

## THE INCREASE IN PULSE PRESSURE IN THE EARLY AGE POST MENOPAUSE WOMEN IN LOCAL POPULATION AS A MARKER OF PRECLINICAL CARDIOVASCULAR DISEASE

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### ABSTRACT

#### Objective:

To determine the post menopausal changes of pulse pressure in the early age menopause women.

#### Methodology:

A cross sectional and comparative study, was performed at the department of Physiology B.M.S.I., J.P.M.C., Karachi in collaboration with the Abbasi Shaheed Hospital and National Institute for Cardiovascular Diseases, Karachi.

This study included a total of 100 women, 50 with early age post menopause and 50 with normal age post menopause. For the statistical analysis , the degree of probability was computed by comparing the calculated value of "t" with tabulated value in the table of "t" distribution against the degree of freedom.

#### Results:

Pulse pressure was found to be significantly increased with a P-value of <0.001 in the early age post menopause women.

#### Conclusion:

This suggests that an early age post menopause is more likely to develop a marker of preclinical cardiovascular disease such as increased pulse pressure.

#### Key words:

Early age post menopause. Normal age post menopause. Pulse pressure.

Marker of preclinical cardiovascular disease. Cross sectional study.

### INTRODUCTION

Pulse pressure (PP) is the change in blood pressure seen during a contraction of the heart. Formally it is the systolic pressure minus the diastolic pressure, measured in mmHg. Usually the resting pulse pressure (PP) in healthy adults is 40 mmHg. Various studies show that a high pulse pressure is linked to an increased risk of heart attack, stroke and heart failure.<sup>1</sup>

Pulse pressure is the strong predictor of primary outcome and all cause cardiovascular mortality.<sup>2</sup> High brachial PP is not a cardiovascular risk factor, such as arterial hypertension, but rather a marker of preclinical cardiovascular disease.<sup>3</sup> The pulse pressure, i-e the difference between systolic and diastolic blood pressures, is a crude but a readily acquired measure of arterial stiffness. For every 10 mmHg rise in the pulse pressure, there was a 15% increase in risk for coronary heart disease and a 32% increase in the risk for death from a stroke.<sup>4</sup>

Prognostic effect of Brachial PP on coronary heart disease was stronger than that of systolic BP. At each level of systolic BP, the risk was in fact higher when diastolic BP was lower, suggesting more severe arterial stiffness. Therefore, there is evidence that both PP and other measures are more

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directly associated with arterial stiffness sharing a similar pattern of relations with CV risk factors and prediction of mortality.<sup>5</sup>

Thus the pulse pressure appears to be the best single measure in predicting cardiovascular mortality in older people and helps in understanding the results for low diastolic blood pressure.<sup>3</sup>

Menopausal age is defined retrospectively when menstrual bleeding has stopped for one year.<sup>6</sup> Cessation of menstruation between the ages 45 to 55 years is said to be a menopause.<sup>7</sup> In Pakistan, the mean age at menopause has been found to be 49 years(+/-3.6 years) in rural areas and 47 years in urban areas.<sup>8</sup> Thus resulting in no ovulation, low or absent estrogen and high levels of FSH and LH, is the picture of menopause.<sup>9</sup>

Women were defined as naturally post menopause or normal age menopause if they had not been menstruating for the past 2 years and reported their menopause was natural. The average age of menopause is around 50 years with majority going through it with 45 - 55 years of life. Age ranges, some as young as 40, other as old as 60. Menopause before 45 years of age, is considered to be early age menopause.<sup>10</sup>

Spontaneous cessation of ovulatory function before age 45 was associated with an increased risk of myocardial infarction as compared with women who had a natural menopause at age 50 or older.<sup>11</sup>

Cardiovascular mortality have been found to be greater in women with age at menopause lower than age 45 years as compared to women with later age at menopause.<sup>12</sup>

Our purpose of study was concerned in finding out the changes of pulse pressure in two different menopausal age groups. As an increased pulse pressure, is a marker of preclinical cardiovascular disease, is likely to be found in the menopausal group which has more chance to develop the incidence of cardiovascular disease.

## METHODOLOGY

This was a cross sectional and comparative study conducted in the department of B.M.S.I., J.P.M.C. in collaboration with Abbassi Shaheed Hospital and National Institute of Cardiovascular Diseases, Karachi.

A total sample of 100 post menopausal women, was selected for the study. 50 women with a history of cessation of menstruation since 2 years, ages between 40 – 45 years, were selected as early age post menopause. Whereas, 50 women as normal age post menopause consisting of women with a history of cessation of menstruation since 2 years ,ages between 50 – 58 years.

Brachial pulse pressure was calculated as the difference between systolic blood pressure and diastolic blood pressure, by a mercury type of sphygmomanometer in mmHg.<sup>13</sup>

2 ml of venous blood was drawn from all participants under aseptic conditions ,after taking their consent. After centrifugation, serum were stored at - 20 degree centigrade. Serum follicle stimulating and serum leutinizing hormones were measured by enzyme linked immunoassay.

## STATISTICAL ANALYSIS

The degree of probability was computed by comparing the calculated value of “t” with tabulated value in the table of “t” distribution against the degree of freedom. The difference with mean values of the two groups was regarded as statistically significant, if the P-value was less than 0.05 and it was taken as highly significant if P-value was less than 0.001. Correlation coefficient was detected using Pearson coefficient of correlation SPSS-10. For data feeding the computer package Microsoft Excel was used. Only P-value (<0.05) are considered significant.

## INCLUSION CRITERIA

Non obese, non hypertensive and non hysterectomized women who were experiencing meno-

pause, were included in our study. All the subjects were having normal electrocardiographs, fasting blood sugar under normal limits and hemoglobin = 11 g/dl or above. Overall, they were apparently healthy subjects.

#### EXCLUSION CRITERIA

All the subjects having history of smoking, any malignancy or psychiatric disorder, were not included in this study. Subjects on hormone replacement therapy and known cardiac patients, were also excluded from this study.

**TABLE 1**  
COMPARISON OF AGE, HEIGHT AND WEIGHT IN NORMAL AGE MENOPAUSE AND EARLY AGE MENOPAUSE.

(Values are expressed as Mean  $\pm$  SEM)

Variables	Normal Age Menopause	Early Age Menopause
Age(years)	53.52 $\pm$ 0.44	42.08 $\pm$ 0.36*
Height(Meters)	1.55 $\pm$ 0.007	1.56 $\pm$ 0.008
Weight(kg)	63.52 $\pm$ 1.36	64.30 $\pm$ 1.51

\*showing a significant difference at P-value<0.05

**TABLE 2**  
COMPARISON OF PULSE PRESSURES BETWEEN NORMAL AGE MENOPAUSE AND EARLY AGE MENOPAUSE

(Values are expressed as Mean  $\pm$  SEM)

Variable	Normal Age Menopause	Early Age Menopause
Pulse Pressure mmHg	35.90 $\pm$ 1.68	50.10 $\pm$ 1.28**

\*\*showing highly significant difference at P-value <0.001

**TABLE 3**

COMPARISON OF BLOOD PRESSURE, FOLLICLE STIMULATING HORMONE (FSH) AND LEUTINIZING HORMONE(LH) BETWEEN NORMAL AGE MENOPAUSE AND EARLY AGE MENOPAUSE

(Values are expressed as Mean  $\pm$  SEM)

Variables	Normal Age Menopause	Early Age Menopause
Systolic Blood Pressure (BP) mmHg	124.62 $\pm$ 2.35	124.38 $\pm$ 1.98
Diastolic Blood Pressure (DBP) mmHg	89.32 $\pm$ 1.35	74.08 $\pm$ 1.53**
FSH( $\mu$ U/ml)	61.93 $\pm$ 4.15*	77.22 $\pm$ 5.16*
LH( $\mu$ U/ml)	54.74 $\pm$ 3.31	55.36 $\pm$ 4.50

\*\*showing highly significant difference at P-value <0.001

\*showing significant difference at P-value<0.05

#### RESULTS

Table 1 shows the comparison of age, height and weight between normal age menopause and early age menopause women.

Age was significantly higher in early age menopause (42.08 $\pm$ 0.36 years) than the normal age menopause(53.52 $\pm$ 0.44 years) women, whereas height and weight show no statistical difference.

Table 2 shows that the mean pulse pressure was significantly higher with a P value of <0.001 in early age menopause (50.10 $\pm$ 1.28 mmHg) than in normal age menopause (35.90 $\pm$ 1.68 mmHg) women.

Table 3 shows that the mean of diastolic blood pressure was highly significant in the early age menopause whereas mean systolic blood pressure remained insignificant on both sides. The mean FSH was significant in early age menopause (77.22 $\pm$ 5.16  $\mu$ U/ml) as well as to the mean value in normal age menopause (61.93 $\pm$ 4.15  $\mu$ U/ml). There was no statistical difference as far as the mean LH values concerned as they remained non significant on both sides.

## DISCUSSION

Women who experience early menopause, are at an increased risk of cardiovascular disease as compared to women in whom menopause occurs routinely, at their normal or standard age. Cardiovascular risk factor changes occurring with menopause at unfavorable levels in the former have been considered as the biological mechanism.<sup>14</sup> Premature ovarian failure following the deprivation of endogenous estrogen, seems to be the most crucial factor, in explanation of this change.<sup>15</sup>

According to Edmunds et al, who have analyzed data from many studies for an early menopause, both natural or surgical, an abrupt cessation of ovarian function and estrogen production following a surgical menopause may have an entirely different effect to a naturally occurring menopause in which ovarian function declines gradually.<sup>16</sup>

In the study of Luoto et al, the cross-sectional association of pulse pressure with the early age of onset of menopause (age < 45 years) was found to be significant as compared to the later menopause or menopause at normal average age and according to Munawar et al. (2007), the pulse pressure has the predicted value as the determinant of cardiovascular disease.<sup>17,18</sup>

Under these circumstances, the current study was performed to analyze and compare the association of marker of preclinical cardiovascular disease such as pulse pressure, in two different ages of post menopause women.

Firstly, the normal age post menopause had females with a history of at least two years of amenorrhea or post menopause and ages between 50-58 years, were taken. Secondly, females of early age post menopause with a history of at least two years of amenorrhea or post menopause with ages between 40-45 years, were taken as early age menopause.

The results of our study suggest that the cardiovascular risk factors were increased with the women who underwent early or premature ovarian

failure i.e the early age post menopause women as compared to the women with the normal age post menopause. These findings were in agreement of the studies done by Fioretti et al and Atsma et al.<sup>19,20</sup>

Pulse pressure is the difference between systolic and diastolic blood pressures and is a measure of pulsatile component of blood pressure as well as a marker of arterial stiffness. It has been found that pulse pressure is a predictor of cardiovascular mortality due to all causes and non-fatal myocardial infarction even after adjusting for baseline covariates like systolic blood pressure, diastolic blood pressure and mean arterial pressure. For the end point of stroke, however, pulse pressure is a strong, predictive risk factor.<sup>2</sup>

Davidson et al, noted that the relative risk of cardiovascular events per 10 mm Hg increase in systolic blood pressure is not equitable to a 10 mmHg increase in pulse pressure. Their comparative statistical analysis also showed the superiority of 10 mmHg increase in pulse pressure Vs 10 mmHg increase of systolic blood pressure.<sup>19</sup> Thus, the pulse pressure appears to be the best single measure in predicting cardiovascular mortality in older people and helps in understanding the results for low diastolic blood pressure. Pulse pressure also had a significant but negative correlation with diastolic blood pressure i.e as the pulse pressure increased, a significant decrease in diastolic blood pressure was found, and this observation is in accordance with the findings of Simone et al. (2005).

In our study, we found highly significant values for the increased pulse pressure in early age post menopausal women than that of the normal age post menopause, suggesting that development of the marker of preclinical cardiovascular disease is more likely to occur in them.

In our study, follicular stimulating hormone and leutinizing hormones levels were significantly higher in the early age post menopause showing an apparent menopausal status in them whereas these levels were significantly decreased in the normal

age post menopause , showing that early age post menopause with a stronger menopausal status than that of normal age post menopause and these observations are in accordance with the study done by Barnett et al.<sup>21</sup>

## CONCLUSION

From this cross-sectional, comparative study, it is concluded that the values of pulse pressure are increased in the early age post menopause women.

It shows that the pulse pressure, a marker of preclinical cardiovascular disease, is more profound in the early age post menopause women than the naturally occurring normal age post menopause women.

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