

## EVALUATION OF SOME INFLAMMATORY AND MUSCLE MARKERS IN PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN

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### ABSTRACT

**Background:** Menopause is associated with an array of metabolic changes which results into the appearance of inflammatory conditions.

**Objectives:** The study evaluated the levels of some inflammatory markers; C-reactive protein (CRP), rheumatoid factor, erythrocyte sedimentation rate (ESR) and uric acid. The muscle markers evaluated were creatine kinase (CK) and aspartate transaminase (AST) as well as body mass index (BMI) and blood pressure (Bp) in premenopausal and

postmenopausal women. **Method:** The study is a case-controlled study involving 50 premenopausal and 50 postmenopausal women in Nnewi metropolis. In both study groups, anthropometric measurements including body mass index ( $\text{Kg/m}^2$ ) and blood pressure (mmHg) were carried out. Serum levels of uric acid, creatine kinase, C-reactive protein, aspartate transaminase, rheumatoid factor and erythrocyte sedimentation rate were measured using appropriate techniques. **Results:** The result showed significant increase ( $p < 0.05$ ) in the mean serum levels of uric acid ( $\mu\text{mol/L}$ ), CRP (mg/L), ESR mm/hr, and AST IU/L but no

significant change was observed in creatine kinase in post menopausal women. A significant positive relationship was observed between CRP and BMI ( $r = 0.562$ ;  $p < 0.01$ ), CRP and ESR ( $r = 0.553$ ;  $p < 0.01$ ). The prevalence of positive rheumatoid factor among postmenopausal women was determined as 16%. **Conclusion:** The study concluded that in postmenopausal women, there is significant increase in the levels of CRP, ESR and uric acid. There is also a significant positive relationship between CRP, ESR and BMI indicating that the degree of changes in metabolites and obesity might have a role in the mediation of inflammation in post menopausal women.

**KEYWORDS:** Premenopausal women, postmenopausal women, inflammatory markers

## INTRODUCTION

Menopause is associated with an array of metabolic changes which results into the appearance of inflammatory conditions. Menopause occurs in most women between 45 and 55 years of age, although it may begin as early as age 40 or be delayed to the late 50s. Menopause has been considered to be premature when it occurs before 40 years of age.<sup>[1]</sup> The hormonal changes that occur during menopause may modulate certain diseases.<sup>[2]</sup> The most common types of arthritis seen in women after menopause are osteoarthritis, rheumatoid arthritis and gouty arthritis to a lesser degree. The culminating effect of these conditions is arthralgia or severe joint pain.<sup>[3]</sup> Menopause is associated with a natural decline in estrogen, increase visceral fat mass, decrease bone mass density, muscle mass, and strength.<sup>[4]</sup> Muscle loss is a natural consequence of aging, inactivity, and their associated metabolic dysfunction, but it is strongly accelerated in critical illness such as organ failure, sepsis, or cancer.<sup>[5]</sup> Therefore, evaluation of these conditions will provide an understanding into the cause and possible management of these conditions.

## MATERIALS AND METHODS

The ethical approval for the research was obtained from the ethical Committee, Faculty of Health Sciences, NAU. Informed consent was obtained from the subjects using questionnaire. Blood specimen was collected for the estimation of the serum levels of C-reactive protein, uric acid, rheumatoid factor and the activities of aspartate aminotransferase<sup>[8]</sup> and creatine kinase.<sup>[6,7,8,9]</sup> The erythrocyte sedimentation rate was determined using whole blood.<sup>[10]</sup> Statistical Package for Social Science (SPSS) version 20.0 was used for the analysis of the results obtained. Data collected was subjected to statistical analysis using student t-test and correlation ( $r$ ). Values were deemed significant at  $p < 0.05$  and  $p < 0.01$ .

## RESULTS

The mean level of Body Mass Index and blood pressure were shown in table 1 while Table 2 shows the mean serum level of the inflammatory and muscle markers in Premenopausal and Postmenopausal Women. Table 3 shows the relationship between the markers in postmenopausal women. Eight out of the fifty women were Rheumatoid factor-positive resulting in 16% positivity.

**Table 1: Anthropometric Data in the Premenopausal and Postmenopausal Women**

PARAMETERS	PRE-MENOPAUSAL MEAN $\pm$ SD	POST-MENOPAUSAL MEAN $\pm$ SD	t-test	p-Value
Body Mass Index (kgm <sup>-2</sup> )	22.59 $\pm$ 3.37	30.70 $\pm$ 6.16	-8.173	0.000*
Systole (mmHg)	121.70 $\pm$ 10.95	154.36 $\pm$ 27.42	-7.821	0.000*
Diastole (mmHg)	75.70 $\pm$ 9.03	90.30 $\pm$ 12.24	-6.787	0.000*

N = 50

\* = Significant at p<0.05

**Table 2: Serum levels of inflammatory and muscle markers in Premenopausal and Postmenopausal Women.**

PARAMETERS	PRE-MENOPAUSAL MEAN $\pm$ SD	POST-MENOPAUSAL MEAN $\pm$ SD	t-test	P-Value
C-Reactive Protein (mg/L)	0.02 $\pm$ 0.04	0.06 $\pm$ 0.05	-4.894	0.000*
Uric acid ( $\mu$ mol/L)	191.86 $\pm$ 47.50	265.56 $\pm$ 77.10	-5.755	0.000*
ESR (mm/hr)	14.26 $\pm$ 8.31	32.20 $\pm$ 18.85	-6.158	0.000*
Creatine kinase (U/L)	155.47 $\pm$ 88.31	156.26 $\pm$ 117.13	-0.038	0.970
AST (U/L)	15.64 $\pm$ 4.96	18.99 $\pm$ 7.75	-2.576	0.011*

N = 50

\* = Significant at p<0.05

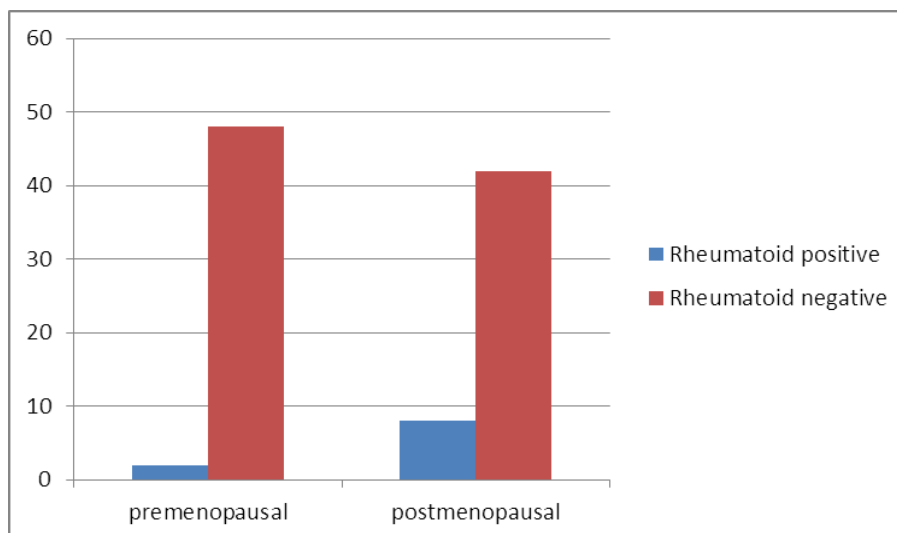
**Table 3: Relationship between the markers in postmenopausal women.**

PARAMETERS	r	p-value
C-reactive protein and Body mass index	0.562	0.000**
C-reactive protein and Erythrocyte sedimentation rate	0.553	0.000**
Body mass index and Erythrocyte sedimentation rate	0.306	0.031*
Erythrocyte sedimentation rate and Uric acid	0.302	0.033*

N = 50

\*\* = Significant at p<0.01

\* = Significant at p<0.05



**Figure 1: Rheumatoid factor in premenopausal and postmenopausal women.**

## DISCUSSION

Metabolic changes and the appearance of many diseases tend to occur following the onset of menopause. These changes include inflammation and muscular damage.<sup>[11,12,13,14]</sup> It was observed that the systolic and diastolic blood pressure increase significantly between premenopausal and postmenopausal women. This increase in blood pressure has been associated with increase in age which reduces the elasticity of blood vessels as well as associated increase in cholesterol level seen in postmenopausal women which leads to vascular stenosis.<sup>[15,16,17,18]</sup> Previous studies have also recorded marked differences in both systolic and diastolic blood pressure with the onset of menopause.<sup>[12,19,20]</sup> The body mass index (BMI) also showed a significant increase in the mean levels in postmenopausal women and this agrees with other researchers.<sup>[21]</sup>

The CRP, ESR and uric acid showed significant increases in the postmenopausal women compared with the premenopausal women and these have been supported by other works.<sup>[22,23]</sup> There was positive correlation between BMI and CRP levels in postmenopausal women. There are several mechanisms which may link adiposity with elevated CRP levels. Adiposity has been shown to be a significant predictor of plasma CRP in post-menopausal women.<sup>[23]</sup> The increase in uric acid in postmenopausal women has been supported by a work on menopause, postmenopausal hormone use and serum uric acid levels in women.<sup>[24]</sup> The work revealed that menopause was associated with higher serum uric acid levels and postmenopausal hormone use was associated with a lower serum uric acid level among postmenopausal women, although, the mechanism is not known.<sup>[24]</sup>

The muscle marker Creatine kinase showed no change between premenopausal and postmenopausal women, whereas aspartate transaminase activity was increased in postmenopausal women. This is in harmony with the work which attributed this rise partly to the liver.<sup>[25]</sup> Some authors suggested that the loss of muscle strength coincides with the estrogen deficit of menopause.<sup>[26]</sup>

It was also observed that the percentage prevalence of positive test for Rheumatoid Factor is 16% within the postmenopausal group. This agreed with the work carried out on prevalence of rheumatoid factor in Nigeria.<sup>[27]</sup> The study found the percentage prevalence in Isheri to be 17% and Igbo-Oro to be 19%.

## CONCLUSION

The study concluded that in postmenopausal women, there is significant increase in the levels of CRP, ESR and uric acid. There is also a significant positive relationship between CRP, ESR and BMI indicating that the degree of changes in metabolites and obesity might have a role in the mediation of inflammation in post menopausal women.

## Conflicts of Interest

The authors declare no conflict of interest.

## REFERENCES

1. Davis, E. M., Utiger, R. D. Menopause (physiology). In *Encyclopedia Britannica*. Encyclopaedia Britannica. Retrieved from (2010) <http://www.britannica.com/EBchecked/topic/375206/menopause>
2. Wluka, A. E., Cicuttini, F. M., Spector, T. D. Menopause, oestrogens and arthritis. *The European Menopause Journal*, 2013; 35(2): 183–199.
3. Samartzis, D. Arthritis (disease). In *Encyclopedia Britannica*. Retrieved from (2013).<http://www.britannica.com/EBchecked/topic/36923/arthritis>
4. Maltais, M., Desroches, J., Dionne, I. J. Changes in muscle mass and strength after menopause. *Journal of Musculoskeletal and Neuronal Interaction.*, 2009; 9(4): 186–197.
5. Nedergaard, A., Karsdal, M., Sun, S., Henriksen, K. Serological muscle loss biomarkers: an overview of current concepts and future possibilities. *Journal of Cachexia and Sarcopenia Muscle.*, 2012; 10: 6–8.

6. Votila, M. High sensitive C-reactive Protein. *Journal of Immunological Methods*. 1981; 42(11): 123–128.
7. Ochei, J., Kolhatkar, A. Common Serodiagnostic Tests. In *Medical Laboratory Science Theory and Practice*, First edition. New Delhi: McGraw-Hill, 2000; 1207–1208.
8. Cheesebrough, M. Measurement of Serum Aspartate aminotransferase. In *District Laboratory Practice in Tropical Countries*, second edition. Cambridge: Cambridge University Press, 2005; 358–361.
9. Panteghini, M. Bais, R. Enzymes. In C. A. Burtis, E. R. Ashwood, D. E. Bruns eds. *Teiz Fundamentals of Clinical Chemistry*. St. Louis: Elsevier Saunders, Sixth edition, 2008; 318–321.
10. Westergren, A. Diagnostic tests: the erythrocyte sedimentation rate range and limitations of the technique. *Triangle; the Sandoz Journal of Medical Science*, 1957; 3(1): 20–25.
11. Sternfeld, B., Wang, H., Quesenberry, C. P., Abrams, B., Everson-Rose, S. A., Greendale, G. A., Sowers, M. Physical activity and changes in weight and waist circumference in midlife women: findings from the Study of Women’s Health Across the Nation. *American Journal of Epidemiology*, 2004; 160(9): 912–922.
12. Coylewright, M., Reckelhoff, J. F., Ouyang, P. Menopause and hypertension: an age-old debate. *Hypertension*, 2008; 51(4): 952–959.
13. Gormsen, L. C., Høst, C., Hjerrild, B. E., Pedersen, S. B., Nielsen, S., Christiansen, J. S., Gravholt, C. H. Estradiol acutely inhibits whole body lipid oxidation and attenuates lipolysis in subcutaneous adipose tissue: a randomized, placebo-controlled study in postmenopausal women. *European Journal of Endocrinology / European Federation of Endocrine Societies*, 2012; 167(4): 543–551.
14. Isayeva, G., Vovchenko, M. [The severity of menopausal symptoms and cardiovascular risk in women]. *Georgian Medical News*, 2014; 231: 21–26.
15. Eferakeya, A. E., Imasuen, J. E. Relationship of menopause to serum cholesterol and arterial blood pressure in some Nigerian women. *Public Health*, 1986; 100(1): 28–32.
16. Casiglia, E., d’Este, D., Ginocchio, G., Colangeli, G., Onesto, C., Tramontin, P., Pessina, A. C. Lack of influence of menopause on blood pressure and cardiovascular risk profile: a 16-year longitudinal study concerning a cohort of 568 women. *Journal of Hypertension*, 1996; 14(6): 729–736.
17. Peter, W. F., Wilson, M. D., Hoeg, J. M., D’Agostino, R. B., Silbershatz, H., Belanger, A. M., Wolf, P. A. Cumulative Effects of High Cholesterol Levels, High Blood Pressure, and

- Cigarette Smoking on Carotid Stenosis — NEJM. *National England Journal of Medicine England Journal Medicus*, 1997; 337: 516-522.
18. Tomiyama, H., Odaira, M., Kimura, K., Matsumoto, C., Shiina, K., Eguchi, K., Yamashina, A. Differences in Effects of Age and Blood Pressure on Augmentation Index. *American Journal of Hypertension*, 2014; 5(1): 54-59.
  19. Schillaci, G., Verdecchia, P., Borgioni, C., Ciucci, A., Porcellati, C. Early Cardiac Changes After Menopause. *Hypertension*, 1998; 32(4): 764–769.
  20. Lima, R., Wofford, M., Reckelhoff, J. F. Hypertension in postmenopausal women. *Current Hypertension Reports*, 2012; 14(3): 254–260.
  21. Suboc, T. M., Dharmashankar, K., Wang, J., Ying, R., Couillard, A., Tanner, M. J., Widlansky, M. E. Moderate Obesity and Endothelial Dysfunction in Humans: Influence of Gender and Systemic Inflammation. *Physiological Reports*, 2013; 1(3): 512-519.
  22. Barinas-Mitchell, E., Cushman, M., Meilahn, E. N., Tracy, R. P., Kuller, L. H. Serum Levels of C-reactive Protein are associated with Obesity, Weight Gain, and Hormone Replacement Therapy in Healthy Postmenopausal Women. *American Journal of Epidemiology*, 2011; 153(11): 1094–1101.
  23. Shende, S. S., Bimanpalli, M. V., Apte, I. C., Mahajan, V. V., Narkhede, H. P. Study of Lipid Profile and C Reactive Protein in Pre- and Post-menopausal Women. *Journal of Clinical and Diagnostic Research*, 2011; 5(8): 1544–1547.
  24. Hak, A. E., Choi, H. K. Menopause, postmenopausal hormone use and serum uric acid levels in US women--the Third National Health and Nutrition Examination Survey. *Arthritis Research & Therapy*, 2008; 10(5): R116.
  25. Suchetha, Kumari, N., Rosario, S. B., Gowda, K. M. Altered Liver Function and the Status of Calcium in Postmenopausal Women in and Around Mangalore. *Al Ameen Journal of Medical Sciences*, 2010; 3(2): 115.
  26. Cooper, R., Mishra, G., Clennell, S., Guralnik, J., Kuh, D. Menopausal status and physical performance in midlife: findings from a British birth cohort study. *Menopause*, 2008; 15: 1079–1085.
  27. Greenwood, B. M., Muller, A. S., Valkenburg, H. A. Rheumatoid factor in Nigerian sera. *Clinical and Experimental Immunology*, 1971; 9(2): 161–173.