



## **Circulating Leptin, Insulin and Thyroid Profile Levels in Different Age Groups of Women Population of Manipur, India**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Age is linked to a number of hormonal disorders. This study was designed to look for changes in leptin, insulin, and thyroid profile concentrations in women of various ages.

**Materials and Methods:** This study was carried out in the Department of Physiology, Regional Institute of Medical Sciences, Imphal. Female subjects (350 participants) between the ages of 20 and 65 were recruited. Subjects were grouped as pre-menopause (< 40 age), menopause (≥ 40 to < 50 age) and post-menopause (≥ 50 age). Blood samples were separated serum and estimated levels of leptin, insulin and thyroid profile levels. Statistical calculation was done using SPSS software version 26, at  $P < 0.05$  as significant.

**Results:** Body mass index (BMI) had significant changes in different age groups ( $P < 0.05$ ), but the levels were not in the higher range of BMI. Serum levels of leptin, insulin, T4 (thyroxine) and TSH (thyroid stimulating hormone) were found no significant differences among the different age groups.

**Conclusion:** Study demonstrates that age has no effect on the levels of leptin, insulin, T4, and TSH in this Manipuri women's group.

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## 1. INTRODUCTION

The older population of world's developing countries are expanding at a far higher rate with increase longevity and declining fertility. A rise in the population of those aged 60 or over will account for half of the increase in global population from 2005 to 2050, but the population (those under the age of 60) will decrease marginally [1]. All body systems, including the endocrine system, undergo changes as one ages. The amount of hormones secreted or the sensitivity of target organs could be the cause of these alterations. As one ages, changes occur in all body systems including the endocrine system. These changes may be due to the amount of hormones secreted or the sensitivity of target organs [2].

After menopause, a huge number of women acquire weight, which is a common clinical observation. This impact has been demonstrated in several studies [3-5]. After menopause, central obesity develops, implying that estrogen deficiency may not only increase body weight and fat, but also alter body fat distribution [6]. Long-term hormone replacement treatment (HRT) has been shown to reduce the rise in body weight and skin-fold thickness that occurs after menopause [7]. However, the specific mechanism of the menopausal effect on body weight and fat distribution after estrogen reduction has yet to be established. In postmenopausal women, it has been suggested that estradiol and leptin metabolism, synthesis, and/or action are linked. Ageing is associated with Central and peripheral leptin resistance, increased fat mass, and a failure to reduce food intake, enhance metabolic rate, and so induce weight loss. Leptin resistance is one of the common feature of obesity and aging [8]. In adult subjects of different body weight, leptin concentrations gradually reduces during aging; that is higher in women compared to men. However, it is unaffected by BMI or other age-related endocrine alterations [9].

Age-related dysfunctions in insulin secretion may have a role in glucose metabolism changes as people become older, contributing to the high incidence of glucose intolerance in the elderly. Several studies have looked at the impact of ageing on pancreatic beta-cell activity in humans, but the results of these investigations have been inconsistent [10]. The lesser magnitude of the

age impact, the use of diverse measurements of insulin secretion, and confounding factors associated with ageing such as decreased physical activity, obesity, and concomitant insulin resistance may all contribute to this variability. Early insulin secretion abnormalities may be undetectable during the transition from normal to reduced glucose tolerance. In view of increased insulin resistance and potential decreased insulin clearance with ageing, studies of the influence of ageing on insulin secretion imply that relative insulin deficiencies are related with advancing age. Insulin secretory abnormalities in aged people have been repeatedly demonstrated when insulin sensitivity is adjusted for [11].

Thyroid dysfunctions are extremely common, affecting mostly older women. The ability to diagnose thyroid illnesses, particularly overt and subclinical hypothyroidism in the elderly, is critical since thyroid-related symptoms are remarkably similar to symptoms associated with the normal ageing process. The interpretation of thyroid function may be influenced by the presence of non-thyroidal disease. Special care needs to be focus on treatment due to variations in thyroid hormone metabolic clearance, medication interactions, and potential adverse responses [12]. The non-specific clinical symptoms of hypo and hyperthyroidism in the elderly also cause misunderstanding in the clinical setting. On the other hand, the thyroid profile result may deviate from the typical ranges for people of a younger age [13]. Furthermore, different studies on the impact of endocrine hormone levels such as leptin, insulin, and thyroid profile on ageing have come to different conclusions in different populations. In the Manipuri population, there is a paucity of study on the effects of ageing on different hormone levels. The aim of this study is to look at the levels of leptin, insulin, and thyroid profile in Manipuri women of various ages.

## 2. MATERIALS AND METHODS

This was a cross-sectional study undertaken at the Department of Physiology, Regional Institute of Medical Sciences, Imphal. A total of 350 women were recruited (ages 20-65 years). The study excluded women who were lactating and those who had known chronic metabolic problems. The subjects' weight and height were recorded, and their BMI was computed. The study was divided into three groups depending

on age as pre-menopause, menopause, and post-menopause. Blood sample was collected in the morning under fasting conditions. After centrifugation, samples were separated serum and stored at  $-20^{\circ}\text{C}$ . Then, samples were estimated levels of leptin, insulin and thyroid profile. Data was analysed using one way ANOVA in SPSS software version 26.  $P < 0.05$  was used to denote significant values.

### 3. RESULTS

Table 1 shows the demographic profile and biochemical characteristics. In the study population, 100 subjects were under the age group of  $< 40$  years (pre-menopause), 150 individuals were in the age of  $\geq 40$  to  $< 50$  years (menopause) and 100 participants were  $\geq 50$  age group (post-menopause). The reference study individuals had significant changes in BMI among different levels of age groups ( $P < 0.05$ ). There were no significant variations in the levels of leptin, insulin, T4 and TSH between the groups.

### 4. DISCUSSION

Menopause is a well known risk factor for obesity among women over the age of 40. According to the reports of World Health Organization (WHO), the incidence rate of obesity is higher during postmenopausal period, between 45 to 55 years of ages. Obesity in postmenopausal women is assumed to be caused by hormonal changes after menopause. In energy homeostasis, estrogen is known to have a substantial anorexigenic effect. After menopause, a decrease in basal metabolic rate and induced metabolic dysfunctions are well-known symptoms of hypoestrogenic conditions, resulting in increased body fat percentage and mass, and hence a shift in body fat distribution from gynoid to android [14-16].

Deficiency of ovarian hormone during menopause may cause an imbalance in energy homeostasis and hyperphagia, which can lead to obesity and other metabolic diseases [17,18]. Obesity was shown to be prevalent in 65 percent of women between the ages of 40 and 65 and incidence rates peaked at 74% beyond the age of 65 [19,20]. In this study, BMI of pre-menopause, menopause and post-menopause groups were  $24.68 \pm 4.84 \text{ kg/m}^2$ ,  $27.29 \pm 4.44 \text{ kg/m}^2$  and  $25.93 \pm 4.51 \text{ kg/m}^2$ , respectively. Menopausal and postmenopausal women have higher tendency of BMI than premenopausal women. Although disparities in BMI ranges are

not yet considered obesity, may be the result of variances in genetic background, dietary habits, and lifestyle.

According to comparative bivariate analysis results, obese and non-obese women had relatively identical levels of estradiol, implying that energy homeostasis is regulated by food and lifestyle factors [21,22]. Leptin's sympathetic excitatory function is amplified by estrogen, resulting in greater leptin levels [23] Several studies have looked into the effects of long-term estrogen deprivation and hormone replacement therapy on leptin concentrations. The findings of this research are highly disparate. In previous investigations, postmenopausal women were shown to have a hypoestrogenic state, which resulted in a considerable drop in leptin levels. Another study of postmenopausal women found that obese women had considerably greater leptin levels than non-obese women [24] These studies signify the influence of menopausal status in leptin concentration. Menopausal status had little effect on leptin levels in a previous study, implying that BMI is the most important predictor determining leptin levels in women [25] Our findings show that there are no significant changes in leptin concentration between different menopausal groups, implying that age is an independent determinant of leptin levels regardless of menopausal status. One study in this Manipuri group found that leptin levels increased as BMI grades increased, implying that BMI is a significant determinant of leptin levels [26] One of the studies also hypothesized that if estradiol takes a role in regulation of leptin production, leptin concentration must vary in absence or presence of estrogen in women. "But, concluded that neither menopause nor serum estradiol alters plasma leptin concentration even after controlling for BMI in a multiple linear regression analyses in healthy pre and post-menopausal women [27] Obesity was found to have no connection with leptin concentrations in people over 65 years old in some studies [28,29] In a study conducted by Ostlund *et al.*, it was found that leptin exhibited a negative connection with age, regardless of body fat, in participants aged 18 to 80 years [30] This shows that circulating leptin concentrations in subjects over 65 years were expected to be much lower than in people under 65. On the other hand, some studies have reported positive correlation between age and leptin levels [31]

Insulin secretion reduces as one gets older [32] This decrease could be caused by islet mass loss as well as beta cell impairment as people

get older. In population studies, post-challenge insulin levels have been found to decrease with age [33,34] Although the findings could be due to beta cell failure as people age, they could also be due to changes in gastric emptying, diet, or even an increase in insulin sensitivity as people become older. With increasing age, glucose tolerance drops, resulting in a high frequency of impaired glucose tolerance and type 2 diabetes in the elderly [35] The factors associated with aging may contribute to change in glucose tolerance in this subjects. The associated factors include decrease physical activity, increased adiposity, co-existing illness and the defects of insulin secretion associated with aging. In the present study, insulin levels in different ages of menopausal status groups found no significant changes. It implies that the impact of ageing on insulin secretion and clearance are unlikely to change. The reason could be that because the study subjects' ages ranged from 20 to 65, women under 65 may not have a reduction in insulin beta activity and may not be affected by menopausal status. Cell function was previously assessed using the hyperglycemic clamp approach, which revealed a decreased or no drop in insulin secretion with age [36,37] Bourey *et al.* [38] Hyperglycemic clamp studies of normal glucose tolerance in young and elderly people with various degrees of glucose tolerance were investigated. During the hyperglycemic clamp, older patients with glucose tolerance exhibited similar insulin responses to youthful subjects. Some studies have found a consistent reduction in insulin clearance in older subjects, which could be due to abnormalities in relative insulin secretion in older people with slightly reduced insulin clearance and relative glucose intolerance, as described in some research [39-41].

In addition, there is a controversy over thyroid function in the older population [42] The concentrations of T3, T4, and TSH in the blood

change with age [43,44] Study of Whickham survey, reported in 1977, demonstrated that TSH levels did not differ with age in males but markedly higher in females after the 45 age [45] In contrast, a research in a specific area with adequate iodine consumption found that TSH levels decreased continuously throughout life, while FT4 levels rose exclusively in participants over 60 [46] There was no significant variation in T4 and TSH concentrations between the different age groups of women in our study. It is most likely not due to ageing, but rather to factors such as weight gain, dietary changes, and lifestyle changes that could influence thyroid profile in this female group. Although, the common understanding is that Thyroid dysfunctions are more prevalent and highly afflicting aging women [47] One study looked into the role of estrogen in thyroid receptors, and how estrogen might affect thyroid function and, as a result, thyroid diseases. The interaction between these hormones, however, necessitates a thorough knowledge [48] Hypothyroidism may exacerbate or exacerbate menopause symptoms, implying that treating thyroid disorders could aid in the management of menopause symptoms [49] Women's sex hormone does not appear to have much of an influence on thyroid profile in our study sample. Thyroid disease, on the other hand, has a well-known impact on disability, cognition, cardiovascular risk, and longevity. In medical societies around the world, there are no common screening protocols for thyroid disorders in elderly women or in different menopausal stages [50].

This study has a sample size constraint, and women's sex hormone estimation should be included for better interlinking processes in this population's various age groups. However, the study revealed that age had no significant impact on the levels of the hormones estimated in these women's population.

**Table 1. Demographic profile and biochemical parameters in pre-menopause, menopause and post-menopause**

Characteristics	Pre-menopause	Menopause	Post-menopause	P - value
Age (years)	28.88±7.30	46.00±7.52	61.58±8.18	0.000*
BMI (kg/m <sup>2</sup> )	24.68±4.84	27.29±4.44	25.93±4.51	0.037*
Leptin ((ng/ml)	12.44±9.36	13.65±8.91	13.47±9.77	0.763
Insulin (µIU/ml)	24.24±23.66	27.42±28.93	26.81±25.06	0.538
T4 (µg/dl)	8.24±1.73	8.04±1.67	8.45±1.78	0.579
TSH (µIU/ml)	2.20±1.59	3.06±3.51	2.88±2.04	0.096

\*Significant at  $P < 0.05$

## 5. CONCLUSION

This research showed that age had no effect on leptin, insulin, or thyroid profile levels in women of various ages who were classed as being in various stages of menopause. As a result, factors such as modifying one's lifestyle, food habits, and weight management may be more effective in controlling these hormone levels.

## CONSENT AND ETHICAL APPROVAL

The study was conducted after receiving clearance from the Institutional Ethical Board. All of the subjects gave their informed consent on an individual basis.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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