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Correlation between Sub-clinical hypothyroidism and Hemoglobin A1c in non-diabetic Patients; A case control study

Khawar Hussain[1], Chetan Dev[2], Muhammad Zarrar Rajput[3], Waseem Raja Memon[4], Mir Tahir Hussain[5], Mukhtiar Ahmed Abro[6]

[1]Medical Officer, People's University of Medical and Health Sciences For Women Nawabshah Pakistan. email: dr_khawarhussain@yahoo.com

[2]General physician Medicine. Zayed military hospital Sharjah UAE. email: Drchetandev@ymail.com

[3]Assistant Professor Medicine, People's University of Medical and Health Sciences For Women Nawabshah Pakistan. email: Zarrarahmed@yahoo.com

[4]Assistant Professor Medicine, People's University of Medical and Health Sciences For Women Nawabshah Pakistan. email: waseemwasfi81@gmail.com

[5]Assistant Professor Medicine, People's University of Medical Health Science For Women Nawabshah Pakistan. email: drtahirhussaintalpur@yahoo.com

[6]Assistant Professor Medicine, People's University of Medical Health Science For women Nawabshah Pakistan. email: drmukhtiarahmed@gmail.com

Corresponding author: Waseem Raja Memon, Assistant Professor Medicine, People's University of Medical and Health Sciences For Women Nawabshah Pakistan. email: waseemwasfi81@gmail.com

Abstract

Aim: To assess correlation between Sub-clinical hypothyroidism and Hemoglobin A1c in non-diabetic individuals

Study Design: case control study

Place and duration: This study was conducted in, People's University of Medical and Health Sciences for Women Nawabshah Pakistan since May 2019 to May 2020

Methodology: A case-control study with a total of 200 individuals was performed in our hospital. In both case and control groups, 100 patients were assigned. Cases were non-diabetics individuals suffering from subclinical hypothyroidism. Controls were patients' family and friends who were age and sex-matched and were without subclinical hypothyroidism. To compare the demographic and biochemical parameters between cases and controls, an independent student's t-test was used. To determine the relationship between serum TSH and HbA1c, a Pearson correlation test was utilized.

Result: No significant association between cases and controls have been observed in terms of gender and Mean age. In the case and control groups, the mean serum TSH level was 7.13 ± 1.29 μIU/ml, and 2.51 ± 0.68 μIU/ml and the mean HbA1c levels were 5.88 ± 0.41 and 5.09 ± 0.22, respectively (p-value of < 0.0001). Pearson's correlation coefficient revealed that the levels of serum TSH (U/L) and HbA1c in all study participants had a significantly positive correlation ($r=0.551$, $p<0.001$).

Conclusion: HbA1c values are higher in hypothyroid persons with subclinical hypothyroidism. The effects of increased serum TSH on the HbA1c must be taken into consideration when assessing the HbA1c for analysis of diabetes or pre-diabetes in subclinical hypothyroid individuals.

Keywords: Sub Clinical Hypothyroidism, Diabetes Mellitus, HbA1c, Non-diabetic individuals

Introduction:

Thyroid diseases are quite prevalent and followed by diabetes mellitus (DM). A diminution in thyroid hormone production describes hypothyroidism. [1] A high blood Thyroid-stimulating hormone (TSH) levels and normal levels of free Triiodothyronine (FT3), free Tetrathyroxine (FT4) are all signs of subclinical hypothyroidism (SCH). Condition including dilutional hyponatremia, anaemia, and hyperlipidemia might make it worse. [2] The majority of the time, subclinical hypothyroidism has no symptoms. When symptoms appear, they are usually nonspecific and widespread, such as anxiety, insomnia, lethargy, goiter, weight gain, loss of hair, and temperature intolerance.[3]

Research suggests that untreated higher TSH levels can lead to hypertension and excessive cholesterol levels.[4, 5] Hypothyroidism has been associated with many cardiovascular diseases, including hypertension and hypercholesterolemia.[6] In an investigation of older individuals, with a blood TSH level of 7 mIU/L or more were twice as likely as those with a normal TSH level to develop congestive heart failure.[7] One more complication is discussed in a study that the rate of spontaneous abortion in pregnant women with Subclinical Hypothyroidism rises in early pregnancy.[5]

SCH affects more women than males and is more common in the elderly. [8] According to a study conducted at the Jinnah Postgraduate Medical Centre (JPMC) in Karachi, 62.05 % of patients had thyroid problems, while 9.42 % had SCH. [9] The same findings were also observed in a recent study conducted in Hyderabad, Sindh. [10] Hypothyroidism affects roughly 10.6% of the population in the United States of America. [11]

The HbA1c concentration is affected by conditions that impact erythrocyte turnover or survival, as well as the prevailing glycaemia. As a result, conditions that influence red blood cells turnover or lifespan may result in HbA1C levels that are incorrectly increased or lowered.[12] Although there is a known link between thyroid abnormalities and Diabetes Mellitus, further research is needed to determine the impact of thyroid diseases on glucose metabolism in individuals free from diabetes. Recent research has revealed that it causes a false increase HbA1c in the absence of diabetes. [13]

The current study aimed to measure HbA1c levels in SCH participants without diabetes, and determine the consequence of SCH on HBA1c levels in individuals without diabetes.

Methodology: -

This study was conducted in, People's University of Medical and Health Sciences for Women Nawabshah Pakistan since May 2019 to May 2020. Permission was taken from the ethical review committee of the institute. This study incorporated two hundred people, including a hundred in each group. Controls were patients' family members and companions who were age and gender-matched but were without subclinical hypothyroidism. There were 100 cases who were non-diabetics and had subclinical hypothyroidism.

Patients with diabetes, anaemia, renal failure, blood disorders, history of blood transfusion in the last three months, severe hypertriglyceridemia, hepatic disease, and patients already on thyroid treatment were all excluded.

The following parameters were measured: Haemoglobin (Hb), fasting blood sugar (FBS), fasting lipid profile, Liver Function Test (LFT), HbA1c, serum T3, T4, TSH, and Complete Blood Count (CBC). All data was gathered and statistically analyzed to assess the importance of various parameters. All values were expressed as mean, standard deviation. Pearson correlation test was executed to find the relationship between serum TSH and HbA1c. The Independent student's t-test was executed to associate the case and control groups. In order to be considered statistically significant, a P-value of less than 0.05 was required.

RESULTS:

There were 200 participants in this research (100 cases and 100 controls). We analyzed that the mean ages were 47.10 ± 13.02 and 47.67 ± 14.39 years, in controls and cases, respectively (p= 0.81). The case groups had 46 males and 54 females, and in the control group, 49 males and 51 females (p-value of 0.67). **(**As shown in Table 1**)**

We evaluated that the case group had a mean fasting blood sugar level of 104.34 ± 5.11, and the control group had a 103.88 ± 4.98. Between the case and control groups, no significant difference was observed. Similarly, hemoglobin levels in the cases and controls were 12.68 ± 1.10 and 12.98 ± 1.08, respectively, with a p-value of 0.88. In the cases and controls, the mean serum TSH level was 7.13 ± 1.29 µIU/ml & 2.51 ± 0.68 µIU/ml, respectively. Among cases and controls, we found a statistically significant difference (P < 0.001). In the case and control groups, the mean HbA1c levels were 5.88 **± 0.41** and 5.09 **± 0.22**, respectively. With a p-value of < 0.0001. (As shown in Table 2)

We also discovered a significant positive link between serum TSH (U/L) and HbA1c as per Pearson's correlation test (r=0.551, p< 0.0001) (As shown in Table 3)

Table 1: Demographic Characteristics of the study participants (n=200)

Variable	**Case (N= 100)**	**Control (N=100)**	**P-value**
Age (Years)	47.10 ± 13.02	47.67 ± 14.39	0.81
Gender			
Males (n=95)	46	49	0.67
Females (n=105)	54	51	

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Table 2: Study parameters in the case and the control groups.

Parameter	Case (mean ± SD)	Control (mean ± SD)	P-value
HbA1c (%)	5.67 ± **0.41**	5.09 ±**0.22**	<0.001
FBS	104.34 ± **5.11**	103.88 ± **4.98**	0.76
Haemoglobin (gm/ dl)	12.68 ± **1.10**	12.98 ± **1.08**	0.88
S. TSH (µIU/ml)	7.13 ± **1.29**	2.51 ± **0.68**	<0.001
S.T3 (ng/ml)	1.13 ± **0.31**	1.19 ± **0.33**	0.69
S.T4 (µg/dl)	7.10 ± **1.03**	7.45 ± **0.98**	0.09

Table 3: The correlation between the levels of serum TSH (µU/L) and HbA1c

		HbA1c	TSH (µU/L)
HbA1c	Pearson Correlation	1	0.551
	P		< 0.0001
	N	100	100
TSH (µU/L)	Pearson Correlation	0.551	1
	P	<0.0001	
	N	100	100

DISCUSSION

We found that the difference between the cases with SCH and the controls, mean serum TSH level was statistically significant (p< 0.001). When comparing the case group, which included SCH patients, to the control group, which included healthy people, blood TSH levels were considerably higher in the case group. The difference between the cases and controls in mean HbA1c levels was statistically significant (p < 0.001). The HbA1c values in the cases were significantly higher than those in the controls.

Since there was no statistically significant variation in demographic characteristics or biochemical parameters between the cases with SCH and controls with healthy persons. As a result, it can be assumed that these variables did not affect HbA1c levels in both groups. Similar findings were reported in another study that further validates our study findings. [14]

We found a significantly correlated association between HbA1c and S. TSH levels. In today's world, SCH is a frequent endocrine disease. The effects of thyroid hormones on HbA1c levels in patients with thyroid dysfunction must be investigated so that their results can be better interpreted. The inclusion and exclusion criteria were developed with the many non-glycemic factors impacting glycosylated haemoglobin in mind. Acute and chronic blood loss, hemolytic and , other anaemia, haemoglobin variations, blood urea, and serum creatinine were all ruled out as confounding medical conditions.[15] In the case group, which included participants with Subclinical hypothyroidism, had considerably higher blood TSH levels than the controls, which included healthy individuals. The difference in mean HbA1c levels between the cases and controls was significant (p <0.001). The case group's HbA1c readings were substantially higher than the control groups. In the current study, we found that when it came to age, gender, FBS, haemoglobin, serum T3, and serum T4 levels, Hba1C, the only difference between the case and control groups were serum TSH. The cases with SCH and the controls persons did not differ statistically significantly in any of the other factors.

Haemoglobin, Fasting Blood Sugar, T3 and serum T4, were all within acceptable limits in both groups. As a result, we can conclude that age, sex, and FBS levels, serum T3, and serum T4 did not affect HbA1c levels in both groups. According to the findings, serum TSH levels were substantially greater in those with SCH than in healthy people, and HbA1c values were significantly higher in the cases than in the controls. According to Pearson's correlation coefficient (r=0.551, p<0.0001), there was a statistically significant link between serum TSH and HbA1c levels in all research individuals. Another study also reported that TSH and HbA1c had a positive and significant association (r=0.46). [16] This could be owing to the link between insulin resistance and SCH in individuals or the action of thyroid hormones on erythropoiesis

There appears to be a link between SCH and hyperinsulinemia and insulin resistance. Insulin resistance and SCH are linked by a number of processes that affect glycemic regulation.[16] A study performed in Kuwait conducted a study on women to see if there was a link between SCH and insulin resistance. They discovered that insulin levels in the SCH group were considerably higher than in the control group. [17]Another study compared hypothyroid, non-diabetic subjects having normocytic normochromic anaemia to euthyroid, & non-diabetic individuals reported normocytic normochromic anemia. Hypothyroid patients had HbA1c of 6.32 compared to 5.87 in the euthyroid group, a statistically significant difference. [18] Similarly, TSH and HbA1c were also found to be substantially associated in a study performed in Pakistan. [19]
Thyroid illness affects about 10-15% of persons with DM. [20] HbA1c were reported elevated in hypothyroid patients in diabetic and non-diabetic individuals. An Indian study stated that thyroid dysfunction is quite prevalent (21.5%) among type 2 DM patients, with SCH being the most common. [21]

Conclusion:

HbA1c values are significantly higher in subclinical hypothyroid patients, according to the findings of this study. Anemia can also cause an increase in HbA1C in hypothyroidism. As a result, it's a good idea to think about it before diagnosing diabetes purely based on HbA1C. However, bigger cohort studies are needed to determine the specific mechanism.

Permission:

It was taken from the ethical review committee of the institute

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Conflict of interest:
None

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