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A prospective evaluation of retinopathy in diabetes patients with coexisting hypothyroidism

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Abstract
Background: Diabetes is the cause of 2.6% of global blindness which occur due to diabetic retinopathy caused by long term accumulated damage of small blood vessels in the retina. Hypothyroidism is common endocrine disorders that coexist with diabetes mellitus. Concurrent hypothyroidism, treated with thyroxin, appears to have a sparing effect on the risk of developing retinopathy among patients with type 2 diabetes.
Material and method: This is a prospective observational study conducted in the department of ophthalmology. During our study period we have enrolled 240 patients with diabetes mellitus based on selection criteria and evaluated for diabetic retinopathy and hypothyroidism. A standard diagnostic criterion was followed for diagnosis of diabetes mellitus and all patients were assessed by two senior ophthalmologists for detection of retinopathy. Classification of diabetic retinopathy was based on the early treatment of diabetic retinopathy study (ETDRS).
Result: Diabetic retinopathy was present in 12(30%) patients in type 2 diabetes mellitus group and 18(45%) patients in type 2 DM plus hypothyroidism group. In DM plus hypothyroidism patients, Mild nonproliferative retinopathy present in 4 (22.22%) patients, Moderate nonproliferative retinopathy 8(44.44%) patients, severe nonproliferative retinopathy 1(5.5%) patients, Early proliferative retinopathy 4(22.22%) patients and High-risk proliferative retinopathy 1(5.5%) patients.
Discussion and conclusion: From present study we can conclude that that prevalence of hypothyroidism was higher among type 2DM mellitus patients in comparison to general population without type 2 DM. Diabetic retinopathy was more common on type 2 DM plus hypothyroidism group then type 2 diabetes mellitus group. We have observed that Moderate nonproliferative retinopathy is more common in both group but early proliferative retinopathy is more common in type 2 DM plus hypothyroidism group then yrs type 2 diabetes mellitus group.

Keywords: Type 2 diabetes mellitus, hypothyroidism, diabetic retinopathy

Introduction
Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The number of cases of diabetes mellitus has increased from 108 million in 1980 to 422 million in 2014. Its Prevalence is increasing more rapidly in low- and middle-income countries than in high-income countries [1]. It is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. Diabetes is the cause of 2.6% of global blindness which occur due to diabetic retinopathy caused by long term accumulated damage of small blood vessels in the retina [2]. It has been reported that individual with diabetes mellitus is 25 times more prone to become blind then non diabetic individual. Diabetic retinopathy is classified into two stages: nonproliferative and proliferative. Nonproliferative retinopathy first decade or early in the second decade of the disease and is marked by retinal vascular micro aneurysms, blot haemorrhages, and cotton-wool spots [3].
Thyroid gland is responsible for physiological functions and developmental processes of various organs including retina. Hypothyroidism is common endocrine disorders that coexist with diabetes mellitus. Talwalkar P, Deshmukh V, Bhole M *et al.* has reported that there is a high (>20%) prevalence of hypothyroidism in patients with T2DM [4]. Palma, C.C.S.S.V., Pavesi, M., Nogueira, V.G. *et al.* conclude that screening for thyroid disease among patients with diabetes mellitus should be routinely performed considering the prevalence of new cases diagnosed and the possible aggravation the classical risk factors such as hypertension and dyslipidemia, arising from an undiagnosed thyroid dysfunction [5]. Various literature reviews suggest that undiagnosed hypothyroidism disrupts thyroid hormone homeostasis to the extent that it may contribute to a higher incidence of DR [6]. Sailesh S, Randeva, Harpal S *et al.* has concluded that concurrent hypothyroidism, treated with thyroxine, appears to have

a sparing effect on the risk of developing retinopathy among patients with type 2 diabetes [7]. Wu J, Yue S, Geng J, *et al.* from his meta-analysis concluded that SCH was associated with DR in diabetes and exposure to SCH can increase the DR risk 2.13 times [8].

Based on above literature we have designed this study with an aim and objective to know the prevalence of thyroid dysfunction in type 2 diabetes mellitus patients, prevalence of diabetes retinopathy and it association with hypothyroidism in coastal district.

Material and method

This is a prospective observational study conducted in the department of ophthalmology Konaseema institute medical science Amalapuram Andhra Pradesh India from October 2019 to May 2021.

Selection of patients

During our study period we have enrolled 240 patients with diabetes mellitus based on selection criteria and evaluated for diabetic retinopathy and hypothyroidism. 240 normal healthy people for the evaluation of prevalence of subclinical hypothyroidism in general population and diabetes mellitus patient based on selection criteria. Out of these patients in diabetes group we have selected two group first DM + Euthyroidism group and second DM+ (diabetes mellitus + hypothyroidism) group. Each group have 40 patients.

Selection criteria: patients were selected based on following inclusion and exclusion criteria,

Inclusion criteria

Age more than18 years
Both sex

Exclusion criteria

Known case of thyroid disorder
Hepatic and renal disorder
Cardiovascular diseases
Malignancy
Glaucoma
Hypertensive
Pregnancy
Patients in whom fundus cannot be examined

Sample size: Considering the prevalence of hypothyroidism to be 20 % based on previous study of Talwalkar P, Deshmukh V, Bhole M *et al.* and prevalence of diabetes mellitus to be 11.8%, precision of 5%, confidance interval of 95% and population of Amalapuram India 141000, sample size was calculated for prevalence of hypothyroidism to be 240 [4]. For calculation of sample size we used calculator for Sample size for a prevalence survey, with finite population correction [9].

Ethics: Present study is approved by the institutional ethics committee. Written informed consent was obtained from all patients or relatives of patients before enrolling them for study.

Method

After enrolment of patients a detailed relevant history of patients were taken and detailed clinical examination was done. All information obtained from patients was recorded in predesigned Performa. After 8 hours of fasting, serum levels of glucose by fully automated clinical biochemistry analyzer EM 200. Serum free T3 free T4 and TSH were measured using standard assay. American Diabetes Association Diabetes Care 2020 was used for the diagnosis of diabetes mellitus and Primary hypothyroidism is defined by TSH concentrations above the reference range (most commonly used 0–4-4–0 mIU/L) and free thyroxin concentrations below the reference range [10, 11]. All patients were assessed by two senior ophthalmologists for detection of retinopathy. Classification of diabetic retinopathy was based on the early treatment of diabetic retinopathy study (ETDRS). Classified as Mild nonproliferative retinopathy, Moderate nonproliferative retinopathy, severe nonproliferative retinopathy, early proliferative retinopathy and High-risk proliferative retinopathy as per specification mentioned [12].

Statistical analysis: Data were recorded in excel sheet and statistical Analysis was done with software SPSS-14 version. Qualitative data were calculated as percentage and proportions and were analyzed by Chi-square test. Quantitative data were expressed as mean ±SD and these data were analyzed by unpaired student t test. The P value less than 0.05 were taken as significant.

Result

As per sample size calculation 240 patients with diabetes and 240 patients without diabetes mellitus from general population were enrolled for this study.

Table 1: Frequency of hypothyroidism in general population and type 2 DM patients

Variable		With DM	Without DM	P value
Hypothyroidism	Absent	186(77.5%)	218(90.83%)	.000
	Present	54(22.5%)	22(9.16%)	

As per table 1, out of 240 patients with diabetes mellitus 186 (77.5%) without hypothyroidism and 54 (22.5%) patients were hypothyroidism. In general population hypothyroidism was present in 22 (9.16%) patients and absent in 218 (90.83%). This difference is significant statistically.

Table 2: Demographic profile of patients with type 2 DM and type 2 DM plus hypothyroidism

Variables		Type 2 DM patients	Type 2 DM plus hypothyroidism	P value
Age (yrs)		47.3±10.28	44.86±12.72	.21
sex	Male	22	14	.07
	Female	18	26	
Duration of diabetes mellitus		6.43±2.96	7.06±3.5	.24
Presence of diabetic retinopathy		12(30%)	18(45%)	

In present study 40 patients with type 2 DM and 40 patients with type 2 DM plus hypothyroidism were enrolled for evaluation of retinopathy. Mean age of patients with type 2 DM was 47.3±10.28 years and with type 2 DM plus hypothyroidism was 44.86±12.72 years. Both groups were statistically similar to each other and the p value was more than .05. Both groups are similar to each other with respect sex distribution (P = .07). But there is male predominance in type 2 diabetes mellitus group and female predominance in Type 2 DM plus hypothyroidism group. Duration of diabetes mellitus was 6.43±2.96 yrs type 2 diabetes mellitus group and 7.06±3.5 years in type 2 DM plus hypothyroidism group. This finding was not significant statistically.
Diabetic retinopathy was present in 12(30%) patients in type 2 diabetes mellitus group and 18(45%) patients in type 2 DM plus hypothyroidism group.

Table 3: Distribution of severity of diabetic retinopathy in type 2 DM patients

Variable	Number	percentage
Mild nonproliferative retinopathy	2	16.6%
Moderate nonproliferative retinopathy	6	50%
severe nonproliferative retinopathy	2	16.6%
Early proliferative retinopathy	1	4.76%
High-risk proliferative retinopathy	1	4.76%

Regarding severity of retinopathy as per ETDRS in type 2 DM patients, Mild nonproliferative retinopathy present in 2(16.6%)patients, Moderate nonproliferative retinopathy 6(50%) patients, severe nonproliferative retinopathy 2(16.6%)patients, Early proliferative retinopathy 1(4.76%) patients and High-risk proliferative retinopathy 1(4.76%) patients.

Fig 1: Diabetic retinopathy in type 2 DM patients

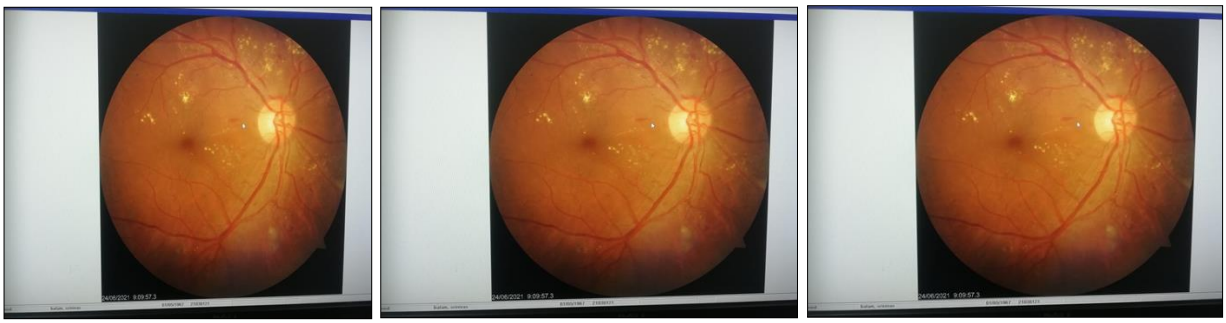

Fig 2: Diabetic retinopathy in DM plus hypothyroidism patients

Table 4: Distribution of severity of diabetic retinopathy in DM plus hypothyroidism patients

Variable	Number	Percentage
Mild nonproliferative retinopathy	4	22.22%
Moderate nonproliferative retinopathy	8	44.44
severe nonproliferative retinopathy	1	5.55%
Early proliferative retinopathy	4	22.22%
High-risk proliferative retinopathy	1	5.55%

Regarding severity of retinopathy as per ETDRS in DM plus hypothyroidism patients, Mild nonproliferative retinopathy present in 4(22.22%) patients, Moderate nonproliferative retinopathy 8(44.44%) patients, severe nonproliferative retinopathy 1(5.5%) patients, Early proliferative retinopathy 4(22.22%) patients and High-risk proliferative retinopathy 1(5.5%) patients.

Discussion

In present prospective observational study we have enrolled 240 patients with type 2 diabetes mellitus as per exclusion and inclusion criteria to study the prevalence of hypothyroidism in type 2 diabetes mellitus patients, prevalence of diabetes retinopathy and it association with hypothyroidism in coastal district.
We have observed that prevalence of hypothyroidism was 22.5% among type 2DM mellitus patients in comparison to 9.16% in general population without type 2 DM. This finding is supported by the study of Talwalkar P, Deshmukh V, Bhole M *et al.*, C. Wang *et al.* and Kamendu A, Aslami AN *et al.* [4, 13, 14]. Khalid SA, Samia AB, Muneera AA, Patan MK, Abdulla MM *et al.* from Kingdom of Saudi Arabia has reported higher prevalence than our study that is 30.7% [15].
Mean age of patients with type 2 DM was 47.3±10.28 years and with type 2 DM plus hypothyroidism was 44.86±12.72 years. But there is male predominance in type 2 diabetes mellitus group and female predominance in Type 2 DM plus hypothyroidism group. Both finding was no significant statistically. This finding corroborates with the study of Afrin G, Rathore B, Kumar V *et al.* and Vikram B Vikhe1, Shubhangi A Kanitkar *et al.* [16, 17].
Duration of diabetes mellitus was 6.43±2.96 yrs type 2 diabetes mellitus group and 7.06±3.5 years in type 2 DM plus hypothyroidism group. This finding was not significant

statistically. This finding corroborates with the study of Ogbonna SU, Ezeani IU *et al.* and Mehalingam V, Sahoo J, Bobby Z, Vinod KV *et al.* [18, 19].

Diabetic retinopathy was more common on type 2 DM plus hypothyroidism group then type 2 diabetes mellitus group. Wu J, Yue S, Geng J, *et al.* From his meta-analysis concluded that SCH was associated with DR in diabetes and exposure to SCH can increase the DR risk 2.13 times which support our study [8]. Zou J, Li Z, Tian F, Zhang Y, Xu C, Zhai J *et al.* has reported that decreased FT3 was significantly related to the prevalence of DR in T2DM with normal thyroid function this finding corroborates with our study [20].

We have observed that Moderate nonproliferative retinopathy is more common in both group but early proliferative retinopathy is more common in type 2 DM plus hypothyroidism group then yrs type 2 diabetes mellitus group. Borooah M, Phukan S *et al.* has reported that Prevalence of severe NPDR and PDR was higher in patients with SCH as compared to euthyroid patients this finding corroborates with our study [21]. George E, Kuriakose S, Chackochan M *et al.* has reported that Proliferative diabetic retinopathy was found to be significantly higher in diabetic patients with thyroid dysfunction [22].

Conclusion

From present study we can conclude that that prevalence of hypothyroidism was higher among type 2 DM mellitus patients in comparison to general population without type 2 DM. Diabetic retinopathy was more common on type 2 DM plus hypothyroidism group then type 2 diabetes mellitus group. We have observed that Moderate nonproliferative retinopathy is more common in both group but early proliferative retinopathy is more common in type 2 DM plus hypothyroidism group then yrs type 2 diabetes mellitus group. A routine thyroid function test is recommended to prevent the development and progress of diabetic retinopathy.

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