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Study on Advanced Oxidation Protein Products (AOPP) as a Novel Marker of Oxidative Stress in Postmenopausal Osteoporosis: A Teaching Hospital Based Study

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ABSTRACT

Background: Micro-structural degeneration along with poor bone density (BMD) results in bone fragility that is characterized in osteoporosis, a multifactorial chronic skeletal condition. **Methods:** Overall 64 participants was selected for the research, in which 32 postmenopausal females as per diagnostic requirements for osteoporosis by the World Health Organization's (WHO) and 32 post-menopausal females without osteoporosis (both of them of the same age; 46-60) with menstrual abstinence for at least a year were enrolled in this study. **Results:** Mean height and BMI were increased in postmenopausal women with OP as compared to postmenopausal without OP women while weight was slight increase in postmenopausal women with OP as compared to postmenopausal without OP women. Mean FBS, MDA, AOPPs, BLAP, TRACP5b level were found increased in postmenopausal women with OP as compared to postmenopausal without OP women while BMD was found to decrease. **Conclusion:** There are higher plasma levels of compared AOPPs and a standard age coordinated comparison population of postmenopausal osteoporotic women. Plasma AOPPs concentrations of postmenopausal women are characterized by bone tragedy and bone turnover markers.

Keywords: MDA, AOPPs, BMD and postmenopausal women.

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INTRODUCTION

Micro-structural degeneration along with poor bone density (BMD) results in bone fragility that is characterized in osteoporosis, a multifactorial chronic skeletal condition. Postmenopausal osteoporosis is a serious health challenge for women that raises morbidity, mortality and health care costs.[2] In the revised point of view of pathogenesis in this disease, the need to distinguish solid markers to suggest oxidative pressure status in this disease from estrogen mediated to oxidative pressure was expressed.[3] Estrogen deficiency decreases the brain's resistance against oxidative fear, meaning that increased bone resorption and reduced bone growth are associated with severe deficiency of these hormones, the major neurotic symptom of postmenopausal osteoporosis.[4] As of late, the relevance of oxidative vulnerability to the development of postmenopausal osteoporosis has been identified in the region.[5] Owing to the rise in ROS as well as failure of cell reinforcing limit,[6] oxidative pressure exists. The exact calculation of ROS to mirror the degree of oxidative concern in vivo is problematic due to the dumbfounding assortment, low abundance, high reactivity, and the very brief half-existence of ROS generated during each phone period.[7] Consequently, the calculation of certain completed peroxidation outcomes is used in vivo to test the oxidative pressure status. The final product of lipid peroxidation, malon di aldehyde (MDA), is commonly used as an oxidative pressure parameter.[8] Be it as it might, the postmenopausal osteoporosis section of MDA is also exceedingly far from being explicitly true.[9] Advanced oxidation protein products (AOPPs) were first observed in the plasma of chronic uremic patients and are known as a remarkable marker of oxidative stress since they are stable and simple to detect. AOPPs are mostly attributed to the activity of ROS (chlorinated compounds) in proteins, which leads to the formation of dityrosine residues and protein crosslinking.[10] Our aim was to determine the levels of advanced plasma oxidation protein products as an indicator of ox datively modified proteins and also to calculate plasma MDA as a lipid peroxidation marker. The association between the above oxidative stressors and indicators of bone mineral density or bone turnover was also examined.

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MATERIALS & METHODS

This new research was carried out in conjunction with the Department of Biochemistry in the Department of Obstetrics and Gynecology at World College of Medical Sciences & Research and Hospital, Jhajjar, during the period January, 2019 to February, 2020. The study was conducted after

getting ethical committee clearance from the institute. Informed, written and understood consent of the participants were taken. A group of 64 participants were recruited in the research, in which 32 postmenopausal women fulfilled the World Health Organization's (WHO) diagnosis requirements for osteoporosis and 32 postmenopausal women without osteoporosis (both of them of the same age; 46-60) were enrolled in the research with menstrual absence for at least one year. Patients of secondary osteoporosis, conditions that are known to be linked of heightened oxidative stress (dementia, cardiovascular disease, diabetes, kidney or liver dysfunction, and inflammatory disease), antioxidant vitamin utilization or malnutrition were removed within 6 months previous to registration. Many who had previously or presently used active bone agents such as selective estrogen receptor modulators or estrogen replacement therapy, strontium ranelate, teriparatide or PTH, calcitonin, and deno-sumab were also omitted if they had taken medicines that could influence bone mineral metabolism within the last 6 months (including corticosteroids, heparin, and anticonvulsants). On all issues, demographic data is revised.

Biochemical Analysis:

Under aseptic settings, 10 ml of a vein puncture blood sample was collected. For clotting, the sample kept at RT for 3-5 minutes. Then centrifugation was done for 10 minutes at 2500 rpm. The following conditions have been examined.

1. Fasting Blood Glucose by GOD POD method
2. MDA by Kei Satoh
3. AOPP by spectrophotometric method
4. Relevant bone resorption markers, BALP and TRACP 5b with ELISA kits and
5. Measuring BMD:

Assessment of BMD by dual-energy X-ray absorptiometry on the spine, hip, and/or forearm is gold standard for the diagnosis of osteoporosis. In this dual-energy X-ray absorptiometry in the lumbar spine area is utilized for BMD measurement (L2-L4). The assessment of osteoporosis is characterized by T score of -2.5 or less, suggesting a BMD lower than the norm for young adults of at least 2.5 SD.

Statistical Analysis:

Posed as values of SD ± Mean. The result processing was done using Microsoft Excel. By independent sample t test, statistical variations between cases and controls were calculated. In order to define the association between parameters, Pearson's correlation coefficient was computed. $p< 0.05$ was regarded as noteworthy.

RESULTS

Mean ages of postmenopausal with OP and postmenopausal without OP women were 44.4 ± 3.27 and 55.8 ± 2.8, respectively. Mean height and BMI were increased in postmenopausal women with OP as compared to postmenopausal without OP women while weight was slight increase in postmenopausal women with OP as compared to postmenopausal without OP women. Mean FBS, MDA, AOPPs, BLAP, TRACP5b level were found increased in postmenopausal women with OP as compared to postmenopausal without OP women while BMD was found to decreased as shown in [Table1].

Table 1: shows the level of different demographic & biochemical parameters

Parameters	Postmenopausal women		P Value
	With Osteoporosis	Without Osteoporosis	
Age in years	57.6 ± 2.9	55.8 ± 2.8	0.04
Height in cm	157.3 ± 2.3	154.5 ± 3.1	0.001
Weight in kg	61.7 ± 3.7	61.5 ± 3.7	0.8
BMI kg/m^2	25.8 ± 1.8	24.9 ± 1.5	0.3
FBS (mg/dl)	97.21±10.1	92.41±9.21	0.01
MDAnmol/L	6.3 ±0.47	5.8 ±0.43	0.21
AOPPs µmol/L	120.3 ±33.5	62.4 ±5.6	0.001
BLAP	45.53±11.5	30.41±13.3	0.001
TRACP5b	5.2±1.4	3.4±1.2	0.001
BMD gm/cm^2	0.62±0.20	0.92±0.6	0.001

Table 2: Correlation between markers of oxidative stress and markers of BMD or Bone Turnover

Variables	AOPPs		MDA	
	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value
MDA	+0.34	0.05	-	
BMD	-0.32	0.07	-0.12	0.51
BALP	+0.46	0.00	-0.15	0.41
TRACP5b	+0.36	0.04	+0.18	0.38

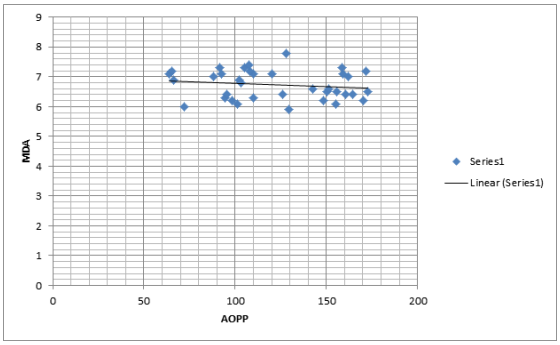

Figure 1: Shows the positive correlation between MDA & AOPP.

[Table 2]shows the plasma AOPP levels were negatively associated with BMD (r=0.32, P<0.07) and the plasma MDA level was positively correlated with AOPPs(r=0.34, P<0.05), BALP (r=0.46, P<0.00) and TRACP5b (r=0.36, P<0.04) bone turnover markers. Plasma MDA amounts, however, were negatively associated with BMD(r=-0.21, P=0.51) & BALP(r=-0.15, P=0.41), while TRACP5b(r=0.18, P=0.38) plasma in postmenopausal osteopoporotic women was positively correlated.

DISCUSSION

As strong criteria for evaluating the oxidative pressure status in vivo,[11,12] oxidative altered particles were used. In the current research, to determine the degree of oxidative pressure, we calculated plasma AOPPs and observed that it increased in postmenopausal ladies without osteoporosis. The levels of AOPPs were adversely related to lumbar BMD and were specifically connected to bone markers, while the levels of MDA were not connected to lumbar BMD. Morphological assessments along with estimations of some markers have revealed that when the two markers of resorption and development are extended, bone redesigning is increased at menopause.[12,13] BALP, which encourages bone mineralization, is known to be basically an indicator of increased osteoblast activity and, optionally, a remedial response due to enhanced bone demineralization.[15] Serum bone turnover marker levels are important in the survey of postmenopausal osterporetic foundational bone turnover.[16]As a bone-explicit compound, osteoclasts comprise TRACP5b, the serum convergence of which often represents the degree of bone demineralization.[17] In our research, we observed that BALP and TRACP5b were higher in contrasting and regulated postmenopausal osteoporotic women. There are many laboratory approaches available in the literature that help to assess the existence of in vivo stress, but none have proven itself unambiguously better than the others.[18] MDA, which is one of the most commonly used measures of lipid peroxidation, is prominent and most harmful penalty of oxidative stress.[19] MDA is recognized as a possible stress biomarker facilitates osteoclast activity. In the past decade, there have been some talks of using MDA as a proxy for OP in postmenopausal women. In a small sample of postmenopausal osteoporotic women, complete femoral BMD mea-surements were reported to be significantly correlated with MDA levels. However, the results of this study show that MDA levels have not been correlated with lumbar BMD or bone turnover markers. It is also not feasible to measure the magnitude of postmenopausal OP using MDA amounts, which is strongly compatible with the findings of existing research of greater sample sizes.[9] Proteins are the primary focus of ROS prior to lipid and other cellular elements.[20] Increased levels of AOPPs, which therefore serve as a novel biomarker of oxidative stress, indicate oxidative damage to proteins.[21] In addition to chronic uremia levels of AOPPs, patients with multiple oxidative stress-related diseases such as diabetes,[22] coronary artery disease and chronic intestinal inflammatory diseases are also elevatedIn the present research,[23] after we examined the interaction between AOPPs and BMD or bone turnover markers, we also discovered that AOPPs seemed to be a more important marker to represent the magnitude of postmenopausal OP than MDA. AOPPs have also been shown to be a novel molecular source for oxidative stress, implicated in many biological activities by causing intracellular ROS production,[24] in addition to being called an oxidative stress producer. Postmenopausal OP is considered to be a form of high-turnover osteoporosis and is characterized by excessive bone resorption and inadequate bone growth controlled by osteoblast and osteoclast coupling.[25] ROS can affect the genesis and longevity of osteoblasts and osteoclasts. RANKL-induced RANK activation in osteoclastic precursors improves ROS growth, which is important for osteoclastogenesis. In osteoblastic cells, ROS is an important apoptosis mea-diator. More recently, an in vitro study demonstrated that OS results in an improved content of AOPPs in cultured mouse MC3T3-E1 osteoblast-like cells. Additionally, AOPPs can inhibit osteoblast cell proliferation and differentiation through the ROS-dependent NF-kB pathway. Overall, these results suggest that AOPPs can be a strong indicator as well as an important factor in the pathogenesis of this condition when determining the severity of postmenopausal OP. A few challenges to our review should be remembered. To begin with, we have been unable to measure BMD in the femoral zone. Besides, we were not checking the plasma levels of any other cell reinforcements. Further examinations should be conducted to examine the link between AOPPs, stages of cell reinforcement, and femoral BMD.

CONCLUSION

These findings indicate that postmenopausal osteoporotic women have higher plasma reference levels of AOPPs and a similar group that is normally age-coordinated. In postmenopausal women, Plasma AOPPs concentrations are distinguished by bone misfortune and markers of bone turnover. Eventually, plasma levels of AOPPs can be used as a novel indicator of oxidative danger to anticipate the incidence of postmenopausal osteoporosis. In addition, their components in osteoporosis pathogenesis warrant further study.

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