BURDEN OF THYROID DYSFUNCTION IN PATIENTS OF TYPE 2 DIABETES MELLITUS

Syed Ihtisham Ul Haque, Tahir Mukhtar Sayed*, Amna Tahir

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Armed Forces Institute of Rehab Medicine/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the frequency of thyroid disorders in patients of type II diabetes mellitus at Pak Emirates Military Hospital Rawalpindi.

Study Design: Cross sectional analytical study.

Place and Duration of Study: The study was conducted at Pak Emirates Military Hospital Rawalpindi, from Jul 2017 to Jun 2018.

Material and Methods: The study focused on patients with type-II diabetes mellitus presenting to outpatient department of Pak Emirates Military Hospital, Rawalpindi. Ages ranged from 30 years to 70 years and patients who had a previous co-existing thyroid disease or taking drugs that affect thyroid function were excluded. Glycosylated hemoglobin levels were done and Thyroid stimulating hormone levels was used to screen patients for thyroid dysfunction.

Results: Mean age of the participants was 54.89 ± 1.10 years. A total of 334 patients [186 (55.7%) males and 148 (44.3%) females] were analysed. Among them 233 patients (69.8%) were euthyroid, 52 patients (15.6%) had subclinical hypothyroidism, 34 patients (10.2%) had subclinical hyperthyroidism, 9 patients (2.7%) had hypothyroidism and 6 patients (1.8%) had hyperthyroidism.

Conclusion: The frequency of thyroid disease was significantly higher in patients with type II diabetes mellitus as compared to the general population and thus patients with type II diabetes mellitus should be screened.

Keywords: Diabetes mellitus, Prevalence, Thyroid dysfunction.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Diabetes mellitus (formerly called non-insulin-dependent) is an endocrine disorder that is characterized by elevated levels of blood sugar due to either inadequate insulin production by pancreas or insulin resistance. Diabetes mellitus is among one of the major health problems of the modern world. The number of people with diabetes has increased from 108 million in 1980 to 422 million in 2014. Urbanisation, sedentary life style and unhealthy diet patterns have greatly increased the incidence of diabetes. The prevalence of diabetes was more in the urban area as compared to rural areas[1-4]. The prevalence of diabetes in adults of age greater than 18 years has increased from 4.7% in 1980 to 8.5% in 2014[5]. Despite advancements in the management of type 2 diabetes mellitus, the mortality and morbidity associated with type 2 diabetes mellitus is still haunting. Diabetes and thyroid disorders are both due to disturbances in endocrine system functions which are contributed to body metabolism. Insulin and thyroid hormones contribute in cell metabolism together; any increase or decrease in each of them can impair the function of the other. There is a close association of thyroid dysfunction and diabetes mellitus and researchers have been investigating their association in different parts of the world[6]. As of now the diagnostic criteria by American Diabetes Association states that following patients be classified as having type 2 diabetes mellitus, all patients with a fasting plasma glucose of ≥126 mg/dL (7.0 mmol/L) where fasting is defined as no caloric intake for at least 8 h, OR 2 hours plasma glucose of ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test. The test should be performed as per guidelines of WHO, with a

Correspondence: Dr Syed Ihtisham Ul Haque, Internal Medicine Department, Pak Emirates Military Hospital Rawalpindi Pakistan
Email: syedihtishamulhaq@gmail.com
Received: 24 Jun 2018; revised received: 30 Jul 2019; accepted: 16 Aug 2019

glucose load of 75-g glucose dissolved in water or glycosylated haemoglobin A1C ≥6.5% (48 mmol/mol). The test should be performed with NGSP certified and standardized to the DCCT assay[7].

In patients with symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L)[7] can also be done.

People of south Asian ethnicity are at increased risk of development of diabetes mellitus and have early age screening thresholds[7]. Diabetes mellitus is associated with a lot of microvascular as well as macrovascular complications which ranges from strokes, myocardial infarctions to devastating microvascular complications of blindness. During the past years it has been found that diabetes mellitus is also associated with thyroid dysfunction[1-3,8]. The underlying thyroid malfunction can lead to clinically important sequelae especially with the background of type 2 diabetes mellitus. Hypothyroidism can cause elevate serum LDL cholesterol and cause worsening of already existing dyslipidemia, ultimately leading to more risk of atherosclerosis[9]. Subclinical hyperthyroidism can also increase the risk of cardiac arrhythmias especially atrial fibrillation and worsening of angina pectoris. Patients with diabetes mellitus are at increased risk of cardiovascular diseases, therefore early diagnosis of thyroid dysfunction has a lot of importance in decreasing the risk of associated problems. The highly sensitive serum TSH (Thyroid stimulating hormone) immunoassay is a great tool in the diagnosis of thyroid dysfunction. It is a valuable and sensitive screening test for thyroid disorders and can help diagnose both hypothyroidism and hyperthyroidism[4]. It is the first marker to get deranged in the development of thyroid disease. Subclinical thyroid dysfunction can be diagnosed by abnormal levels of TSH because the serum T3 and T4 are normal and as can be inferred from the term "subclinical" itself, the patients are asymptomatic. HbA1c is considered a reliable tool for diagnosis and monitoring control of diabetes mellitus by American Diabetes Association[7,10-12] Australian recommendations also coincide with the ADA guidelines for use of HbA1C[11]. Because of the close association between diabetes and thyroid dysfunction and possible implications of thyroid dysfunction on body that may further complicate further type 2 diabetes mellitus, we organized a study at Pak Emirates Military Hospital Rawalpindi to study the frequency of thyroid dysfunction in patients of type 2 diabetes mellitus and thus help rationalize the need for getting patients with type 2 diabetes mellitus screened for thyroid dysfunction.

MATERIAL AND METHODS

It was a prospective cross sectional anaytical study conducted at Medical department, of Pak Emirates Military Hospital Rawalpindi from July 2017 to Jan 2018. A total of 334 patients of type 2 diabetes mellitus were studied. Probability sampling technique was used. Sample size was calculated by using online openepi calculator[13]. Approval of ethical committee was sought and patients were informed about the study. Confidence interval was taken as 95%. Blood samples for TSH and HbA1c and necessary details including age, gender, area of residence and a full history were taken from patients attending the general medical out patient department at Pak Emirates Military Hospital, Rawalpindi.

Following patients were included in the study

- Age 30-70 years
- Type 2 diabetes mellitus
- Following patients were excluded from the study
- Pre-existing thyroid disease
- Taking drugs, like amoidarone, interferon and lithium

Samples were sent to the hospital laboratory and close liaison was made with the laboratory staff. Patients belonged to different areas of Punjab and Kashmir. The study subjects were divided into 5 groups: Euthyroid who had a normal TSH level, subclinical hypothyroidism who had high levels of TSH with normal free T4

levels, subclinical hyperthyroidism who had low TSH levels with normal T4 levels, hypothyroid who had low T4 and high TSH levels and hyperthyroid who had high T4 levels and low TSH levels. Laboratory reference values were adhered to. TSH levels were done along with HbA1c. Patients with HbA1c levels >7% were considered as having uncontrolled diabetes mellitus and those with HbA1c <7% were taken as controlled diabetes. Those having normal TSH levels were not subjected to further testing whereas patients with abnormal TSH levels were further evaluated with T3 and T4 levels. Patients suffering from preexisting thyroid disease or drugs affecting thyroid function like amoidarone, interferon, etc were excluded from the study. SPSS 16.0 was used for assessing different variables. Frequencies *p*-value and other descriptive analysis were done to calculate the mean and standard deviation. A *p*-value was calculated using the chi-square formula.

RESULTS

Mean age of the participants was 54.89 ± 1.10 years. A total of 334 patients (186 males 55.7% and 148 females 44.3%) were analyzed out of whom 233 patients (69.8%) were euthyroid, 52 patients (15.6%) had subclinical hypothyroidism, 34 patients (10.2%) had subclinical hyperthyroidism, 9 patients (2.7%) had hypothyroidism and 6 patients (1.8%) had hyperthyroidism as shown in table. Among them 219 (65.6%) patients had uncontrolled diabetes based on HbA1c levels and 115 (34.4%) had controlled diabetes. Moreover it was also seen that patients with uncontrolled diabetes had more thyroid dysfunction (*p*-value <0.05). It was also seen that patients with uncontrolled diabetes mellitus had more frequency of thyroid dysfunction as shown in figure.

Table: Frequency of thyroid dysfunction and related percentages.

Thyroid dysfunction	Frequency	Total (%)
Euthyroid	233	69.8
Subclinical hypothyroidism	52	15.6
Subclinical hyperthyroidism	34	10.2
Hypothyroidism	9	2.7
Hyperthyroidism	6	1.8

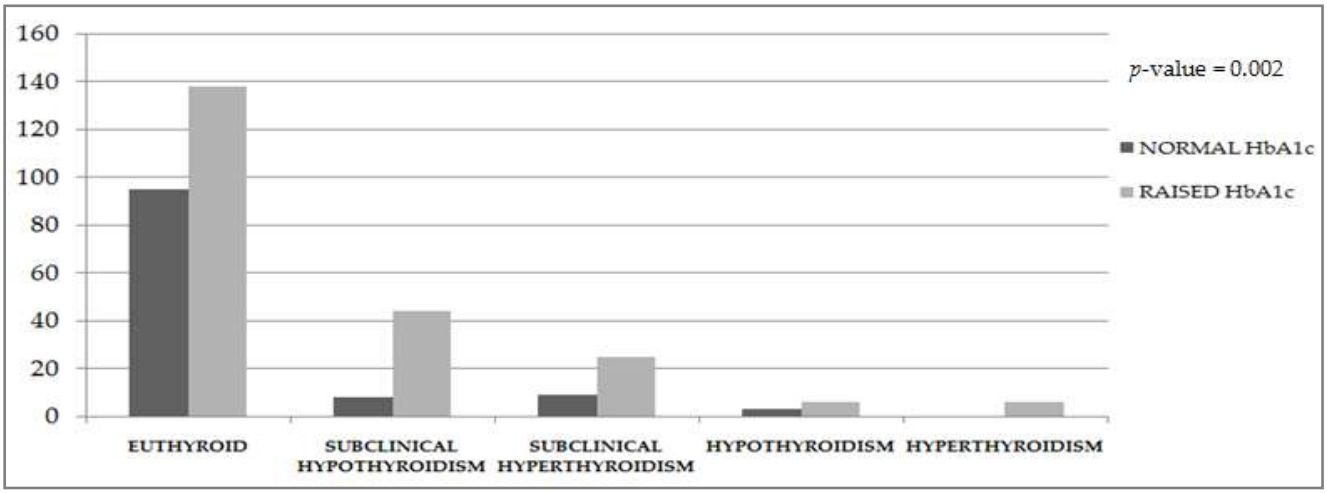

Figure: Frequency of thyroid dysfunction in relation to HbA1c.

DISCUSSION

We found that the incidence of thyroid dysfunction in our study among patients of type 2 DM was significantly higher 15.6% as compared

to the general population which is 4.78%. Moreover we observed that thyroid dysfunction was more common among patients with raised glycosylated hemoglobin. The most plausible explanation for thyroid dysfunction in patients with type 2 diabetes is the development of insulin resistance that is attributable to a number of factors at genetic and physiological level, this insulin resistance in turn causes thyroid dysfunction[8]. One of the largest trials on association of type 2 diabetes mellitus and thyroid dysfunction were done by Hanne F. Fleinerin their Population based-HUNT trail Norway concluded that increased surveillance for thyroid dysfunction in T2DM is not necessary[2].

Metab Al-Geffari *et al* in their study on Saudi population demonstrated that thyroid dysfunction occurred in more than 25% of Saudi population with Type 2 diabetes mellitus. They also found those who had family history of thyroid dysfunction with type 2 diabetes mellitus and female gender had more chances of thyroid dysfunction[14].

Laloo Demitrost in his study of 202 patients of type 2 diabetes mellitus in India found that the burden of thyroid dysfunction was significantly higher in patients of type 2 diabetes mellitus especially those with increased body mass index[13]. Moreover, increased body mass index is related to the development of a lot of co-morbidities which includes type 2 diabetes mellitus, all cancers except prostate and esophageal cancer, bronchial asthma, all cardiovascular diseases, osteoarthritis, gall bladder disease and back pain[15]. BMI (Body mass index) greater than 25 is a risk factor for development of diabetes mellitus, Hypertension and ischemic heart disease[16-18].

Aung WP found in their study that the prevalence of diabetes was more in the urban area as compared to rural areas[19]. This very well correlates with the use of junk food (which includes processed red meat, fried potatoes) sedentary habits which all contribute to the development of diabetes[20-22]. Odegaard AO also concluded that Western-style fast food had an associated with increased risk of development of type 2 diabetes mellitus and heart disease[23].

The strong area of our study was an adequate sample size. Among the weak areas were the less diverse ethnicity, patients mainly from suburbs of Rawalpindi and adjoining Kashmir.

CONCLUSION

Patients with type II diabetes mellitus have an increase incidence of developing thyroid dysfunction, more studies are required in the South Asian population to authenticate the validity of routine screening of thyroid dysfunction in patients of type 2 diabetes mellitus.

ACKNOWLEDGEMENT

We are thankful to all the authors and Pak Emirates Military Hospital Rawalpindi in particular.

Funding Source

All patients were entitled for free treatment at Pak Emirates Military Hospital and all the investigations, medicines were funded by Hospital.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Maxzud CM, Fregenal M, Calafiore AF, Lanus CM, D'Urso M, Luciardi H. Prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus. Medicina (B Aires) 2016; 76(6): 355-58.
2. Hanne F. Fleiner TB, Midthjell K, Grill V, Bjørn O. Åsvold. Prevalence of thyroid dysfunction in autoimmune and type 2 diabetes: The Population-Based HUNT study in norway. J Clini Endocrinol Metabol 2016; 101(2): 669-77.
3. Palma. Prevalence of thyroid dysfunction in patients with diabetes mellitus. Diabetology & Metabolic Syndrome 2013; 2013 (5): 58.
4. Waqar Azim AAASA. Thyroid stimulating hormone assay as a screening tool of Thyroid disease. Biomedica 2006/Bio-15 22(Jul-Dec).
5. Mathers CD LD. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006; 3(11): e512.
6. Hage M, Azar ST. Thyroid disorders and diabetes mellitus. J Thyroid Res 2011; 2011: 439463.
7. Association AD. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2019. Diabetes Care 2019; 42(Suppl-1): S13-S28.
8. Wang C. The Relationship between type 2 diabetes mellitus and related thyroid diseases. J Diabetes Res 2013; 2013: 390534.

9. Rizos C, Liberopoulos effects of thyroid dysfunction on lipid profile. Open Cardiovascular Med J 2011; 5(1): 76-84.
10. Diagnosis and classification of diabetes mellitus. Am Diabet Assoc Diabe Care 2011; 34-Suppl (1): S62-9.
11. The role of HbA1c in the diagnosis of diabetes mellitus in Australia. Royal College of Pathologists of Australasia. Australasian Assoc Clini Biochem Med J Aust 2012; 197(4): 220-1.
12. D'Emden MC, Colman PG, Colagiuri S, Twigg SM, Jones GR, Goodall I, et al. The role of HbA1c in the diagnosis of diabetes mellitus in Australia, Australian Diabetes Society., Royal College of Pathologists of Australasia, Australasian Association of Clinical Biochemists. Med J Aust 2012; 197(4): 220-1.
13. Demitrost L RS. Thyroid dysfunction in type 2 diabetes mellitus: A retrospective study. Indian J Endocr Metab 2012; 16(1): 334-35.
14. Al-Geffari MNAA, Al-Sharqawi AH, Youssef AM, Al-Naqeb D, Al-Rubeaan K. Risk factors for thyroid dysfunction among type 2 diabetic patients in a highly diabetes mellitus prevalent society. Int J Endocrinol 2013; 1-6.
15. Guh DP, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. BMC Public Health 2009; 9(1): 88-108.
16. Gray N, Sloan F, Yashkin A. The Relationship between BMI and onset of diabetes mellitus and its complications. South Med J 2015; 108(1): 29-36.
17. Dua S, Sharma P, Dhall M, Kapoor S. Body Mass Index Relates to Blood Pressure Among Adults. North Am J Med Sci 2014; 6(2): 89-95.
18. Lamon-Fava S, Schaefer EJ. Impact of body mass index on coronary heart disease risk factors in men and women. The Framingham Offspring Study. Arterioscler Thromb Vasc Biol 1996; 16(12): 1509-15.
19. Aung WP, Bjertness E. Urban–rural differences in the prevalence of diabetes mellitus among 25–74 year-old adults of the Yangon Region, Myanmar: Two cross-sectional studies. BMJ Open 2018; 8(3): e020406.
20. Pan P, Malik V, Hu FB. Exporting diabetes to asia: The impact of western-style fast food. Circulation 2012; 126(2): 163-5.
21. Pan ASQ, Bernstein AM, Schulze MB, Manson JE, Willett WC, Hu FB. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. Am J Clin Nutr 2011; 94(4): 1088-96.
22. Halton TL, Liu S, Manson JE, Stampfer MJ, Hu FB. Potato and french fry consumption and risk of type 2 diabetes in women. Am J Clin Nutr 2006; 83(2): 284-90.
23. Odegaard AO, Yuan JM, Gross MD, Pereira MA. Western-style fast food intake and cardiometabolic risk in an Eastern country. Circulation 2012; 126(2): 1-5.