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Original Research Article

Correlation of Dyslipideamia among Hypothyroidism and Type II Diabetes Mellitus

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Abstract: Hypothyroidism and diabetes mellitus (DM) are the two most common endocrine disorders, which are on simultaneous rise. Dyslipidemia is common metabolic abnormalities in hypothyroidism and diabetes mellitus with marked increase in circulating low density lipoprotein (LDL-C). Several studies have demonstrated significant variations in dyslipidemia in Type II Diabetes Mellitus with Hypothyroidism**.** This study was carried out on patient attending in Katihar Medical College & Hospital. The entire subjects were categorised into three groups. The lipid profile of all the groups were estimated and compared with normal control groups without having any type of diabetic or thyroid complication. All the lipid profile parameters were significantly increased except HDL among the diabetics, hypothyroidism, and diabetics with hypothyroidism subjects. Increase was more in cholesterol and LDL values among subjects suffering from both diabetes and hypothyroidism. HDL levels were lowest among the diabetics and further decreased among the diabetic hypothyroids. Finally it appeared that both the endocrine disorders are equally responsible for the alteration in lipid profile & theirs cumulative effects further added fuel to the fire.
Keywords: T2DM, Hypothyroidism, TC, TG, LDL-C, VLDL-C, HDL-C.

INTRODUCTION:

The occurrence of diabetes mellitus (DM) has increased dramatically over past two decades from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, more than 360 million individuals will have diabetes by the year 2030 [1].

'Diabetic dyslipidaemia' is characterised by high level of plasma triglyceride (TG), and low density lipoprotein (LDL) concentrations with low level of High density cholesterol (HDL-C) due to reduced action of insulin at the tissue level or due to insulin resistance [2]. Diabetic dyslipidemia increases the risk of atherosclerosis particularly, if glycaemic control is poor, which in-turn is an important risk factor for coronary heart disease (CHD) [3].

Hypothyroidism is by far the most common thyroid disorder in the adult population and is more common in older women [4]. Thyroid disease is associated with various metabolic abnormalities due to effect of thyroid hormones on all major metabolic pathways by directly or indirectly modifying the other regulatory hormones such as insulin or catecholamine [5]. Hypothyroidism is associated with hypercholesterolemia, hypertriglyceridemia with marked increased in circulating cholesterol concentration and low density lipoprotein (LDL-C) and apolipoprotein B(ApoB) due to decreased LDL receptor in the liver [6,7,8]. In hypothyroidism dyslipidemia, co-existing metabolic abnormalities in combination of hormone induced hemodynamic alterations lead to cardiovascular diseases.

Thyroid dysfunction and diabetes mellitus (DM) are the two most common endocrine disorders. DM and thyroid disease appear to be closely linked [9]. Thyroid hormone enhances the absorption, production and utilization of glucose. Often latent diabetes may be unmasked by hyperthyroidism, while hypoglycaemia is sometimes a manifestation of hypothyroidism. Diabetes mellitus appears to influence thyroid function at several sites, from hypothalamic control of TSH, release to T3, production from T4 in the target tissue. The best studied effect is the lowering of circulating T3 in diabetics **[**10, 11**].** Apart from genetic link between thyroid disorders

and Diabetes mellitus, thyroid hormones (TH) also have well described effects on glucose and lipid metabolism. Thyroid hormones have short- and long-term interaction with the regulatory network for energy homeostasis and via direct interaction with insulin regulation causes glucose disposal in peripheral tissues [12].

RESEARCH DESIGN AND METHODS:

Subjects:

This cross-sectional study was conducted on 150 subjects & 50 control having same socioeconomic status, cultural and food habits in the Department of Biochemistry in Katihar Medical College and Hospital in collaboration with the Department of Medicine.

The patients were divided into four groups. Group A consisting of 50 subjects presented with only Type 2 Diabetes Mellitus (T2DM) Group B having 50 subjects who were suffering from only Hypothyroidism (HY). Group C consisted of patients suffering from both type 2 Diabetes mellitus and Hypothyroidism. Age and sex matched fifty healthy people without any history or symptoms of diabetes & hypothyroidism and other metabolic disorders were chosen as the controls were kept in D group.

The diagnosis of diabetes mellitus was based on World Health Organization (WHO) criteria i.e. a fasting plasma glucose of 126 mg/dl (7.0 m mole/L) after a minimum 12-hour fast, with symptoms of diabetes and a 2 hours of post prandial glucose level of more than or equal to 200 mg/dl (11.1mmole/L) [14].

Study Design:

All the biochemical estimations (Plasma Glucose & S. Lipid Profile) were done by using fully automated biochemistry analyzer Turbo-Chem by Awareness Technology, Inc. Reagents were used commercially available ready to use Kits supplied by CPC Diagnostics[17-22]. Instructions from manufacturers were followed for the estimations. Thyroid hormones were estimated by Chemiluminescence Immunoassay methods, machine and kits supplied by Monobind Inc USA [15-16].

Interpretation of the data was done by statistical Software like SPSS-19.0 and Microsoft Office Excel.

RESULT ANALYSIS AND DISCUSSION:

The present study is an attempt to establish a correlation in the alteration of the lipoproteins within the study groups. The table shown here focussed the mean with standard error of mean of Fasting glucose, Serum TSH, total cholesterol (TC), triglycerides (TG), very low density Lipoprotein cholesterol(VLDL-C), low density Lipoprotein cholesterol (LDL-C) and high density Lipoprotein cholesterol (HDL-C) were compared among the three study groups (T2DM, HY, and T2DM with HY) and the control group. In T2DM with hypothyroidism group there was marked increase in TG level (350.02±5.12mg/dl) with lowest HDL level (31.74±0.28 mg/dl). The lipoprotein parameters were significantly increased among the Diabetic subjects except serum HDL level which was significantly decreased when compared to their non-diabetic control group. The HDL cholesterol was high in the HY group when compared with the control and other groups (40.22±0.24 mg/dl). All other parameters were significantly increased among the hypothyroid subjects (HY) when compared to control subject. In T2DM + HY group all the serum lipoprotein parameters were significantly increased among the Diabetic hypothyroid subjects except serum HDL level which was significantly decreased when compared to their non-diabetic control group.

Table-I Mean and standard error of mean for the Fasting P. Glucose, serum TSH & Serum Lipid Profile among study groups and control

Groups	P. Glucose (F) mg/dl	TC (mg/dl)	TG (mg/dl)	VLDL (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TSH (µIU/ml)
Type-2Diabetes Mellitus(T2D)	192.72±3.82	310.12±4.26	329.46±4.63	65.89±0.92	216.92±4.12	30.28±0.27	3.93±0.11
Hypothyroidism(HY)	92.50±1.00	312.58±1.77	321.86±2.49	64.37±0.49	207.76±1.68	40.22±024	21.06±1.57
T2DM With Hypothyroidism (T2DM+HY)	191.86±1.00	337.92±4.79	350.02±5.12	70.00±1.02	23617±4.09	31.74±0.28	24.32±0.99
Control (C)	86.7±1.007	175.66±1.38	169.62±1.76	33.82±0.36	99.58±1.52	40.80±0.53	3.94±0.109

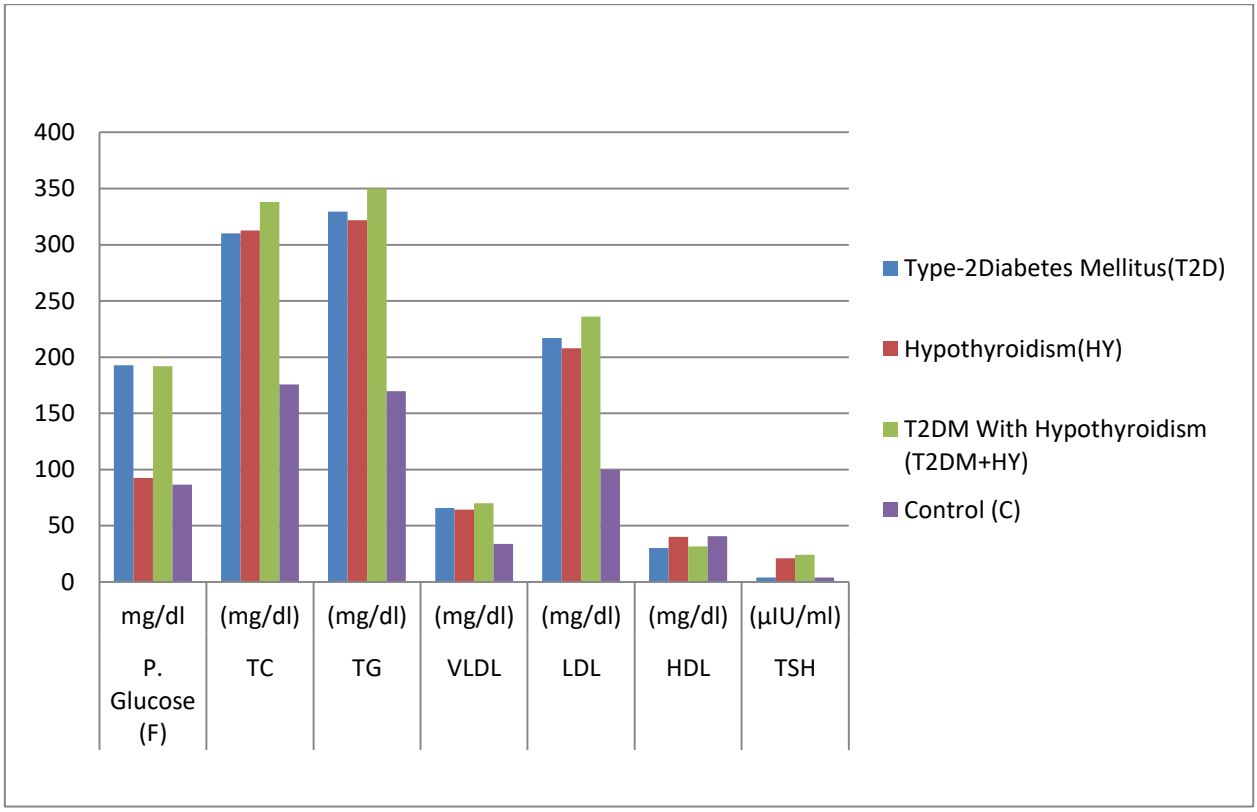

Fig-1: Graph showing Mean for the Fasting P. Glucose, serum TSH & Serum Lipid Profile among study groups and control

Thyroid hormone enhances the absorption, production and utilization of glucose. Diabetes mellitus appears to influence thyroid function at several sites, from hypothalamic control of TSH, release to T3, production from T4 in the target tissue. **[**10, 11**]** There is a lowered T3:T4 ratio in the diabetic group. Uncontrolled hyperglycemia with ketosis lowers T4 and T3 levels and rT3 is elevated. The mechanisms of carbohydrate derangements in hypothyroidism are unclear [3**].**

The diabetic (T2DM), hypothyroid (HY) and diabetic with hypothyroidism (T2DM with HY) groups have been compared with the control group (C) to find the changes in the lipoprotein parameters.

The table reflects that all the serum lipoprotein parameters were significantly increased among the Diabetic subjects except serum HDL level which was significantly decreased when compared to their non-diabetic control group. Our findings were consistent with findings of studies by Miller *et al.;* [23] and The Framingham Study [24]. They established that serum total cholesterol increases in diabetics with age secondary to increasing LDL-C. Arshag D Mooradian in 2009 [3] supported our findings that Dyslipidemia is one of the major risk factors for cardiovascular disease in diabetes mellitus. The characteristic features of diabetic dyslipidemia are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased concentration of small dense LDL-cholesterol particles. The lipid changes associated with diabetes mellitus are attributed to increased free fatty acid flux secondary to insulin resistance.

The present studies also showed that all the serum lipoprotein parameters were significantly increased among the hypothyroid subjects when compared to control subject. The Rotterdam population-based cohort study showed that in hypothyroidism, with its accompanying hypercholesterolemia and hypertension shows a strong association with cardiovascular diseases in elderly population especially in women [25]**.** Parle *et al.;* made a cross-sectional study in southern UK found that dyslipidemia was a singular risk factor for development of atherosclerosis even though HDL level was not reduced [26] **.**Whickham survey studied the thyroid function in a large cohort of randomly selected adult subjects [27]. This mainstay study identified that, after 20 year of follow-up, the progression of subclinical to overt hypothyroidism occurred with major changes in the lipoprotein fractions which lead to complications [28].

In this study it was observed that all the serum lipoprotein parameters were significantly increased among the Diabetic hypothyroid subjects except serum

HDL level which was significantly decreased when compared to their non-diabetic control group. The serum HDL level in diabetic hypothyroid group was (31.74±0.286) which is slightly higher than the diabetic group. B M Singh and Goswami in 2010 in their study found that Patients with hypothyroidism demonstrated insulin resistance and dyslipidemia as observed by higher cholesterol and triglyceride levels respectively as compared to the controls. Thyroid dysfunction leads to alterations in glucose and lipid metabolism which is an important risk factor for cardiovascular diseases [29].

A study was conducted in Regional Hospital Hamirpur, Himachal Pradesh, India where the level of high density lipoprotein (HDL) was significantly decreased and level of low density (LDL), triglycerides and very low density lipoprotein (VLDL) increased in subclinical and clinical hypothyroid diabetic patients. We concluded that insulin sensitivity act as a mediator of thyroid induced lipid changes in diabetic patients [30]. Jeong Rang Park *et al.;* in his study showed Primary hypothyroidism and type 2 diabetes are both typically associated with the increased level of triglycerides [27].

In this study it is found that all the serum lipoprotein parameters were significantly increased among both the Diabetes mellitus subjects and diabetic hypothyroid subjects except HDL which was significantly lower in Diabetics than diabetic hypothyroids. The triglyceride levels were more in only diabetic with hypothyroidism patients. The characteristic features of diabetic dyslipidemia are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased concentration of small dense LDL-cholesterol particles [3]. The prevalence of low HDL cholesterol level in those with diabetes mellitus was almost twice as high as the prevalence in non-diabetic. Thus, both men and women with diabetes had an increased prevalence of hypertriglyceridemia and low HDL cholesterol levels, but their total cholesterol and LDL cholesterol levels did not differ from those in patients with both endocrinal disorders [31]. The hypercholesterolemia of hypothyroidism is a well-known risk factor for cardiovascular atherosclerotic disease that will aggravate the macroangiopathic and perhaps also the microangiopathic complications of long-standing diabetes mellitus. Studies done by Mason *et al.;* as early as 1930 had first revealed the fact which was further justified by studies done by Rosenman in 1952,Kurland *et al.;* in 1955, Dorey *et al.;* in 1981 and Abrams JJ in 1981 [32-36].

All the serum lipoprotein parameters were significantly increased among the diabetic mellitus subjects when compared with only hypothyroid subjects except serum TC level which was raised in both the groups but did not show a significant variability. Our findings of this study among T2DM and HY groups were corroborating with the Miller GJ *et al.;* in 1977, Arshag D Mooradian in 2009, Jeong Rang Park *et al.;* in 2005 and others [23, 3, 27]. Studies under taken by, Hecht and Gershberg in 1968, Lendrum *et al.;* in 1975, Saunders *et al.;* in 1978, Weissel *et al.;* in 1980 Gavin *et al.;* in 1981 support the findings of our study [37-41].

The benefits of identifying thyroid dysfunction at an early stage in Type 2 DM, and even in a symptomatic patient are considerable because progression to overt thyroid dysfunction is associated with consequent morbidity including the adverse effects on lipid and bone metabolism which proves that overt hypothyroidism in T2DM has much more deleterious effects [42, 43]. Consecutively many studies done by Tunbridge *et al.;* in 1977, Feely in 1979, Gray *et al.;* in 1980 in the same decade supported our findings [28, 44-46].

CONCLUSION

This study finally concluded a marked alteration in lipoprotein parameters in the subjects suffering from both T2DM with HY. Hypothyroidism is found to occur commonly in T2DM subject's mostly subclinical variant (SH). Although, triglyceride levels were significantly increased in all three cohorts, but it was highest in diabetic subjects with hypothyroidsm. The level of Total cholesterol, LDL and VLDL were increased among diabetics and Hypothyroidism and it was further enhanced among the subjects suffering from Diabetes and hypothyroidism both. So that the whole work may be summarized that the diabetes and hypothyroidism both have a significant role in alteration of lipoprotein levels and their collective presence have greater effect.

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