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Original Research

Prevalence Of Subclinical Hypothyroidism Among Patients Of Diabetes Mellitus Attending Tertiary Care Centre

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ABSTRACT

Background-. Early detection and treatment of SCH in diabetes patients may be beneficial in better control of diabetes and improvement of quality of life.

Objectives- To screen diagnosed diabetes mellitus patients for subclinical hypothyroidism and assess correlation between SCH with duration of diabetes in patients of diabetes mellitus. To assess correlation between TSH and HbA1c in diabetes mellitus patients.

Methodology: This study wasconductedas a facility based observational cross-sectional study on patients with diabetes mellitus attending outpatient department,Department of Medicine, People's College of Medical Sciences and Research Centre&associatedPeople'sHospitalBhopal,duringthestudyperiodof18months,i.e.from1st November2022 to 30th April2024.All patientsunderwent blood investigations including blood glucose estimation, HbA1c levels, TSH, FT3 and FT4.

Results: The present study was conducted on a total of 250 patients with diabetes with meanageof51.06±14.4 years. 9.2% cases had subclinical hypothyroidism. We observed a significant association of subclinical hypothyroidism with age, duration of diabetes, fasting blood glucose, postprandial blood glucose and HbA1c levels ($p<0.05$). We observed a weak positive correlation of TSH levels with duration of diabetes as well as HbA1clevels ($r=0.30$-0.50; $p<0.05$).

Conclusions-Thyroid disorders, particularly subclinical hypothyroidism are common in patients with diabetes mellitus. Advancing age, prolonged duration of diabetes, poor glycemic control (raised FBS, PPBS and HbA1c) levels are significantly associated with subclinical hypothyroidism. Both duration of diabetes and raised HbA1c levels showed correlation with TSH levels. All the patients with diabetes must be screened for thyroid dysfunctions especially patients with advancing age, females, prolonged diabetes and uncontrolled hyperglycemia.

Keywords- Subclinical hypothyroidism, thyroid disorders, diabetes, glycaemic index.

INTRODUCTION

Diabetes mellitus is one of the commonest chronic metabolic disorder, characterized by persistent hyperglycemia, which have been attributed to mainly two factors i.e. impaired insulin secretion and/ or resistance to insulin action.[1,2] According to Indian Diabetes Federation (2021), approximately 531 million adults are living with diabetes globally. However, due to significant increase in burden of diabetes in our country, India is considered as "Diabetic Capital of the World". One in 11 adults (approximately 90 million adults) are known to be suffering from diabetes according to International Diabetes Federation (IDF-2021) in Southeast Asian region. Overall the prevalence of diabetes is projected to increase to 113 million adults by the year 2030 and more than 150 million by 2045.[3]

Thyroid disorders are second most common endocrinal disorders worldwide,[4] characterized by abnormal levels of thyroid hormones (T3 and T4) and abnormal thyroid stimulating hormone (TSH) levels. Thyroid disease are reported to be more common in females than males.[5] Thyroid dysfunction and diabetes may have common link and coexistence of both the disorders may have significant negative impact on overall health status of an affected individual. On one hand, thyroid hormones have antagonist action on insulin receptors and may directly affect insulin secretion, on the other hand, diabetes may affect thyroid functions by their influence on hypothalamic thyroid stimulating

hormone (TSH) and thyroid hormones at thyroid gland level.[6] Literature suggest that irrespective of the level of glycemia and glycemic control, the nocturnal peak of TSH is absent among diabetics and thyroid dysfunction is known to impede the control of blood glucose levels.[6]

The association between diabetes and hypothyroid disorders have been established in previous studies. Overall, the prevalence of overt hypothyroidism is reported to be higher in type 2 diabetes mellitus(T2DM) cases as compared to general population.[4,7] However, the data depicting relationship between diabetes mellitus and subclinical hypothyroidism is scarce and controversial.[8] Screening of Subclinical hypothyroidism (SCH) in patients with diabetes mellitus is essential as majority of patients may be asymptomatic and the co-existence of both these conditions may worsen the glycemic control, increasing the risk of microvascular and macrovascular complications of diabetes.[9] Early detection and treatment of SCH in diabetes patients may be beneficial in better control of diabetes and improvement of quality of life. The present study was therefore conducted at tertiary care centre to screen diagnosed diabetes mellitus patients for subclinical hypothyroidism and assess correlation between SCH with duration of diabetes in patients of diabetes mellitus. We also assessed correlation between TSH and HbA1c in diabetes mellitus patients.

METHODOLOGY

This study was conducted as a facility based observational cross sectional study on patients with diabetes mellitus attending outpatient department, Department of Medicine, People's College of Medical Sciences and Research Centre & associated People's Hospital Bhopal, during the study period of 18 months, i.e. from 1st November 2022 to 30th April 2024. All willing patients of the diabetes mellitus belonging to more than 18 years of age were included whereas pregnant women, patients with known thyroid disorders and on drugs which interfere with thyroid function e.g. Amiodarone, Lithium, Iodides Glucocorticoids, propanolol, TCA (tricyclic antidepressants), SSRI, Dopamine agonists Phenobarbitone, Rifampin, Phenytoin, Carbamazepine were excluded from the study.

After obtaining ethical clearance from Institute's ethical committee, all the patients with diabetes mellitus fulfilling the inclusion criteria and willing to participate in the study were enrolled. Detailed history was obtained and all the patients were subjected to detailed general and systemic examination and findings were documented. Further, patients underwent blood investigations including blood glucose estimation, HbA1c levels, TSH, FT3 and FT4. Subclinical hypothyroidism was defined according to European thyroid journal guidelines as TSH >4-10mU/l (grade1B hypothyroidism) with normal FT3 and FT4 levels with absence of clinical signs of hypothyroidism.

STATISTICAL ANALYSIS

Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and proportions whereas continuous data was expressed as mean and standard deviation. All the patients were screened for presence of subclinical hypothyroidism and expressed in proportion. Correlation of SCH with duration of diabetes and HbA1c was assessed using Pearson Correlation Coefficient whereas association was noted using Chi square test. P value of less than 0.05 was considered statistically significant.

RESULTS

The present study was conducted on a total of 250 patients with diabetes seeking care at our hospital. In present study, mean age of patients with diabetes enrolled in our study was 51.06±14.4 years and 64% cases with diabetes were females. 9.2% cases had subclinical hypothyroidism in our study (Figure 1). However, 68% cases were euthyroid. 20% cases had overt hypothyroidism, whereas 1.6% and 1.2% cases had subclinical and overt hyperthyroidism respectively.

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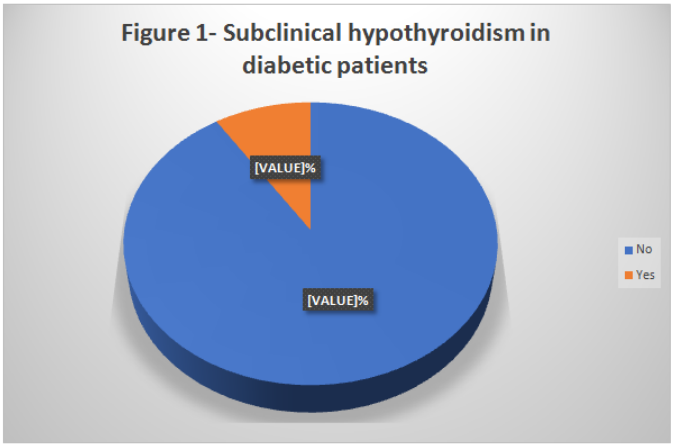

Table1-Association of subclinical hypothyroidism with baseline variables and diabetes characteristics in diabetic patients

Variables		Subclinical hypothyroidism				P value
		Absent		Present		
		Frequency	Percentage	Frequency	Percentage	
Age	≤30	21	95.5	1	4.5	**0.01**
	31-40	33	91.7	3	8.3	
	41-50	49	96.1	2	3.9	
	51-60	73	93.6	5	6.4	
	61-70	41	85.4	7	14.6	
	>70	10	66.7	5	33.3	
Sex	Male	80	88.9	10	11.1	0.43
	Female	147	91.9	13	8.1	
Duration of diabetes	≤5	122	94.6	7	5.4	**0.003**
	>5-10	85	86.7	13	13.3	
	>10-15	20	90.0	2	9.1	
	>15	0	0.0	1	100.0	
	Mean±SD	4.64±2.06		6.83±3.87		
Fastingbloodsugar(mg/dl)	<100	52	98.1	1	1.9	**0.044**
	100-125	64	92.8	5	7.2	
	>125	111	86.7	17	13.3	
	Mean±SD	155.26±72.4		166.74±90.45		
Post prandial bloodsugar(mg/dl)	<140	64	98.5	1	1.5	**0.046**
	140-199	81	88.0	11	12.0	
	≥200	82	88.2	11	11.8	
	Mean±SD	196.25±82.5		238.30±91.9		
HbA1c(%)	≤7.5	120	95.2	6	4.8	**0.036**
	7.5-8.5	47	88.7	6	11.3	
	>8.5	60	84.5	11	15.5	
	Mean±SD	8.08±1.94		10.07±3.44		

As observed from table 1, we observed a significant association of subclinical hypothyroidism with age, duration of diabetes, fasting blood glucose, postprandial blood glucose and HbA1c levels ($p<0.05$).

Table 2- Correlation of TSH levels with duration of diabetes, FBS, PPBS andHbA1clevels

Correlation of TSH with	R	R Square	Adjusted RSquare	Std. Errorof the Estimate	F	Sig.
Duration	0.301	0.040	0.037	3.092	**10.435**	**0.001**
FBS	0.093	0.009	0.005	73.951	2.161	0.143
PPBS	0.049	0.002	-0.002	84.176	0.602	0.439
HbA1c	0.378	0.077	0.073	2.108	**20.741**	**0.0001**

We observed a weak positive correlation of TSH levels with duration of diabetes as well as HbA1clevels ($r=0.30$-0.50; $p<0.05$) (Table 2).

DISCUSSION

Literature suggests a common link between thyroid disorders and diabetes. Co- existence of both the conditions is associated with significant negative impact on health of an affected individual.[6] As hypothyroidism patients may be asymptomatic, screening for thyroid disorders especially subclinical hypothyroidism is essential as both the disease can affect each other. Coexistence of thyroid disorders in patients with diabetes may worsen their glycemic control and increase the risk of microvascular as well as macrovascular complications.[9] The present study was conducted on a total of250 diabetic patients. In this study, we aimed to screen diagnosed diabetes mellitus patients for subclinical hypothyroidism and to assess correlation between SCH with duration of diabetes in patients of diabetes mellitus. We also assessed correlation between TSH and HbA1c in diabetes mellitus patients.

The development of thyroid dysfunction in individuals with type 2 diabetes mellitus is mostly attributed to insulin resistance, which is commonly observed in these patients. Hypothyroidism and hyperthyroidism are two conditions that can result from thyroid malfunction. Patients with diabetes may also experience sub-clinical hypothyroidism, which

can exacerbate diabetic consequences such as neuropathy, retinopathy, and cardiovascular disease.[10]

Literature suggest that prolonged duration of hyperglycemia may have cumulative effect on Thyroid disorders in patients with Diabetes.[11] In our study, mean duration ofdiabetes was 6.83±3.86 years. Duration of diabetes was less than 5 years in 51.6% cases whereas it ranged between 6 to 10 years in 39.25 cases. We observed a significant association of subclinical hypothyroidism with prolonged duration of diabetes ($p<0.05$), however, no such association was observed between overt hypothyroidism and duration of diabetes ($p>0.05$). We also observed a weak positive correlation of duration of diabetes with serum TSH levels ($r=0.301$; $p<0.05$). Our study findings were consistent with the findings of Mehalingam et al in which, for individuals with hypothyroidism, the length of diabetes (more than five years) was a significant contributing factor.[12]. According to a study by Al-Geffari et al, having diabetes for more than ten years was a significant risk factor for the development of thyroid dysfunction.[13] Ogbonna et al also found a significant association of thyroid dysfunctions with increasing duration of diabetes ($p<0.05$).[14] However, Kamendu et al observed hypothyroidism prevalence to be higher in patients with duration of disease more than 5 years, but the difference was statistically insignificant ($p>0.05$).[15] Reshdat et al also found duration of diabetes to have no impact on prevalence of SCH.[16] Mean FBS and PPBS in our study group was 166.74±90.45 and 238.30±91.89 mg/dl. FBS levels were more than 100 in 78.8% cases and among them FBS levels were raised above 125 mg/dl in 51.2% cases. Only half of the patients with diabetes had FBS levels above 125 mg/dl, and this could be attributed to diabetic awareness among the study participants as patients are advised and motivated for strict glycaemic control with dietary modification and lifestyle changes at each visit at our hospital. Similarly, PPBS levels were more than 140 mg/dl in 74% cases, of them levels above 200 mg/dl were noted in 37.2% cases. Our study found a significant association of subclinical hypothyroidism with elevated FBS and PPBS levels ($p<0.05$), however, no such association was observed between overt hypothyroidism and blood glucose levels ($p>0.05$). We found no significant correlation of serum TSH with FBS and PPBS levels ($p>0.05$). Mean HbA1c levels in our study group were 10.07±3.45%. HbA1c levels were >7.5% in 49.6% cases with elevated levels above 8.5% in 28.4% cases. We found a significant association of HbA1c levels with both subclinical as well as overt hypothyroidism ($p<0.05$). Also we found a weak positive correlation of HbA1c levels with TSH levels ($r=0.378$; $p<0.05$). Our study findings were supported by the findings of Billic-Komarica et al, in which the authors found a significant positive correlation of HbA1c with serum TSHlevels ($r=0.46$; $p<0.05$).[17] Manjunath et al observed a significant association of subclinical hypothyroidism with diabetic retinopathy[18], which may be proxy indicator of uncontrolled glycemic status as complications are more common in patients with uncontrolled blood glucose levels.[18] Kamendu et al also documented a significant association of hypothyroidism with higher HbA1c levels (>7%) supporting our study findings.[15] According to research by Sharma et al, the mean HbA1c for diabetics without SCH was 7.89%, whereas it was 8.33% for those with SCH. According to statistics, this difference was not substantial. There was no discernible correlation between TSH and HbA1c.[19] The findings of our study were consistent with the findings of Cho et al, whereby the authors observed a higher frequency of SCH, particularly in the group with the highest HbA1c than in the well-controlled group. A lower glycemic control group was associated with a higher risk of SCH; the odds ratio for SCH in patients with HbA1c $\geq$ 9% compared to < 7% was 2.52.[20] Makadia et al observed significantly higher levels of HbA1c in patients with non diabetic subclinical hypothyroidism as compared to controls 5.70±0.35 vs. 5.26±0.17%; $p<0.0001$).[21] Reshdat et al on the other hand observed no significant association of subclinical hypothyroidism with FBS, PPBS as well as HbA1c, which was contrasting to our study.[16]

Our study had certain limitations, first our study had small sample size therefore further studies need to be done to validate the results. Second, selection bias was inevitable in our study as evident from a greater number of females as compared to males. Third, our study was conducted in a tertiary care center and had cases from endocrine department hence it is not representative of population at large. Fourth, our study had less number of type 1 diabetes mellitus patients hence no clear association between type 1 diabetes mellitus and thyroid disorders was found. Fifth, anti-thyroid peroxidase (anti TPO) antibody quantification was not carried out. Therefore, it was not possible to evaluate the involvement of thyroid auto-immune antibodies in individuals with type 2 diabetes who developed thyroid dysfunction. Sixth, the study was conducted on diabetic patients, lack of control group is anobvious limitation. Seventh, effect of treatment of diabetes on thyroid dysfunctions was not assessed in our study.

CONCLUSIONS

Thyroid disorders are common in patients with diabetes mellitus and the spectrum of thyroid disease may range from subclinical to overt hyperthyroidism and hypothyroidism. Subclinical Hypothyroidism is common in diabetic patients. Advancing age, prolonged duration of diabetes, poor glycemic control (raised FBS, PPBS and HbA1c) levels are significantly associated with

subclinical hypothyroidism. Both duration of diabetes and raised HbA1c levels showed correlation with TSH levels. All the patients with diabetes must be screened for thyroid dysfunctions especially patients with advancing age, females, prolonged diabetes and uncontrolled hyperglycemia.

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