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Original Research Article

A Cross-Sectional Evaluation of Serum Calcium, Magnesium in Hypothyroid Subjects in Rohilkhand Region of Western Uttar Pradesh

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Abstract:

Background: Thyroid hormones have a very significant role in the metabolic processes that occur in the human body. Hypothyroidism is the commonest form of thyroid dysfunction. Mineral metabolism is frequently disturbed in thyroid dysfunction.

Aim: To evaluate the Serum calcium, magnesium in the newly diagnosed cases of hypothyroidism as compared to the euthyroid subjects.

Methods: The present study was conducted 60 cases and 60 healthy subjects who attended the OPD of Rohilkhand Medical college and Hospital, Bareilly. The serum calcium levels were done by Ortho-cresolphthalein complexone method and serum Magnesium was assessed by calmagite method. Data was analyzed statistically using SPSS software.

Result: We found decreased levels of serum calcium and increased levels of serum magnesium in hypothyroidism patients as compared to the euthyroid subjects. Our study shows statistically insignificant positive correlation of serum magnesium with TSH and there is no correlation between serum TSH and serum magnesium was observed in hypothyroid cases as compared to the controls.

Conclusion: Our study found that serum Calcium levels are lower and serum Magnesium are higher in hypothyroid cases when compared to healthy subjects. A strong negative correlation between serum TSH levels and serum calcium was observed among hypothyroid individuals.

Keywords: Serum Calcium, Magnesium, Hypothyroid.

Introduction

Thyroid hormones have a very important function in the human body. These hormones regulate body temperature and the metabolism of carbohydrates, proteins, lipids and minerals. Thyroid hormones play an important role in hemodynamic, thermoregulation and metabolism of body. Among all the endocrine disorders, thyroid disorders are the most common disorders which is prevalent worldwide as well as in India out of which hypothyroidism is the most common. Serum T_3 and T_4 levels are reduced in primary hypothyroidism resulting in pituitary TSH hyper secretion and elevated serum TSH levels. Abnormal activity of thyroid gland slows metabolic processes and causes a variety of clinical and physiological abnormalities. [1] Hypothyroidism is characterized by a generalized reduction in metabolic functions that most often manifest as a slowing of physical and mental activities. In most of the cases, a decrease in thyroid function occurs gradually, with sub-clinical hypothyroidism progressing over time to overt hypothyroidism. [2] Hypothyroidism may present sub-clinically with raised level of serum TSH and normal free T_4 levels. It occurs more repeatedly in women; with an overall incidence of ~3% of the general population. [3] Hypothyroidism has a wide clinical spectrum ranging from an unconcealed stage of myxedema, end- organ effects & multiorgan failure to an asymptomatic or subclinical state with normal ranges of thyroxine & triiodothyronine & mildly increasing levels of serum thyrotropine. [4] Subclinical hypothyroidism is explained as a serum TSH above the defined upper range of the reference range, with a serum free thyroxine within the reference range. Subclinical hypothyroidism (SCH), also called mild thyroid failure, is diagnosed when peripheral thyroid hormone levels are within normal reference laboratory range but serum thyroid – stimulating hormone (TSH) levels are mildly elevated. This

condition occurs in 3% to 8% of the general population. Its more common in women than man, and its prevalence increase with age. Of patients with SCH, 80% have a serum Thyroid stimulating hormone of less than 10μIU/L. The most important implication of subclinical hypothyroidism is high likelihood of progression to clinical hypothyroidism. Currently, the practical approach is routine levothyroxine therapy for the persons with a persistent serum TSH of more than 10.0μIU/L. [5] Overt hypothyroidism is as low thyroxine levels and elevated serum TSH levels with clinical features. [6] Overt hypothyroidism refers to cases in which the serum thyroid stimulatory hormone (TSH) concentration is elevated and serum thyroxine is below the reference range. The progression to overt hypothyroidism is approximately 2 – 5 % / year. Thyroid hormones bring to bear direct cellular effects on almost all tissues of the body. It causes multi organ failure secondary to deranged metabolism. The cardiac dysfunction ranges from functional systolic/diastolic dysfunction to overt failure and coronary artery disease. This is as a consequence of the direct effect of the disease. It can cause a number of symptoms, such as tiredness, poor ability to tolerate cold, and weight gain. In children, hypothyroidism leads to delay growth and intellectual development, it is known as cretinism in most of the severe cases. The diagnosis of hypothyroidism, when suspected, can be confirmed with blood test is done in measuring TSH and thyroxine level. Worldwide, less quantity of iodine in diet is the most common cause of hypothyroidism. In most of the countries with enough dietary iodine is the most common cause of hypothyroidism which is an autoimmune state of Hashimoto's thyroiditis and less common causes includes the following: Previous treatment with radioactive iodine, Injury to the hypothalamus or the anterior pituitary gland, Certain medications, A lack of a functioning at birth or previous thyroid surgery. Hypothyroidism can be well treated with manufactured levothyroxine; the dose is adjusted according to symptomsand normalization of the thyroxine and thyroid stimulating (TSH) levels. [7] Calcium and Magnesium are divalent metal ions, which are necessary for metalloenzymes and many important metabolic pathways regulated by thyroid hormones. [8] Thyroid dysfunction causes disturbances in metabolism of calcium and minerals. Thyroid hormones increase serum calcium levels by stimulating bone resorption and inhibiting parathyroid hormone (PTH) activity. Opposite effects are seen in hypothyroidism. [9]

Decreased synthesis & low levels of circulating thyroid hormones in clinical hypothyroidism causes many processes of metabolism to slow down. [10] Hypothyroidism is associated with weight gain, cold intolerance & constipation. It is a well-established fact that thyroid hormone influence mostly all the metabolism in the body such as – carbohydrate, protein, lipids & maintenance of water & electrolytes homeostasis. [11] Disturbance of calcium homeostasis was frequently seen with dysfunction of thyroid gland. [12] Thyroid hormones regulate the levels of calcium in blood by releasing calcium from the cells. Since thyroxine level is found to be decreased in primary hypothyroidism, so the out flux of calcium from the cells is also decreased. [13] In hypothyroidism there is a depressed turnover due to impaired mobilization of calcium into the bone which leads to decrease in blood calcium levels. In hypothyroidism increased production of calcitonin can increase tubular excretion of calcium. [14] Low calcium level in hypothyroidism is caused by poor calcium mobilization into the bone as evidenced by numerous recent studies. Calcitonin synthesis is increased resulting in the reabsorption of phosphate and excretion of calcium from the renal tubules. Serum calcium level is regulated by thyroid hormones by releasing it from the para - follicular cells of thyroid gland. [15] In hypothyroidism, disturbances in the levels of serum magnesium have also been discovered. [16] Serum magnesium levels are higher in hypothyroid disorders. [17] Magnesium stimulates cyclic 3, 5 nucleotide phosphodiesterase. Since the action of thyrotropin on the thyroid gland is mediated by cyclic AMP, the availability of magnesium could affect the response of the gland to the pituitary hormone. [18] The hormones of thyroid glands regulate many metabolic pathways & also the divalent metal ions like – calcium & magnesium which are required for several metalloenzymes. Hypocalcemia is a similar detection in the patients of hypothyroidism. These hormones regulate the levels of calcium in the bloodstream by releasing the calcium ions from cells, so the levels of thyroxine hormone are decreases in hypothyroidism & outflow of calcium ion is also reduced from the cells. [19] Despite the fact that increase in Ca and Mg report for low levels in thyroid disorders, the disturbances were found to be censorious in the long run for the patients. [20] Decreased thyroid hormone synthesis is due to decreased calcium ions in blood. The changes in the calcium levels may be slight in hypothyroidism cases in some conditions & may not be an acute problem for them but it may be possible that these changes are illustrious for the hypothyroid patients in the long term. [21] Magnesium has a major role in the regulation of membrane permeability & thereby affecting the secretion of thyroid hormones. These hormones also in turn affect the metabolism & clearance of the levels of serum calcium & magnesium which gets altered in hypothyroidism & this is eminent for the hypothyroid patients in the long run. [22] Moreover, calcium & magnesium deficiency may be risk factors for the hypothyroidism which is a condition

that is highly prevalent in the women. [23] We undertook this study to investigate the serum calcium and magnesium levels in hypothyroidism. Calcium has been reported to be essential for the optimal thyroid gland functioning and is also essential for the normal conversion of the thyroid hormones. Many studies have reported that decreased levels of calcium in the case of hypothyroidism. [24]

Moreover, very less studies have revealed its effect on serum calcium and magnesium. Therefore, the present study is undertaken to evaluate whether there is any alteration in the status of calcium, magnesium in hypothyroid subjects.

Materials and Methods

Place of study: The study was carried out in the Department of Biochemistry in collaboration with Department of Medicine, Rohilkhand Medical College and Hospital, Bareilly.

Type of Study: An analytical cross-sectional study.

Study Duration: Study was conducted for duration of 12 months (October 2021 – September 2022), after obtaining the ethical clearance from the Institutional Ethics Committee.

Study Population: The study population comprised of two groups, the hypothyroid cases with TSH ≥ 6.16 μIU ⁄ L& controls as euthyroid subjects with TSH range between 0.28 – 6.16 μIU ⁄ L.

Sample Size: After calculation, the sample size obtained was 60. Soin this study, 60 cases and 60 controls weretaken.

Criteria for Selection of Cases: The subjects for the study were selected from patients with hypothyroidism who fulfil the inclusion and exclusion criteria, attending the Medical OPD & IPD of RMCH, Bareilly.

Inclusion criteria: The patients newly diagnosed with hypothyroidism with TSH > 6.16μIU ⁄mL in age group of 20 – 60 years.[25]

The patients of hypothyroidism who have given their consent to participate in the study.

Exclusion criteria:

- Already diagnosed cases of

a) Renal disorders
b) Liver disorders

- Diabetic patients
- Pregnant and lactating women.
- Patients on drugs for hypothyroidism
- Patients on medication and supplementation affecting mineral metabolism.

Methods:

Patients attending IPD & OPD of Medicine department in Rohilkhand Medical College & Hospital, Bareilly satisfying the inclusion & exclusion criteria were taken for the study.

Detailed history & findings of the complete physical examination were noted on patient information sheet. The required investigations were done in Biochemistry laboratory as follows-

Specimen collection & processing: After getting approval from Institutional Ethics Committee (IEC), a written informed consent was taken from subjects or their Legally authorized representative. The demographic and clinical profile was documented in the proforma attached.

Under all aseptic conditions 4 ml of venous blood after 10 hours of fasting was collected from the cases & control in a serum separating tube.

Blood was allowed to clot for 30 minutes at 37^0C & then centrifuged at 2000 rpm for a period of 10 minutes and obtained serum stored at 2 – 8^0C for further analysis maximum to 7 days.

The obtained serum was used for determination of TSH, Calcium, Magnesium and liver function tests

Serum calcium was estimated by O – Cresolphthalein Complexone, End point assay method on semi-autoanalyser Chem-7 by Transascia.

Serum magnesium was estimated by Calmagite, End point assay method on semi-autoanalyser Chem – 7 by Transascia.

Liver function tests (ALT, AST, ALP, Total & Direct bilirubin, total protein & albumin) parameters was estimated on autoanalyser EM 360 by transascia by following method –

AST & ALT- by modified IFCC method

ALP – by paranitrophenol phosphate, amino methyl propanol (Pnpp, Amp) by IFCC kinetic assay methods

Bilirubin – by Malloy &Evelyn method by using Vanden Berg reaction

Albumin – by Bromo Cresol Green dye binding method

Serum total protein – by Biuret method

Determination of thyroid hormone: TSH estimation was done by Sandwich ELISA method & T_3 & T_4 estimation were done by competitive ELISA method & reading was taken by Erba Manngeim LISA SCAN II

Statistical Analysis: Data was collected and entered in software SPSS 23.0 and analyzed for descriptive statistics. The results are presented in

mean ± SD. Unpaired t- test was used to compare the study parameters between hypothyroid cases and euthyroid as control. Pearson correlation coefficient was calculated among the study parameters p-value <0.05 was considered significant.

Observations and Results

This study was conducted in the Department of Biochemistry at RMCH, Bareilly. The study was conducted from October 2021 to September 2022. This study included 60 newly diagnosed hypothyroid cases and 60 euthyroid as control with the age group of 20 – 60 years.

The mean age in the controls and cases were 35.05± 13.21 years and 34.86±12.25 years respectively. The mean serum TSH among controls and cases were 2.38±1.37 and 21.06±35.19 µIU/L.

Table 1: Age distribution of cases and control

Age	Euthyroid	Cases
20 – 30	30 (50%)	26 (43.3%)
31 – 40	12 (33.3%)	15 (25%)
41 – 50	8 (13.3%)	11 (18.33%)
51 – 60	10 (16.66%)	8 (13.33%)
Total Mean±SD	35.05±13.21	34.86±12.25

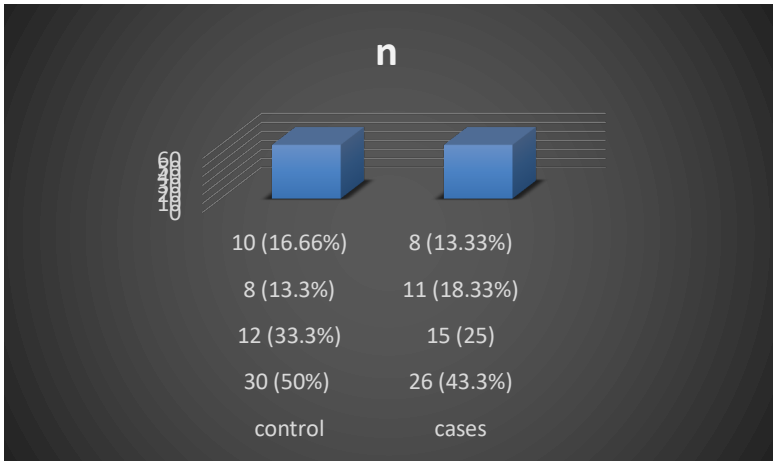
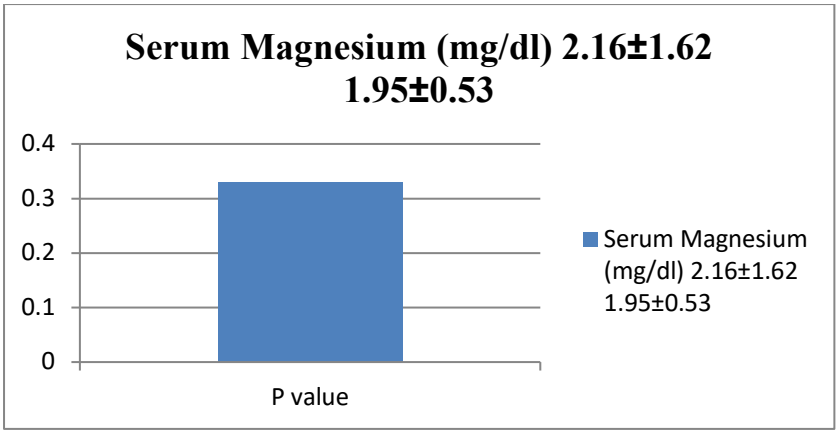


Figure 2: Age distribution in cases and control

The highest number (50%) of the cases belonged to the age group 20 – 30 years. The mean age group of the cases was 34.86±12.25. the highest number of hypothyroidism (43.3%) and euthyroidism(50%) were found in group 20 – 30 years of age in control groups. The mean age of control was 35.05±13.21.

Table 2: Comparison of Age, TSH, Serum Calcium and Magnesium in controls and Cases

Parameter	Euthyroid (n=60)	Cases (n = 60)	P value
Age (years)	35.05±13.21	34.86±12.25	
TSH (µIU/L)	2.38±1.37	21.06±35.19	
Serum Calcium(mg/dl)	9.57±1.00	8.31±0.53	0.00*
Serum Magnesium (mg/dl)	2.16±1.62	1.95±0.53	0.33



The mean serum TSH among controls and cases were 2.38 ± 1.37µIU/L and 21.06 ± 35.19µIU/L respectively. A significant increase was observed among cases compared to the controls. The mean serum Calcium in controls and cases were 9.57±1.00mg/dl and 8.31±0.53mg/dl respectively (the p value was 0.00. In our study we considered p value <0.05.) A significant hypocalcemia was seen in cases compared tocontrols. The mean serum Magnesium in controls and cases were2.16±1.62mg/dl and 1.95±0.53mg/dl respectively. The increase was highly statistically insignificant in cases compared to controls.

Discussion

Thyroid hormones maintain body hemodynamics, thermoregulation and several metabolic reactions. They have an influence on renal hemodynamics, glomerular filtration and electrolyte handling. Hypothyroidism being the most prevalent endocrine disease which can lead to a group of clinical situations including electrolyte and mineral disturbances.

Calcium and magnesium homeostasis were frequently disturbed in thyroid dysfunctions. Thyroid hormones affecting the glomerular filtration rate and blood flow, have direct effect on calcium and magnesium reabsorption. [26]

Our study demonstrated a significant lower levels of serum calcium in cases as compared to the controls. Our study revealed a significant negative correlation of serum calcium with TSH . Our study was in accordance with study conducted by Shivaleela et al. [27]

Thyroid hormones are the most essential for normal growth and maturation of skeletal system. Depressed turnover due to impaired mobilization of calcium into the bone was seen in hypothyroidism leading to decreased blood calcium. [28]

Present study demonstrates increased levels of serum magnesium in hypothyroidism. Which is in agreement with Kaur J et al, and Gupta A et al. [29]

Our study shows insignificant positive correlation of serum magnesium with TSH and there is no correlation between serum TSH and serum magnesium was observed in hypothyroidism. But some studies shows that decreased levels in hypothyroidism compared to euthyroid subject and show negative correlation with thyroid hormones. [30]

Our findings were contradictory to Abedelmula M, et al. who mentioned a significant decrease in serum magnesium levels in hypothyroid group compared to controls in their study. [31]

The major concern with subclinical hypothyroidism has been risk of progression to overt hypothyroidism.

Conclusion

Our study concludes that serum calcium levels were decreased in hypothyroidism compared to the euthyroid subjects. A strong negative correlation between serum TSH levels and serum calcium was observed among hypothyroid individuals. Serum magnesium levels were increased in hypothyroidism. Hypothyroidism patients need to be regularly evaluated for serum calcium and magnesium as early detection and correction can prevent further complications from mineral metabolism dysfunction.

The limitation of the study was small sample size which may be the reason for insignificant correlation for serum magnesium

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