)	407 ± 106*	97.1 ± 54.7	<0.0001
Serum CXC12 (ng/L)	328.8 ± 84.4*	179.6 ± 64.2	<0.0001
Serum Calcium (mg/dL)	9.287 ± 0.916	9.055 ± 0.701	p = 0.318
Serum Alkaline Phosphatase (U/L)	52.4 ± 12.4	57.7 ± 12.1	p = 0.14

p-value < 0.05 considered significant
p-value < 0.01 considered high significant

Table 3: Correlations (r) Results for Group A

Variable Group A N = 70		*Age*	*BMI*	*WC*	*Yr. of menopause*	*T Score*	*Z score*	*IL17A*	*FGF 21*	*CXC 12*	*Total Ca*	*ALP*
Age	R	1	-0.217	0.068	0.825	-0.203	0.263	0.044	0.085	0.015	0.019	-0.109
	P	0	0.071	0.576	0.0001*	0.092	0.028*	0.718	0.485	0.903	0.873	0.371
BMI	R	-0.21	1	0.325	-0.154	0.209	-0.068	-0.183	-0.001	0.066	0.233	0.051
	P	0.07	0	0.006*	0.202	0.083	0.574	0.13	0.995	0.589	0.052	0.676
WC	R	0.068	0.325	1	-0.017	0.031	-0.029	-0.029	-0.078	-0.057	0.029	0.051
	P	0.57	0.006*	0	0.890	0.801	0.80	0.811	0.522	0.639	0.812	0.676
Yr. of menopause	R	0.82	-0.154	-0.017	1	-0.11	0.187	0.073	0.069	-0.051	-0.024	-0.065
	P	0.0001*	0.202	0.890	0	0.365	0.122	0.55	0.568	0.673	0.844	0.592
T score	R	-0.119	0.258	0.123	-0.038	1	0.349	-0.403	-0.495	-0.441	0.156	-0.056
	P	0.326	0.031*	0.311	0.755	0	0.003	0.001**	0.0001**	0.0001**	0.197	0.646
Z score	R	0.263	-0.068	-0.029	0.187	0.349	1	-0.344	0.113	-0.169	0.073	-0.021
	P	0.028*	0.574	0.810	0.122	0.003	0	0.004**	0.354	0.163	0.546	0.862
IL17A	R	0.044	-0.183	-0.029	0.073	-0.403	-0.402	1	0.163	0.134	-0.285	0.093
	P	0.718	0.13	0.811	0.55	0.001*	0.004	0	0.179	0.268	0.017*	0.442
FGF21	R	0.085	-0.001	-0.078	0.069	-0.495	0.113	0.163	1	0.401	-0.058	-0.016
	P	0.485	0.995	0.522	0.568	0.0001*	0.354	0.179	0	0.001**	0.633	0.898
CXC12	R	0.015	0.066	-0.057	-0.051	-0.441	-0.169	0.134	0.401	1	-0.025	0.177
	P	0.903	0.589	0.639	0.673	0.0001**	0.163	0.268	0.001**	0	0.837	0.143
Total Calcium	R	0.019	0.233	0.029	-0.024	0.156	0.073	-0.285	-0.058	-0.025	1	-0.002
	P	0.873	0.052	0.812	0.844	0.197	0.546	0.017*	0.633	0.837	0	0.988
ALP	R	-0.109	-0.008	0.051	-0.065	-0.056	-0.021	0.093	-0.016	0.177	-0.002	1
	P	0.371	0.946	0.676	0.592	0.646	0.862	0.442	0.898	0.143	0.988	0

(*) Correlation is significant at 0.05 level (2-tailed)
(**) Correlation is high significant at 0.01 level (2-tailed)

Table 4: Correlations (r) Results for Group A1

Variable Group A1		*Age*	*BMI*	*WC*	*Yr. of menopause*	*T score*	*Z score*	*Il17A*	*FGF 21*	*CXC 12*	*Total Ca*	*ALP*
Age	R	1	-0.300	0..064	0.806	-0.287	0.499	0.089	0.142	0.018	-0.007	-0.116
	P	0	0.06	0.695	0.0001**	0.073	0.001**	0.587	0.382	0.913	-0.964	0.476
BMI	R	-0.300	1	0.432	-0.206	0.216	-0.017	-0.168	0.08	0.144	0.195	0.046
	P	0.06	0	0.005**	0.202	0.181	0.915	0.299	0.622	0.376	0.229	0.776
WC	R	0.064	0.432	1	-0.029	0.086	0.099	-0.111	-0.028	-0.005	0.07	0.201
	P	0.695	0.005	0	0.858	0.598	0.543	0.496	0.862	0.974	0.669	0.214
Yr. of Meno-pause	R	0.806	-0.206	-0.029	1	-0.251	0.321	0.154	0.2	-0.047	-0.049	-0.096
	P	0.0001**	0.202	0.858	0	0.119	0.043	0.343	0.215	0.775	0.765	0.555
T score	R	-0.287	0.216	0.086	-0.251	1	0.382	-0.313	-0.386	-0.374	0.041	0.146
	P	0.073	0.181	0.598	0.119	0	0.015*	0.049*	0.014*	0.018*	0.801	0.369
Z score	R	0.499	-0.017	0.099	0.321	0.382	1	-0.365	0.154	-0.204	0.147	-0.117
	P	0.001*	0.915	0.543	0.043*	0.015*	0	0.02*	0.342	0.207	0.367	0.472
IL17A	R	0.089	-0.168	-0.111	0.154	-0.313	-0.365	1	0.055	0.031	-0.295	0.109
	P	0.587	0.299	0.496	0.343	0.049*	0.02	0	0.736	0.848	0.065	0.503
FGF21	R	0.142	0.08	-0.028	0.2	-0.386	0.342	0.055	1	0.294	-0.036	-0.129
	P	0.382	0.622	0.862	0.215	0.014*	0.154	0.736	0	0.065	0.824	0.426
CXC12	R	0.018	0.144	-0.005	-0.047	-0.374	-0.204	0.031	0.294	1	0.016	0.168
	P	0.913	0.376	0.974	0.775	0.018*	0.207	0.848	0.065	0	0.922	0.299
Total Calcium	R	-0.007	0.195	0.07	-0.049	0.041	0.147	0.295	-0.036	0.016	1	0.216
	P	0.964	0.229	0.669	0.765	0.801	0.367	0.065	0.824	0.922	0	0.18
ALP	R	-0.116	0.046	0.201	-0.096	0.146	-0.117	0.109	-0.129	0.168	0.216	1
	P	0.476	0.776	0.214	0.555	0.369	0.472	0.503	0.426	0.299	0.18	0

(*) Correlation is significant at 0.05 level(2-tailed)
(**) Correlation is high significant at 0.01 level(2-tailed)

DISCUSSION

There is clinical and molecular evidence suggests that inflammation also exerts significant influence on bone turnover, inducing OP. Several pro-inflammatory cytokines have been implicated in the regulation of bone cells and an activated immune profile has been considered an important risk factor in the occurrence of OP.[14] In this study serum IL17A levels were significantly higher in group A and subgroup patients (A1 and A2) compared to healthy controls, respectively, this was following several studies.[15,16] IL17A correlates negatively with BMD in Group A and groupA1. This result was in agreement with Zhang, J. *et al.* study.[17] IL17A affects the bone and induced bone loss is initiated through RANK ligand-mediated osteoclastgenesis; this occurs by activation of T cell also its has a role in local inflammatory processes by regulating neutrophil production and recruitment.[18] In this study, serum FGF21 was significantly higher in group A and subgroup patients (A1 and A2) compared to healthy controls, respectively, FGF21 correlates negatively with BMD in Group A and group A1 this results agreed with recent studies[19-21] and disagree with other studies.[22,23] Fibroblast growth factor 21 (FGF21) is an atypical member of the FGF family, which functions as a powerful endocrine and paracrine regulator of glucose and lipid metabolism, in addition to liver and adipose tissue. Whether FGF21 has a positive or detrimental effect on bone in mice and humans remains unclear. recent studies have shown that FGF21 can also be produced in skeletal muscle and bone.[24] The mechanism could be explained by the following facts: physiological or pharmacological elevation of FGF21stimulate IGFBP1 expression, which could be secreted into circulation and induced osteoclast differentiation, bone resorption and reduce bone mass.[25] Also, the present study found that the serum CXC12 was significantly higher in group A and subgroup patients (A1 and A2) compared to healthy controls respectively, CXC12 correlates negatively with BMD in Group A and groupA1 this results was accordance with several studies.[26,27] Dysregulation of the immune system is associated with the beginning of various inflammatory autoimmune disorders, which cause antagonistic effects on bone integrity.[28] CXC12 has a role in bone resorption, during osteoclast differentiation, the expression of CXCL12 and its receptor CXCR4 increase, indicating an autocrine/paracrine mechanism of action of CXCL12 throughout the osteoclast differentiation process.[29] Although calcium is the primary nutrient of interest in bone health, the information from previous studies linking serum calcium and BMD is limited. Our study shows no significant difference in serum level of total calcium in all group patients compared to healthy control, total

Table 5: Correlations (r) Results for Group A2

Variable Group A2		*Age*	*BMI*	*WC*	*Yr. of menopause*	*T score*	*Z score*	*Il17A*	*FGF21*	*CX12*	*Total ca*	*ALP*
Age	R	1	-0.057	0.092	0.850	-0.159	0.108	-0.147	-0.245	-0.188	0.077	-0.136
	P	0	0.765	0.626	0.000	0.402	0.569	0.439	0.193	0.320	0.685	0.473
BMI	R	-0.057	1	0.056	-0.081	-0.272	0.194	-0.019	0.148	0.203	0.238	-0.005
	P	0.765	0	0.769	0.672	0.145	0.305	0.919	0.436	0.281	0.205	0.981
WC	R	0.092	0.056	1	0.003	-0.399	0.251	0.342	-0.218	-0.273	-0.055	-0.142
	P	0.626	0.769	0	0.987	0.029	0.181	0.064	0.248	0.145	0.788	0.455
Yr. of menopause	R	0.850	-0.081	0.003	1	-0.040	0.153	-0.107	-0.366	-0.186	0.002	-0.041
	P	0.000	0.672	0.987	0	0.833	0.418	0.573	0.047	0.325	0.990	0.831
T score	R	-0.159	-0.272	-0.399	-0.04	1	-0.189	-0.240	0.162	0.187	-0.063	-0.194
	P	0.402	0.145	0.029	0.833	0	0.318	0.201	0.392	0.321	0.742	0.305
Z score	R	0.108	0.194	0.251	0.153	-0.189	1	0.034	-0.258	-0.12	0.256	0.061
	P	0.569	0.305	0.181	0.418	0.318	0	0.860	0.168	0.528	0.172	0.748
IL17A	R	-0.247	-0.019	0.342	-0.107	-0.240	0.034	1	0.012	0.134	-0.223	-0.102
	P	0.439	0.919	0.064	0.573	0.201	0.860	0	0.949	0.479	0.237	0.593
FGF21	R	-0.245	0.148	-0.218	-0.366	0.162	-0.258	0.012	1	0.513	0.224	-0.04
	P	0.193	0.436	0.248	0.047	0.392	0.168	0.949	0	0.004	0.234	0.833
CXC12	R	-0.188	0.203	-0.273	-0.186	0.187	-0.12	0.134	0.513	1	0.204	0.057
	P	0.320	0.281	0.145	0.325	0.321	0.528	0.479	0.004	0	0.279	0.765
Calcium	R	-0.077	0.238	-0.051	0.002	-0.063	0.256	-0.223	0.224	0.204	1	-0.133
	P	0.685	0.205	0.788	0.99	0.742	0.172	0.237	0.234	0.279	0	0.483
ALP	R	-0.136	-0.005	-0.142	-0.041	0.194	0.061	-0.102	-0.04	0.057	-0.133	1
	P	0.4	0.981	0.455	0.831	0.305	0.748	0.593	0.833	0.765	0.483	0

(*) Correlation is significant at 0.05 level(2-tailed)
(**) Correlation is high significant at 0.01 level(2-tailed)

calcium shows no correlation with BMD in all group patients; these results agree with several studies.[30,31] and disagree with other.[32] Also, the current study shows the serum level of ALP in all group patients was lower compared to healthy control but no significant difference; this agree with Zhao et al. study[33] and disagrees with others.[34,35]

CONCLUSION

According to the present study, which includes:

- Serum levels of IL17A, FGF21 and CXC12 is significantly increased in Group A and sub group patients
- Serum levels of total calcium and ALP is a non-significant difference in a Group A and sub group patients
- Significant negative correlation between serum levels of IL17A and T score, FGF21 and T score, CXC12 and T score in Group A
- In the future, IL17A, FGF21 and CXC12 levels may be used to evaluate, diagnose, and follow up of high-risk patients with osteoporosis and osteopenia.

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