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Relationship between Osteoprotegrin and estrogen serum level with osteoporosis in postmenopausal Iraqi women

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Abstract Osteoporosis can define as a major bone disease especially in older women, it correlated with decrease bone density and change in the bone structure that may be increase in bone fragility. Osteoporosis more prevalence in women with age over 50 years old (post menopause), this correlate with estrogen hormone deficiency, this bone loss may be rapid and lead to accelerate bone resorption because of lack of balance occur between osteoclast and osteoblast, increasing in the osteoblast differentiation lead to osteoporosis activation. After menopause estrogen level will decrease due to the lacking occur in eggs produced by ovaries and this will lead to increase synthesis of IL-1, IL-6 and tumor necrosis factor and OPG level will decreased and this will lead to increase bone turnover and osteoporosis, at the same time promote vascular calcification due to increase action of RANKL one bone and vascular cell. Two group included in this study divided into patient group (n=25), age 50 years and over postmenopausal women and control group (n=50), age between 30-50 years' premenopausal women. 5ml of blood was taken from both postmenopausal and premenopausal women. All blood samples for both groups was tested for calcium, alkaline phosphtase and OPG level. OPG level was determined by ELISA technique. Serum level of alkaline phosphatase was found to be higher in postmenopausal group than premenopausal women group ($p<0.001$). serum calcium level is lower in postmenopausal group than premenopausal women group ($p<0.001$). serum osteoprotegerin level was higher in postmenopausal group than premenopausal women group ($p<0.001$). osteoprotegerin (OPG) can be used as indicator of osteoporosis and useful for early diagnosis in postmenopausal women.

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Keywords: *osteoprotegrin, osteoporosis, menopaused women, estrogen, calcium*

1. INTRODUCTION

Osteoporosis can define as a major bone disease especially in older women, it correlated with decrease bone density and change in the bone structure that may be increase in bone fragility. (1)

Osteoporosis more prevalence in women with age over 50 years old (post menopause), this correlate with estrogen hormone deficiency, this bone loss may be rapid and lead to accelerate bone resorption because of lack of balance occur between osteoclast and osteoblast, increasing in the osteoblast differentiation lead to osteoporosis activation. (2,3)

Osteoprotegrin OPG it is soluble glycoprotein also known as tumor necrosis factor receptor 11 B (TNFRSF11B), or osteoclastogenesis inhibitory factor (OCIF) and it is also a decoy receptor of receptor activator of nuclear factor kappa-b (RANK). (4)

OPG expressed in bone cells, vascular cells, lung and skin. OPG considered as anti resorpative factor because it leads to neutralizing NFkb (RANKL) which considered as a cytokine with strong osteoclast suppression effect and inhibit bone resorption. (5,6)

OPG / RANKL is an important regulatory mechanism for mineral metabolism in bone and vascular tissue because RANKL promote bone resorption and vascular calcification; while OPG inhibit bone resorption and had protective effect. (7,8)

OPG expression controlled and regulated by estrogen, so estrogen will suppress osteoclastogenesis by increasing OPG expression in osteoblast. Also estrogen lead to increase calcium absorption. (9) Because estrogen receptor found highly in bone cells, so estrogen when bind to estrogen receptor this will lead to expression of IL-1, insulin like growth factor IGF-1 and TGF-β, also suppress action of RANKL and this mean inhibition of osteoclast formation and inhibit bone resorption. (10,11)

After menopause estrogen level will decrease due to the lacking occur in eggs produced by ovaries and this will lead to increase synthesis of IL-1, IL-6 and tumor necrosis factor and OPG level will decreased and this will lead to increase bone turnover and osteoporosis, at the same time promote vascular

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calcification due to increase action of RANKL one bone and vascular cell. (12,13)

It thought that serum level of postmenopausal women of OPG was decreased but there is paradoxical role that increase level of OPG as protective mechanism of body to decrease bone resorption and decease vascular calcification. (14)

The aim of the study was to determine if we can use serum osteoprotegerin (OPG) in early diagnosis of osteoporosis in postmenopausal women.

2. Subject and Method

Two group included in this study divided into patient group (n=25), age 50 years and over postmenopausal women and control group (n=50), age between 30-50 years' premenopausal women. Patient collected from medical city hospital in Baghdad from October 2022 to march 2023. 5ml of blood was taken from both postmenopausal and premenopausal women. Vein blood of each individual was collected and stored in freeze (-20) C for analysis.

Patient group already diagnosed with osteoporosis with DXA machine to measure bone mineral density. All blood samples for both groups was tested for calcium, alkaline phosphtase and OPG level. OPG level was determined by ELISA technique. All data were statistically processed by using SPSS program.

3. RESULT

It was found that the value of mean level of ALP in the postmenopausal patient group was higher than in the premenopausal control group as shown in table (3-1) and fig (3-1) below.

Table (3-1): *Mean level of ALP in Study groups*

ALP Level (U/L)	Patient group	Control group	P value
Min-Max	231-263 U/L	54-148 U/L	P< 0.01
Mean±SD	243±7.6 U/L	88±15.5 U/L	

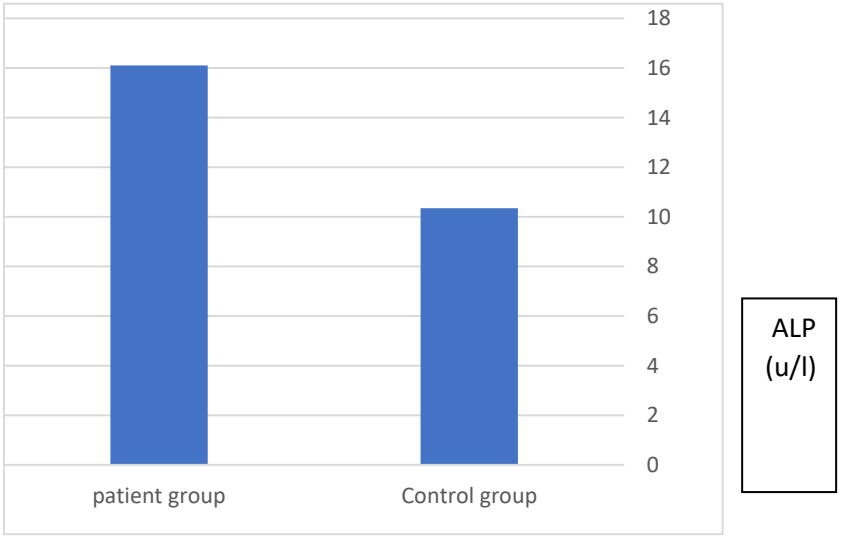

Fig:(3-1) *Mean level of ALP in Study groups.*

It was found that the value of mean serum level of calcium in the postmenopausal patient group was lower than in the premenopausal control group as shown in table (3-2) and fig (3-2) below.

Table (3-2): *Mean level of calcium in Study groups*

calcium Level (mg/dl)	Patient group	Control group	P value
Min-Max	6.9-8.1 mg/dl	8.3-10.1 mg/dl	P< 0.01
Mean±SD	7.5± 2.1	9.2± 1.5	

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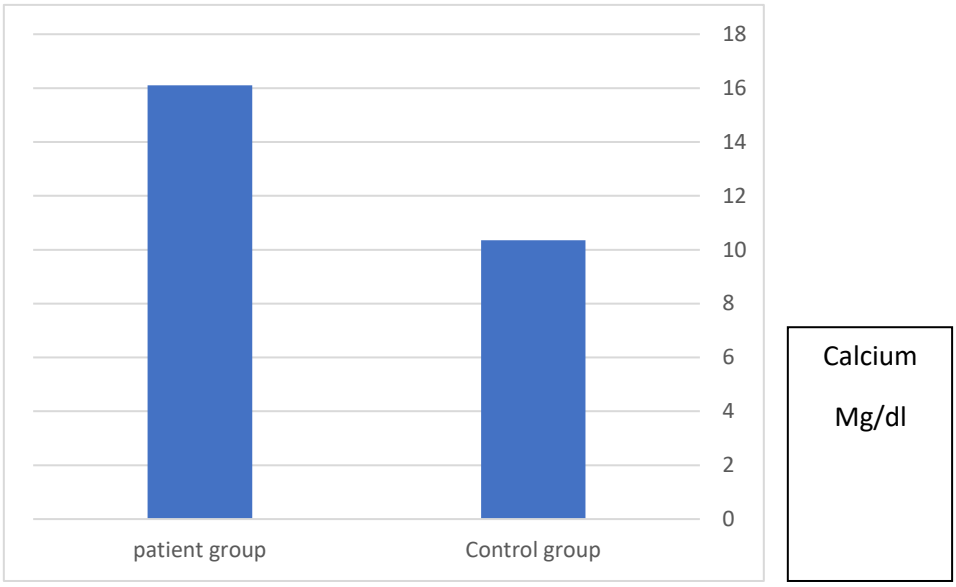

Fig:(3-2) *Mean level of Calcium in Study groups.*

We found that the value of mean level of osteoprotegerin in the postmenopausal patient group was higher than in the premenopausal control group as shown in table (3-3) and fig (3-3) below.

Table (3-3): *Mean level of OPG in Study groups*

OPG level (pmol/l)	Patient group	Control group	P value
Min-Max	13.7 – 19.8 pmol/l	9.5 – 11.9 pmol/l	P< 0.01
Mean±SD	16.1 ± 2.75	10.35 ± 2.4	

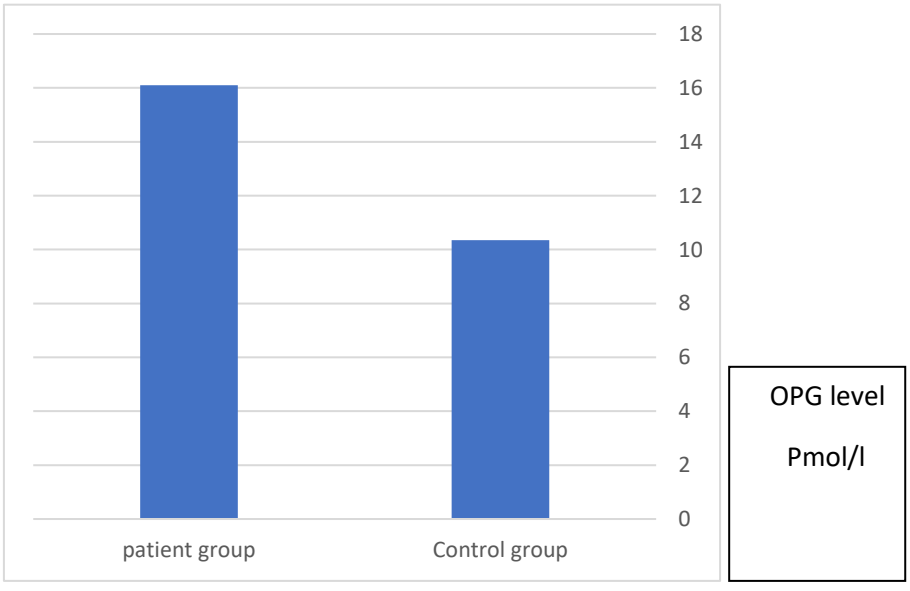

Fig:(3-3) *Mean level of OPG in Study groups*

4. Discussion

According to table (3-1) the alkaline phosphatase level is greater in the postmenopausal patient group than premenopausal control group (p<0.001) because of increased activity of osteoclast due to low estrogen level and lead to bone resorption (15,16). Alkaline phosphatase enzyme level increase when there is increasing in the metabolic activity of bone and liver, as well as according to table (3-2) the serum calcium level is fewer in postmenopausal patient group than premenopausal control group (p<0.001) because of increased activity of osteoclast that will break down bone (bone resorption),

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releasing the minerals, resulting in a transfer of calcium from bone fluid to the blood (17,18), also low level of estrogen lead to reduction of absorption of calcium at the same time increase loss of calcium by kidney(urine) . According to table (3-3) the serum osteoprotegerin level is greater in the postmenopausal patient group than premenopausal control group ($p<0.001$) and this is considered as a reflection of the body to the increasing of bone turnover so it is act as compensatory response to excessive osteoclastogenesis, inhibits of differentiation of osteoclast and also its function by inhibiting the interaction occur between RANKL and RANK (19,20).

5. CONCLUSION

Osteoprotegerin (OPG) can be used as indicator of osteoporosis and useful for early diagnosis in postmenopausal women.

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