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Prevalence of Insulin Resistance and its Effects in Cases of Hypothyroidism

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Abstract:

Background: Insulin tolerance, despite its normal or elevated blood concentration, can be defined as impairedglucose values, reducedtolerance ofliver, muscles, adipose tissues and other body tissues to insulin hormone . resistanceto insulin could be symptomless or manifest as a number of conditions, like failure of glucose metabolism,hypercholesterolemia, hypertriglyceridemia, diabetes mellitus II type,obesity and hypertension. This study aims to measure the prevalence of IR in hypothyroidism and to co relate IR with various anthropometric variables clinical (blood pressure) , biochemical (FBS, lipid profile) and (BMI, Waist circumference) with cases of hypothyroidism.

Objectives :

- To estimate prevalence of Resistance to insulin among sub clinical hypothyroidism usingThyroid stimulating hormone[TSH], free triiodothyronine[fT3] Thyroid stimulating hormone[TSH], free triiodothyronine[fT3]
- To estimate the prevalence of resistance to insulin in overt hypothyroidism
- To estimate prevalence of resistance to insulin in overt hypothyroidism
- Clinically correlate resistance to insulin

Methods:A cross-sectional research will be based among 100 cases of hypothyroidism over 16 years of age who attend or are admitted to this hospital opd within a span of 3 years.

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TSH(THYROID STIMULATING HORMONE), free thyroxine, IR, Fasting Lipid Profile, Fasting Glucose, fasting insulin levels, kidney function tests would be assessed for all patients.
Expected Results:HOMA -IR ,insulin, glucose levels substantial rise relative to controls is expected, in case of hypothyroidism. Significant increase in cholesterol,Low density lipid,Very Low density lipidand triglycerides and significantly associated High density lipidwill be seen in low thyroid level.In hypothyroidism patients, insulin would be moderately associated with cholesterol,. When compared to controls, Homa-IR is expected to be significantly associated with TSH in hypothyroidism situations. In contrast to the controls, TSH is expected to be significantly associated with cholesterol and low density lipid in cases of hypothyroidism.
Conclusion: Will be drawn as per the results obtained.

Keywords: thyroid hormones, insulin resistance, TSH

INTRODUCTION:

Hypothyroidism is caused by low thyroid hormone levels with varying etiology and symptoms. Morbidity and mortality are increased by untreated hypothyroidism. Autoimmune thyroid syndrome is the most frequent cause of hypothyroidism in the US., However, worldwide dietary iodine deficiency is the primary important cause. The appearance of the patient will be different from myxoedema coma to asymptomatic disease. Today, with clear blood tests, the diagnosis of hypothyroidism is easy and can be managed via exogenous thyroid hormones.

Hypothyroidism, predominant and secondary (central) hypothyroidism, is often divided into two groups. If the primary hypothyroidism is a condition in which thyroid gland itself is unable to produce sufficient thyroid hormone, . Where the thyroid gland itself is healthy, the pituitary gland or hypothalamus is diagnosed with the condition, secondary or central hypothyroidism is marked.
The major causes of hypothyroidism are autoimmune thyroid diseases in the United States both in iodine-sufficient nations. The most common etiology in the US isHashimoto thyroiditis, and it has a significant correlation with lymphoma. Emergence of new iodine-deficient areas will affect etiology locally along with iodine fortification.

Failure of the thyroid gland to release sufficient thyroid hormone is the most common cause of hypothyroidism, but thyroid deficiency can also result due to pituitary and hypothalamus abnormality which is less common .The hypothalamus secretes (TRH) that stimulates (TSH) production in the anterior pituitary gland. Thyroid-stimulating hormone induces development and secretion of the thyroid gland, primarily T4 and minute amounts of T3. T4 has a half-life of seven to ten days and finally, through 5'-deiodination, peripherally T4 changes into T3 .In turn, the levels of T3 and T4 exert, to some degree, negative feedback on output of Thyroid Releasing Hormone and Thyroid Stimulating Hormone .

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Risk factors for insulin resistance, hypercoagulability , hyperlipidemia and low-grade inflammation have been identified for subclinical hypothyroidism (SCH) and overt hypothyroidism (OH)[1,2].
Several studies have shown that insulin resistance and hypothyroidism are associated with overt hypothyroidism.

Resistance to insulin in thyroid disease

Insulin resistance is characterized, despite its normal or enhanced blood concentration, As a state of glucose homeostasis that includes decreased insulin sensitivity of adipose tissue, muscles, liver and various tissues.Resistance may be symptomless, or a range of diseases may arise, such as: Impairment of glucose metabolism, diabetes type II, along with hyperlipidemia, obesity, hypertriglyceridemia and arterial hypertension. Insulin operates on the surface of most of the body's cells through unique receptors. On adipocytes, liver cells and striated muscle cells, the largest number of these receptors are located. Insulin resistance has three mechanisms: pre-receptor resistance, receptor resistance and post-receptor resistance. The various approaches to insulin resistance testing are focused on coordinated blood serum glucose and insulin levels measurements.Glucose and insulin tests are carried out under baseline conditions or after a set amount of glucose or insulin is administered I.V.

Either a thyroid hormone deficiency or an overload can disrupt the normal metabolism of glucose, leading to carbohydrate disorders.
Monocyte insulin receptors, in the presence of glucose react rapidly to variations in blood serum glucose levels and increase the rate of glucose removal quickly. [3-5]

Thyroid condition has revealed the prevalence of glucose metabolism abnormalities causing either overt hyper or hypo-thyroidism. [6] The period of the sickness is equal to the difference of these effects.[6,7,8]

(b) Hypothyroidism

Clinical hypothyroidism is characterised as a risk factor for resistance to insulin.[09-12)
There is a decline in the rate of absorption of intestinal glucose in hypothyroidism, as adrenergic activity decreases, resulting in a decrease in muscle and liver glucose breakdown, along with a reduction in new glucose synthesis and secretion of insulin. HoweverDue to massive peripheral insulin resistance associated with higher free fatty acid concentrations, impaired glucose absorption and elevated glucose oxidation, there has been a post-prandial rise in insulin secretion [13].

In patients with hyperthyroidism, there are less findings on the impact of decreased thyroid level on glucose metabolism than those examining insulin resistance.
Subclinical hypothyroidism (SHO) is characterised as elevated plasma Thyroid stimulating hormone levels, followed by normal plasma of thyroid hormone (free T3 and free T4) levels. The impact of insulin on glucose metabolism in hypothyroidism is unclear according to the study.

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The reduced sensitivity to fasting insulin estimated using the HOMA index has also been found to be lower in several other studies in patients Subclinical hypothyroidism.[14,15,16] However, the findings of some researchers suggest normal insulin sensitivity in that patient cohort [17,18]
However it should be acknowledged that in some of these trials, fasting elevated insulin levels were reported in which insulin tolerance was not found in patients. [16,19]
These findings can be interpreted as an early indication of glucose metabolism impairment. In this study, we will summarize the prevalence and effects of resistance of insulin in cases of hypothyroidism.

MATERIAL AND METHOD

PLACE OF STUDY
The research will be undertaken by the Department of Medicine at the Sawangi (Meghe) Hospital of AcharyaVinobaBhave, a tertiary care teaching hospital located in rural Central India.
DURATION-

- The duration of the study will be from September 2020 To September 2022

STUDY DESIGN:

- A Cross sectional study

Participants:
Cases: 1. All patient's who are attending medicine opd or are admitted to ward with symptoms of hypothyroidism or on clinical examination have signs of hypothyroidism and diagnosed as hypothyroidism by Free T3, free T4 and TSH levels.
2 . Patients already diagnosed of hypothyroidism and are on treatment for same .
CRITERIA:
INCLUSION CRITERIA
Criteria for inclusion:
Subclinical thyroid disorder, defined as normal serum free T4 and free T3 levels and increased serum Thyroid Stimulating Hormone levels.
Patients with elevated Thyroid stimulating hormone and low Free Thyroid hormone 3 (< 2pg / ml) and/or Free Thyroid hormone 4 (< 0.93 ng / dl) arecategorised as overt hypothyroids.
In patients with normal TSH, FT3, and FT4, the euthyroid condition was considered.
Exclusion Criteria
• Pregnancy
• Cases with diabetes mellitus
• Hypothalamic diseases
• AKI
• Myxedema Coma
• Sepsis
Any drug proven to impair resistance to insulin

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METHODS:

A cross-sectional study will be performed among 100 cases of hypothyroidism over 16 years of age who attend or are admitted in this hospital within a span of 2years.
TSH, fT3, free thyroxine, IR, Fasting Lipid Profile, Fasting Glucose, for both patients, kidney function tests would be assessed.
Consecutive sampling will be carried out in order to gather subjects for analysis. The research will include someone who has diagnosed hypothyroid patients without any complications who comes to the hospital during this period and meets the inclusion criteria.

Estimation of kidney function tests

Estimation of HOMA-IR

$$\text{HOMA-IR} = \frac{\text{fasting glucose values (mmol/L)} \times \text{fasting insulin values}(\mu U/mL)}{22.5}$$

The physiological value (Index)= 1.0.
Values>1 indicate resistance to insulin.

SAMPLE SIZE:

P = Prevalence of hypothyroidism = 5.9 % = 0.059
Z= Level of significance at 5% i.e 95% confidence interval 1.96
D = desired error of margin = 5% = 0.05
N = 100 patients needed in the study,
Reference: VK Chadha, sample size determination in health studios NIT bulletin 2006, 42/394 ,55-62

Expected Outcomes/Results:

In cases of hypothyroidism, substantial rise in insulin, Homa-IR, and glucose levels relative to controls is expected . Cholesterol, Low density lipid, very Low density lipid and triglycerides will be eventually increased, and high density lipid will be significantly reduced in cases of hypothyroidism relative to controls.
In hypothyroidism patients, insulin would be moderately associated with cholesterol, When compared to controls, Homa-IR is expected to be significantly associated with TSH in hypothyroidism situations. In contrast to the controls, TSH is expected to be significantly associated with cholesterol and low density lipid in cases of hypothyroidism.

DISCUSSION:

Thyroid disease alters the metabolism of glucose and lipids, a significant risk factor for cardiovascular diseases. An elevated level of insulin in low level of thyroid has been documented in numerous studies. This balance could be disrupted by a deficiency or thyroid hormone excess leading to changes in the metabolism of carbohydrates. Glucose sensitivity and even ketoacidosis have been linked with overt hypothyroidism. As for hypothyroidism,
In the literature, cases of hypoglycemia have been recorded, considering the presence of peripheral insulin resistance. Following the first findings of unregulated glucose metabolism

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in thyrotoxic diabetic patients, new methods of glucose homeostasis control by thyroid hormones have been recognized. Novel results include thyroid hormone stimulating the production of hepatic glucose via the sympathetic pathway through the hypothalamus.

Thyroid hormones in our research can have a negative correlation with insulin and Homeostatic Model Assessment of Resistance to Insulin, suggesting that lower plasma thyroid hormones decrease tissue sensitivity to insulin.
Kim et. al. [20] claimed in his research that thyroid hormone-T3 and insulin play complementary roles in glucose homeostasis at both cellular and molecular levels. It has been indicated that insulin-induced impaired glucose disposal results from diminished serum T3 intracellular levels.Therefore, even a small drop of thyroid hormone levels, as in SCH, correlates inversely with Homeostatic Model Assessmentof Resistance to insulin.
Homeostatic Model Assessment of Resistance to insulinis an insulin resistance fasting index correlating with hepatic insulin resistance, while the Matsuda Index is an insulin sensitivity index that partly estimates muscle insulin sensitivity after glucose loading . By binding to common nuclear receptors [TSH receptor] of which the TRβ isoform is specific to the liver, thyroid hormones exert their physiological effects and have been considered a putative target for dyslipidemia and fatty liver treatment . Lowering Lower density Lipid cholesterol, reducing whole-body fat and weight are the beneficial effects of TRβ activation. This could speculate that this happens to have no measurable influence in healthy adolescents with adequate muscle metabolic activity. A number of related studies were rereported. Jose et. al. assessed profile of thyroid dysfunctions among the female population in a rural community of Wardha [21]. Raniwalaet. al. studied the correlation of clinical, radiological, cytological, and histopathological findings in the diagnosis of thyroid swellings [22]. Similar related studies were reviewed [23-26].

The effect of thyroid status on insulin sensitivity is of high importance, but among different research, there is conflicting evidence on this aspect.Throughout the study population, subjects with subclinical hypothyroidism, overt hypothyroidism, and euthyroid controls would be considered.Thyroid profile, insulin and lipid profile, serum samples assays in every patientwill be done.The evaluation model of homeostasis (HOMA-IR) will be used to assess the degree of resistance to insulin. Patients with lower thyroid leveldemonstrated insulin resistance and dyslipidemia, as demonstrated by the elevated amounts of Homeostatic Model Assessment of Resistance to insulinand cholesterol and triglycerides relative to controls.In the hypothyroidism community, a highly positive association was also observed between TSH and HOMA-IR levels. Thyroid disorder results in glucose and lipid metabolism changes, which are a major effects factor for CVS disorders.

Another theory is that IR-related metabolic hepatic dysfunction may impair thyroid hormone metabolism High glucose production and raised Very Low Density Lipid-cholesterol . Hepatic IR, exacerbating hyperglycemia and increasing serum insulin content.
The association between HOMA-IR values and TSH levels was strongly positive in obese patients. Our results validate the HOMA-IR cutoff value of 2.5 with respect to TSH levels, which was higher in obese patients with IR than in those without IR. Although serum cortisol

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was associated with HOMA-IR and serum TSH levels, the association between HOMA-IR and TSH was retained even after the cortisol had been modified.

CONCLUSION :

We hope that insulin resistance will be present in both clinical and subclinical hypothyroidism. In both types, an increased Homeostatic Model Assessment of Resistance to insulin index and a decreased Matsuda index would indicate that resistance to insulin is present in both fasting and post-glucose conditions. These results would be in line with previous reports showing an increased risk of cardiovascular disease under these conditions.

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