

## Deciphering the Clinico-Biochemical Mileau of Perimenopausal and Postmenopausal women with a note on beneficial effects of Yoga and Exercise

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### Abstract

**Background & Objectives:** Psychosomatic disturbances faced by women approaching their fifth decade have been a matter of concern since many years. Many approaches have been tried to help them, including nutritional, pharmacologic and hormone replacement therapies. However, the importance of regular yoga practice is not much debated though it is believed to improve blood glucose levels & serum lipid concentrations and also to combat oxidative stress. The current study was designed to broadly analyze the clinico-biochemical challenges encountered by such women and to suggest better measures to face them.

**Methods:** A total of 90 women aged around 40-60 years were grouped into perimenopausal, postmenopausal and healthy control groups and were checked for anthropometric and biochemical parameters like FBS, HbA1c, lipid profile, calcium, magnesium, copper, ceruloplasmin, TSH, uric acid, alkaline phosphatase (ALP) and total proteins.

**Results:** Age of the subjects, their BMI, blood pressure and waist hip ratio (WHR) together with levels of glycated Hb, LDL cholesterol, TGs, calcium, magnesium, copper, ceruloplasmin and uric acid levels exhibited significant variation among the groups.

**Conclusions:** Several psychosomatic changes encountered in and around menopause and few biochemical changes can be better handled by persistent yoga practice, either alone or in combination with conventional treatment, as it can effectively bring down the oxidative stress levels, chances of developing metabolic syndrome, risk of CVD events and improve the quality of life in such women.

**Keywords:** Perimenopause, Postmenopause, FBS, HbA1c, Lipid profile, Calcium, Yoga

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### Introduction

Cessation of menstrual cycling process for a year in row would be aptly called Menopause and this happens at around 45-55 years<sup>1</sup>. Perimenopausal period, lasting for nearly 7 years, is merely the time period around menopause, which includes before menopause, during and after menopause<sup>2</sup>. This period of worsening ovarian functions is characterized by a steady decline in estrogen level and rising levels of progesterone, FSH and LH, leading to various major issues like increased risk of cardiovascular events, vascular complications, altered bone and lipid metabolism, changes in coagulation pathway & fibrinolytic system, alteration in the volume & frequency of bleeding<sup>1,2</sup>.

Most common problems encountered due to menopause induced hormonal changes are hot flushes, depression, incontinence of urine, its urgency, infections of bladder, urethra & vagina, painful coitus, atrophy of epithelial cells and tissues, oral dryness and intense burning sensation affecting lips, tongue & gums

and osteoporosis<sup>1,3</sup>. Thus, perimenopausal women are affected by numerous general and systemic problems like anxiousness and mood disturbances thus affecting their day to day activities. Further, these symptoms start encroaching their lives slowly and cause significant problem over a span of time<sup>4</sup>.

Menopause is not without changes in body composition such as an increase of fat mass, changes in glucose homeostasis and changes in mineral metabolism, thus interfering with optimum functioning of various organ systems. In this context, the role of physical activity in counteracting the changes in body composition has been well established. Moreover, many observational and interventional studies have demonstrated that hormonal therapy combined with an exercise program can produce a synergistic effect on fat mass and insulin sensitivity<sup>5</sup>. This provoked several researchers to try solving the issues with little variation in day to day practices like consuming nutritious food and skipping the junk, indulgence into spiritual practices, physical exercise, Ayurveda and homeopathy therapies<sup>2</sup>.

Yoga is one such better alternative, consisting of several yogasanas, pranayama and meditation that can effectively improvise psychosomatic symptoms associated with deadly diseases like hypertension, diabetes, musculo-skeletal, neuroendocrine, excretory, cardiovascular, respiratory and GI system disorders. It is also effective in counteracting stress and reducing

body weight<sup>2,4</sup>. Thus, present study was designed keeping in mind various biochemical alterations and physiological risk factors in perimenopausal and menopausal age groups.

### Materials and Methods

This study was conducted at a tertiary care hospital in Karnataka, after obtaining approval by its IEC committee. The study was conducted in 30 women with perimenopausal symptoms, aged between 40-52 years and 30 postmenopausal women between the age groups 50-60 years. 30 age matched women with no known risk factors and having normal levels of biochemical parameters were considered as controls<sup>3</sup>. Excluded from the study were those women who underwent uterine resection, those receiving hormone replacement therapies and those having other systemic disorders. The study procedure was explained to those women and consent was obtained. The importance of regular exercise and yoga practice was stressed to them.

The study procedure and its purpose were explained to each of the participant. After taking their anthropometric measurements and measuring their blood pressures, fasting blood sample was collected from their antecubital vein. Randox Daytona Autoanalyzer was used to measure Glucose (Glucose oxidase-peroxidase method), HbA1C (Ion Exchange Method), serum cholesterol (cholesterol oxidase method), HDL-cholesterol (measured by same enzymatic assay using the supernatant obtained after precipitating other components) and serum triglycerides (GPO-PAP method). Friedwald's formula was then

used to calculate LDL-cholesterol. Serum copper, calcium and ceruloplasmin were analyzed spectrophotometrically. Magnesium (Xylidyl Blue Method), TSH (Two-site sandwich immunoassay), Uric acid (Uricase Method), Alkaline phosphatase (ALP AMP method) and total protein (Biuret rmethod) were also measured using same autoanalyzer. Statistical analysis was performed using Microsoft Excel 10 and SPSS version 16 and the values were reported in terms of mean and standard deviation (mean±SD). 95% confidence level was used as cut off to know if the difference obtained was significant.

### Results

The study was conducted on 90 subjects: 30 each of perimenopausal (group 1), postmenopausal (group 2) and age matched controls (group 3). Age of the subjects under various groups, together with their blood pressures and anthropometric measurements exhibited high statistical significance, as has been summarized in the Table.

Glycated Hb, LDL cholesterol, TGs, calcium, magnesium, copper, ceruloplasmin and uric acid levels exhibited significant variation among the groups. Differences were also found in levels of FBS, Total Cholesterol and TSH, but they were not statistically significant. Although ALP level was relatively increased in perimenopausal women, it exhibited no significant significance. Total serum protein was more or less same in all three groups. Results have been summarized in Table 1.

**Table 1: Table showing clinical data and biochemical parameters of subjects under various groups**

Parameters	Perimenopausal women (group 1, n = 30)	Postmenopausal women (groups 2, n = 30)	Control group (group 3, n = 30)
Age (yrs) ¥	44.07±4.01	55.75±1.71	46.8±13.5
BMI (kg/m <sup>2</sup> ) ¶	27.0±0.3	27.3±0.5	26.9±0.5
Systolic BP (mm Hg) ¥	131.45±9.23	142.25±12.23	118.00±10.43
Diastolic BP (mm Hg) ¥	85.69±9.04	89.90±9.34	78.70±8.87
FBS (mg/dl)	108.59±29.22	110.26±31.95	106.59±26.88
HbA1c (%) P	6.28±0.81	6.34±0.84	6.22±0.83
Total Cholesterol (mg/dl)	206.31±33.92	208.27±35.85	204.00±35.02
HDL Cholesterol (mg/dl)	49.12±11.32	48.92±12.64	49.77±10.86
LDL Cholesterol (mg/dl) P	130.64±30.36	132.20±31.76	127.68±29.32
Triglycerides (mg/dl) ¥	109.36±9.2	113.8±10	103.1±7.8
Calcium (mg%) ¥	7.34±0.35	7.50±1.73	8.24±0.12
Magnesium (mg/dl) P	1.924±0.418	2.071±0.363	1.871±0.434
Copper (µg/dl) ¥	110.926±20.629	99.972±24.245	126.559±29.823
Ceruloplasmin (mg/dl) P	36.924±9.27	38.151±12.777	31.923±10.029
TSH (µIU/ml)	2.87±0.3	2.98±0.3	2.8±0.4
Uric acid (mg%) P	5.33±1.44	5.00±0.89	4.66±0.26
ALP (KAU)	11.29±18.29	7.25±3.50	7.15±2.46
Total Protein (g%)	7.33±0.47	7.55±0.30	7.18±0.11

¥ -  $p < 0.001$ , ¶ -  $p = 0.002$ , P -  $p < 0.05$

## Discussion

Menopause is one of the key events in a woman's life. Effective addressal of health care issues of menopausal women involves two vital issues, i.e., control of menopause associated symptoms on one side and prevention & management of disorders secondary to menopause like metabolic syndrome, osteoporosis, cancer, neuro-degenerative diseases, cardiovascular diseases etc on the other side. All these disorders can also be due to menopause induced hormonal variation, one of its biggest consequences being oxidative stress. Thus, special care and attention are needed to tackle these issues, so that these women lead a healthy life<sup>2</sup>.

Depression complained by postmenopausal women can be because of the loss of the effect of estrogen in regulating neuronal excitability and synaptic plasticity. Further, irregular uterine bleeding, a characteristic symptom of perimenopausal women could be due to exhaustion of ovarian receptors & its resistance to the action of gonadotropins and also due to raised FSH levels. Further, estrogen deficient state causes skin thinning (by decreasing its collagen and elastic fibers), dehydration, reduces vascularity thus compromising nutrient supply and oxygen delivery. Additionally, aging factor by itself declines the physiological functions further, like reduced muscle mass and strength<sup>1</sup>. Oxidative stress is also well known to result in estrogen deficiency<sup>2</sup>.

A recent study found that aerobic exercise training even in a low intensity promoted reductions in blood pressure in postmenopausal women by improving their endothelial functioning, showing how change in lifestyle is favorable in preventing cardiovascular events. Health benefits of exercise training are related to activation of NO/cGMP signaling pathway<sup>6</sup>. Physical activity helps prevent osteoporosis not only by regulating bone metabolism & by stimulating osteogenesis (by increased mineral accumulation), but also by concomitantly restoring the balance through muscle strengthening action, thus reducing the overall incidence of fractures due to falls<sup>3</sup>. Persistent practice of yoga leads to reduced activation of HPA axis and the sympatho-adrenal system, thus improving parasympathetic tone and reduced cardiovascular morbidity and mortality and even insulin resistance syndrome (IRS)<sup>2</sup>.

An abnormal atherogenic lipid profile, together with an elevated serum glucose and Glycated Hb is almost always encountered with progressing menopause. This may be due to one or more of the following reasons: ovarian failure leading to estrogen deficiency, advanced age, central redistribution of body fat contributing to progression of coronary atherosclerosis etc<sup>1</sup>. It also results in the development of hyperglycemia, hyperinsulinemia, obesity and even hypertension<sup>1,4</sup>. Thus, menopause can aptly be considered as an independent factor for development of metabolic syndrome<sup>1</sup>. Also, psychosomatic stress in such women leads to increased secretion of cortisol, resulting in hyperglycemia, insulin resistance and risk of metabolic syndrome<sup>2</sup>. Altogether, this phase of

menopausal transition is representative of changes in hormonal balance<sup>1</sup>.

Immediate symptoms and long term consequences of menopause, including visceral fat deposition could be managed successfully with hormone replacement therapies (HRT), which helps prevent the gain of fat mass and alterations in lipid profile & insulin sensitivity<sup>2,5</sup>. But, unfortunately it raises new worries about risk of developing endometrial & breast cancers, vaginal bleeding etc<sup>2</sup>. Furthermore, one of the studies showed that estrogen-progestin combination therapy may even increase the risk of CVD among otherwise healthy postmenopausal women. Thus, the use of hormone therapy has become controversial<sup>5</sup>. Since a number of clinical features of perimenopausal women are shared with those of adult growth hormone (GH) deficiency, the use of recombinant human growth hormone (rhGH) to increased serum IGF-1 levels was proposed in elderly subjects<sup>7</sup>.

Oxidative stress related issues observed in peri- and postmenopausal women is mainly due to hypoestrogenism, since estrogen has an antioxidant effect during reproductive span of a woman<sup>2</sup>. Oestrogen deficiency due to oophorectomy without hormone replacement contributes to low postmenopausal bone mass and osteoporotic fracture<sup>3</sup>. With advancing age in women, decreased level of estrogen reduces the calcification process. Further, a longitudinal study has demonstrated decreased calcium absorption during perimenopause<sup>4</sup>. Hypocalcemia in both perimenopausal and postmenopausal groups may also be due to low dietary calcium intake during childhood or adolescence, which will also be reflected in premenopausal BMD levels. Dietary calcium is thought to function as an 'enabler', allowing the skeleton to interact with both genetic and environmental characteristics. Calcium deficiency in perimenopausal women not only leads to osteoporosis, but also restlessness and wakefulness. Raised level of serum calcium can also be associated with hypertension and could be a risk factor for cardiovascular events. Oestrogen deficiency even in premenopausal women may induce excessive bone resorption and result in reduced peak bone mass<sup>3</sup>. Magnesium intake not only relieves mood disorders, but also helps in preventing osteoporosis, bone mineral density loss and in regulating body temperature. It also takes care of menopause associated palpitations and hot flushes. Copper cross links collagen and elastin fibres. Copper deficiency causes bone growth arrest and thus

osteoporosis<sup>4</sup>. Ceruloplasmin, in addition to being a late response acute phase reactant, acts as a free radical scavenger<sup>4</sup>.

Nearly, a quarter of perimenopausal women experience hypothyroidism, which acts as an independent risk factor for MI in these women<sup>2</sup>. However, we didn't encounter this. Level of serum uric acid was low in postmenopausal group when compared to perimenopausal group, although both were within normal limits. A study reported that antioxidant defences are markedly decreased in osteoporotic women. Our results, in liaison with few other studies, show a decreased level of ALP in postmenopausal women as compared to perimenopausal women, although both fall within the reference range. A study observed that ALP acts as a phenotypic marker too, for early-stage differentiated osteoblasts. Total serum protein was found to be normal in both groups of patients. This study is in contrast to the study which observed low protein level in both groups of patients. Few other studies also found a normal level of protein but one such study debated that animal proteins are associated with an increased incidence of osteoporotic fractures<sup>3</sup>.

Various efforts have been put to combat oxidative stress: dietary therapy (nutritional supplements rich in antioxidants) and pharmacologic therapy (Menopause hormonal therapy, Selective estrogen receptor modulators etc). Old traditional methods, describing yoga, is one of the important therapies to counter oxidative stress, that caused due to menopause too. Physically active subjects are known to have more longevity and less morbidity<sup>2,6</sup>. It is also vital in slimming the individual (by reducing waist circumference), improving BMI, glycemic index (by increasing sensitivity of pancreatic  $\beta$ -cells to glucose, increasing insulin binding receptors as well as by inducing insulin- receptor interaction), hypertension, insulin resistance, and lipid metabolisms<sup>2</sup>. Thus, an overall improvement in mineral status and climacteric symptoms of peri- and postmenopausal women suggests that regular yoga practice can definitely improve their quality of life. Irrespective of improvement in bone mineral status, muscular strength, endurance & balance, yoga practice reduces fracture risk to a great extent by reducing the risk of falling<sup>4</sup>.

Yoga is believed to increase calcium absorption too. Serum copper status is also believed to improve after yoga sessions. Copper, a component of superoxide dismutase (an antioxidant enzyme) might combat oxidative stress. Following yoga intervention, magnesium concentration in serum of perimenopausal women markedly reduced in one of the studies and is thought to be because of its role in improvement of vasomotor symptoms (by regulating body temperature), thus making them feel more comfortable, with less mood swings. Serum ceruloplasmin levels are found to increase as the menopause approaches. Yoga

intervention decreases serum ceruloplasmin levels also, and this is due to its antioxidant function. Ceruloplasmin might have thus been utilized to reduce stress, depression and anxiety. Several studies have clearly shown the beneficial effects of yoga in managing several systemic diseases including musculoskeletal, gastrointestinal, neuroendocrine, respiratory and cardiovascular systems<sup>4</sup>.

## Conclusion

Following a plethora of observations, our study conveys the message that certain inevitable physical and psychological changes encountered in and around menopause, together with significant biochemical changes can be better handled by persistent yoga practice. Not only the symptoms, but also the root causes of menopause induced changes including oxidative stress can be mitigated effectively by yoga. Timely intervention into issues related to modifiable risk factors is important even in menopause related changes as in any other systemic disease. Thus yoga sessions alone or in combination with conventional treatment methods can effectively decrease the incidence of complications due to oxidative stress, CVD disasters, metabolic syndrome and improve the quality of life in perimenopausal and postmenopausal women. Nonetheless, further studies with more robust designs may yield better outcomes by means of better understanding.

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