Original article:

A comparative study of hematocrit & mean arterial blood pressure in perimenopausal women

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ABSTRACT:
Background: Pre-menopausal women have decreased risk of atherosclerosis & coronary heart disease compared to age matched males. The aim of this study was to compare between Hematocrit & Mean arterial pressure, with increase of age in women.

Materials & Methods: 90 healthy women of age group 25-55 years were selected from the general population & the data is collected by grouping them in to 3 groups, based on their age: 25 – 35 years age; 36 - 45 years age & 46 - 55 years age. A general physical examination involved the measurement of height & weight. Body Mass Index, Hematocrit (Hct)  & Mean Arterial Blood pressure ( MABP ) were measured.

Results: When the MABP was compared between group I and group II , group I and group III , group II and group III women , we found a significant increase in the MABP in group II women , group III and group III respectively . When the Hct was compared between group I and group II women, group I and group III, group II and group III women, we found a significant decrease in Hematocrit in group II women , group III and group III respectively.

Conclusion: The significant findings of this study were that pre and postmenopausal women did not present a significant difference in Hematocrit and weight (in all age groups) with the exception of blood pressure, which was significantly elevated in the Postmenopausal women.

Keywords: Mean Arterial Blood pressure (MABP) , Hematocrit (Hct), Body Mass Index (BMI), Menopause

INTRODUCTION:
Menopause refers to the cessation of menstruation permanently due to loss of ovarian follicular activity which leads to a decrease in estrogen secretion, which is responsible for majority of the features seen in menopausal women. The steep rise of cardiovascular morbidity & mortality in menopause, related to coronary artery disease & stroke, was due to cardiovascular risk factors such as dyslipidemia, diabetes, obesity & hypertension leading to arterial stiffening & consequent decreased baroreflex sensitivity. Variations in hematocrit and blood viscosity change shear stress on the endothelium leading to the production of vasoactive substances such as nitric oxide (NO), prostacyclin, and endothelin, which have a direct effect on diameter of micro vascular vessels. Menopause was associated with a reduction in estradiol and a decrease in estrogen to testosterone ratio. This leads to endothelial dysfunction and increase in body weight.
(body mass index i.e., BMI) or type II diabetes, which cause an increase in sympathetic activation, seen in Post Menopausal Women. Sympathetic activation can result in increased renin release and increases in angiotensin II (Ang II).

In the absence of chronic pre-existing conditions such as diabetes, pre-menopausal women have a favorable cardiovascular phenotype compared with age-matched men, largely due to the vasoprotective role of ovarian steroids such as estrogen. An alteration in circulating sex hormones at menopause, like a decrease in estrogens and a relative excess of androgens, was associated with the conversion to high risk cardiovascular profile.

Ageing of the Vascular system is a complex process characterized by sustained proinflammatory and proconstrictor changes in the vascular microenvironment leading to structural and functional alterations seen in systemic vasculature and increased risk of cardiovascular diseases such as hypertension, myocardial infarction and stroke in the ageing population. In ageing, increased oxidative stress and inflammatory activity lead to changes in the cardiovascular system. This affects vessel wall structure, passive mechanical properties. The process of vascular ageing includes endothelial dysfunction accompanied by reduction in Nitric Oxide (NO) and increase in endothelin, which is common in Post Menopausal Women. The increase in Angiotensin II and endothelin and the reduction in NO may all lead to increased oxidative stress which contributes to renal vasoconstriction leading to hypertension.

According to existing literature, it was observed that a slight but significant increase of BMI is seen in menopausal women when compared to reproductive group. Also, menopausal women showed a higher prevalence of visceral adipose tissue distribution than fertile women & visceral fat influences sympathetic activity. Increased BMI & redistribution of the adipose tissue contribute to blood pressure variability in menopausal women.

Endothelial cell activation by stressful stimuli such as pro-inflammatory cytokines and reactive oxygen species (ROS), impair many endothelium-dependent vasoprotective functions, which precede the onset of symptomatic cardiovascular disease. A progressive decline in nitric oxide (NO) mediated vascular relaxation with age has been documented by numerous studies in humans and animal arteries. In females, estrogen regulates various signaling pathways in the vascular cells which are protective to the vessel structure and function, both long term and rapid. These include modulation of vascular tone by both the endothelium-dependent mechanisms and the mechanisms inherent to the Vascular Smooth Muscle Contraction. In addition, antioxidant, anti-inflammatory and antiproliferative pathways modulated by estrogen protect against vessel injury from exposure to the vascular risk factors. The relationship between blood viscosity and Mean Arterial Pressure was shown to be mediated by NO production by Martini et al.

Ageing was also associated with changes in the coagulation and fibrinolysis (DeSouza CA, Jones PP, and Seals DR). Postmenopausal women exhibit higher fibrinogen levels and lower levels of endogenous fibrinolysis [manifested as higher tissue plasminogen activator (tPA) antigen and lower plasminogen activator inhibitor-1 (PAI-1) activity] compared with pre-menopausal women, which partially explain their increased risk of Cardiovascular Disease. Clinical studies conclude that estradiol reduces circulating levels of homocysteine...
in postmenopausal women. Homocysteine contributes to vascular disease by inducing endothelial cell damage, inhibiting endothelial cell growth and inducing smooth muscle cell growth.

**MATERIALS & METHODS:**

90 healthy women aged 25-55 years were selected from the general population & the data is collected by grouping them in to 3 groups, based on their age: GROUP-1: Women of 25 – 35 years age GROUP-2: Women of 36 - 45 years age GROUP-3: Women of 46 - 55 years age. An approval was obtained from Institutional Ethical committee.

**Exclusion criteria:** Women receiving oral contraceptive pills / hormone replacement therapy, Women who underwent hysterectomy with or without oopherectomy, Women with any family history of hypertension/ diabetes or women undergoing anti-hypertensive treatment, Women with any history of hematological diseases/ ovarian & uterine dysfunctions (Menstrual disorders).

**RESULTS:**

<table>
<thead>
<tr>
<th>Group</th>
<th>BMI Kg/m²</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
<th>MAP (mm Hg)</th>
<th>Hct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>21.57 ±2.28</td>
<td>117.67 ± 8.17</td>
<td>77.6 ± 6.61</td>
<td>90.8 ± 5.58</td>
<td>39.6±2.24</td>
</tr>
<tr>
<td>Group II</td>
<td>22.58 ±2.65</td>
<td>128 ± 6.64</td>
<td>79.33 ± 8.68</td>
<td>95.53 ± 6.96</td>
<td>37.93±2.85</td>
</tr>
<tr>
<td>Group III</td>
<td>25.29 ±3.95</td>
<td>139.33± 7.39</td>
<td>88 ± 7.14</td>
<td>105.16 ± 6.18</td>
<td>36.5±2.73</td>
</tr>
</tbody>
</table>
The systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and packed cell volume in women of age group 25-36 (Group I) is 117.67 ± 8.17 mmHg; 77.6 ± 6.61 mmHg; 90.8 ± 5.58 mmHg and 39.6 ± 2.24 respectively. The systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and packed cell volume in women of age group 36-45 (Group II) is 128 ± 6.64 mmHg; 79.33 ± 8.68 mmHg; 95.53 ± 6.96 mmHg and 37.93 ± 2.85 respectively. The systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and packed cell volume in women of age group 46-55 (Group III) is 139.33 ± 7.39 mmHg; 88 ± 7.14 mmHg; 105.16 ± 6.18 mmHg and 36.5 ± 2.73 respectively.

When the MABP was compared in group I and group II women, we found an increase in the MABP in group II women (5.2% increase) (p value = 0.0052). When the MABP was compared in group I and group III women, we found a significant increase in the MABP in group III women (15.81% increase) (p value < 0.0001). When the MABP was compared in group II and group III women, we found a significant increase in the MABP in group III women (10.08% increase) (p value < 0.0001).

When the Hct was compared in group I and group II women, we found a decrease in Hct in group II women (4.21% decrease) (p value = 0.0146). When the Hct was compared in group I and group III women, we found a significant decrease in Hct in group III women (7.8% decrease) (p value < 0.0001). When the Hct was compared in group II and group III women, we found a decrease in Hct in group III women (3.77% decrease) (p value = 0.0513). This study shows that there is a significant change in Hct between pre- and postmenopausal healthy women.

**DISCUSSION:**

Several studies have reported adverse effects of menopause on serum concentrations of triglycerides, low density lipoprotein cholesterol (LDL cholesterol), diastolic blood pressure, and body mass index. Although it is difficult to segregate the effect of menopause on cardiovascular risk factors from that of age, changes in hemorheological profile in menopausal women was not clearly understood. However age, smoking, obesity & menopausal status could be the possible mechanism. Blood viscosity and its determinants were important risk factors for the development of early atherosclerosis in menopausal women. Menopausal women are at increased risk of development of Coronary artery disease.

In general the prevalence of hypertension increase more steeply in women than men after middle age. The risk of coronary heart disease in women rises with increasing age, body weight, blood pressure, cigarette smoking & decreased exercise 19, 20, 21. The changes related to increased age were deleterious as Serum triglycerides, diastolic pressure, weight (BMI), and LDL cholesterol showed significant increase. The older the women were premenopausally, the greater the increase in serum triglycerides adjusted for HDL cholesterol levels and the greater their rise in blood pressure; the younger the women, the greater their increase in relative weight 22. Cardiovascular Disease (CVD) is the major cause of death in women (American Heart Association) and the risk of developing CVD increases after menopause 23.

Although the mechanisms which appear to be involved in the antioxidant properties of estrogen were not clear, many hypotheses have been put forward regarding the role of estrogens. Estrogens act
as free radical scavengers interacting with the free radical chain formation produced from membrane oxidation processes and inhibiting lipid peroxidation.

One longitudinal study suggested that in healthy normotensive women, ovarian senescence protects against increasing BP with a negative association between years after menopause and systolic and diastolic BP. Ageing was associated with an insignificant increase in systolic BP only; however, increased BMI was associated with hypertension. Increased arterial stiffness coincides with menopause. Postmenopausal women more frequently have many traditional vascular disease risk conditions (e.g., diabetes, obesity, hypertension, inactivity, etc) which occur and cluster more frequently in women than men. Ageing attenuates many estrogen-related potentially beneficial responses. The renin-angiotensin (RAS) system is an important regulator of BP, Fluid and Electrolytes. Estradiol may provide cardiovascular protection by controlling components of the RAS, including decreasing AT1 receptor expression in vessels and kidney and reducing the activity of angiotensin 1-converting enzyme (ACE). Owens JF, Stoney CM, Matthews KA et al. studied about the influence of menopause and stress on blood pressure. They observed that Postmenopausal women had higher stress-induced SBP & DBP rise than premenopausal women or men. Diastolic BP was higher in post-menopausal women and men compared to pre-menopausal women. Staessen JA, Ginocchio G, Thijs L et al. prospectively studied the relation between blood pressure and menopause in pre, peri and post menopausal women. They concluded that the increase in SBP was 5 mm Hg per decade which is more in peri and postmenopausal than in premenopausal women. Simmi Kharb conducted studies in menopausal women and found that Menopausal women had significantly higher total cholesterol as compared to premenopausal women. Also, fibrinogen and hematocrit levels were higher in menopausal women as compared to premenopausal women. Blood viscosity was significantly higher in menopausal women. Triglyceride, LDL-cholesterol and HDL-cholesterol levels were higher in menopausal women and a positive correlation between hematocrit and viscosity levels was observed in menopausal women. Letcher RL, Chien S, Pickering TG, and Laragh JH et al. observed that higher Hct values in Hypertensive patients than normotensive control individuals. Aging is associated with an increased incidence of cardiovascular disease. Premenopausal women are relatively protected from vascular alterations compared with age-matched men, likely due to higher levels of the female sex hormones. However, these vasoprotective effects in women are attenuated after menopause. Thus, the vascular system in aging women is affected by both the aging process as well as loss of hormonal protection, predisposing women of this age group at a higher risk for cardiovascular diseases such as hypertension, myocardial infarction, and stroke. The endothelin system and endothelin-1 (ET-1) in particular plays an important role in the pathogenesis of vascular dysfunction associated with aging. Female sex steroids can interfere with the vascular expression and actions of ET-1 by several mechanisms, which may further contribute to pathological processes in the vasculature of aging women. Postmenopausal women are at a dual disadvantage related to their cardiovascular health: aging by itself contributes to increased oxidative stress and vascular degenerative processes, which are further aggravated by the loss of vasoprotective effects of the female sex hormones at menopause.
CONCLUSION: The major limitation of the present study is the cross sectional design and it is important that future longitudinal studies be conducted to confirm our findings from this cross-sectional design. The principle findings of this study were that pre and postmenopausal women did not present a significant difference in Hematocrit and weight (in all age groups) with the exception of blood pressure which was significantly elevated in the Postmenopausal women.

REFERENCES:
3) Lewis SJ ; Cardiovascular disease in postmenopausal women: myths and reality; Am J Cardiol 89: 5E–10E; discussion 10E–11E, 2002.
19) Correa JM, Becker RC, Hamilton GA; Coronary heart disease in women; Cardiology 1990; 77 (Suppl.):8-24.
26) Dubey RK, Oparil S, Imthurn B, Jackson EK; Sex hormones and hypertension; Cardiovasc Res.2002;53;688-708.
27) Owens JF, Stoney CM, Matthews KA; Menopausal status influences ambulatory blood pressure levels and blood pressure changes during mental stress; Circulation. 1993; 88:2794 –2802.
29) Simmi Kharb; Association Between Rheology and Lipoproteins in Menopausal Women; JK Science ;Vol. 10 No. 1, January-March 2008.