ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Interaction Between Thyroid Hormones and Glucose Homeostasis in Post-Menopausal Diabetic and Non-Diabetic Women.

CH Kalashilpa[1]*, Sumangala M Patil[1], and Manjunatha Aithala[2].

[1]Department of Physiology, B.L.D.E.U Shri BM Patil Medical College, Bijapur, Karnataka, India.
[2]Department of Physiology, B.L.D.E.U Shri BM Patil Medical College, Bijapur, Karnataka, India.

ABSTRACT

To evaluate the interaction between Thyroid hormones and Glucose homeostasis in post menopausal Diabetic and Non-Diabetic women. Sixty women aged between 46-65 years were selected for the present study & further divided into 2 groups. 30 post menopausal diabetic women were compared with equal number of post menopausal Non-diabetic women. Anthropometric & Physiological parameters were taken. Complete blood picture count, Fasting blood glucose(FBS),Glycosylated haemoglobin(HbA1C), Oestradiol, progesterone, Follicle stimulating hormone(FSH), Luteinizing hormone(LH) levels were analyzed. Unpaired "t" test, is used for the analysis of data between Diabetic and Non-Diabetic group. $P<0.05$ considered statistically significant. In our study we found, there is significant increase in weight, BSA, BMI, where as significant decrease in DBP of diabetic group compared to Non-Diabetics & there is significant increase in FBS, HbA1C levels of Diabetic group & significant decrease in LH levels of Diabetics compared to Non-Diabetics. However T3 levels of Diabetic and Non-Diabetic group were almost same, where as T4, Oestradiol and progesterone levels of diabetic group non-significantly increased and FSH and TSH levels non-significantly decreased in Diabetics. There is frequent co-existence of thyroid dysfunction and diabetes mellitus among post menopausal diabetic women. So in conclusion, screening of all post menopausal diabetic women for thyroid disorders should be included in routine investigation for better diagnosis and prognosis of the patients.

Keywords: Thyroid hormones, Diabetes, Glucose regulatory hormones, Post Menopause, Glucose Homeostasis

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Menopause is the permanent cessation of menstruation due to loss of ovarian function. This transition is gradual which takes place over a period of time from the reproductive to non-reproductive phase of life. The transition from pre to post-menopause is often associated with the emergence of metabolic syndrome features. These risk factors may be due to the direct result of ovarian failure or an indirect result of the metabolic consequences of central fat redistribution with estrogen deficiency [1-3].

Diabetes and thyroid have showed to mutually influence each other and association between both the conditions have long been reported[4,5].Diabetic patients have higher prevalence of thyroid disorders compared with the normal population because patients with one organ-specific autoimmune disease are at high risk of developing other autoimmune disorders[6].The presence of thyroid disorders usually affects diabetes control.

Thyroid Hormones, namely Tri-iodothyronine (T3) and Thyroxin (T4); either or both of which may be elevated or reduced have both direct and indirect effects on blood glucose homeostasis. Elevated levels of free circulating thyroid hormone (hyperthyroidism) produce hyperglycemia by causing polyphagia, enhancing glucose absorption from the gastro-intestinal tract, accelerating insulin degradation and stimulating glycogenolysis. Reduced level of hormones(hypothyroidism) may cause hypoglycemia[7].The prevalence of thyroid disorders has been found to increase linearly with age and virtually all thyroid disorders are common in women[8].

In women, thyroid disorders are also associated with menopause. Menopause is the time of life when menstrual cycles ceases and is caused by reduced secretions of ovarian hormones, oestrogen and progesterone [9]. Menopause is also one of the most important period which favors weight gain and leading to obesity. Obesity can also be considered as a condition of exaggerated estrogen production. It has been demonstrated that the conversion of androgens to estrogen in peripheral tissues is significantly correlated with body weight and the amount of body fat [10]. There are many studies on thyroid hormones and diabetes and the relation between them. But very few studies are there on interaction of thyroid hormones and glucose regulatory hormones in postmenopausal diabetic and non-diabetic women.

So, Aim of the present study is to know the interaction between thyroid hormones and glucose regulatory hormones in post menopausal diabetic and non-diabetic women.

MATERIAL AND METHODS

The study was conducted at Shri B.M Patil Medical College, Hospital& Research center, BLDE University. 30 Post menopausal Non-diabetic women attending OPD, Department of OBG and 30 Post menopausal Diabetic women attending the out-patient clinic of Diabetes, aged between 46-65 years were selected for the study. Written informed consent was obtained from the subjects. Ethical clearance was obtained from the Research Ethical Committee of Shri B.M Patil medical college and Hospital, BLDE University.

Inclusion and Exclusion criteria

Post menopausal Diabetic and Non-Diabetic women aged 46-65 years old with resting blood pressure (BP<139/89) according to WHO hypertension guidelines and who were Non-smokers were included in this. For diabetic patients, duration of diabetes mellitus longer than one year or more have been included and where as the subjects with evidence of Hypertension (BP>139/89), with a history of alcohol intake, or they were taking any thyroid supplements, or they have undergone Hysterectomy, use of any oral contraceptives within the previous six months, and pregnant women were excluded from this study.

A detailed history of diabetes and menopause was taken from the subjects and complete physical examination was done at the time of recruitment. Menopause was confirmed by the criteria that women are not menstruating for a period of 12 consecutive months with no other abnormality noticed.

The following Physical Anthropometric & Physiological Parameters were assessed from the patients: Age, Height, weight, Body surface area, Body Mass Index, Waist to Hip Ratio, Blood pressure and Pulse rate. Height was measured in cm. Weight was measured nearest to 0.1 kg. Body mass Index was calculated by using the following formula:

$$\text{Body Mass Index (BMI)} = \frac{\text{Weight in kg}}{\text{Height in meter square}}$$

Body Surface Area (BSA) is calculated using Duboi's formula [11]

$$BSA\ (m^2) = 0.007184 \times \text{Height (cm)}^{0.725} \times \text{Weight (kg)}^{0.425}$$

Waist to Hip ratio was calculated by measuring waist at narrowest point under lowest rib and hips at the widest portion of buttocks using a tape and the ratio was calculated in cm by dividing waist measurement by hip measurement.

$$\text{Waist-Hip Ratio} = \frac{\text{Waist (cm)}}{\text{Hips (cm)}}$$

Blood pressure was measured by using mercury sphygmomanometer and Systolic Blood pressure (SBP, mmHg), Diastolic Blood pressure was recorded and Pulse Rate (beats per min, bpm) was also recorded.

Blood samples from patients were obtained at the morning hours after a 12 hour overnight fast for biochemical, Hormonal analysis. Haematological parameters like complete blood picture count (CBC) was analyzed by using SYSMEX XN-1000 Automated Haematology cell counter. Biochemical parameters like Fasting Blood Glucose(FBG) was analyzed by using Glucose oxidase-peroxidase method, with MISPO UNO(AGAPPE)-semi-auto analyzer, where as HbA1C was analyzed by Turbidimetric Inbition Immunoassay method by using fully auto analyzer(ROCHE COBAS C 311) and the hormonal analysis like thyroid profile(T3,T4,TSH) and Reproductive Hormonal profile (FSH, LH) were analyzed by the method ELFA(Enzyme linked fluorescent assay) by using Mini VIDAS, where as Estrogen and progesterone hormones were analyzed by the method C.L.I.A(Chemi Luminescent Immuno Assay).

Statistical analysis

It was done by using SPSS statistical software 16 version. Data was expressed as Mean±SD (standard deviation). Significance of difference between Diabetic group and Non-Diabetic group was determined by using student's unpaired (independent) sample "t" test. $P<0.05$ is considered statistically significant (two tailed).

RESULTS

Table 1 shows Comparison of Anthropometric and physiological parameters of Post Menopausal Diabetic and Non-diabetic women. There was no significant difference in height of both groups. Here it was shown that weight was significantly increased in Diabetic Group compared to Non-diabetic group. At the same time, Body surface area, Body Mass Index significantly increased in diabetic group where as Diastolic blood pressure (DBP) of diabetic group significantly decreased compared to Non-diabetic group, where as Waist to hip ratio, pulse rate, systolic blood pressure was non- significantly increased in diabetic group.

Table 2 shows comparison of Biochemical and Hormonal parameters of Post menopausal Diabetic and Non-diabetic women. Here it was shown that Fasting blood glucose(FBS) levels and Glycosylated hemoglobin(HbA1C) levels were significantly increased in diabetic group compared to non-diabetic group($P<0.0001$) where as Luteinizing hormonal(LH) level significantly decreased in diabetic group compared to non-diabetic group($P<0.007$) . However T3 levels of diabetic and non-diabetic group showed were almost same,where as T4, Oestradiol and progesterone levels of diabetic group non-significantly increased in diabetic group and Follicle stimulating hormone(FSH) and TSH levels non-significantly decreased in diabetic group.

ISSN: 0975-8585

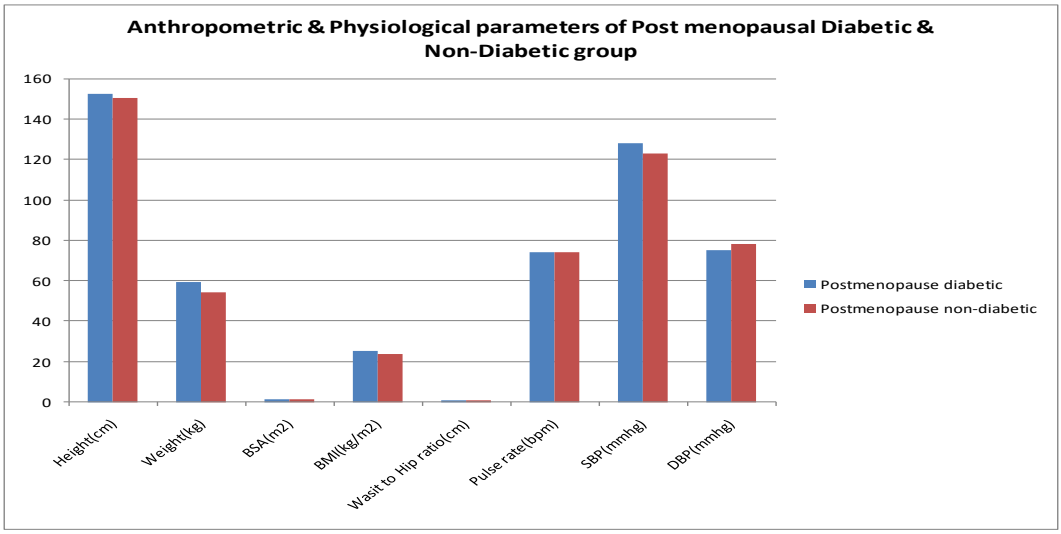
Table 1: Anthropometric and physiological parameters of Post Menopausal Diabetic and Non-Diabetic women.

Parameter	Post menopause Diabetic (n=30)	Post menopause non-diabetic (n=30)	P Value
Height(cm)	152.29±5.55	150.16±6.83	0.19(NS)
Weight(kg)	59.56±7.35	54.10±8.48	0.009**(HS)
BSA(m^2)	1.55±0.11	1.47±0.12	0.01*(S)
BMI(kg/m^2)	25.64±2.45	23.95±3.16	0.02*(S)
Wasit to Hip ratio(cm)	1.00±0.12	0.95±0.10	0.06(NS)
Pulse rate(bpm)	74.06±3.87	74.00±4.51	0.08(NS)
SBP(mmhg)	128±11.90	123±10.22	0.08(NS)
DBP(mmhg)	75.33±3.83	78.20±5.71	0.02*(S)
Data is presented as Mean±SD(standard deviation) SBP-systolic blood pressure, DBP-Diastolic blood pressure, BMI-Body mass index, BSA-Body surface area, bpm- beats per minute, mmhg-millimeters of mercury P<0.05 considered significant(S). P>0.05 considered Non significant(NS) P<0.001 considered Highly significant(HS). *indicates level of significance. *P<0.05(S), **P<0.001(HS)			

Table 2 : Biochemical and Hormonal parameters of Post Menopausal Diabetic and Non-Diabetic women.

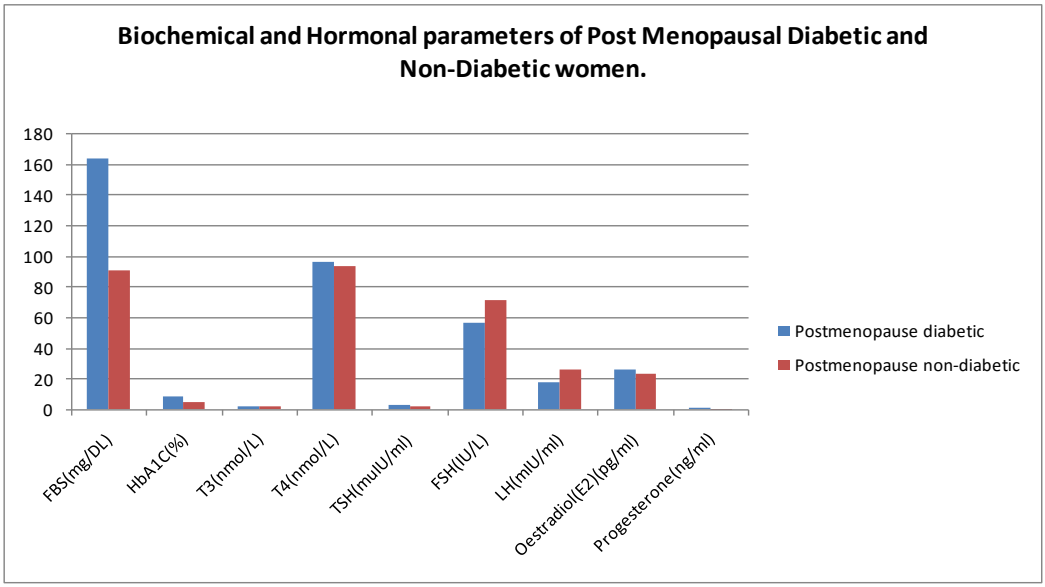
Parameter	Post menopause Diabetic (n=30)	Post menopause non-diabetic (n=30)	P Value
Fasting blood glucose(mg/DL)	163.83±53.06	90.76±12.68	0.0001**(HS)
HbA1C(%)	8.14±2.16	5.24±0.76	0.0001**(HS)
T3(nmol/L)	1.71±0.75	1.71±0.36	0.96(NS)
T4(nmol/L)	96.74±15.31	93.77±19.07	0.50(NS)
TSH(muIU/ml)	2.37±1.40	2.54±2.30	0.73(NS)
FSH(IU/L)	56.62±27.34	71.46±33.21	0.06(NS)
LH(mIU/ml)	17.71±7.70	25.87±14.31	0.0079*(HS)
Oestradiol(E2)(pg/ml)	25.78±28.65	23.69±16.52	0.73(NS)
Progesterone(ng/ml)	0.62±2.40	0.24±0.17	0.38(NS)
Data is presented as Mean±SD(standard deviation) mg/DL- Milligrams per deciliter, nmol/L- Nanomoles per liter, muIU/ml- millimicrons-International units per milli liter, IU/L-International unites per leter, mIU/ml-milli-International units per milli liter. Pg/ml- Picograms per milliliter, ng/ml-nanograms per milli leter. P<0.05 considered significant(S). P>0.05 considered Non significant(NS) P<0.001 considered Highly significant(HS). *indicates level of significance. *P<0.05(S), **P<0.001(HS)			

Figure 1



ISSN: 0975-8585

Figure 2



DISCUSSION

Menopause in women leads to many physiological changes in the body. Here in our study, significant changes have been observed in post menopausal diabetic women compared to Non-diabetics. There was a significant increase in weight of the Post menopausal diabetic women. Obesity is one of the commonest cause of post menopausal diabetic women. Excess insulin causes polyphagia,so persons eat more to try to maintain a balance[12].women tend to gain weight and undergo an alteration to their fat distribution in mid-life[13,14].Obesity acts as a diabetogenic factor and leads to decrease in insulin receptors on the insulin responsive cells[15]. At the same time, there is a central redistribution of fat with a decrease in gluteo femoral fat and an increase in intra abdominal fat. Moreover, during climacteric, often appears an associated muscle mass loss. Likewise for weight gain, changes in body composition are related to aging. Different factors (diet - physical activity - GH secretion) could be involved. This tendency to visceral fat accumulation clearly favors the increased cardiovascular risk observed after menopause [16]. Changes in the body fat distribution at menopause may be due to decreased production of estrogen. Changes in body fat distribution with declining estrogen are likely due to changes in adipose tissue metabolism since estrogen is known to influence adipose tissue lipoprotein lipase (LPL) activity and lipolysis[17].

There was a significant increase in BSA, BMI in Diabetic group compared to Non-Diabetic group. This may be because of relationship between BMI, insulin resistance, blood glucose and HPG axis functions are complex. It is commonly accepted that the volume of fat mass increases with age results into the higher BMI noted during aging. Similar observation was reported by Forbes GB et al., [18]. However, we did not find any significant change in the waist to hip ratio between Diabetics and Non-diabetics.

There was a significant decrease in DBP of diabetic group compared to Non-diabetic group ($P<0.02$). It may be due to the age related decline in diastolic pressure is presumed to result from early recoil of the pressure wave, because of increasing arterial stiffness and lack of proper large artery compliance. Such shift of the reflection wave from the diastole to the systole increases systolic and decreases diastolic pressure. Here in this study we also found that SBP increased in Diabetic group compared to Non-diabetics, but it did not differ significantly. These observations were supported by Ronnback M et al., [19]. Pulse rate was almost similar in both the groups.

There was a significant Increase in Fasting blood glucose levels and HbA1C in Diabetic group. The increase in HbA1C during diabetes, may be due to the excess glucose present in blood reacts with hemoglobin.[20,21].There was a marked increase in HbA1C levels in diabetic patients, which could be due to excessive glycosylation of hemoglobin. Our finding is supported by Saha HR et al., [22].

There was a significant decrease in LH levels in diabetic group compared to non-diabetic group(P<0.007).At the same time There was a Non significant decrease in FSH levels in diabetic group. The decreased levels of these hormones may be due to increased level of estrogen and progesterone in diabetic group. It is well established that aging is associated with dramatic changes in gonadotropin secretion in healthy subjects. In women, after the initial elevation of serum gonadotropins that characterizes the menopause, a progressive decline in both follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels occurs with age in the later post-menopausal years[23-27]. However there were no significant differences of estrogen and progesterone levels in both the groups. There were no significant differences in Thyroid hormones (T3,T4,TSH) of diabetic group compared to Non-diabetic group. T3 levels were almost similar in both groups. T4 levels Non-significantly increased in diabetic group where as TSH levels decreased in diabetic group compared to non-diabetic group.

The frequency of thyroid disorders rises with age and is higher women. In our study, TSH is low and T4 is high. Low levels of TSH may indicate “Hyperthyroidism”. The occurrence of hyperthyroidism in patients with diabetes is greater than in general population. Thyroid hormones may influence glucose control through a variety of actions on intermediatory metabolism. Some of these effects become clinically relevant in patients with co-existent diabetes and hyperthyroidism. Excess Thyroid hormones promote hyperglycemia by facilitating glucose intestinal absorption, increasing insulin clearance, and enhancing glycogenolysis and gluconeogenesis also, Hyperthyroidism is associated with increased hepatic output, reduced insulin action and increased lypolysis in diabetics [28].

CONCLUSION

The interaction between thyroid hormones and glucose homeostasis among postmenopausal diabetic & Non-diabetic women is a typical phenomenon. The physiological basis and the complex interaction between thyroid hormones and glucose regulatory hormones and their relation with female reproductive hormones among postmenopausal diabetic women trigger the glycaemic control mechanism. So clinicians should be aware of the frequent co existence of thyroid dysfunction and diabetes mellitus among post menopausal diabetic women. Periodic thyroid screening should be targeted for post menopausal diabetic women. Recognition and prompt correction of thyroid dysfunction will optimize glycaemic control among postmenopausal diabetic women. So routine annual thyroid screening should be Mandatory.

This study will serve as a valuable guideline for physician to proceed for diagnosis and management of thyroid dysfunction in postmenopausal diabetic women. From our study, we found more prevalence of “Hyperthyroidism” among Postmenopausal diabetic women. So screening of all postmenopausal diabetic women for thyroid disorders should be included in routine investigation for better diagnosis and prognosis of the patients.

ACKNOWLWDGEMENT

We would like to thank all the patients and healthy subjects of Shri B.M. Patil Medical Hospital and Research Center, BLDE University, Vijayapur for participating in this study.

REFERENCES

[1] Carr MC. J Clin Endocrinol Metab 2003;6:2404-11.
[2] Fu CH, Yang CC, Lin CL, Kuo TB. Chin J Physiol 2008;2:100-5.
[3] Pellizzer AM, Straznicky NE, Lim S, Kamen PW, Krum H. Clin Exp Pharmacol Physiol 1999;8:656-60.
[4] Feely J, Isles TE. BMJ 1979; 6179:1678.
[5] Gray RS, Irvine WJ, Clarke BF. BMJ 1979; 6202: 1439
[6] Perros P, MC Crimmon RJ, Shaw G, Frier BM. Diabet med 1995; 7:622-627.
[7] Ghazali SM and Abbiyesuku FM. Niger J Physiol sci 2010;2:173-179.
[8] Der EM, Quayson SE, Clegg-Lamptey JN, Wiredu EK, Ephraim RKD, Gyasi RK. Journal of Medical and Biomedical Sciences 2013; 1: 1-7.
[9] Dr Heidi D Nelson, MD. THE LANCET 2008; 9614: 760-770.
[10] Siiteri PK. J Endocrinol 1981; 89: 119P—129P

[11] DuBois D, DuBois EF. Arch Int Med 1916; 17: 863-71.
[12] Rosenthal S. The type 2 diabetic women. Lincolnwood,Illinois:Lowell House. 1999.
[13] Wing RR, Malthews KA, Kuller LH, Meilahn EN, Plantinga PL. Arch Int Med 1991; 1:97-102.
[14] Svendesen OL, Hassager C,Christiansen C. Metabolism 1995;44:369-73.
[15] Satyanarayana U, Chakrapani U. Biochemistry, 3rd edition, 2006.
[16] Castelo-Branco C. Obstetrics and Gynaecology 2009;1-136
[17] Rebuffe-Scrive M, Eldh J, Hafstrom LO, Bjorntorp P. Metabolism 1986;9:792–797.
[18] Forbes GB, Reina JC. Metabolism. 1970; 9: 653-63.
[19] Ronnback M, Fagerudd J, Forsblom C, Pettersson-Fernholm K, Reunanen A, Groop PH. Finnish Diabetic Nephropathy(Finn Diane) Study Group age-related blood pressure pattern in type 1 diabetes.2004; 9:1076-1082.
[20] Gloria-Bottini F, Antonacci E, Bottini N, Ogana A, Borgiani P, et al. Hum Biol 2000;2: 287-294.
[21] Sampson MJ, Gopaul N, Davies IR, Hughes DA, Carrier MJ. Diabetes Care 2002; 3:537-541.
[22] Saha HR, Sarkar BC, Khan SA, Sana NK, Choudhury S. A Comparative study of Thyroid Hormone and Lipid Status in Diabetic and Non Diabetic Adults 2012;9:450.
[23] Kwekkeboom DJ, De Jong FH, Van Hemert AM, Vandenbroucke JP, Valkenburg HA &Lamberts SWJ. Journal of Clinical Endocrinology and Metabolism 1990 ;70: 944-950
[24] Rossmanith WG, Scherbaum WA & Lauritzen C. Neuroendocrinology 1991;3: 211–218.
[25] RossmanithWG. Exp Gerontol 1995; 3-4: 369–381.
[26] Lamberts SWJ, van den Beld AW & van der Lely AJ. Science 1997; 5337: 419–424.
[27] Santoro N, Banwell T, Tortoriello D, Lieman H, Adel T & Skurnick J. Am J Obstet Gynecol 1998;4:732–41
[28] Potenza M, Via MA, Yanagisawa RT. Endocr Pract 2009; 3: 254–62.

.