



EFFECT OF THYROID HORMONES ON GLUCOSE REGULATION IN PRE AND POST MENOPAUSAL DIABETIC WOMEN

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ABSTRACT

There is a mutual influence of thyroid and diabetes and the association between them reported long back. Prevalence of thyroid on diabetics is increasing worldwide. The presence of thyroid usually affects diabetic patients. Aim of the study is to evaluate the relationship between Thyroid hormones and Glucose Regulation in pre and post menopausal diabetic women. Total Sixty women, among them 30 pre menopausal diabetic aged between 25-45 years & 30 Post menopausal diabetic women aged between 46-65 years were selected for the present study. Anthropometric & Physiological parameters were taken. Complete blood count, Fasting blood glucose (FBS), Glycosylated hemoglobin (HbA1C), Thyroid hormone profile (T3, T4, TSH) levels were analyzed. In our study we found, there is significant increase in BSA, BMI, Waist to Hip ratio of Pre menopausal diabetic group compared to post menopausal diabetics where as significant increase in SBP of Post menopausal diabetic group compared to pre menopausal Diabetics & there is non-significant increase in HbA1C levels of post menopause Diabetic group. However, there is non-significant decrease in T3, T4 and significant increase in TSH levels of Pre menopause Diabetic group compared to post menopause diabetics. We found more prevalence of "Hypothyroidism" among pre menopausal diabetic women. So prompt recognition of thyroid dysfunction in premenopausal diabetic women and controlling the blood glucose level is necessary and also routine thyroid screening should be recommended for pre menopausal diabetic and post menopausal diabetic women to detect thyroid abnormalities in most of the patients in subclinical stage.

KEYWORDS : *Thyroid Hormones, Glucose Regulation, Pre Menopausal Diabetic, Post Menopausal Diabetic.*



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INTRODUCTION

Thyroid diseases and diabetes mellitus are the two most common endocrine disorders encountered in clinical practice.^{1,2}The physiological and biochemical interrelationship between insulin and influence of both insulin and iodothyronines on the metabolism of carbohydrates, proteins, and lipid have been recorded.³ ⁴such records indicate that iodothyronines are insulin antagonist with high levels being diabetogenic while absence of hormone inhibits the development of diabetes.⁴Diabetes mellitus is a common endocrine disorders rising in India and has reached approximately 20% in urban populations and approximately 10% in rural Population.⁵ The first report showing the association between diabetes and thyroid dysfunction was published in 1979. Few studies also estimated much higher prevalence of thyroid dysfunction in diabetes.^{6,7} Diabetes mellitus appears to influence thyroid function at two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissue.⁸ The term 'thyroid diabetes' was coined in the early literature to depict the influence of thyroid hormone alterations in the deterioration of glucose control.⁹ Thyroid dysfunction may lead to hypothyroidism or hyperthyroidism in diabetic patients. In women thyroid disorders are also associated with pre menopause and post menopause. Thyroid hormones play an important role in normal reproductive function both through direct effects on the ovaries and indirectly by interacting with sex hormone binding proteins. Thyroid dysfunction can lead to menstrual irregularities and infertility.¹⁰ Many studies were there on the thyroid and diabetes but very few studies were there on the relationship between thyroid hormones and glucose homeostasis among women. So our aim of the present study is to evaluate the relationship between thyroid hormones and glucose Regulation in pre menopausal diabetic and postmenopausal diabetic women.

MATERIALS AND METHODS

The study was conducted at Shri B.M Patil Medical College, Hospital & Research center, BLDE University. Total 60 women were selected. Among them 30 Pre menopausal diabetic women, aged between 25-45 years

and 30 Post menopausal Diabetic women aged between 46-65 attending the out-patient clinic of Diabetes, 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. A detailed history of diabetes taken from the subjects and pre menopause was confirmed by women having regular menstrual cycle every month and post menopause was confirmed by the women who were not menstruating for a period of 12 consecutive months and complete physical examination was done at the time of recruitment.

Inclusion criteria

Pre menopausal Diabetic & Post menopausal-Diabetic women with

- i. Regular menstruation every month (for pre menopausal diabetic)
- ii. Women not menstruating for a period of 12 consecutive months (for post menopausal diabetic)
- iii. With Resting Blood pressure (BP < 140/90)¹¹ (according to WHO guidelines)
- iv. Non-smokers
- v. Duration of Diabetes mellitus longer than one year or more (For Diabetic patients)

Exclusion criteria

Pre menopausal Diabetic & Post menopausal Diabetic women with

- i. Evidence of Hypertension (BP > 140/90)
- ii. History of alcohol intake
- iii. Intake of Thyroid supplements
- iv. Hysterectomy
- v. Use of any oral contraceptives within the previous six months
- vi. Pregnant women

The following Physical Anthropometric & Physiological Parameters were assessed from the patients: Age, Height, weight, and 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.¹²

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 Inhibition Immunoassay

method by using fully auto analyzer (ROCHE COBAS C 311) and the hormonal analysis like thyroid profile (T3, T4, TSH) were analyzed by the method ELFA (Enzyme linked fluorescent assay) by using Mini VIDAS.

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).

diabetic women. There was no significant difference in height and weight of both groups. But BSA, BMI, Waist to Hip Ratio of Pre menopause diabetic group is significantly more compared to Post menopause-Diabetic group. Pulse rate shows non-significant increase in post menopause diabetics, Whereas Systolic blood pressure (SBP) of post menopausal diabetic group significantly increased but diastolic blood pressure was non-significantly decreased in post menopausal diabetic group compared to Pre menopausal Diabetics. The same results were shown here in the form of graphical representation in Graph 1.

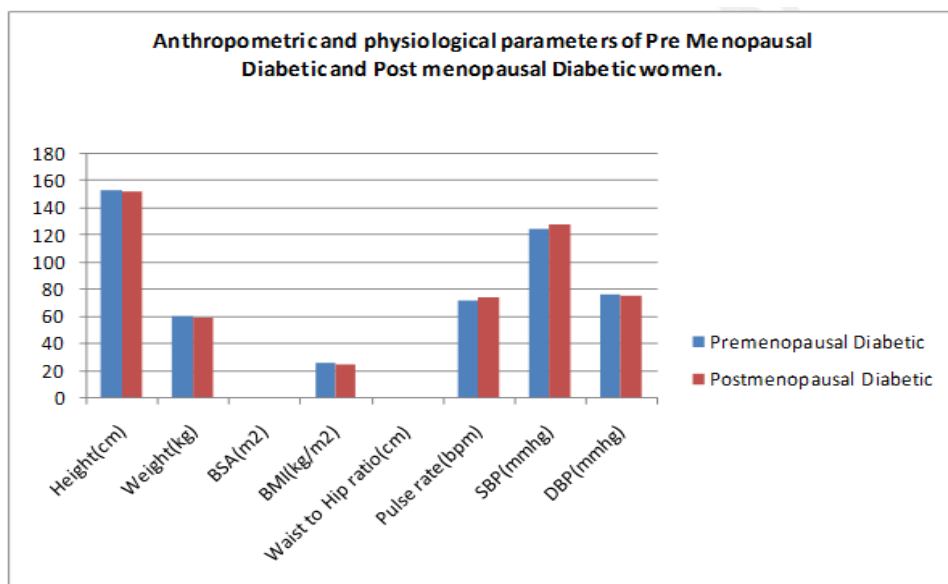
RESULTS

Table 1 shows Comparison of Anthropometric and physiological parameters of Pre and Post menopausal

Table 1
Anthropometric and physiological parameters of pre menopausal diabetic and Post menopausal diabetic women

Parameter	Pre menopause Diabetic(n=30)	Post menopause Diabetic (n=30)	p value
Height(cm)	153.82±4.16	152.29±5.55	0.10
Weight(kg)	60.93±6.18	59.56±7.35	0.38
BSA(m ²)	1.58± 0.08	1.55±0.11	0.03*
BMI(kg/m ²)	25.93±2.83	25.64±2.45	0.000**
Waist to Hip ratio(cm)	1.07±0.21	1.00±0.12	0.000**
Pulse rate(bpm)	71.96±4.05	74.06±3.87	0.94
SBP(mmHg)	124.73±6.79	128±11.90	0.05*
DBP(mmHg)	76.53± 5.79	75.33±3.83	0.35

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
*indicates level of significance. *P<0.05(S), **P<0.001



Here there is graphical representation of Comparison of Anthropometric and physiological parameters of Pre Menopausal Diabetic and Post menopausal diabetic women in Graph 1

Graph 1
Anthropometric and physiological parameters of Pre Menopausal Diabetic and Post Menopausal Diabetic women

Table 2
Biochemical and Hormonal parameters of Pre Menopausal Diabetic

and Post Menopausal Diabetic women.

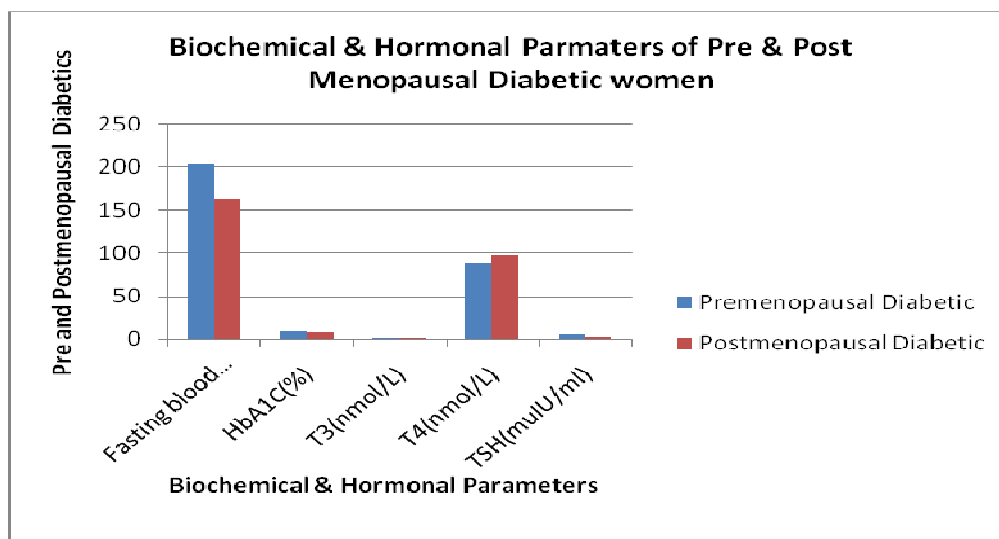
Parameter	Pre Menopause Diabetic (n=30)	Post menopause Diabetic (n=30)	p value
Fasting blood glucose(mg/DL)	204.1+76.90	163.83+53.06	0.18
HbA1C(%)	8.3+1.52	8.14+2.16	0.15
T3(nmol/L)	1.40+0.48	1.71+0.75	0.54
T4(nmol/L)	88.32+13.72	96.74+15.31	0.39
TSH(mulU/ml)	4.86+10.97	2.37+1.40	0.05*

Data is presented as Mean±SD(standard deviation)mg/DL- Milligrams per deciliter, nmol/L- Nanomoles per liter, mulU/ml- millimicrons-International units per milli liter, *Indicates the level of significance. *P<0.05, **P<0.001

Table 2 shows comparison of Biochemical and Hormonal parameters of Pre menopausal Diabetic and Post menopausal diabetic women. Fasting blood Sugar (FBS) levels non-significantly increased in Pre menopausal diabetic group. Glycosylated hemoglobin (HbA1C) levels were non-significantly increased in Post

menopausal diabetic group .T3 and T4 levels Non-significantly decreased and TSH levels significantly increased in Pre menopausal Diabetic group compared to Post menopausal -Diabetic group . The same results were shown here in the form of graphical representation in Graph 2.

Graph 2
Biochemical and Hormonal parameters of Pre Menopausal Diabetic and Post Menopausal Diabetic women.



Here there is graphical representation of Comparison of Biochemical and Hormonal parameters of Pre Menopausal Diabetic and Post menopausal diabetic women in Graph 2

DISCUSSION

In our study, significant changes have been observed in Pre menopausal diabetic and Post menopausal diabetic women. There were no significant changes observed in height and weight of both groups but BSA, BMI, and Waist to Hip Ratio of Pre menopause diabetic group were significantly more compared to Post menopause-Diabetic group. It may be due to obesity which in turn may be associated with high BMI, BSA and waist hip ratio. Twin studies have shown important (up to 75%) genetic explanation to BMI.^{13,14} With the exception of the rare mutations that cause severe morbid obesity, it seems that numerous genes, each with modest effect contribute to an individual's predisposition toward the more common forms of obesity.¹⁵ The risk of diabetes increases by 9% for each kg gained in weight¹⁶ and generally starts to increase at a BMI of 22¹⁷ and is 40 times higher at a BMI over 35.^{18,19} Insulin resistance is widely recognized as a fundamental defect seen in obesity and type 2 diabetes. The development of diabetes is strongly associated with overweight and

obesity. Over 90% of diabetics are overweight or obese²⁰ Weight gain and insulin resistance usually precede the onset of diabetes. Current theories indicate that diabetes develops when pancreatic beta cell output can no longer satisfy the demands imposed by increased insulin resistance.²¹ Kissebah et al showed that regional body fat distribution was associated with glucose intolerance and hyperinsulinemia in premenopausal women.²² There was significant increase in SBP and Non-significant decrease in DBP of Post menopausal diabetic group. It may be due to the age related decline in diastolic blood pressure. It 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 blood pressure. In our study, we also found that SBP increased in Post Menopausal-Diabetic group compared to Pre-menopausal diabetics. These observations were supported by Ronnback M et al.²³ There was no significant change in pulse rate. There was a non-significant Increase in HbA1C in Post

menopause Diabetic group. It may be due to the excess glucose present in blood reacts with hemoglobin.^{24, 25} There was a marked increase in HbA1C levels in diabetic patients, which could be due to excessive glycosylation of hemoglobin. Our observations are supported by Saha HR et al.²⁶ In our study, T3 and T4 levels are non-significantly decreased and TSH levels were significantly increased in Pre menopause-Diabetic group compared to post menopause-diabetic group. Decrease in T3,T4 and increase in the TSH level may indicate "Hypothyroidism". The frequency of "Hypothyroidism" in pre-menopausal diabetic women is more than in general population. In pre menopausal diabetic women, Hypothyroidism may influence metabolic control through effects on glucose metabolism which include reductions in hepatic glucose output, gluconeogenesis and peripheral glucose utilization.²⁷ Glycaemic status may inturn influence thyroid function. A low T3 state is observed in patients with severe hyperglycaemia.²⁸ Celani et al. reported a high frequency of thyroid function abnormalities in acute hospital admissions with poorly controlled diabetes.²⁹

CONCLUSION

REFERENCES

1. Feely J, Isles TE. Screening for thyroid dysfunction in diabetics. *BMJ*.1979Dec 1;2(6202):1439.
2. Gray RS, Irvine WJ, Clarke BF. Screening for thyroid dysfunction in diabetics. *BMJ*.1979 Dec 1;2(6202):1439.
3. Dias CM, Nogueira P, Rosa AN, De-Sa JV, Gouvea MF, Mannho-Falcos CM. Total cholesterol and high-density cholesterol in patients with insulin dependent diabetes mellitus. *Acta Medica*.1995; 8(11):619-28.
4. Murray RK, Granner DK, Mayes PA, Rodwell VW. *Harpers' Biochemistry*, New York: McGraw-Hill , 2000:1
5. Ramachandran A, Snehalatha C. Current scenario of diabetes in India. *Journal of diabetes*. 2009 Mar 1;1(1):18-28.
6. Celani MF, Bonati ME, Stucci N. Prevalence of abnormal thyrotropin concentrations measured by a sensitive assay in patients with type 2 diabetes mellitus. *Diabetes Res(Edinburgh, Scotland)*. 1993 Dec;27(1):15-25.
7. Udiong CE, Udoh AE, Etukudoh ME. Evaluation of thyroid function in diabetes mellitus in Calabar, Nigeria.*IJCB* 2007 Sep 1;22(2):74-8.
8. Shah SN. Thyroid disease in diabetes mellitus. *J Assoc Physicians India*1984 Dec;32(12):1057-9.
9. Güney E, Efe B, Akalin A, Kebapçı MN, Erenoğlu E. Thyroid disease in diabetes mellitus. *Turk J Endocrinol Metab*. 1999;3(3):119-22.
10. Poppe K, Glinoe D. Thyroid autoimmunity and hypothyroidism before and during pregnancy. *Human reproduction update*. 2003 Mar 1; 9(2):149-61.
11. World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society

of Hypertension (ISH) statement on management of hypertension. *J Hypertension*. 2003 Nov 1;21(11):1983-92.

From our study we found more prevalence of "Hypothyroidism" among pre menopausal diabetic women. So, prompt recognition of thyroid dysfunction in premenopausal diabetic women and controlling the blood glucose level is necessary to avoid further complications in future. So, routine thyroid screening should be included as a part of investigations in pre menopausal as well as post menopausal diabetic women. It will help in detection of thyroid abnormalities in subclinical stage itself.

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CONFLICT OF INTEREST

Conflict of Interest declared none.

12. DuBois D, DuBois EF. A formula to estimate the approximate surface area if height and weight be known. *Arch Int Med*. 1916; 17: 863-71.
13. Stunkard AJ, Harris JR, Pedersen NL, McClearn GE. The body-mass index of twins who have been reared apart. *N Eng J med*1990 May 24;322(21):1483-7.
14. Moll PP, Burns TL, Lauer RM. The genetic and environmental sources of body mass index variability: the Muscatine Ponderosity Family Study. *Am.J.Hum.Genet* 1991 Dec; 49(6):1243.
15. Damcott CM, Sack P, Shuldiner AR. The genetics of obesity. *Endocrinol Metab Clin North Am* 2003; 32:761-86.
16. Ford ES, Williamson DF, Liu S. Weight change and diabetes incidence: findings from a national cohort of US adults. *Am J Epidemiol* .1997 Aug 1;146(3):214-22.
17. Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol*. 1990 Sep 1;132(3):501-13.
18. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med*.2001 Sep 13;345(11):790-7.
19. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *Jama*. 1999 Oct 27;282(16):1523-9.
20. Albu J, Pi-Sunyer FX. Obesity and diabetes. In: Bray GA, Bouchard C, James WPT. *Handbook of Obesity*, Marcel Dekker New York, NY.1998:697-707.

21. DeFronzo RA. The triumvirate: β -cell, muscle, liver. A collusion responsible for NIDDM. *Diabetes*. 1988;37(6):667-87.
22. Kissebah AH, Vydelingum N, Murray R, Evans DJ, Kalkhoff RK, Adams PW. Relation of Body Fat Distribution to Metabolic Complications of Obesity*. *J Clin Endocrinol.Metab*1982 Feb;54(2):254-60.
23. Rönneck M, Fagerudd J, Forsblom C, Pettersson-Fernholm K, Reunanen A, Groop PH, Finnish Diabetic Nephropathy (FinnDiane) Study Group. Altered age-related blood pressure pattern in type 1 diabetes. *Circulation*. 2004 Aug 31;110(9):1076-82.
24. Gloria-Bottini F, Antonacci E, Bottini N, Ogana A, Borgiani P, De Santis G, Lucarini N. RH blood groups and diabetic disorders: Is there an effect on glycosylated hemoglobin level? *Hum Biol* .2000 Apr 1:287-94.
25. Sampson MJ, Gopaul N, Davies IR, Hughes DA, Carrier MJ. Plasma F2 Isoprostanes Direct evidence of increased free radical damage during acute hyperglycemia in type 2 diabetes. *Diabetes care*. 2002 Mar 1;25(3):537-41.
26. 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;1:450.
27. Mouradian M, Abourizk N. Diabetes mellitus and thyroid disease. *Diabetes Care* 1983;6(5):512-20.
28. Naeije R, Golstein J, Clumeck N, Meinhold H, Wenzel KW, Vanhaelst L. A low T3 syndrome in diabetic ketoacidosis. *Clin Endocrinol*. 1978 Jun 1;8(6):467-72.
29. Celani MF, Bonati ME, Stucci N. Prevalence of abnormal thyrotropin concentrations measured by a sensitive assay in patients with type 2 diabetes mellitus. *Diabetes Res(Edinburgh, Scotland)*. 1993 Dec;27(1):15-25.

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