Original Article

Diabetic Retinopathy

# Frequency of Subclinical Hypothyroidism in Patients with Proliferative Diabetic Retinopathy

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## ABSTRACT

**Objectives:** To determine the frequency of subclinical hypothyroidism in patients with proliferative diabetic retinopathy.

**Study Design:** Cross Sectional Study.

**Place and duration of study:** This study was conducted in Dow University Hospital, Dow University of Health Sciences , Karachi from 1st January 2012 to 31st December 2012.

**Materials and Methods:** One hundred and nineteen patients attending the medical OPD Dow University of Health Sciences were included in study.

**Results:** 119 patients were enrolled in study .47.1% were male and 52.9% were female patients mean age was 55.75±7.85 years , Mean $HbA1_c$ value was 8.02 ± 1.46%,Subclinical hypothyroidism was identified in 26.9% the patients.

**Conclusion**: Subclinical hypothyroidism is associated with the development of proliferative diabetic retinopathy in the patients suffering from type 2 diabetics.

**Key Words:** Subclinical hypothyroidism, Proliferative diabetic retinopathy, type 2 diabetes mellitus, $HbA1_c$

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## INTRODUCTION

Type 2 diabetes is a global public health burden causing great load on the economy of developing nations.[1] Diabetic retinopathy is a common complication of diabetes that affect blood vessels of the retina and leads to blindness2 Its frequency ranges from 15.7% to 28.9% in Pakistan.[3,4] Risk factors include duration of diabetes, poor glycemic control and dyslipidemia and they are amenable to therapeutic intervention.[5] Subclinical hypothyroidism is defined when peripheral thyroid hormone levels are within the normal range but serum thyroid stimulating hormone levels are elevated (>4.0µU/ml).[6]

subclinical hypothyroidism is associated with atherogenic lipid profile, impaired vascular function and increased systolic blood pressure[7].Researchers have investigated and found that the presence of subclinical hypothyroidism in type 2 diabetics not only needs to be screened but treated as it causes an increased risk of development of proliferative diabetic retinopathy, leading to blindness in such patients. In a recent study Guang-Ran Yang found that the prevalence of subclinical hypothyroidism increased to 27.3% in patients with proliferative diabetic retinopathy and showed that subclinical hypothyroidism was independently related to proliferative diabetic retinopathy The recent international evidence of the relationship between subclinical hypothyroidism and proliferative diabetic retinopathy warrants the need of further studies locally to evaluate and substantiate this very crucial relationship. Therefore, this study aims to determine the frequency of subclinical hypothyroidism in patients with proliferative diabetic retinopathy to verify the need of routine screening of type 2 diabetics for subclinical hypothyroidism, so as to identify patients at risk of a severe morbidity (proliferative diabetic retinopathy leading to blindness) and help develop a national guideline for routine surveillance of subclinical hypothyroidism in type 2 diabetics for early recognition and treatment of subclinical hypothyroidism so that they do not develop proliferative diabetic retinopathy

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## MATERIALS AND METHODS

This is a cross sectional study was conducted in medical OPD Dow University of Health Sciences, Karachi from 1st January 2012 to 31st December 2012

**Inclusion Criteria:** Patients of either gender, 40-70 years of age group, diagnosed as having proliferative diabetic retinopathy on fundoscopyand diabetes mellitus for more than 10 years.

**Exclusion Criteria:**

1. Patients who are on thyroid medications or have history of thyroidectomy or radioactive iodine.
2. Patients who were found to have goiter on examination.
3. Patients who turned out to have clinical hypothyroidism or subclinical hyperthyroidism after investigation.

119 patients fulfilling the inclusion criteria were included in the study their fundoscopic findings were recorded on pre designed proformawhich included patients demographics (age and gender) , duration of diabetes , duration of proliferative diabetic retinopathy , thyroid stimulating hormone value , haemoglobin A1c , status of diabetes (controlled or uncontrolled ), and final outcome that is presence of subclinical hypothyroidism.

**Operational Definitions:** Subclinical hypothyroidism defined as when peripheral thyroid hormone levels are within the normal range but serum thyroid stimulating hormone levels are elevated (>4.0µU/ml).[7]

**Proliferative diabetic Retinopathy: proliferative diabetic retinopathy** defined as when there is presence of: neovascularization (tiny, abnormal leaky blood vessels inside the eye) and vitreous hemorrhage (leakage of blood around the vitreous humor of the eye), on fundoscopic examination.[15]

**Controlled Diabetes:** $HbA1_c$ level of less than 6.5%.

Data was analyzed using SPSS Version 13; P-value at 5% confidence interval was calculated with 0.05 taken as significant.

## RESULTS

Between 1stJanuary 2012 to December 2012, 119 known diabetic patients with proliferative diabetic retinopathy, who visited outpatient clinics of medicine, Dow University Hospital were identified and were investigated for subclinical hypothyroidism, which fulfilled the inclusion criteria. Frequency of subclinical hypothyroidism was determined.

**Age Distribution:** The mean age of the one hundred and nineteen participants of this study was 55.75 ± 7.85 years. (Table 1).

**Gender Distribution:** Fifty six participants of the study were male accounting for 47.1% of the study group, while sixty three participants were female representing 52.9% of the study population. The male to female ratio of this study was 1:1.12.

**Duration of Diabetes Mellitus:** In this study, eighty patients had a history of diabetes mellitus less than 15 years. This represented 67.2% of the study group. Thirty nine patients had duration of diabetes mellitus of more than 15 years accounting for 32.81% of the group. The mean duration of diabetes in this study group was 13.80 ± 2.50 years. (Table 2)

**Heamoglobin $A1_c$ and Thyroid Stimulating Hormone:** The mean value of the haemoglobin$A1_c$ in this study population was 8.02 ± 1.46%. The mean value of serum thyroid stimulating hormone was 2.52 ± 1.73 µU/ml (Table 3).

**Status of Diabetes Mellitus:** Out of the 119 participants of this study 49 participants had controlled diabetes mellitus accounting for 41.2% of the group. 70 participants had uncontrolled diabetes mellitus representing 58.8% of the study group (Table 4).

**Final Outcome:** Subclinical hypothyroidism was identified in 32 of the study participants accounting for 26.9% of the group. The rest of the 87 participants (73.1%) did not have SCH (Table 5).

**Table No.1: Age Distribution**

| Age of Patients (Years) | Frequency (n=119) | Percentage (%) |
|---|---|---|
| **<55** | 57 | 47.9 |
| **>55** | 62 | 52.1 |

**Mean age +S.D = 55.5 + 7.85**

**Table No.2: Duration of Diabetes Mellitus**

| Duration (Years) | Frequency (n=119) | Percentage (%) |
|---|---|---|
| **<15** | **80** | **67.2** |
| **>15** | **39** | **32.8** |

**Mean ± Standard Deviation = 13.80 ± 2.50**

**Table No.3: Mean HBA1C and mean thyroid stimulating hormon**

| | Mean | Standard deviation (+) |
|---|---|---|
| Hba1c (%) | 8.02 | 1.46 |
| Thyorid stimulationg hormone (µu/ml) | 2.52 | 1.73 |

**Table No.4: Status of diabetes mellitus**

| Diabetes Mellitus | Frequency (n=119) | Percentage (%) |
|---|---|---|
| **Controlled** | **49** | **41.2** |
| **Uncontrolled** | **70** | **58.8** |

**Table No.5: subclinical hypothyroidism (final outcome)**

| Subclinical Hypothyroidism | Frequency (n=119) | Percentage (%) |
|---|---|---|
| **Yes** | 32 | 26.9 |
| **No** | 87 | 73.1 |

## DISCUSSION

The current study reveals the prevalence of subclinical hypothyroidism in the patients suffering from proliferative diabetic retinopathy to be 26.9%.

In this study the mean age of the one hundred and nineteen participants was found out to be 55.75 ± 7.85 years. This observation is similar to the observations of Sato et al.[8]They in their of 108 patients suffering from proliferative diabetic retinopathy calculated the mean age to be 57.6 ± 11.8 years. The observation of this study was also comparable to the observation of Yang et al[9]who in their study found the mean age to be 59.94 ± 10.61. Observation of this study and the above studies reveal the average age of patients suffering from proliferative diabetic retinopathy to be in the mid to late 50's.

47.1% of the participants of this study were male. The male to female ratio was identified to be 1:1.12. This observation is in contrast to the observation of He and colleagues[10], who observed that 47.6% of their study patients were female. This contrast may be accounted by the comparatively larger sample size of their study which included 2099 participants. However, the female predominance of this study group is comparable to the similar observation of higher female ratio in patients as observed by Yang and associates.[11]

67.2% of the participants of this study had a history of diabetes mellitus of more than 15 years. The mean duration of diabetes in this study group was 13.80 ± 2.50 years. This observation is very similar to El-Bab and colleagues[12], who in their study of over six hundred patients found the mean duration of diabetes to be 13.35 ± 8.17 years. Similarly the observation of this study was also very much similar to the observation of Yang et al[9], who in their study found the mean duration of duration of diabetes mellitus to be 13.20 ± 7.04 years. Zavrelova and associates[13], in their study also stated that the average duration of diabetes in proliferative diabetic retinopathy patients of their study was 12.5 years. This relationship between duration of diabetes and proliferative diabetic retinopathy was also stated by Kim et al[14], who observed that 52.3% of the patients of proliferative diabetic retinopathy had a history of diabetes of more than 10 years. The observations of all these studies consolidate duration of diabetes as a risk factor for proliferative diabetic retinopathy.

The mean $HbA1_c$ value observed in this study was 8.02 ± 1.46%. El-Bab and colleagues[12] in their study observed a comparable value of $HbA1_c$that is 7.4 ± 1.4%. In other study this value was observed to be 7.5 ± 1.7 by Kim and associates.[14] Paine and colleagues[15]also observed a similar $HbA1_c$ 7.5 ± 1.2 %. Zavrelova and associates[13], however observed a slightly higher but still comparable value of 9.0 ± 1.8%. Sato et al[16], also observed a higher value of 9.4%. Yang and colleagues[9] also noted a mean $HbA1_c$ value of 9.16 ± 2.0%. These studies affirm that $HbA1_c$ is a risk factor for proliferative diabetic retinopathy, an observation affirmed by a study conducted in Tehran.[17]

The mean value of serum TSHof one hundred and nineteen participants was 2.52 ± 1.73 µU/ml. This value is similar to the observations of Yang and associates[9] who found an average value of 2.10 µU/ml. In another study by Yang JK et al[11], it was observed that the majority of the patients of their study had serum TSH levels between 2-4 µU/ml.

It was observed in this study that 58.8% that is 70 participants are uncontrolled diabetes mellitus. This is contrast to the observations of Javadi and colleagues[17], who reported in their study that 40.3% of their patients had uncontrolled diabetes. This contrast may be accounted by the different cultures leading to different life styles in addition to the difference in sample size of the two studies. Javadi and colleagues[17] in their study had 240 patients of diabetic retinopathy.

In this study subclinical hypothyroidism was identified in thirty two (26.9%) of the participants suffering from proliferative diabetic retinopathy. These observation is very similar albeit marginally lower to that reported by Yang and associates[9] who in their study observed this frequency to be 27.3%. The relationship between SCH and PDR was also demonstrated by Jin-Kui Yang[11] who observed that type 2 diabetics who had subclinical hypothyroidism had a significantly higher frequency of proliferative diabetic retinopathy.

## CONCLUSION

Subclinical hypothyroidism is associated with the development of proliferative diabetic retinopathy in the patients suffering from type 2 diabetics. It is therefore suggested that type 2 diabetics should be screened for subclinical hypothyroidism so as to identify those at risk for development of proliferative diabetic retinopathy and take measures to prevent its onset.

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