Original Article

Idiopathic post prandial glucose lowering, a whistle blower for subclinical hypothyroidism and insulin resistance. A cross-sectional study in Tertiary Care Centre of northeast India

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Abstract

Background and Aims: There has been a lot of confusion in management of apparently healthy individuals whose post prandial plasma glucose levels were lower than fasting levels. It has been observed that many clinicians do send for repeat tests to rule out analytical error since there is common knowledge that post prandial glucose should be higher than fasting glucose level. Blood glucose level is regulated by a fully integrated mechanism with complex interplay of hormones and enzymes on metabolic pathways. Increase or decrease of thyroid hormones can break this equilibrium leading to alterations of carbohydrate metabolism. The objective for this study was to look for subclinical hypothyroidism (SCH) and insulin resistance (IR) in Idiopathic Post prandial glucose lowering and the correlation between thyroid stimulating hormone (TSH) with IR in them. **Methods**: A cross-sectional study with subgroup analysis, 34 cases and 34 controls. Cases comprises of otherwise healthy individuals whose post prandial glucose is lower than fasting glucose and controls as those healthy individual whose post prandial glucose is higher than fasting. Thyroid hormones and insulin were measured in fasting serum samples. Homeostasis model assessment for IR was calculated as per formula. **Results**: Among the 34 cases with idiopathic post prandial glucose lowering, 76% (n = 26) had subclinical hypothyroidism and 61% (n = 21) had insulin resistance. A positive correlation (r = 0.55) was observed between Thyroid-Stimulating hormone (TSH) and Index of insulin resistance and homeostatic model assessment (HOMA-IR) and was statistically significant with $P < 0.1$. **Conclusions**: The study highlights the importance of evaluating glycoregulatory hormones like thyroid hormones and insulin in cases with idiopathic post prandial glucose lowering for early diagnosis and prevention of overt clinical diseases like Hypothyroidism and Diabetes Mellitus.

Keywords: Idiopathic post prandial glucose lowering, insulin resistance, subclinical hypothyroidism, thyroid stimulating hormone

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Introduction

Studies have reported that some apparently healthy individuals showed lower post prandial plasma glucose levels than fasting levels.[1,2] There has been a lot of confusion in management of these apparently healthy individuals whose post prandial

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plasma glucose levels were lower than fasting levels. It has been observed that many clinicians do send for repeat tests to rule out analytical error since there is common knowledge that post prandial glucose should be higher than fasting glucose level. Blood glucose level is regulated by a fully integrated mechanism with complex interplay of hormones and enzymes on key metabolic pathways.[3] An intimate relationship between thyroid hormones and carbohydrate metabolism has long been established. Influence of thyroid hormones on insulin action to different organs can be both agonistic and antagonistic, however, maintaining a fine balance between these opposing actions is required for normal glucose metabolism. An increase or decrease of thyroid hormones can break this balance leading to alterations of carbohydrate metabolism.[4,5] Recently, increased interest has focused on the association between thyroid dysfunction and obesity, diabetes, metabolic syndrome and other cardiovascular risk factors [6-8] Previous studies have established overt hypothyroidism as a risk factor for insulin resistance (IR).[9] Subclinical hypothyroidism (SCH) often goes unrecognized due to lack of signs and symptoms.[10] Various studies have suggested the possible adverse clinical outcomes of subclinical hypothyroidism, including cardiac dysfunction, dyslipidaemia leading to an increased risk of atherosclerosis, and neuropsychiatric symptoms. Several more recent meta-analyses of observational studies found an association between SCH and coronary artery disease.[11] There are various studies of post prandial glucose lowering and various hormonal counter regulatory response to hypoglycaemia[1,3] but sparse study on whether idiopathic post prandial glucose lowering is related to thyroid dysfunction and insulin resistance.

In the light of these reports, this study was conducted to find out if post prandial glucose lowering is a whistle blower indicating some subclinical conditions. Once the correlation is determined, it should be aimed to correct the disorder, or if that is not possible, to attain measures to reduce and treat it before development of overt clinical disorder or complication.

Methods

This hospital-based study was started after obtaining clearance from NEIGRIHMS Scientific Advisory Committee (NSAC) and Institute Ethics Committee (IEC) 2/07/2019. A cross sectional design with subgroup analysis, 34 cases and 34 controls, were enrolled prospectively from outpatient department of General Medicine Department of our hospital within a time period of 8 months between July 2019 -February 2020. Cases comprises of otherwise healthy individual whose post prandial glucose is lower than fasting glucose and healthy individual whose post prandial glucose is higher than fasting, were taken as control.

Inclusion criteria

1. Adults (18-60 years) whose fasting blood glucose >post prandial blood glucose in otherwise normal individual with no prior history of Diabetes Mellitus or Impaired Fasting Glucose or Impaired Glucose tolerance
2. Willingness to participate in the study.

Exclusion criteria

1. Strenuous exercise
2. Smoking
3. Known case of Diabetes Mellitus, hypothyroidism, hyperinsulinemia, adrenocortical hypofunction, decreased gastrointestinal absorption like sprue and coeliac disease
4. Medication: oral hypoglycemic drugs, anti- diabetic, anti-inflammatory drugs.

About 5ml of fasting blood sample was drawn from all subjects after an overnight fast, also after 2 hours post prandial. The serum was separated by centrifuging the blood at 3000 rpm for 10 minutes. Serum glucose and lipid profile levels was estimated by spectrophotometric method. (AU2700 Chemistry auto-analyser, Beckman Coulter, Inc.), while serum FT3, FT4, TSH, and Insulin were measured by Chemiluminescence immunoassay method (UniCel DxI 800, Beckman Coulter, Inc.).

Insulin resistance was estimated using following calculated parameters:

Homeostatic model assessment in assessing insulin resistance (HOMA-IR) = [Fasting glucose (mg/dl) * fasting insulin (micro IU/ml)]/405.

Patient were considered as insulin resistant when HOMA-IR ≥ 1.4.[12]

And diagnosed to have subclinical hypothyroidism when their free triiodothyronine (FT3) and free thyroxine (FT4) were normal, but thyroid stimulating hormone (TSH) was >4 mU/I.[13]

Statistical analysis

Database was constructed in Microsoft Excel 2007, and statistical analysis was done using IBM Statistical Package for the Social Sciences (SPSS) MacOS version 23 (SPSS Inc., Illinois, USA), *t*-test and Pearson's correlation test were done to analyse the data. $P < 0.05$ was considered statistically significant.

Results

In this study, there were in total 68 participants, which was sub-grouped into 34 cases and 34 controls.

Table 1: This table shows that majority of cases were in age group 31-40 years (44.1%). Also more than half of the cases (64.7%) were females.

Table 2: This table shows that that out of the 34 cases, 76% (n = 26) had subclinical hypothyroidism (SCH) and 61% (n = 21) had insulin resistance (HOMA-IR).

Discussion

Glucose is an essential fuel for the brain, therefore, adequate uptake of glucose from the plasma is key for normal brain function and survival. Despite wide variations in glucose flux (i.e. fed state, fasting state, etc), blood glucose is maintained in a very narrow range. This is accomplished by a series of hormonal and physiologic responses. As a result, hypoglycaemia is a rare occurrence in normal individuals.[3] It is well understood how this glucose counter-regulatory responses are altered in patients with diabetes, but this is not the case in a healthy normal individual. In this regard, keeping in mind the various interplay of hormones in glucose metabolism, in our study we found that out of the 34 cases, 76% (n = 26) had subclinical hypothyroidism (SCH) and 61% (n = 21) had insulin resistance (HOMA-IR) [Table 2]. A positive correlation (r = 0.55) was observed between TSH and HOMA IR and was statistically significant with $P < 0.01$[Figure 1]. This is in accordance with the study done by Maratou E *et al.*[14], AL Sayed *et al.*[15]

The maximum prevalence of cases was seen in age group 31-40 years (44.1% of cases) and more common in women than in men (64.7%, n = 22) [Table 1]. This is in accordance with study done by AL Sayed *et al.*[15] and BM Singh.[16]

Elevated LDL cholesterol, total cholesterol level, and triglycerides has been widely used to assess lipid atherogenesis and Insulin resistance. Thyroid disease can also increase the risk of cardiovascular disease. In the present study, we found a significantly higher proportion of total cholesterol and LDL cholesterol levels among cases [Table 3], which is an important risk factor for cardiovascular disorders.[11,17,18]

It is not clear as to whether SCH is related to risk for cardiovascular disease (CVD), although it has been concluded recently that mild thyroid failure is associated with an increased risk for development of atherosclerosis[19] and that SCH is a strong indicator for risk of atherosclerosis and myocardial infarction in women.[15]

Continuous exposure to a plethora of cardiovascular risk factors including hyperinsulinemia, dyslipidaemia and undetected SCH may lead to overt and complicated metabolic disease.

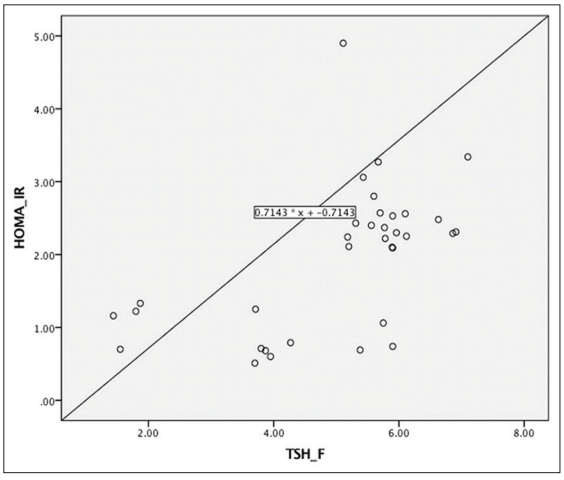

Figure 1: Correlation test was done between TSH and HOMA-IR among the cases and was found to be positively associated (r = 0.55) and significant at 0.01 level

Table 1: Age and sex distribution of the study group/ respondents

	Study Group				Total	
	Case		Control			
	%	*n*	%	*n*	%	*n*
Age in years						
18-30	8.8	3	11.8	4	10.3	7
31-40	44.1	15	20.6	7	32.4	22
41-50	26.5	9	41.2	14	33.8	23
51-60	20.6	7	26.5	9	23.5	16
Sex						
Male	35.3	12	52.9	18	44.1	30
Female	64.7	22	47.1	16	55.9	38
Total	100.0	34	100.0	34	100.0	68

Table 2: Prevalence of the subclinical hypothyroidism and insulin resistance by study group

Parameter	Study Group				Total	
	Case		Control			
	%	*n*	%	*n*	%	*n*
TSH						
Hypo	76.5	26	0.0	0	35.3	24
Normal	23.5	08	100.0	34	64.7	44
HOMA_IR						
High	61.8	21	0.0	0	30.9	21
Normal	91.2	13	97.1	33	67.6	46
Low	0.0	0	2.9	1	1.5	1
Total	100.0	34	100.0	34	100.0	68

Table 3: Mean with standard deviation (SD) in case and control groups

Parameter	Study Group	
	Cases (*n*=34)	Control (*n*=34)
AGE (Mean±SD)	40.23±9.51	44±8.5
TSH (Mean±SD)	5.01±1.52	1.87±0.913
FT4 (Mean±SD)	0.83±0.11	0.81±0.13
FT3 (Mean±SD)	3.32±0.44	2.94±0.28
HOMA-IR (Mean±SD)	1.94±0.99	0.68±0.16
FBS (Mean±SD)	98.32±10.70	84.32±6.5
PPBS (Mean±SD)	85.32±9.8	112.67±17.13
T. CHOL (Mean±SD)	195±26	154±27
TRIG (Mean±SD)	150.7±42	93±29
HDL (Mean±SD)	48±12	43±10
LDL (Mean±SD)	115±21	91±20

TSH=Thyroid Stimulating Hormone, FT4=Free Thyroxine, FT3=Free Triiodothyronine; HOMA-IR=Homeostasis Model Assessment of Insulin Resistance, FBS=fasting Blood Sugar; PPBS=Post Prandial Blood Sugar, T. CHOL=total cholesterol; TRIG=triglyceride, HDL=High Density Lipoprotein, LDL=Low Density Lipoprotein

Therefore, there is a need for routine assay of thyroid hormones and Insulin resistance in patients with idiopathic post prandial glucose lowering so as to diagnose subclinical disorders as early as possible and reduce morbidity and prevent them from overt clinical disorder like Diabetes, Hypothyroidism and related complications.

Conclusion

The results of the studies we conducted on the 34 cases and 34 controls clearly highlights the importance of evaluating glycoregulatory hormones like thyroid hormones and insulin in cases with idiopathic post prandial glucose lowering. This is especially true for early diagnosis and prevention of overt clinical diseases like Hypothyroidism and Diabetes Mellitus.

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Conflicts of interest

There are no conflicts of interest.

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