INTRODUCTION

Considerable evidences from studies on female rats have showed that ovariectomy decreased insulin-stimulated skeletal muscle glucose uptake.\(^1\)\(^-\)\(^3\) Ovarian hormone deficiency is associated with the development of insulin resistance. Moreover, ovarian hormones may influence glucose uptake by regulating nonoxidative glucose disposal in skeletal muscle.\(^4\) In humans, the menopause transition marks the cessation of ovarian function and dramatic reductions in circulating estrogen and progesterone concentrations.\(^3\)

Accordingly, as ovarian hormone levels are reduced after the menopause transition in women, researchers had hypothesized that postmenopausal state might be associated with reduced insulin sensitivity. In support of this hypothesis, an American study by Lindheim et al., 1994\(^6\) measured the insulin sensitivity by insulin tolerance test in 18 premenopausal women and ten postmenopausal women with Insulin tolerance test and frequently sampled intravenous glucose tolerance test (FSIVGTT) and observed a reduction in insulin sensitivity in postmenopausal compared to premenopausal women. Similarly, another cross-sectional observation study involving 28 obese premenopausal and 142 postmenopausal Swedish women also found that postmenopausal women are relatively more insulin resistant than premenopausal ones in comparison with same degree of overall obesity.\(^7\) In this study, insulin sensitivity was measured by IVGTT and EHC methods. Contrary to this hypothesis, Walton et al., 1993\(^8\) measured insulin sensitivity in 66 premenopausal and 92 postmenopausal women.
non-obese Caucasian women with FSIVGTT and reported that measured insulin sensitivity in postmenopausal non-obese Caucasian women was 50% greater than insulin sensitivity in premenopausal women. On other hand, Toth et al., 2000 found that there was no change in insulin sensitivity measured by hyperinsulinemic-euglycemic clamp technique between 43 early postmenopausal and 40 premenopausal women from Burlington. A study from North Taiwan measured insulin sensitivity in 380 premenopausal and 234 postmenopausal women with HOMA-IR and showed no significant difference between them. These conflicting and equivocal findings cannot draw definite conclusion about the effect of postmenopausal status on insulin sensitivity and further confirmation studies are needed. Moreover, evidences from Asian populations are limited. Because of ethnic differences in insulin sensitivity, the findings from Western populations could not be extrapolated directly to Asian population.

Thus, this study was intended to evaluate the effect of postmenopausal status on insulin sensitivity in Myanmar women.

MATERIALS AND METHODS

Selection of participants
This was a cross sectional analytical study conducted in the department of Physiology University of Medicine 2, Yangon, Myanmar. Apparently healthy 33 premenopausal women (between 25 and 40 years of aged) and 42 post menopausal women (between 45 and 60 year of age) were recruited in this study. Like previous studies women with self reported lack of menstruation or spotting for at least 1 year prior to enrolment were classified as post menopausal women. Ethical clearance for conducting the study was obtained from the institutional Ethics committee. Written informed consent was obtained from all subjects. All subjects were examined for a complete medical history taking and physical examination including BMI calculation. Healthy subjects without family history of diabetes, history of chronic smoking and alcohol drinking were included in this study. Then, all participants underwent oral glucose tolerance test (OGTT). After 10-hour overnight fasting, a venous blood sample was taken and then a solution containing 75 gm of glucose anhydrous, in 300 ml of drinking water was given orally. Venous blood was taken again at two hours after the glucose ingestion. Subjects with BMI >25 kg/m², fasting blood glucose >6.1 mmol/L and post-prandial blood glucose >7.8 mmol/L were excluded from this study.

Blood sample analysis
Fasting blood sample were taken after fasting for at least 10 hours. 5 ml of venous blood samples were taken an

Fasting blood glucose was measured by glucose oxidase method (Glucose Liquicolor, Human, D-65205 Wiesbaden, Germany) and serum insulin level was measured by Insulin ELISA (DSL-10-1600, Diagnostic System Laboratories, Inc., Texas, USA) kit method. Insulin sensitivity was calculated by following formulas described by Matthews et al.

HOMA-IR = Insulin (μIU/mL) × glucose (mmol/L)/22.5.

Statistical analysis
Data were analyzed using by SPSS software for Window (version 16.0, SPSS Inc., Chicago, IL, USA). All data were expressed as mean ± standard deviation. Skewed data were expressed as median and interquartile range. Difference between those with premenopausal and post-menopausal women were analyzed by using independent two sample t-test or Mann-Whitney U-test, considering it significant at the p<0.05. Statistical analysis of the three sets of data (non-obese premenopausal, non-obese postmenopausal and overweight postmenopausal) for each analysis was carried out by Bonferroni post-hoc test.

RESULTS

Postmenopausal women were older than premenopausal women significantly (p<0.001). Postmenopausal women have significantly (P <0.001) more BMI, WC and WHR than premenopausal women. SBP and DBP were significantly higher in the postmenopausal women compared to the premenopausal women (Table 1). FBG, PPB, fasting serum insulin level and HOMA-IR value were not significantly different between postmenopausal women and the premenopausal women (Table 2).

DISCUSSION

Present study observed that postmenopausal women have no significant differences in FBG, fasting serum insulin level as compared to premenopausal women. Contrary to this present result, two previous studies reported that mean fasting serum insulin level in postmenopausal women were significantly higher than that in premenopausal women. The postmenopausal women participated in the study of Razay et al., 1992 and Poehlman et al., 1995
were associated with higher cholesterol level, higher BMI and higher waist hip ratio. Accordingly hyperinsulinemia, is well established feature of obesity; their increased fasting insulin level may be due to increased level of total and intra-abdominal fat. In the present study, BMI and WC were 21.3±2.8 kg/m² and 77.19±2.29 cm in all postmenopausal women and 19.7±2.2 kg/m² and 75.85±2.06 cm in all premenopausal women (BMI <25 kg/m²). They were within normal Asians values (normal BMI range is 18.5 to 22.9 kg/m² and WC <80 cm) of BMI and WC for premenopausal women (BMI <25 kg/m²). They were recruited the obese premenopausal (BMI: 66±9 kg) women having normal body weight and Akin et al., 2007 recruited the non-obese postmenopausal women (BMI: 36.2± 6.1 kg/m², WC: 96.4 ±10.1 cm). In their finding, it was shown that there was no significant difference of insulin sensitivity between premenopausal and postmenopausal women. Similarly, present study intentionally recruited all the non-obese premenopausal and postmenopausal women. Contrary to this, two studies of Lindheim et al., 1994 and Nilsson et al., 2000 have reported that insulin sensitivity was reduced in post menopausal women. Post menopausal women have increased tendency to be obese with advancing age and more sedentary life style. It was also noted that postmenopausal women recruited in previous studies were associated with increased BMI and central adiposity. Accordingly, HOMA-IR was significantly and positively correlated with BMI and WC. It can be assumed that increased insulin resistance of these postmenopausal women may be due in part to increased BMI and central obesity and did not entirely reflect the effect of menopausal status. Many studies required to evaluate whether decrease in insulin sensitivity after the menopause is related to menopause itself or change in body composition.

On this regard, Toth et al., 2000 recruited both premenopausal (61±8 kg) and postmenopausal (66±9 kg) women having normal body weight and Akin et al., 2007 recruited the obese premenopausal (BMI: 35.5±6.9 kg/m², WC: 95.8±11.7 cm) and postmenopausal women (BMI: 36.2± 6.1 kg/m², WC: 96.4 ±10.1 cm). In their finding, it was shown that there was no significant difference of insulin sensitivity between premenopausal and postmenopausal women. Similarly, present study intentionally recruited all the non-obese premenopausal and postmenopausal women. Contrary to this, two studies of Lindheim et al., 1994 and Nilsson et al., 2000 have reported that insulin sensitivity was reduced in post menopausal women. Post menopausal women have increased tendency to be obese with advancing age and more sedentary life style. It was also noted that postmenopausal women recruited in previous studies were associated with increased BMI and central adiposity. Accordingly, HOMA-IR was significantly and positively correlated with BMI and WC. It can be assumed that increased insulin resistance of these postmenopausal women may be due in part to increased BMI and central obesity and did not entirely reflect the effect of menopausal status. Many studies required to evaluate whether decrease in insulin sensitivity after the menopause is related to menopause itself or change in body composition.

Like previous studies, the present study also showed that there was no significant difference between premenopausal and postmenopausal women. Contrary to this, two studies of Lindheim et al., 1994 and Nilsson et al., 2000 have reported that insulin sensitivity was reduced in post menopausal women. Post menopausal women have increased tendency to be obese with advancing age and more sedentary life style. It was also noted that postmenopausal women recruited in previous studies were associated with increased BMI and central adiposity. Accordingly, HOMA-IR was significantly and positively correlated with BMI and WC. It can be assumed that increased insulin resistance of these postmenopausal women may be due in part to increased BMI and central obesity and did not entirely reflect the effect of menopausal status. Many studies required to evaluate whether decrease in insulin sensitivity after the menopause is related to menopause itself or change in body composition.

### Table 1: General characteristic of subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Premenopausal women (n=33)</th>
<th>Postmenopausal women (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>32.7±4.9</td>
<td>52.6±4.4*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.7±2.2</td>
<td>21.3±2.8*</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>75.85±2.06</td>
<td>77.19±2.29*</td>
</tr>
<tr>
<td>WHR</td>
<td>0.8±0.07</td>
<td>0.8±0.05*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>106.2±8.93</td>
<td>120.12±9.03*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>68.79±3.76</td>
<td>76.55±4.56*</td>
</tr>
</tbody>
</table>

Significantly different from Premenopausal women (P<0.05), *P<0.001. Data presented as mean±SD. SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

### Table 2: Plasma FBG level, plasma PPBG level, serum insulin level and HOMA-IR in premenopausal women and post menopausal women

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Premenopausal women (n=33)</th>
<th>Postmenopausal women (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mmol/L)</td>
<td>4.87±0.51</td>
<td>4.76±0.63</td>
</tr>
<tr>
<td>PPBG (mmol/L)</td>
<td>4.92±0.94</td>
<td>5.24±1.11</td>
</tr>
<tr>
<td>Insulin (μU/ml)</td>
<td>8.1 (6.7-11.8)</td>
<td>8.1 (8.5-9.9)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.7 (1.4-2.8)</td>
<td>1.7 (1.2-2.2)</td>
</tr>
</tbody>
</table>

NS indicates not significant different. Data presented as mean±SD for FBG and PPBG, median (IQR) for insulin and HOMA-IR. SD: Standard deviation, IQR: Interquartile range, FBG: fasting blood glucose, PPBG: post-prandial blood glucose, HOMA-IR: homeostasis model assessment – insulin resistance.
resistance. In the present study, 45% of postmenopausal women were overweight according to BMI>=23 kg/m² (Asian people). The HOMA-IR value of overweight postmenopausal women (19 out of 42 postmenopausal women) was significantly higher than that of non-obese premenopausal (n=29) and postmenopausal women (n=23) (Table 4). Not only obese postmenopausal women but also overweight postmenopausal women resulted in insulin resistance after menopause. So BMI and WC were significant predictors of insulin resistance in post menopausal women. It could be assumed that menopause itself does not affect insulin sensitivity.

**CONCLUSION**

This study shows that there was no significant difference of insulin sensitivity between non-obese premenopausal and non-obese postmenopausal women. Observed decrease of insulin sensitivity in overweight postmenopausal women may be due to increased total and intra-abdominal fat. Only hormonal imbalance after menopause does not influence insulin sensitivity. BMI and WC are also strong predictors of insulin resistance. In the light of present study, it could be assumed that menopause itself do not affect insulin sensitivity.

**RECOMMENDATION**

Significant reduction in insulin sensitivity was not found until 60 years of age and decreased insulin sensitivity was noted only in more than 60 years old women who were 10-15 years postmenopausal. Physical activity, diet and genetic factor also influence the insulin sensitivity, and insulin sensitivity varies between individuals. So, further longitudinal study is also recommended to examine the change of insulin sensitivity from premenopausal to postmenopausal state in the same individual.

**REFERENCES**

117:1336-1340.


**Authors Contribution:**

LAT - Conceptualized and executed the study, literature search, collected data and statistically analyzed and interpreted, prepared first draft of manuscript;

MTS - Concept and design of the study, reviewed the literature, statistical analysis and Interpretation of data, participated in drafting, reviewing, and revising the manuscript for intellectual content; TSL - Concept and design of the study, review of study, critical revision of the manuscript, approved the manuscript to be published.

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