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RELATIONSHIP BETWEEN MALONDIALDEHYDE AS AN OXIDATIVE STRESS MARKER AND TOTAL ANTIOXIDANT STATUS IN PRE AND POSTMENOPAUSAL WOMEN TO ASSESS THEIR PREDISPOSITION TO OXIDATIVE STRESS INDUCED DISORDERS

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Abstract

Introduction:-Menopause is the natural step in the process of aging. Women face various physiological, psychological and sociological changes which impair the quality of life during menopause. The risk of nutritional disturbances, particularly trace elements and vitamin deficiencies are high during menopause.

Aims & objectives:- To compare the Serum level of Oxidative Stress Marker along with the level of total antioxidant status in Pre & Post-menopausal Women. **Observation and Result:-**The Oxidative stress marker (MDA) level was significantly lower (1.5 ± 0.46), (p-value-0.0001) in Premenopausal women than that of Postmenopausal women (2.84 ± 0.69). But Antioxidant status level was found to be significantly higher (15.1 ± 2.4) in Premenopausal women than that of Postmenopausal women (10.53 ± 2.54).

Conclusion:-Menopause is associated with oxidative stress which predisposes to the development of various diseases like osteoporosis, depression, diabetes, and hypertension. Dietary, management, antioxidant supplementation, and moderate physical activity would help to prevent diseases related to menopause.

Keyword:-MDA- Malondialdehyde, ROS -Reactive Oxygen Species

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INTRODUCTION

Menopause is the natural step in the process of aging.¹ Women face various physiological, psychological and sociological changes which impair the quality of life during menopause.² The risk of nutritional disturbances, particularly trace elements and vitamin deficiencies are high during menopause. Several trace elements are essential in bone metabolism.³ The adverse effects of menopause are attributed by decrease in estrogen level which leads to alterations in lipid profile, body mass index, insulin levels along with increased risk of hypertension, cardiovascular diseases, osteoporosis, diabetes mellitus, cancer and other degenerative changes in postmenopausal females.⁴ There is increased production of free radicals after menopause which is due to sudden alterations in hormonal status.⁵ There is enhanced oxidative stress along with decreased antioxidant defense in postmenopausal females as compared to premenopausal females which play an important role in the pathogenesis of the various diseases related to menopause.⁶

Menopause is defined as the cessation of menstruation due to complete loss of ovarian follicle with no production of progesterone but less amount of estrogen is produced from adrenal steroid, which are grossly inadequate.⁷ Menopause mostly occurs between the ages of 45 to 50 years; the average age being 47. Menopause before the age of 40 is called as premature menopause. About 60 million Indian women are above the age of 55 years, a majority would spend 1/3rd of their life in postmenopausal stage.⁸

Antioxidants are compounds capable to either delay or inhibit the oxidation processes which occur under the influence of atmospheric oxygen or reactive oxygen species. Antioxidants are involved in the defense mechanism of the organism against the pathologies associated to the attack of free radicals. Endogenous antioxidants are enzymes, like superoxide dismutase, catalase, glutathione peroxidase or non-enzymatic compounds, such as uric acid, bilirubin, albumin, metallothioneins.⁹

When endogenous factors cannot ensure a rigorous control and a complete protection of the organism against the reactive oxygen species, the need for exogenous antioxidants arises, as nutritional supplements or pharmaceutical products, which contain as

active principle an antioxidant compound. Amongst the most important exogenous antioxidants, vitamin E, vitamin C, β -carotene, flavonoids, Selenium are wellknown, but also vitamin D and vitamin K₃.¹⁰

Oxidative stress is defined as the imbalance between the production of free radicals, in particular reactive oxygen species (ROS), and the capacity of disposing them through antioxidants. It leads to progressive accumulation of ROS related damage in cells. This process is inevitably linked to aging and appears to be involved in the onset of several diseases affecting the elderly.¹⁹ In the female population, postmenopausal individuals are regarded as more vulnerable to Oxidative stress than those in reproductive age, because their oxidative balance is deranged not only by the generally older age but also by a lower level of 17 β -estradiol (E2), believed to act as an antioxidant.¹¹

Therefore this study was conducted to compare Serum level of Oxidative Stress Marker along with the level of total antioxidant status in Pre & Post-menopausal Women.

MATERIALS & METHODS

The present cross-sectional study was conducted at Department of Biochemistry, L.N Medical College & Hospital, Bhopal, Madhya Pradesh, India. The present study was approved by the ethics Committee of LNCTU. The approval was on the agreement that patient anonymity must be maintained, good laboratory practice, quality control ensured, and Finding would be treated with utmost confidentiality and that every for the purpose of this research only. All the work was performed according to the International Guidelines for Human Experimentation in Biomedical Research.

Sample size: The sample size was calculated by considering the prevalence to be 27 % (varying 21.5 to 32.5%). According to which minimum of 310 women will be enrolled in the study of L.N Medical College & Hospital, Bhopal, Madhya Pradesh, India. These were divided into two groups-

- **Cases:** 155 Post-menopausal women (46-60 years)
- **Controls:** 155 Pre-menopausal women (30-45 years)

Study Population: All women attending OPD in the Department of Obstetrics & Gynecology, L.N Medical College & Hospital, Bhopal, Madhya Pradesh, India and fulfilling the defined criteria were included in the study till the desired sample size is reached.

Inclusion and Exclusion criteria:

The women who were apparently healthy and they should be non-smoker, non-alcoholic & ambulatory, neither pregnant nor oral contraceptive pills. The patients with any fracture in previous 1 year or on hormonal replacement therapy or any other medication was not included in this study. Initial evaluations were made by detail questionnaire that included demographic information, medical & reproductive history, major life style habits, hormone therapy & diet. All subjects were divided in two groups:

- a. Premenopausal women (known cases) – Control Group.
- b. Postmenopausal women (known cases) – Research Group

Any patient who is under any estrogen therapy or any supportive treatment for menopausal symptoms for at least 6 months prior to study, alcohol abuse, supplementation with nutritional antioxidants, chronic pathogens (e.g. diabetes,

hypertension, malabsorption etc.) & any bone diseases was excluded. Control subjects with some sort of menstrual disorders e.g. irregular menses, menorrhagia etc. were also excluded from the study.

Sample Collection: After obtaining informed written consent, 10ml of blood sample was drawn using disposable syringe under aseptic conditions into a sterile vacutainer from selected subjects with label. Collected blood was allowed to stand at room temperature for 30 minutes to clot. Then serum was separated by centrifugation at 3000 rpm for 5 minutes.

RESULT

The comparison of oxidative stress marker and antioxidant status among premenopausal women and postmenopausal women. Total 310 women were included in this study, out of which 155 were grouped as control (premenopausal women) and 155 were grouped as case (postmenopausal women) who were not on any hormonal replacement therapy, oral contraceptives, smoker, alcoholic, under any estrogen therapy. Oxidative stress marker and antioxidant status were measured in all the groups.

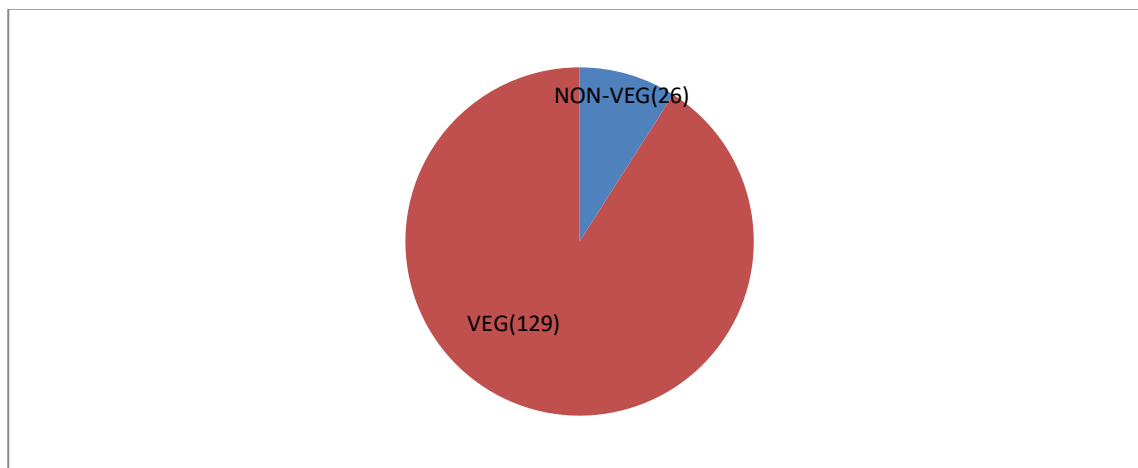


Fig 1: Frequency distribution of Vegetarian and Non-vegetarian in post Menopausal Woman.

It has been observed that there are significant changes in the level of MDA & antioxidant status of Menopausal women. The Oxidative stress marker (MDA) level was significantly lower (1.5 ± 0.46), (p-value-0.0001) in Premenopausal women than that of Postmenopausal women (2.84 ± 0.69). But Antioxidant status level was found to be significantly higher (15.1 ± 2.4) in

Premenopausal women than that of Postmenopausal women (10.53 ± 2.54). (Table-1)

S. No	Parameters	Postmenopausal women (CASE)		Premenopausal women (CONTROL)	
		MEAN	SD	MEAN	SD
1.	MDA ($\mu\text{mol/ml}$)	2.84 \pm 0.69		1.55 \pm 0.46	
2.	Antioxidant Status ($\mu\text{mol/L}$)	10.53 \pm 2.54		15.12 \pm 2.42	

We found the Pearson's correlation between the levels of MDA and serum total antioxidant status in pre and post menopausal women. Statistical analysis showed highly significant negative correlation between serum MDA levels and serum total antioxidant status with p value -0.0001 (Case). And also found same negative significant correlation between MDA and Total Antioxidant status, with p-value -0.0001 (Control). (Fig 2-5)

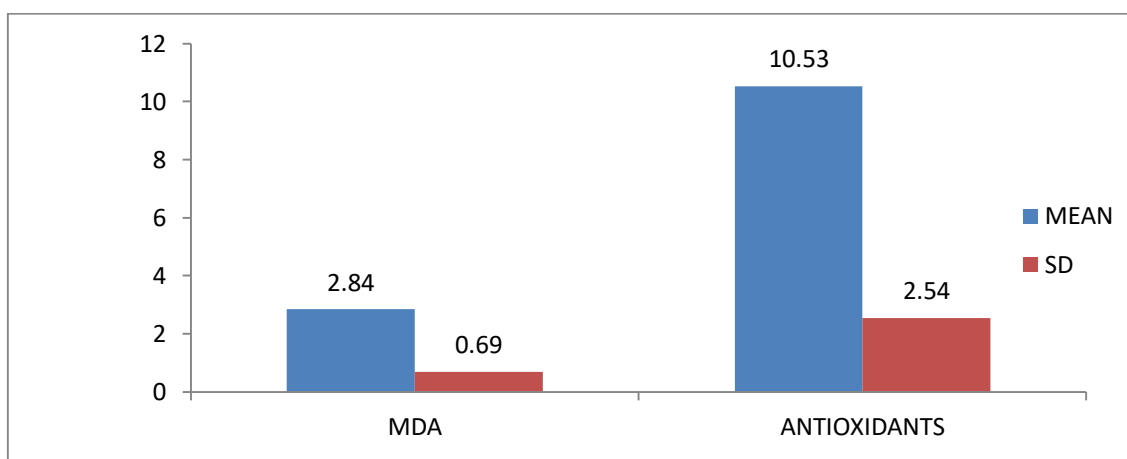


Fig 2 : Graph showing Mean & SD of Postmenopausal Woman(Case).

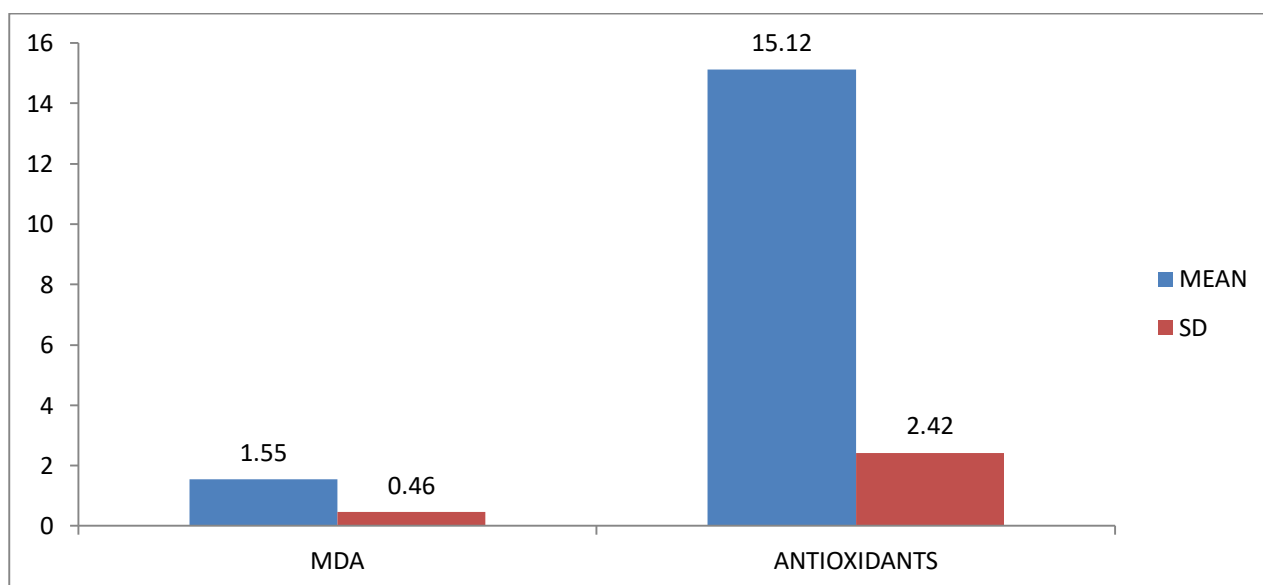


Fig 3: Graph showing Mean & SD of Premenopausal Woman(Control).

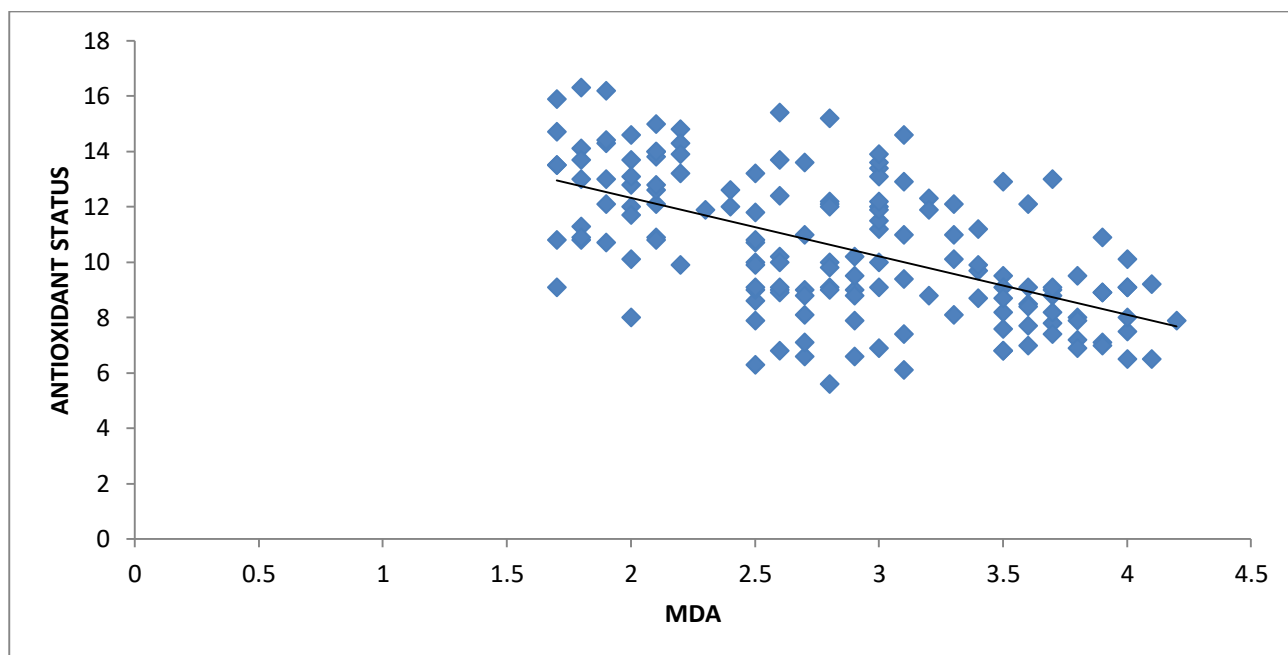


Fig 4:Graph showing Correlation between MDA and Antioxidant status in Premenopausal Woman(Control).

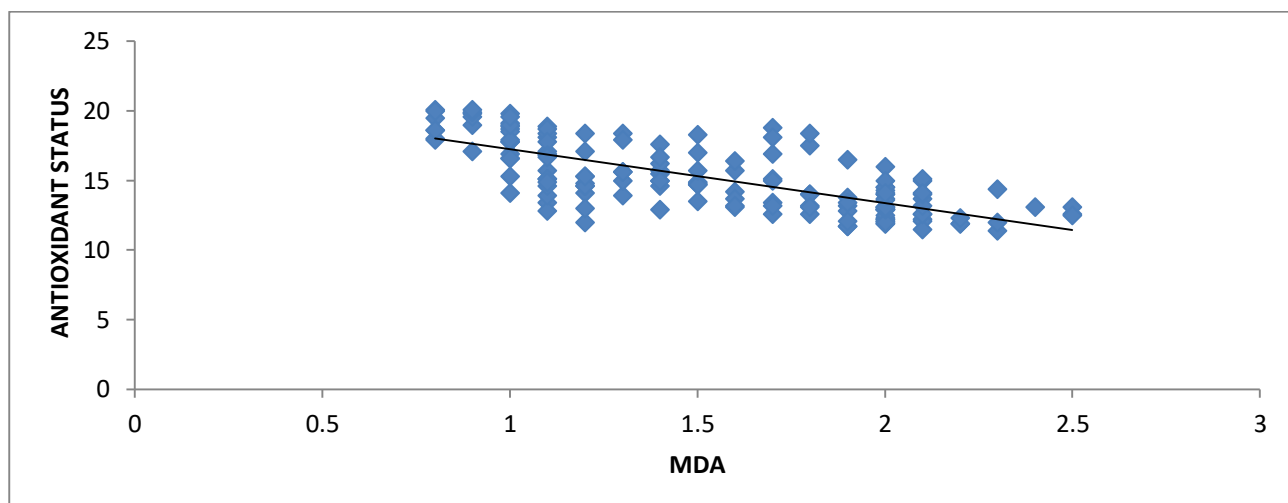


Fig 5:Graph showing Correlation between MDA and Antioxidant status in Postmenopausal Woman(Case).

DISCUSSION

In the present study, the MDA levels were found to be higher in postmenopausal women as compared to premenopausal women. This study results are consistent with the findings of a previous study comparing MDA levels between fertile and postmenopausal age groups.¹² Furthermore, two recent studies report, investigating the effect of surgical menopause on oxidant and antioxidant status of premenopausal patients, revealed that MDA levels were increased after surgical menopause.¹³ Oxidative stress probably

accompanies the process of aging. A variety of oxidative stress markers have been demonstrated to change due to the aging process.¹⁴ Although oxidative vascular stress of young women has been known to be lower as compared to men,¹⁵, the combined effect of aging and menopause in older women as compared to men is less certain. Thus, comparison of oxidative stress markers between the two genders in the elderly is needed to evaluate the independent effect of menopause on oxidative stress. MDA is one of the most often used biomarkers of oxidative stress on lipid associated with aging. An age related

increase in plasma concentration of MDA has been reported in several studies.¹⁶ The present study results are consistent with the findings of a previous study of the similar type where MDA was proposed as an effective prognostic tool for an early detection of cardiovascular disease in Menopausal women. The increased level of MDA marks the index of assessing oxidative stress. Furthermore, recent two study done on lipid peroxidation and lipid metabolism in postmenopausal women and the results of the study suggest that the aging and lack of estrogen may be responsible for the increase in MDA levels. However further studies should be carried out to explain the increased lipid peroxidation in postmenopausal women and assess the effectiveness of treatment with diet and hormone replacement therapy, both with and without antioxidant supplementation.¹⁷

In the present study, mean antioxidant status in postmenopausal women was significantly lower than that of the premenopausal women. This decrease in antioxidant status is in contrast with finding of Bertrand and colleagues¹⁸ but similar to the report by Olisekodiaka MJ et.al¹⁹ and Vincent & Allison²⁰ which showed that antioxidant status was lowered in postmenopausal women when compared with premenopausal women and suggested that this could be due to estrogen deficiency. Structurally, estrogen has a phenol-hydroxyl group at position 3. The presence of this phenol hydroxyl group contributes estrogen its antioxidant property which acts directly neutralizing oxygen free radicals. A decrease in estrogen concentration could result in decreased antioxidant status and accumulation of free radicals. Oxidative stress could then result when the balance between the rate of free radical production and the mop up by the body's antioxidant defense system is altered in favor of the former. Oxidative stress has been implicated in the etiology of over 100 diseases including aging process, hypertension, CVD, diabetes Mellitus (DM) and many forms of cancer.²¹ Menopause is a natural step in the process of aging hence; postmenopausal women are likely to develop oxidative stress because of estrogen deficiency and an advancing age, accompanied with age related changes.²² In postmenopausal women, ovaries stop making estrogen hormone and circulating concentrations of estrogen decrease. The antioxidant enzyme system can also be altered due to deficiency of estrogen, which has got antioxidant properties. The

human RBC has an effective mechanism to prevent and neutralize the oxidative stress induced damage. There are certain naturally occurring antioxidants in our body which neutralize the effects of these free radicals and protect the body against their deleterious effects.²³ Our study shows that there are changes in the serum biochemical profiles in postmenopausal women. It is evident from our study that there is decreased antioxidant defense in postmenopausal women as compared with premenopausal women which play an important role in the pathogenesis of the various diseases related to menopause.

Conclusion:

Menopause is associated with oxidative stress which predisposes to the development of various diseases like osteoporosis, depression, diabetes, and hypertension. Dietary, management, antioxidant supplementation, and moderate physical activity would help to prevent diseases related to menopause.

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