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Original Article

A study of serum calcium, phosphorous and magnesium level in hypothyroid cases

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ABSTRACT

Background: Hypothyroidism is an endocrine disorder occurred either due to its impaired activity or hormonal deficiency. Trace elements are required as a cofactor for many enzymes in various metabolic pathways which are regulated by thyroid hormone. Hence, thyroid disorders are linked with disturbances in various metabolisms. So, the purpose of this study is to evaluate whether serum calcium, magnesium, and phosphorus level are deranged or not in hypothyroid cases.

Materials and Methods: A prospective study was carried out in a total of 112 cases of hypothyroid and euthyroid subjects aged 20-50 years involving both male and female individuals. Thyroid function test, serum calcium, phosphorous and magnesium activities were measured in both the study population.

Results: Serum calcium was significantly lower while serum phosphorous and magnesium levels were significantly higher in hypothyroidism ($p<0.001$). There was a significant negative correlation between Thyroid Stimulating Hormone (TSH) and calcium (r-value -0.282, p0.035) while, there was a significant positive correlation between TSH and serum phosphorous and magnesium (r-value 0.593, $p<0.001$) and (r-value 0.513, $p<0.001$) respectively.

Conclusions: Our study, suggests that there was a significant change in the levels of serum calcium, phosphorous, and magnesium in thyroid dysfunction. Assessing the level of serum calcium and phosphorous can be fairly used as an index of bone resorption. So, preventive measures like supplementation of minerals can be initiated early in those who are at risk of rapid bone loss and to prevent osteoporotic fractures.

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INTRODUCTION

Hypothyroidism is a chronic disease or a common pathological condition that is associated with a deficiency in the thyroid hormones, thyroxine (T4), and triiodothyronine (T3).[1,2] However, it may lead to many metabolic processes slowing down causing many clinical, psychological, and biochemical alterations.[3] Thyroid hormones play a vital role in metabolic and physiologic homeostasis and regulate cardiac output, heart rate, basal metabolic rate, effects of catecholamines, brain and endometrium development as well as catabolism of proteins and carbohydrates.[4,5] The consequences of untreated or inadequately treated

hypothyroidism leads to infertility, cardiovascular disease, and the disorders related to neurological and musculoskeletal symptoms[6, 7]

The divalent ions like calcium, phosphate, and magnesium, are required for many enzymes as a cofactor in various metabolic pathways which are directly or indirectly regulated by thyroid hormones. It has been implicated in disturbances of mineral metabolism influencing bone turnover leading to osteoporosis and has also been related to metabolic syndrome and cardiovascular diseases.[8,9] Magnesium has a role in influencing membrane permeability thereby secretion of thyroid hormones. Thyroid hormones also in turn affect its metabolism and clearance. Serum levels of calcium and magnesium are altered in thyroid disorders and this alteration may be vital for the patients in the long run.10 Therefore, this study is undertaken to evaluate whether there occurs any alteration in the status of minerals or not in diagnosed cases of hypothyroidism.

MATERIALS AND METHODS

The present prospective study was carried out from June 2021 to October 2021 at the medicine in an outpatient department where 56 diagnosed cases of hypothyroid and 56 euthyroid as control ranging from 20-50 years of both sexes were included using a consecutive sampling technique. Thyroid function tests, such as free Tri-iodothyronine (fT3), free thyroxin (fT4), Thyroid-stimulating hormone (TSH), serum calcium, phosphorous, and magnesium level were estimated on the blood sample.

Ethical clearance approval was obtained from the institutional review committee (IRC), reference (0504202105), and written consent was taken from the patients who wish to participate in this study. The blood sample was collected from all the participants by venipuncture from a cubital vein and the sample was collected in a vial under aseptic conditions for biochemical analysis. Thyroid function test was done by Chemiluminescent Immunoassay (CLIA) methods and serum calcium, and phosphorous were estimated by Selectra Pro S auto analyzer using Elitech reagents and serum magnesium level was analyzed by semi autoanalyzer. Values of fT3=1.21-4.18 pg/ml, fT4=8.90-17.20 pg/ml, TSH=0.30-4.50µIU/ml, Serum calcium=8-11mg/dl Phosphorous=2.5-4.5mg/dl and Magnesium=1.6-2.5mg/dl level were the normal reference range for biochemical parameter. Patients suffering from renal diseases, hepatic diseases, pituitary adenomas, bone diseases, diabetes mellitus, alcoholism, other serious medical conditions, and patients on mineral supplementation or any drugs that will affect mineral metabolism were excluded from the study.

The sample size was calculated as follows:

The sample size was determined from the study conducted by Al-Hakeim. 9 Sample size was calculated using the following information.

$$n = \frac{z^2_{1-\alpha/2} XSD^2}{d^2}$$

Z= statistic for a level of confidence. (For the level of confidence of 95%, which is conventional, the Z value is 1.96).

SD= standard deviation of variables

d= absolute error or precision. (d is considered 0.05)

SD of serum total magnesium is 0.19 which is the average number of S.D among all parameters such as total calcium, ionized calcium, and ionized magnesium in the article by Al-Hakeim et al. Thus keeping in consideration not taking higher or lower values, we had taken average value for SD to calculate sample size

So, putting these values

n= 1.962 X 0.192/0.052
= 3.84X0.0361/0.0025
= 0.138624/0.0025
= 55.47

For this study 56 cases diagnosed with hypothyroidism and 56 control samples from the normal euthyroid population will be taken.

Statistical analysis was done by SPSS (Statistical package for social science) version 15. Student t-test was used to compare the means between different groups.

RESULTS

This study included 56 diagnosed hypothyroid cases and the same number of euthyroid control with the mean age of (male= 37.71 and female= 34.47) and (male= 38.95 and female= 34.61) respectively. Out of which 25% of males and 75% of females were enrolled as cases and 36% of males and 64% of females were included under control. Among which 24% of patients had a history of muscle pain and 21% gave a history of weight gain while 16% had a tingling sensation case while 20% had muscle pain, 11% had a tingling sensation in the control group which is as depicted in table 1.

Serum calcium level was significantly lowered in Subclinical hypothyroidism when compared with control p=<0.01. While serum phosphorous and magnesium level was raised significantly when compared with control at p=<0.001 and p=0.001 respectively as shown in table 2. Furthermore, serum calcium level was significantly decreased in hypothyroidism when compared with control at p=<0.001. Whereas serum phosphorous and magnesium

Table 1: Demographic profile of the patients

		Case (56)		Control (56)	
Age (mean SD)	Male	37.71±8.42		38.95±7.80	
		34.47±7.95		34.61±7.83	
Sex	Male	14 (25%)		20 (36%)	
	Female	42 (75%)		36 (64%)	
Clinical history presented by patients		Yes	No	Yes	No
Constipation		3(5%)	53 (95%)	2(4%)	54(96%)
Tingling sensation		9 (16%)	47(84%)	6 (11%)	50 (89%)
Muscle Pain		24 (43%)	32 (57%)	11(20%)	45 (80%)
Weight Gain		**12 (21%)**	**44 (79%)**	**5(9%)**	**51 (91%)**

Table 2: Stastical analysis of data of various biochemical parameters in Subclinical Hypothyroidism and control

Parameter	Diagnosis	Number of patients	Mean ± SD	P-value
fT3	SCH	28	2.93±0.40	0.345
	Control	56	2.84±0.38	
fT4	SCH	28	9.57±1.96	0.021
	Control	56	10.45±1.39	
TSH	SCH	28	9.89±4.41	<0.001
	Control	56	2.45±1.16	
Calcium	SCH	28	8.30±0.17	<0.001
	Control	56	8.93±0.46	
Phosphorous	SCH	28	3.73±0.30	<0.001
	Control	56	3.19±0.43	
Magnesium	SCH	28	1.82±0.10	0.001
	Control	56	1.73±0.10	

Table 3: Stastical analysis of data of various biochemical parameters

Parameter	Diagnosis	Number of patients	Mean ± SD	P-value
fT3	Hypothyroidism	28	2.00±0.85	<0.001
	Control	56	2.84±0.38	
fT4	Hypothyroidism	28	5.32±2.83	<0.001
	Control	56	10.45±1.39	
TSH	Hypothyroidism	28	84.06±28.75	<0.001
	Control	56	2.45±1.16	
Calcium	Hypothyroidism	28	8.04±0.56	<0.001
	Control	56	8.93±0.46	
Phosphorous	Hypothyroidism	28	4.08±0.40	<0.001
	Control	56	3.19±0.43	
Magnesium	Hypothyroidism	28	1.91±0.15	<0.001
	Control	56	1.73±0.10	

levels were raised significantly in the hypothyroid patent when compared with control as p=<0.001 as shown in table 3.

This study found a negative correlation of serum calcium with TSH (r value= -0.282, p =0.035) but the serum phosphorous and magnesium showed a positive correlation with TSH (r value= 0.593 and 0.513, respectively p=<0.001) which is depicted in table 4.

DISCUSSION

In the present study, 56 normal euthyroid and the same number of diagnosed cases of hypothyroid were included. The thyroid gland produces a vital hormone, which plays a major role in the metabolism, growth, and development of the human body. Various body functions are regulated by their constant release in the bloodstream.[11] Hypothyroidism is the most prevalent endocrine disease that can lead to a

Table 4: Correlation of serum calcium, phosphorus, and magnesium with serum TSH

Parameter	Correlation coefficient (r-value)	p-value
TSH v/s Calcium	-0.282	0.035
TSH v/s Phosphorous	0.593	<0.001
TSH v/s Magnesium	0.513	<0.001

variety of clinical situations like congestive heart failure, electrolyte and mineral disturbances, osteoporosis, and coma.[12,13] Due to hypothyroidism there is an influence on renal hemodynamics, as well as glomerular filtration.[14]

In our study, among the hypothyroidism cases, serum calcium level was found to be decreased significantly which was negatively correlated with TSH (r-value -0.282, p0.035). These findings are in agreement with the study done by Murgod R et al.[15], Bharti A et al.[16], Sridevi D et al.[17], Saxena S et al.3, and Athkpham D et al.18 Serum calcium level was significantly decreased in SCH cases when compared with control as 8.30±0.17 and 8.93±0.46 respectively (p<0.001). A similar type of findings was also reported in a study conducted by Shivallela et al.[19] and Bharti A et al.[16] Thyroid hormones have shown a vital role in skeletal growth and maturation and Thyroid-stimulating hormone (TSH) also acts as a direct regulator of bone remodeling.[3] The release of thyroid hormones determines the mineral pool in the blood by influencing their mobilization into the blood and also affects their clearance through glomerular filtration rate. There is increased renal blood flow leading to increased clearance of calcium as well as decreased extracellular release of calcium in hypothyroidism.20 Depressed turnover due to impaired mobilization of calcium into the bone was observed in hypothyroidism leading to reduced blood calcium.[17] The study conducted by Murgod R et al.[15] reported that thyroxin normally regulates blood calcium levels by releasing calcium from cells. Therefore, in hypothyroidism, decreased T4 enters the cells which in turn release less calcium. Additionally, increased renal calcium excretion was obtained in rats with high TSH levels.[21] A study conducted by Bouillon R et al.[22] observed that the sensitivity of bone and kidney to Parathormone (PTH) decreases in hypothyroidism which further leads to hypocalcemia. Due to this, hypocalcemia may cause neuromuscular irritability including perioral paraesthesia, tingling of toes & fingers, and spontaneous or latent tetany.[19]

In the present study, the serum phosphorous levels were markedly increased in cases of hypothyroidism when compared to healthy euthyroid controls at 4.08±0.40 and 3.19±0.43 respectively, likewise, the level of phosphorous was also increased in SCH when compared with control as 3.73±0.30 and 3.19±0.43 respectively (p value<0.001). A significant positive correlation between TSH and a serum phosphorous level was observed in this study (r-value 0.593, p<0.001) which is in accordance with the study conducted by Schwarz C et al[23], Gohel MG et al.[24], Sridevi D et al.[17] Whereas, a contradict finding was reported by Gammage MD et al.[25] where serum phosphorous level was decreased in hypothyroidism. It could be due to increased production of calcitonin which favours the tubular excretion of calcium and promotes the tubular reabsorption of phosphate from the kidney leading to hypocalcemia and hyperphosphatemia due to compensatory effect of calcitonin and PTH.3, 20 Serum T3 which is the active form of thyroid hormone is required for the stimulation of phosphorus reabsorption from renal tubules mediated through Na/P co-transporters, therefore hyperphosphataemia is due to T3 mediated action on kidneys tubules. They also propose thyroid hormones as long term regulators for phosphate metabolism.[18]

In our study serum, magnesium was significantly increased in the hypothyroid case when compared with control as follows 1.91±0.15 and 1.73±0.10 (p=<0.001) respectively. Similarly, serum magnesium level in SCH when compared with control was also significantly increased which is as follows 1.82±0.10 and 1.73±0.10 (p=0.001) respectively. There was a significant positive correlation with TSH observed (r-value 0.513, p<0.001). A similar type of findings was also reported by Saxena S et al.[3] and Bharti A et al.[16] In a study conducted by McCaffrey et al.[12] observed that thyroid hormone affects the glomerular filtration rate, blood flow and tubular sodium transport. It has a direct effect on renal tubules for retention of sodium and magnesium; where magnesium retention is increased by 15-30% from kidneys due to increased reabsorption in renal tubules.

We were unable to estimate serum vitamin D3, serum anti-thyroperoxidase antibody, serum parathyroid hormone concentration which would help to avoid some confounding factors, as well as the study could be extended by measuring serum ionized calcium levels instead of total calcium levels and could be correlated with duration and severity of thyroid disorders for better understanding the biochemical basis of mineral metabolism and associated disorders.

CONCLUSIONS

Hypothyroidism is an endocrine disease that is associated with impaired metabolism of minerals, bone complications, and other clinical manifestations. Impaired metabolism, may lead to a contributory role in the progression of thyroid disease and later development of complications. So, regular monitoring or evaluation of thyroid function activity and mineral status provides a great advantage in assessing the level of progression in thyroid dysfunction. The serum calcium, phosphorous, and magnesium activity were found to be significantly deranged in hypothyroid cases. Assessing the level of serum calcium and phosphorous can be fairly used as an index of bone resorption. So, regular monitoring may be helpful for the better management of the disease and to prevent further complications associated with it. If necessary, preventive measures like supplementation of minerals or hormone replacement therapy can be initiated

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early in those who are at risk for rapid bone loss and to prevent osteoporotic fracture.

Conflict of interest: None

REFERENCES

1. Chiovato L, Magri F, Carle A. Hypothyroidism in Context: Where We've Been and Where We're Going. Adv Ther. 2019 Sep;36(Suppl 2):47-58. Crossref
2. Visser TJ. Pathways of thyroid hormone metabolism. Acta Med Austriaca. 1996;23(1-2):10-6. PMID: 8767510
3. Saxena S, Srivastava PR, Katyal R, Das B, Pannu SJ. Evaluation of mineral status in hypothyroidism in a tertiary care centre. Int J Res Med Sci. 2020;8(2):667-71. Crossref
4. Mohamedali M, Reddy MS, Vyas A, Iyer V, Cheriyath P. Thyroid disorders and chronic kidney disease. Int J Nephrol. 2014;2014:520281. Crossref
5. Kinsella J, Sacktor B. Thyroid hormones increase Na+-H+ exchange activity in renal brush border membranes. Proc Natl Acad Sci U S A. 1985 Jun;82(11):3606-10. Crossref
6. Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet. 2017 Sep 23;390(10101):1550-62. Crossref
7. Gaitonde DY, Rowley KD, Sweeney LB. Hypothyroidism: an update. Am Fam Physician. 2012 Aug 1;86(3):244-51. PMID: 22962987
8. Huerta MG, Roemmich JN, Kington ML, Bovbjerg VE, Weltman AL, Holmes VF, et al. Magnesium deficiency is associated with insulin resistance in obese children. Diabetes Care. 2005 May;28(5):1175-81. Crossref
9. Al-Hakeim HK. Serum levels of lipids, calcium and magnesium in women with hypothyroidism and cardiovascular diseases. J Lab Physicians. 2009 Jul;1(2):49-52. Crossref
10. Ford HC, Crooke MJ, Murphy CE. Disturbances of calcium and magnesium metabolism occur in most hyperthyroid patients. Clin Biochem. 1989 Oct;22(5):373-6. Crossref
11. Informedhealth.org. How does the thyroid gland work? Colonge, Germany: Institute for quality and efficiency in health care; 2018; Website
12. McCaffrey C, Quamme GA. Effects of thyroid status on renal calcium and magnesium handling. Canad J Compara Med. 1984;48(1):51. Website
13. Kargili A, Turgut FH, Karakurt F, Kasapoglu B, Kanbay M, Akcay A. A forgotten but important risk factor for severe hyponatremia: myxedema coma. Clinics (Sao Paulo). 2010;65(4):447-8. Crossref
14. Mariani LH, Berns JS. The renal manifestations of thyroid disease. J Am Soci Nephrol. 2012;23(1):22-6. Crossref
15. Murgod R, Soans G. Changes in Electrolyte and Lipid Profile In Hypothyroidism. International Journal of Life Science & Pharma Research. 2012;2(3):185-94.
16. Bharti A, Shrestha S, Rai R, Singh MK. Assessment of serum minerals and electrolytes in thyroid patients. International Journal of Advances in Scientific Research. 2015;1(6):259-63. Crossref
17. Sridevi D, Dambal AA, Sidrah, Challa AS, Padaki SK. A Study of Serum Magnesium, Calcium and Phosphorus in Hypothyroidism. International Journal of Clinical Biochemistry and Research. 2016;3(2):236-9. Crossref
18. Aathokpham D, Mmohanty S, Ppinnelli VB. Status of Serum Calcium, Phosphorus, Magnesium and Copper in Hypothyroid Patients- A Case Control Study. Journal of Clinical and Diagnostic Research. 2020;14(10):5-8. Crossref
19. Shivallela MB, Poornima RT, Jayaprakash MDS. Serum calcium and phosphorous levels in thyroid dysfunction. Indian journal of fundamental and applied life science. 2012;2(2):179-83.
20. Suneel B, Nagendra DR, Aparna RR, Balakrishna D, Naidu JN. Mineral status in thyroid disorders (hypo & hyper). International Journal of Applied Biology and Pharmaceutical Technology. 2011;2(4):423-29.
21. Kumar V, Prasad R. Molecular basis of renal handling of calcium in response to thyroid hormone status of rat. Biochim Biophys Acta. 2002;1586(3):331-43. Crossref
22. Bouillon R, De moor P. Parathyroid Function in Patients with Hyper- or Hypothyroidism. The Journal of Clinical Endocrinology & Metabolism. 1974;38(6). Crossref
23. Schwarz C, Leichtle AB, Arampatzis S, Fiedler GM, Zimmermann H, K.. EA, et al. Thyroid function and serum electrolytes: does an association really exist? Swiss Med Wkly. 2012;142:01-7. Crossref
24. Gohel MG, Shah AM, Shah AM, Makadia JS. A study of serum calcium, magnesium and phosphorus levels in hypothyroidism patinets. Int J Med Health Sci. 2014;3:308-12.
25. Gammage MD, Parle JV, Holder RL, Roberts LM, Hobbs FD, Wilson S. Association between serum free thyroxine concentration and atrial fibrillation. Arch Intern Med. 2007;167(9):928-34. Crossref