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Relationship between Overt Hypothyroidism and Hypocalcemia: A Cross-Sectional Study in the Rural Population of Bankura, West Bengal

Sumanta Banerjee[1], Subhayan Lahiri[2*], Tanima Mandal[3], Pinaki Sarkar[4]
[1]*Post graduate trainee, Department of Biochemistry, B.S. Medical College,Bankura, West Bengal, India.*
[2]*Post graduate trainee, Department of Biochemistry, B.S. Medical College,Bankura, West Bengal, India.*
[3]*Demontrator, Department of Biochemistry, B.S. Medical College,Bankura, West Bengal, India.*
[4]*Professor & HOD, Department of Biochemistry, B.S. Medical College, Bankura, West Bengal, India.*
**Corresponding Author: Dr. Subhayan Lahiri*

Abstract: *Hypothyroidism is one of the most common endocrinal abnormalities found in India and is coexisted with various metabolic disorders and mineral imbalances. Calcium deficiency is one of them, occurring due to uncorrected hypothyroidism for prolonged period. Present study was conducted with the aim to find relationship between thyroid profile and calcium level, among the rural population suffering from overt hypothyroidism of Bankura district, West Bengal. Subsequently, it was found that 67.9% participants suffering from overt hypothyroidism were found to have subnormal calcium level. Male preponderance (57.9% of all overt hypothyroid cases) was noted in hypocalcemia among hypothyroid persons. Serum calcium level was found to be in high significant negative correlation with TSH level (correlation coefficient= -0.626; Significance <0.001) and in high significant positive correlation with T4 level (correlation coefficient= 0.594; Significance <0.001). Low calcium might depress the activity of thyroid gland and produce hypothyroidism.*

Key Words: *Hypocalcemia, hypothyroidism, T4, TSH.*

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I. Introduction

Thyroid gland is an integral part of human endocrine system .The butterfly shaped gland consists of two lobes connected by an isthmus, situated in the anterior aspect of neck below the Adam's apple. The gland produces mainly two hormones, thyroxine (T4) and triiodothyronine (T3). These two hormones have prominent effects on different metabolic pathways, cellular development and differentiation. Thyroid gland is under direct control of the pituitary gland which is regarded as 'Master gland' of endocrine system. Pituitary gland liberates thyroid stimulating hormone (TSH) which induces the secretion of thyroid hormones from the thyroid gland. T4 and T3 have negative feedback action over adenohypophysis, which down regulate the liberation of TSH. Thyrotropin releasing hormone (TRH), secreted from hypothalamus, enhances the secretion of TSH from adenohypophysis. Primary hypothyroidism results due to diminished activity of thyroid gland that results in decreased production of T4 and T3 and Secondary hypothyroidism is due to certain pathology in hypothalamo-pitutary-thyroid axis or receptor abnormality or defect in signal transduction mechanism of the hormones. Hypothyroidism is one of the most common endocrinopathy in India (prevalence ~11%).[1] Overt hypothyroidism is defined as TSH level >10 mIU/L, and serum T4 level is subnormal/ normal. Subclinical hypothyroidism is defined as TSH level 5.5 -10 mIU/L and T4 within normal range. Calcium is a very important electrolyte in our body conducting various cellular functions. The reference level of total serum calcium is very narrow, 9-11 mg/dL. Hypothyroidism is a well known cause of cellular metabolic disturbances and also impairs the electrolyte balance which may produce disastrous effect on body. Keeping this in mind we had aimed a study to find out the relationship between thyroid profiles and calcium level in serum in a population belonged to the rural area of Bankura district, West Bengal, India.

II. Materials And Methods

A descriptive, cross-sectional, tertiary care hospital based study was conducted in Bankura Sammilani Medical College and Hospital, Bankura over a period of six months (from October, 2017 to March, 2018) among 120 participants, out of which 60 patients were suffering from overt hypothyroidism taken as cases and rest 60 participants were taken as age and sex matched controls, without any obvious disease. All participants belonged to the rural area of Bankura district. They were selected from Medicine out-patient department by systematic random sampling. After getting Ethical clearance from the Institutional Ethics committee a predesigned, pretested questionnaire was framed for each agreed participants for history taking, giving information and taking written consent. Five mL blood was collected with aseptic precautions in properly labeled plain vial and stored as per standard laboratory protocol. Clotted blood samples were centrifuged at 3000 rpm for 10 minutes to obtain serum.

Thyroid function like serum thyroid stimulating hormone (TSH) was assayed by sandwich enzyme-linked immunosorbent assay (ELISA) and serum total tetra-iodothyronine (T4) was assayed by competitive ELISA method. Serum calcium (Ca^{++}) was measured by colorimetric o-Cresolphthalein complexone (oCPC) method using 570 nm filter by semi-automatic chemistry analyzer at the department of Biochemistry, B.S.Medical College, Bankura.

Inclusion Criteria: Patients who were voluntarily agreed to take part in the study and having history of adequate exposure to the sun during last 1 year.

Exclusion Criteria:

i. Critically ill and moribund patients.
ii. Patients suffering from malignancy.
iii. Patient on treatment for any thyroid disease.
iv. Pregnant, lactating and postmenopausal women.
v. Patient having inadequate sun exposure.
vi. Patient extra of vitamin D or Calcium as supplementations duration during last one year.
vii. Patient was on any therapy that might change thyroid, liver or kidney function or produce vitamin or electrolyte imbalance.

After obtaining the data, those were compiled in MS excel sheet and codified accordingly. Statistical calculations were done by suitable statistical methods like central tendencies, correlation, cross-tabulations and chi-square tests etc. by appropriate software package (SPSS ver.20). Shapiro-Wilk tests were done to know the normality distribution of the parameters and it was found that all parameters were skewed and hence, non-parametric tests were mandate for statistical analyses.

III. Results

Total no of participants were 120, out of which 60 were cases and 60 were age and sex matched controls. In cases, Male: Female ratio was 34: 26= 1.308: 1; whereas in controls Male: Female= 30: 30= 1: 1.

Table-1: Distributive statistics of different parameters of cases and controls

Attributes	**Cases Age**	**Control Age**	**Cases T4**	**Control T4**	**Cases TSH**	**Control TSH**	**Cases Ca^{++}**	**Control Ca^{++}**
Mean	42.630	40.500	5.047	7.578	12.074	2.272	7.332	9.890
Standard Deviation	18.755	16.584	1.047	1.049	2.753	1.287	1.091	1.070
Standard Error of Mean	2.421	2.141	0.135	0.135	0.355	0.166	0.141	0.138
Median	40.500	44.000	4.780	7.610	11.605	1.925	7.275	9.965
Significance of difference between cases and controls: *p* value	**--**		**0.005**		**0.020**		**<0.001**	

Significant increase was noted in TSH of cases and significant reduction was noted in serum T4 and calcium (Ca^{++}) in cases with respect to controls.

Table-2: Cross-tabulation between Calcium groups and Thyroid parameters (TSH and T4)

Calcium groups (mg/dL)		TSH groups (mIU/L)		T4 groups (µg/dL)	
		5.5-10	≥10	<4.5	4.5-11
<9	Count	18	38	22	34
	% within Calcium group	32.1%	**67.9%**	39.3%	60.7%
9-11	Count	2	2	2	2
	% within Calcium group	50.0%	50.0%	50.0%	50.0%

Table-2 showed that hypocalcemia was found to be more in hypothyroidism (TSH ≥10 mIU/L).

Table-3: Correlation table of different parameters in all participants (N=120)

Spearman's Correlations		T4 (µg/dL)	TSH (mIU/L)
Ca^{++} (mg/dL)	Correlation Coefficient	0.594	-0.626
	Significance (2-tailed)	**<0.001**	**<0.001**

In all participants (Cases+Controls), serum calcium showed a highly significant negative correlation with serum TSH and highly significant positive correlation with serum T4. TSH level was found to be significantly and negatively correlated with T4 (correlation coefficient= -0.715; significance= **<0.001**).

IV. Discussions

In the present study, it was obvious from the results that hypocalcemia was significantly associated with hypothyroidism. In a previous study, serum calcium was found to be decreased significantly in participants with high TSH level in comparison to normal TSH.[2] It was also shown that low calcium can decrease the activity of the thyroid and its iodine absorption which might lead to insufficient production of thyroid hormones.[2] But this finding was contradicted by a research from the Endocrine Journal which showed that hypothyroidism was not associated with disturbed metabolism of calcium.[3] Scientists also discovered that hypothyroidism was associated with some changes in ionized calcium but not total calcium and represents a simple negative feed-back loop.[4] By the calcium sensing receptor (CaSR) parathyroid cells detect change in blood ionized calcium concentration and modulate parathyroid hormone (PTH) secretion to maintain serum calcium levels within physiological range.[4] Thyroid hormone could potentiate the osteoclastic effects of PTH and exacerbate hypercalcemia, which then led to a relative suppression of PTH secretion by the abnormal parathyroid tissue.[5] Rise in calcium concentration is caused principally by two eff ects: PTH stimulates bone resorption releasing calcium and decreases the excretion of calcium by the kidneys.[6] Renal calcium excretion is increased in hypothyroidism.[4,7]

V. Conclusion

Hypothyroidism had a significant increased risk of developing hypocalcemia. Hence, Calcium estimation might be a good practice to give the supplementation in proper time to avoid complications due to subnormal calcium level, related to hypothyroidism. Further extensive study with more number of sample size will provide causal relationship and better result on this aspect.

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