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Original Research Paper

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STUDY OF SERUM GHRELIN IN THYROID PATIENTS

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ABSTRACT

Background: Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormone by the thyroid gland. Ghrelin is octanoylated peptide containing a 28 amino acid act as an energy balance regulator & play an important role in metabolic process .The aim of the study was to establish possible relationship between them. **Materials and methods:** The present study is a cross sectional study, was conducted in the Department of Biochemistry, J.L.N. Medical college and associated group of Hospitals, Ajmer (Raj.). 65 hypothyroid subjects (group-II) and 65 hyperthyroid subjects (group-III) attending Medical OPD of J.L.N. Hospitals were included and 130 age-sex matched euthyroid controls (group-I) were selected. **Results:** In hypothyroid subjects, mean serum Ghrelin levels were found to be significantly higher in comparison to healthy subjects ($p<0.0001$). In hyperthyroid subjects, mean serum Ghrelin levels were found to be significantly lower in comparison to healthy subjects ($p<0.0001$). **Conclusion:** The overall findings of the present study thus confirm that serum Ghrelin level is significantly higher in Hypothyroid subjects and the level is significantly lower in the Hyperthyroid subjects, thus we have found positive association between serum TSH level and Ghrelin level. However, further experimental and observational studies are needed to illustrate the role of Ghrelin in Hypothyroidism and Hyperthyroidism.

KEYWORDS : Triiodothyronine(T_3), Thyroxine(T_4), Thyroid stimulating Hormone(TSH), Enzyme linked immunosorbent assay (ELISA), Chemiluminescence Immunoassay (CLIA).

INTRODUCTION

Thyroid hormone production is regulated by thyroid stimulating hormone (TSH), which is made by the pituitary gland in the brain. The hypothalamus and the pituitary gland communicate to maintain T_3 and T_4 balance. The hypothalamus produces TSH Releasing Hormone (TRH) that signals the pituitary gland which in turn signals thyroid gland to produce T_3 and T_4 by either increasing or decreasing the release of TSH.

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. It is often the primary process in which the thyroid gland produces insufficient amounts of thyroid hormone. It can also be secondary, i.e., lack of thyroid hormone secretion due to the failure of either adequate thyrotropin (TSH) secretion from the pituitary gland or thyrotropin-releasing hormone (TRH) from the hypothalamus (secondary or tertiary hypothyroidism). The patient's presentation may vary from asymptomatic to, rarely, coma with multisystem organ failure (myxoedema coma) [1].

Hypothyroidism is particularly prevalent in women older than 40 years of age and also prevalent in debilitated geriatric patients of both sexes. Primary hypothyroidism is a commonly encountered clinical problem. Treatment is indicated if thyroid -stimulating hormone (TSH) is more than 10 μIU/ml [2]. The mean annual incidence of hypothyroidism is up to 4 per 1000 women, 1 per 1000 men and 1 in 4000 newborns. The prevalence of overt hypothyroidism increases with age. The most common cause of hypothyroidism is autoimmune thyroiditis. Hypothyroidism can cause slowing in physical and mental activity but may be asymptomatic. Symptoms and signs are often subtle and neither sensitive nor specific [3].

Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormones by the thyroid gland, which leads to the hyper metabolic condition of thyrotoxicosis[4]. Graves' disease is the most common cause of Hyperthyroidism. In Hyperthyroidism the level of T_4 and T_3 are higher than the normal and the level of TSH is lower than the normal.

Ghrelin is octanoylated peptide containing a 28 amino acid which is chiefly produced by the stomach, is the natural ligand of the type 1a growth hormone secretagogue receptor (GHS-R1a) [5]. The gastric Ghrelin hormone originates from 117 amino acid, and its precursor preproghrelin encoded by the Ghrelin gene (GHRL) found on chromosome [6]. Ghrelin is a participant in regulating the complex process at which both energy has to be adjusted. Energy input by adjusting hunger signals and energy output by adjusting the proportion of energy going to ATP production, glycogen storage, fat storage and short term heat loss. Natural and synthetic Ghrelin system(GHS) stimulate GH release from somatotroph cells in vitro, by depolarizing the somatotroph membrane and by increasing the amount of GH secreted per cell. At the hypothalamic level, Ghrelin and GHS act via mediation of growth hormone-releasing hormone (GHRH)-secreting neurons in which showed by signal that passive immunization against GHRH, as well as pretreatment with GHRH antagonists, reduces their stimulatory effect on GH secretion [7].

In hyperthyroid patients, in which Ghrelin levels are also suppressed, according to the degree of thyrotoxicosis and to glucose levels. Moreover the hyper-insulinemic hyperglycemic state or excess of thyroid hormone (hyperthyroidism) itself is leading to decline the Ghrelin level in turn, affecting on carbohydrate metabolism that shift away from energy storage and towards energy use which may have a role in the hyper catabolic state. Ghrelin has an effect on the Hypothalamus–Pituitary–Thyroid (HPT) axis in humans. Thus, the early free thyroxine (fT4) increase was possibly induced by direct ghrelin action on the thyroid gland wherever Ghrelin receptors have been well-known [8].

In a state of severe hypothyroidism, high Ghrelin concentration may lead to appropriate use of energy resources. In hyperthyroidism, which is accompanied by increased metabolic rate and energy expenditure, low ghrelin level may be associated with the transition to a more energy-efficient state [9] .

MATERIALS AND METHOD

A cross sectional study was carried out in department of biochemistry , J.L.N. Medical college, Ajmer , Rajasthan, India.

Total 130 patients with hypo (65) and hyperthyroidism (65) , without having medical history of any chronic disease such as diabetes, hypertension, inflammatory disorder, etc. were included for the study. The results were compared with age matched 130 healthy controls of either sex (group-I). Serum concentration of free T_4 (fT_4), fT_3, TSH and serum Ghrelin were estimated in all subjects. Every subject of control group as well as patients of both hypo & hypothyroidism group given a written consent before participating in the study . serum sample of all subjects were collected to estimate the biochemical parameters. Enzyme linked immunosorbent assay (ELISA) method was used to measure serum Ghrelin. Chemiluminescence immunoassay (CLIA) was used to measure fT_3, fT_4, and TSH. The present study was approved by Institutional Ethical Committee.

Statistical Analysis

All data were analysed by SPSS-13 version. P<0.01 were considered as significant.

RESULTS

The present study was conducted on 65 hypothyroid subjects (group-II) and 65 hyperthyroid subjects (group-III). The results were compared with age matched 130 healthy controls of either sex (group-I). Serum fT_3, serum fT_4, serum TSH, and serum Ghrelin were estimated. The results are summarised in Table and figures.

Table-1 Anthropometric parameters of Healthy subjects (controls), Hypothyroid and Hyperthyroid subjects

Parameters	GROUP-I Healthy subjects (controls) Mean ± SD (n=130)	GROUP-II Hypothyroid subjects Mean ± SD (n=65)	GROUP-III Hyperthyroid subjects Mean ± SD (n=65)
AGE (yrs)	35.00 ± 9.5	39.80 ± 11.4	40.14 ± 12.6
WEIGHT (kg)	53.69 ± 6.7	64.32 ± 5.4	42.44 ± 4.6
HEIGHT (cm)	154.60 ± 4.8	155.80 ± 5.1	156.50 ± 4.9
BMI (kg/m^2)	22.50 ± 5.1	23.20 ± 4.9	20.50 ± 3.9

Table-2 Biochemical parameters of Healthy subjects (controls), Hypothyroid and Hyperthyroid subjects

Parameters	GROUP-I Healthy subjects (controls) Mean ± SD (n=130)	GROUP- II Hypothyroid subjects Mean ± SD (n=65)	GROUP-III Hyperthyroid subjects Mean ± SD (n=65)
fT_3(pg/ml)	3.16 ± 0.54	1.79 ± 0.38	12.50 ± 2.20
fT_4(ng/dl)	0.96 ± 0.19	0.25 ± 0.07	3.10 ± 0.50
TSH (μIU/ml)	2.90 ± 1.50	81.10 ± 16.80	0.01 ± 0.00
S. Ghrelin (pg/ml)	489.00 ± 48.0	541.00 ± 41.0	350.00 ± 43.0

The present study was undertaken in three groups viz group-I, group-II and group-III i.e. normal healthy controls, Hypothyroid subjects and Hyperthyroid subjects respectively.

Basic anthropometric parameters of all subjects in normal healthy controls, Hypothyroid and Hyperthyroid subjects are summarized in table-1. The anthropometric parameters viz, age in years was (35.00 ± 9.5), (39.80± 11.4), (40.14± 12.6) in group-I, group-II and group-III respectively, BMI mean ± SD in kg/m^2 in the group-I, group-II and group-III was (22.50 ± 5.1), (23.20 ± 4.9)and (20.50 ± 3.9) respectively (Table-1).

Table-2 shows the biochemical parameters viz, serum fT_3 (pg/ml), serum fT_4 (ng/dl), serum TSH (μIU/ml), serum Ghrelin (pg/ml) levels in normal healthy controls, Hypothyroid subjects and Hyperthyroid subjects.

In Fig. 1, Comparison of mean serum Ghrelin levels in normal healthy controls and hypothyroid subjects is shown. The mean serum Ghrelin level in hypothyroid subjects (541.00±41.0 pg/ml) is found to be higher than healthy controls (489.00±48.0 pg/ml; P < 0.0001) (Fig. 1).

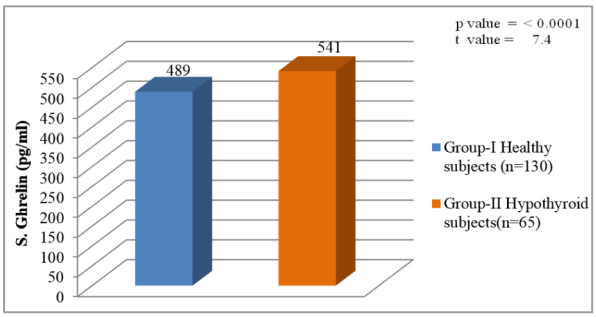

Fig-1 Comparison of S. Ghrelin levels of Healthy subjects (controls) and Hypothyroid subjects

In fig.2, Comparison of mean serum Ghrelin levels in normal healthy controls and hyperthyroid subjects is shown. The mean serum Ghrelin level in hyperthyroid subjects (350.00±43.0 pg/ml) is found to be lower than healthy controls (489.00±48.0pg/ml; P < 0.0001).

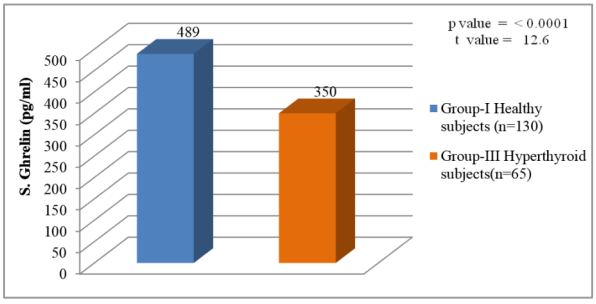

Fig-2 Comparison of S. Ghrelin levels of Healthy subjects (controls) and Hyperthyroid subjects

DISCUSSION

In recent years, thyroidism is unknowingly emerging as a major public health problem in India and it produces an enormous burden on the economy of the country due to high prevalence, risk of progression to overt hypothyroidism and it can lead to adverse cardiovascular consequences [10].

Many studies have shown that Ghrelin levels are affected in thyroid dysfunction like hypothyroidism and hyperthyroidism. The present study evaluates the status of Ghrelin in patients with hypothyroidism and hyperthyroidism and to establish possible relationship between them.

The main factor that regulates the ghrelin secretion are food intake and body weight. we expected that ghrelin concentration would be high in hyperthyroid patients, who complain of increased appetite and weight loss and low ghrelin level in hypothyroid patients, who usually gain weight. But our results are compatible with most of the previous studies that also revealed a low plasma ghrelin concentration in hyperthyroid patients [11-15] and high ghrelin level in hypothyroid patients [9,15-17].

Metabolic disturbances could also be responsible for plasma ghrelin changes in hyperthyroid patients, whose metabolism rate, energy expenditure and thermogenesis are considerably increased. Plasma ghrelin changes in thyroid dysfunction may indicate a compensatory role of this peptide in metabolic disturbances. In a situation of severe hypothyroidism, high ghrelin concentration may direct to proper use of energy resources. In hyperthyroidism, which is accompanied by increased metabolic rate and energy expenditure, low ghrelin level may be associated with the transition to a more energy-efficient state, as previously suggested by Riis et al. [9].

CONCLUSION

The overall findings of the present study thus confirm that serum Ghrelin level is significantly higher in Hypothyroid subjects and the level is significantly lower in the Hyperthyroid subjects, thus we have found positive association between serum TSH level and Ghrelin level.

However, further experimental and observational studies are needed to illustrate the role of Ghrelin in Hypothyroidism and Hyperthyroidism. Confirmation of the level of Ghrelin in thyroid disorder is one more minor step in the direction of understanding the role of ghrelin in human energy homeostasis and may perhaps in the long run contribute to the improvement of new therapeutic strategies in thyroid and metabolic disorders.

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