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RESEARCH ARTICLE

SERUM CHEMERIN LEVELS IN OVARIECTOMIZED OSTEOPOROTIC RAT MODEL.

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Key words:-

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Abstract

Background: Chemerin is an adipocytokine that controls adipocyte differentiation and related to immune and inflammatory functions. Post-menopausal osteoporosis (PMOP) is the most common bone disease in females characterized by decreased bone mineral density (BMD); relationship between chemerin and osteoporosis remains unclear.

Objective: To assess serum chemerin levels in osteoporotic rat model induced by ovariectomy, and to investigate the interplay between serum chemerin levels and BMD, also the impact of estradiol replacement therapy on chemerin levels and its association with BMD parameters.

Material and methods: Three equal groups of adult female albino rats (n=12) were used; sham operated control (sham), ovariectomized (OVX) and OVX with estrogen replacement (OVX-ER) groups. Nine weeks after ovariectomy, serum analysis, bone BMD measurements and histopathology were done.

Results: In OVX osteoporotic rat model, serum levels of chemerin were significantly elevated ($P < 0.001$) when compared to other groups, and negatively correlated with BMD, Changes in OVX chemerin levels were significantly associated with the elevated insulin resistance. However, they were not associated with FSH or estradiol levels.

Conclusion: OVX induced osteoporosis was associated with significant rising in chemerin levels which were associated with changes in insulin resistance rather than sex hormones. It can be hypothesized that the exact causative of PMOP extends beyond pituitary; ovarian axis to be metabolic and adiposity cross talks which needs more detailed investigations.

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Introduction:-

Osteoporosis is a major health problem that characterized by reduction of the bone mineral density (BMD), disruption of the bone micro-architecture that increases the possibility of fractures and osteopathology (Xin et al., 2014; Iliou et al., 2015). Postmenopausal osteoporosis (PMOP) is known to be secondary to changes in the pituitary-bone axis, while postmenopausal deficient estrogen is claimed as the leading pathogenesis (Seibel et al., 2006).

Chemerin is one of these adipokines which plays a role in adipocyte differentiation, insulin signaling and resistance (Roh et al., 2007). Also, related to the development of obesity and metabolic syndrome (Ye et al., 2014).

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Chemerin/chemokine-like receptor 1 (CMKLR1) signaling pathway may perform an essential role in regulating osteoblastogenesis of bone marrow-derived precursor cells (Muruganandan et al., 2010). Chemerin expression and secretion in bone marrow stromal cells significantly induced by Peroxisome proliferator-activated receptor gamma (PPAR γ) (Muruganandan et al., 2011). Chemerin and its receptor CMKLR1 are expressed in hematopoietic stem cell and secreted into the extracellular media. Moreover, chemerin stimulates osteoclastogenesis (Muruganandan et al., 2013). Controversial published studies about the link between serum chemerin and BMD in subjects with osteoporosis have been reported (Terzoudis et al., 2014 & 2016; He et al., 2015; Shi et al. 2016). Also, the mechanisms that regulate serum levels of chemerin in postmenopausal women with osteoporosis are not known. Accordingly, this work was planned to investigate the relationship between serum chemerin levels and BMD in ovariectomy induced osteoporotic rat model, also the impact of estradiol replacement therapy on chemerin levels and its association with BMD parameters.

MATERIAL AND METHODS:

Animals:-

From 4th of March 2016 to 30th of June 2016, this study was carried out on a total number of 45 healthy adult female albino rats weighing 180 ± 10.5 gm. They were obtained from the animal house in Faculty of Veterinary medicine -Zagazig University. Rats were kept in steel wire cages under hygienic conditions in animal house of faculty of Medicine- Zagazig University. All animals received care in agreement with the guide to the care and use of experimental animals (CCAC 1993). The experimental protocol was approved by the Institutional Review Board and research ethics committee of Faculty of Medicine Zagazig University (IRB). Animals were fed standard chow and had free access to water. Animals were accommodated to animal house situations for one week before the experiments going on. Rats divided randomly into three groups (n=15 rats per group); sham operated control (SHAM), ovariectomized (OVX) and OVX with estrogen replacement (OVX-ER). One week after ovariectomy rats in OVX-ER group were subcutaneously injected with 17 β - estradiol valerate (30 μ g/kg bw; sigma) dissolved in 0.2 mL sesame oil (ADWIC Laboratory Chemicals, Egypt), five days a week for eight weeks. (Babaei et al., 2010). Sham operated and OVX rats were injected with the same amount of sesame oil as a vehicle five days a week for eight weeks. Four rats died from OVX and OVX-ER groups; the statistical analysis was done concerning 12 experiments (12 rats) of each group as the recommended sample of IRB.

Rat model of osteoporosis:-

Bilateral ovariectomy:-

Animals were fasted overnight, then anaesthetized by i.m injection of pentobarbital (50mg/kg bodyweight) (Pharma .Misr CO. Ind. S.A.A., Cairo-A.R.E.). After removing hair from lower abdomen and sterilizing bare are of skin, midline incision was made, the ovaries and uterus were exposed with fat around them, the oviduct and blood vessels supplying the ovaries were tied up, and the ovaries were removed. The uterus and oviducts were placed back with fat around them, and the incision was closed with catgut thread suture then the skin incision was repaired with sterile silk suture and the wound was painted with garamycin cream (. (Pharm Misr CO. Ind. S.A.A. Cairo-A.R.E.), and covered with sterile gauze (Gui et al., 2004)

Sham ovariectomy:-

after midline abdominal cut ,the oviducts, ovaries and uterus were exposed with fat and were put back, followed by closure with catgut thread suture, and then the skin incision was repaired with sterile silk suture and the wound was painted with garamycin cream, and covered with sterile gauze (Gui et al., 2004).

At the end of experiments (9 weeks after ovariectomy), rats weighed and BMI were calculated according to the equation: body weight (gm)/length² (nose to anus length) (cm²) (Novelli et al., 2008), and then blood and tissue samples were obtained.

Blood sampling:-

All animals were fasted overnight, anesthetized by diethyl ether, and sacrificed by capitation; blood was immediately collected in clean centrifuge tubes, and was left to clot for 2 hours at room temperature before centrifuging for 15 minutes at nearly 3000 rpm. The separated serum was kept at -80° C until used.

Serum is analyzed for chemerin levels according to Tan et al. (2009) by using rat enzyme-linked immunoassay kits from Usn Life Science., (USA), Follicle stimulating hormone (FSH), Estradiol (E2), and Progesterone (PROG)

according to the method of **Tietz (1995)**, using ELISA rat kits: BC-1029 and BC-1115, respectively, BioCheck Inc 323 Vintage Park Dr. Foster City, CA 94404, serum glucose level, according to **Tietz (1995)** using glucose enzymatic- liquizyme rat kits (Biotechnology, Egypt), insulin level according to **Temple et al. (1992)** using KAP1251-INS-EASIA rat Kits (BioSource Europe S.A., Belgium), then we calculate homeostatic model assessment of insulin resistance index (HOMA-IR) based on serum insulin level ($\mu\text{IU/ml}$) and serum glucose level (mg/dl) according to the formula described by **Matthews et al. (1985)** as $\text{HOMA-IR} = \text{fasting serum glucose (mg/dl)} \times \text{fasting serum insulin (}\mu\text{IU/ml)} / 405$. serum Calcium (Ca^{++}) levels by colorimetric method according to **Gindler et al. (1972)** using kits supplied by Bio-diagnostic Co. (Cairo, Egypt), serum Phosphorus (P) levels by colorimetric method according to **Goldenberg et al. (1966)** using kits supplied by Bio-diagnostic Co. (Cairo, Egypt), Alkaline phosphates (ALP) levels according to **Belfied and Goldberg (1971)**.

Bone density determination according to **Doster et al. (1969)** method: right femur of animals were removed and cleaned then extracted 2 times with a 1:1 mixture of absolute ethanol and diethyl for 48h and one time with diethyl ether for 24h. the dehydrated and defatted bones were dried in 80°C oven for 48h to measure the dry weight. The bones were ashed in a muffle furnace at 600°C for 48h after putting each bone in a clean porcelain dish, after that bone ash weights were measured. Calcium and phosphorus levels in bones were detected by colorimetric methods using spectronic 21 according to **Garcia-Contreras et al., 2000**: bone ashes were acidified by hydrolyzing in 6N HCL, filtration and dilution by distilled water.

Bone histopathological examination:-

Left femur was dissected from each rat separately, cleaned carefully of adhering tissues; fixed and placed in 10% formaline solution for one day (**Raab et al., 1991**), tissues were processed in ascending grades of alcohol, cleaned in xylol and embedded in paraffin blocks, 4 microns sections were cut on a standard rotatory microtome and stained by Heamatoxylin and Eosin (H and E) stain as described by **Bancroft and Cook (1984)**.

Statistical Analysis:-

Results were presented as mean \pm standard deviation (SD). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 20.0 (SPSS Inc., Chicago, IL, United States). Repeated measures of analysis of variance (ANOVA) were applied followed by the Student-least significant deference (LSD), post hoc test to compare means of each two different groups. Pearson's correlation analysis was performed to screen potential relations between serum levels of chemerin and all measured parameters. For all statistical tests done, P value < 0.05 was considered to be statistically significant.

Results:-

Regarding table 1, no significant difference could be detected between sham operated group and OVX-ER group in all parameters measured ($P > 0.05$). OVX group showed significant elevation of the mean values of serum levels of chemerin ($35.2 \pm 5.57 \text{ pg/ml}$), FSH ($8.82 \pm 1.03 \text{ mIU/ml}$) and alkaline phosphatase "ALP" ($169.65 \pm 8.72 \text{ I}\mu\text{/L}$) in comparison to those of sham operated group (16.02 ± 4.6 , 4.99 ± 0.79 and 141.63 ± 7.02 respectively) ($P < 0.001$). Serum levels of estradiol ($5.36 \pm 1.11 \text{ pg/ml}$) in OVX group was significantly lower when compared to that of sham operated group ($27.06 \pm 4.88 \text{ mg/dL}$) ($P < 0.001$). Moreover, among the three studied groups, serum levels of Ca^{++} and P showed non-significant difference ($P > 0.05$).

Concerning table 2, no significant difference could be detected between sham operated group and OVX-ER group in all parameters measured ($P > 0.05$). OVX group revealed significant increase in the mean values of BMI ($0.66 \pm 0.46 \text{ gm/Cm}^2$), serum insulin ($13.59 \pm 2.05 \mu\text{IU/mL}$) and calculated HOMA-IR (5.13 ± 0.53) when contrast to those of sham operated group ($0.48 \pm 0.02 \text{ gm/Cm}^2$, $8.17 \pm 1.16 \mu\text{IU/mL}$, 2.03 ± 0.15 respectively) ($P < 0.001$, $P < 0.05$ and $P < 0.01$ respectively). However, BMD parameters of OVX group were significantly lower (Dry weight $337.08 \pm 37.81 \text{ mg/femur}$, Ash weight $194.66 \pm 23.76 \text{ mg/femur}$, Bone Ca^{++} $93.33 \pm 7.68 \text{ mg/femur}$ and Bone P $32.16 \pm 1.6 \text{ mg/femur}$) than those of sham operated group ($523.22 \pm 32.13 \text{ mg/femur}$, $320.91 \pm 32.41 \text{ mg/femur}$, $151.18 \pm 8.6 \text{ mg/femur}$, $41.81 \pm 2.89 \text{ mg/femur}$ respectively) ($P < 0.001$). However, serum glucose levels (mg/dL) did not show any significant changes among the three studied groups ($P > 0.05$).

Table 3 represents the Pearson's correlation analysis between serum chemerin and the measured parameters in all groups, in OVX group there was a significant positive correlation between the serum chemerin levels and BMI ($r = 0.614$, $P < 0.05$), insulin ($r = 0.622$, $P < 0.05$), HOMA-IR (-0.702 , $P < 0.01$), however a negative correlation with serum

ALP ($r = -0.771$, $P < 0.01$), dry femur weight ($r = -0.891$, $P < 0.0001$), ash femur weight ($r = -0.701$, $P < 0.01$), bone Ca^{++} ($r = -0.691$, $P < 0.01$) and bone P ($r = -0.873$, $P < 0.001$), however, no significant association, could be detected between serum chemerin and serum FSH ($r = 0.191$, $P > 0.05$) or serum estradiol ($r = 0.152$, $P > 0.05$). In sham operated and estradiol treated groups serum chemerin were positive correlated with BMI ($r = 0.604$, $P < 0.05$; $r = 0.632$, $P < 0.05$ respectively) however a negative correlation with serum ALP ($r = -0.602$, $P < 0.05$; $r = -0.621$, $P < 0.05$ respectively), dry femur weight ($r = -0.703$, $P < 0.01$; $r = -0.632$, $P < 0.05$ respectively), ash femur weight ($r = -0.612$, $P < 0.05$; $r = -0.699$, $P < 0.01$ respectively), bone Ca^{++} ($r = -0.599$, $P < 0.05$; $r = -0.601$, $P < 0.05$ respectively) and bone P ($r = -0.612$, $P < 0.05$; $r = -0.621$, $P < 0.05$ respectively) while no significant association could be detected between serum chemerin and serum FSH ($r = 0.111$, $r = 0.245$, $P > 0.05$ respectively), estradiol ($r = 0.121$, $r = 0.254$, $P > 0.05$ respectively), insulin ($r = 0.212$, $r = 0.324$, $P > 0.05$ respectively) and HOMA ($r = 0.217$, $r = 0.212$, $P > 0.05$ respectively).

Histopathological examination:-

The photomicrographs of sham operated group showed normal compact bone tissues normal calcified bone with osteoblasts and osteocytes with normal marrow spaces (figure 1). The OVX group showed thin atrophic bone trabeculae with wide marrow spaces (figure 2). The OVX with estrogen replacement group showed normal calcified bone with osteoblasts and osteocytes with normal lining of bone marrow spaces (figure 3).

Table 1: Statistical analysis of serum levels of chemerin (pg/ml), FSH (μ IU/ml), E2 (pg/ml), Ca^{++} (mg/dL), P (mg/dL), and ALP activity (Iu/L) in the three studied groups. a = p value of significance versus sham operated, b = p value of significance versus OVX group.

n =15	SHAM	OVX	OVX-ER
Chemerin (pg/ml)	16.02±4.6	35.2±5.57 P<0.001 ^a	18.98±5.99 P> 0.05 ^a , P<0.001 ^b
FSH (mIU/ml)	4.99±0.79	8.82±1.03 P<0.001 ^a	4.87±0.68 P> 0.05 ^a , P<0.001 ^b
Estradiol (pg/ml)	27.06±4.88	5.36±1.11 P<0.001 ^a	27.28±4.61 P> 0.05 ^a , P<0.001 ^b
Serum Ca^{++} (mg/dL)	10.51± 0.38	10.11±0.51 P> 0.05 ^a	10.12±0.37 P> 0.05 ^{a,b}
Serum P (mg/dL)	5.39±0.68	5.07±0.87 P> 0.05 ^a	5.31±0.77 P> 0.05 ^{a,b}
ALP (Iu/L)	141.63±7.02	169.65± 8.72 P<0.001 ^a	146.22±5.05 P> 0.05 ^a , P<0.001 ^b

Table 2: Statistical analysis of calculated BMI (gm/Cm^2), serum glucose (mg/dL), serum insulin (μ IU/mL) and calculated HOMA-IR and bone mineral density (BMD) parameters in all studied groups. a = p value of significance

N= 15	SHAM	OVX	OVX-ER
BMI (gm/Cm^2)	0.48±0.02	0.66±0.46 P<0.001 ^a	0.49±0.02 P> 0.05 ^a , P<0.001 ^b
Glucose (mg/dL)	76.32±8.33	80.22±8.66 P> 0.05 ^a	74.11±8.61 P> 0.05 ^{ab}
Insulin (μIU/mL)	8.17±1.16	13.59±2.05 P< 0.05 ^a	7.27±1.26 P> 0.05 ^a , P<0.05 ^b
HOMA-IR	2.03± 0.15	5.13± 0.53 P< 0.01 ^a	2.13± 0.15 P> 0.05 ^a , P<0.01 ^b
Dry weight (mg/femur)	523.22 ± 32.13	337.08±37.81 P<0.001 ^a	500.91±36.62 P> 0.05 ^a , P<0.001 ^b
Ash weight (mg/femur)	320.91±32.41	194.66±23.76 P<0.001 ^a	297.75±31.74 P> 0.05 ^a , P<0.001 ^b
Bone Ca^{++} (mg/femur)	151.18±8.6	93.33±7.68 P<0.001 ^a	147.89±9.07 P> 0.05 ^a , P<0.001 ^b
Bone P (mg/femur)	41.81±2.89	32.16±1.6 P<0.001 ^a	39.97±3.63 P> 0.05 ^a , P<0.001 ^b

versus sham operated, b = p value of significance versus OVX group.

Table 3:- Pearson's correlation analysis between serum chemerin (pg/ml) levels with calculated BMI (gm/Cm²), serum insulin (μ IU/mL), calculated HOMA-IR, serum FSH (μ IU/ml), serum E2 (pg/ml), Serum ALP ($I\mu$ / L), dry weight (mg/femur), ash weight (mg/femur), bone Ca⁺⁺ (mg/femur), bone Phosphorus (P) (mg/femur) in all groups.

parameters	SHAM		OVX		OVX-ER	
	R	P	R	P	r	P
BMI (gm/Cm²)	0.604	P< 0.05*	0.614	P< 0.05*	0.632	P< 0.05*
Insulin (mIU/mL)	0.212	P> 0.05	0.622	P< 0.05*	0.324	P> 0.05
HOMA-IR	0.217	P> 0.05	0.702	P<0.01**	0.212	P> 0.05
FSH (mIU/ml)	0.111	P> 0.05	0.191	P> 0.05	0.245	P> 0.05
E2 (pg/ml)	0.121	P> 0.05	0.152	P> 0.05	0.254	P> 0.05
Serum ALP ($I\mu$/ L)	-0.602	P< 0.05*	-0.771	P<0.01**	-0.621	P<0.05**
Dry weight (mg/femur)	-0.703	P< 0.01*	-0.891	P<0.001***	-0.632	P<0.05*
Ash weight (mg/femur)	-0.612	P< 0.05*	-0.701	P<0.01**	-0.699	P<0.01**
Bone Ca⁺⁺ (mg/femur)	-0.599	P< 0.05*	-0.691	P< 0.01*	-0.601	P<0.05**
Bone P (mg/femur)	-0.612	P< 0.05*	-0.873-	P<0.001***	-0.621	P<0.05*

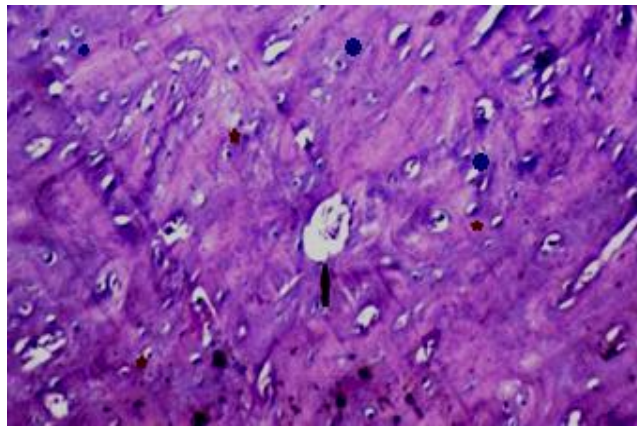


Figure 1: Microscopic picture in the diaphysis of long bone in sham operated group (group I) showing normal calcified bone with osteoblasts (◆) and osteocytes (●) with normal marrow spaces (↑) [H&E stain, LM, focus 400].

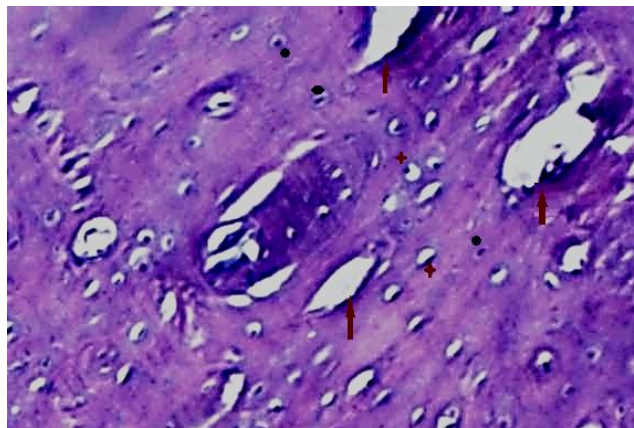


Figure 2: Microscopic picture in the diaphysis of long bone in OVX induced osteoporosis (group II) showing decalcified bone and bluish coloration of osteoblasts (◆) and osteocytes (●) indicate demineralized bone with wide marrow spaces (↑) [H&E stain, LM, focus 400].

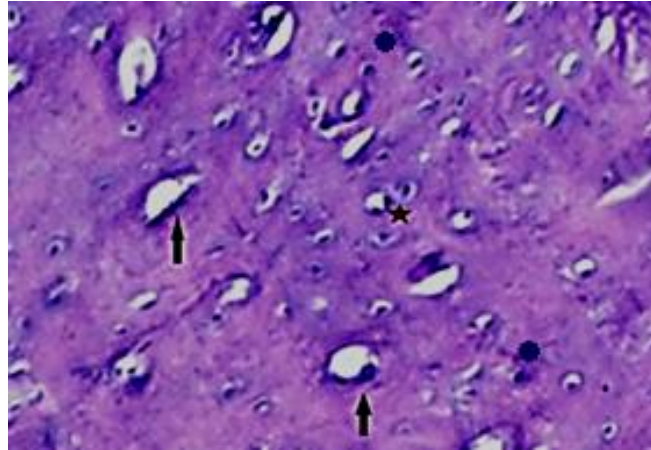


Figure 3: Microscopic picture in the diaphysis of long bone in OVX-ER (group III) showing aberrant normal bone and matrix with osteoblasts (◆) and osteocytes (●) plus normal marrow spaces (↑) [H&E stain, LM, focus 400].

Discussion:-

The present study revealed that BMD decreased in OVX rats in the form of significant decrease in the mean values of femur ash weight, dry weight and bony ashes calcium and phosphorus contents accompanied with a significant increase in serum alkaline phosphatase activity in comparison with that of sham operated rats, These diagnostic criteria of decrease in BMD are in line with the results of OVX rat model of osteoporosis done by **Jiang et al (2003)** and **Yang et al. (2005)**.

Serum FSH levels were significantly increased, while estradiol significantly decreased in OVX rats compared with that of sham operated and OVX with estrogen replacement groups. These results come in accordance with previous studies of **Cheung et al. (2011)**, **Garcia-Martin et al. (2012)** and **Wang et al. (2015)** who reported that serum FSH levels were significantly elevated and negatively correlated with BMD in PMOP independently of estrogen, in addition they concluded that FSH may induce an essential role in the acceleration of bone loss in postmenopausal women and enhance osteoclastogenesis (**Wang et al., 2015**). This hypothesis is supported by **Sun et al. (2006)** investigation which proved that female mice deficient either in FSH receptors or FSH β were unaffected by bone loss although hypogonadism. **Imai (2014)** and **Sowers et al. (2013)** also stated that the proportion of bone mass loss during perimenopause is higher than that in postmenopause, while estrogen serum levels during perimenopause are normal (**Sowers et al., 2006**). However, inconsistent studies of **Ritter et al. (2008)** and **Gourlay et al. 2012** indicated that FSH does not seem to affect bone mass regulation in vivo and does not modulate osteoclastogenesis in vitro.

Rouach et al. (2011) reported that estrogen lack is the leading cause of bone loss in ovariectomized rats; however FSH may be closely related to hypogonadal bone loss. **Liu et al. (2010)** showed that FSH can exacerbate alveolar bone loss by FSHR independently of estrogen; in addition, bone loss in OVX rats was prevented by FSH inhibitors. However, the etiology of postmenopausal osteoporosis extends beyond pituitary and ovarian sex hormones.

Current results showed a significant rising in serum chemerin levels in OVX rats in comparison to both sham operated and OVX -ER groups, moreover, it was found that the elevated serum chemerin had significant negative correlations with BMD parameters in OVX group, these results were in accordance with those of **He et al. (2015)** who suggested that men with osteoporosis present higher concentrations of serum chemerin than in healthy subjects and chemerin levels were negative correlated with femoral BMD and lumbar BMD both in patients with osteoporosis and in healthy controls. Also, **Shi et al. (2016)** showed that serum chemerin levels had significant negative correlations with BMD at the lumbar site in obese postmenopausal women. And they suggested that chemerin served as an independent negative predictor of BMD, and may play a significant role in regulating bone mass in obesity.

Moreover, Serum chemerin levels were significantly raised in subjects with irritable bowel disease in comparison to controls and correlated significantly with the osteoporosis (**Terzoudis et al., 2014 and 2016**). In contrast to these results, in a recent study, **Engin-Üstün et al. (2016)** showed that women with postmenopausal osteoporosis had decreased circulating chemerin than healthy age matched subjects, and they revealed that chemerin might play a role

in the pathogenesis of osteoporosis. This discrepancy between current results and others may be due to difference in subjects (human Vs. animal).

Chemerin is a negative regulator during bone formation (Liu et al., 2013). Chemerin encourages adipocyte differentiation of bone marrow stromal cells by activation of CMKLR1. Knock-down of chemerin gene increased osteoblast marker gene expression and mineralization after osteoblastogenic stimulation (Muruganandan et al., 2010). In vivo, rosiglitazone elevated chemerin mRNA levels in adipose tissue and bone marrow along with an increase in circulating chemerin levels in mice. (Muruganandan et al., 2011). Additionally, Muruganandan et al. (2013) showed that chemerin has an autocrine/paracrine role in modulating osteoclast differentiation of hematopoietic stem cell through regulating intracellular calcium. Chemerin may negatively affect bone metabolism by inhibiting bone formation in the bone marrow (Shi et al., 2016).

According to the results of this study, chemerin level in OVX rats was positively correlated with BMI, insulin levels and HOMA-IR and failed to be correlated with FSH or estradiol. These findings were supported by He et al. (2015) who suggested a relationship of chemerin with obesity and insulin resistance.

Ovariectomy in the present study is accompanied by significant elevation in HOMA-IR (decrease in insulin sensitivity), in same context Saengsirisuwan et al. (2009), reported metabolic alterations mimicking features of the insulin resistance syndrome in ovariectomy rats. Siri and Ginsberg (2003) reported significant increase in insulin resistance in human after ovariectomy, Moreover, Prasannarong et al. (2012) stated that prolonged ovariectomy resulted in dyslipidemia, impaired glucose tolerance and reduced insulin-stimulated skeletal muscle glucose transport. Thus increased serum chemerin levels in OVX rats in this study may possibly attributed to the state of insulin resistance because chemerin has been proposed to be an insulin-sensitizing adipocytokine and its secretion has been shown to raise (possibly as a compensatory mechanism) in insulin-resistant conditions (EL-Mesallamy et al., 2011; Fatima et al., 2013; Van Poppel et al., 2014).

Hormone replacement therapy in postmenopausal women reduced abdominal fat (Kanaley et al., 2001) and insulin resistance (Saengsirisuwan et al., 2009), also induced up regulation of GLUT4 in ovariectomized rats and postmenopausal women (Zoth et al., 2012; Visseres et al., 2013).

Further studies are required to prove whether chemerin plays a role in the pathophysiology of osteoporosis and whether it is qualified as a marker or predictor of osteoporosis.

Conclusion:-

Ovariectomy induced osteoporosis was associated with increase in serum levels of chemerin which were negatively associated with BMD, while positively correlated with insulin resistance. These changes in serum chemerin levels may be related to metabolic rather than sex hormones disturbance. It can be hypothesized that the exact causative of postmenopausal osteoporosis extends beyond pituitary and ovarian sex hormones to be metabolic and adipose tissue cross talks which need more detailed investigations.

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