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RESEARCH ARTICLE

A STUDY OF THE LEVELS OF SERUM MAGNESIUM AND SERUM ZINC IN PATIENTS OF SUBCLINICAL HYPOTHYROIDISM

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Abstract

Background: Subclinical Hypothyroidism (SCH), according to the endocrine web is defined as an elevationin in Thyroid Stimulating Hormone (TSH) level (4.6-10 m I U/L) with thyroid hormone levels in the normal range. Magnesium (Mg2+) is an essential macro-mineral in human body, which acts as a cofactor for more than 300 enzymes. Zinc (Zn^{+2}) is required for proper functioning of 5'-deiodinase & it is a cofactor for Thyrotropin -Releasing Hormone (TRH). Transcription factorsbind to thyroid hormones which are fundamental for modulation expression of gene, also contain Zn^{2+} bound to cysteine residues.

Aim and objectives: This study aim to estimate the levels of serum magnesium and zinc in patients of SCH.

Material and methods: The serum TSH, Total Triiodothyronine (T3)& Thyroxine (T4) levels were estimated by ELISA method to identify the cases of SCH. The concentration of serum magnesium was analyzed using semiautomated analyzerbyspectrophotometry. Serum zinc was analyzed by fully automated analyzer (Vitros 5600) in patients of SCH**.**

Results: In SCH, both T3, T4 were within the normal range and TSH in the range of 4.6-10 m I U/L, there was a statistically significant ($p<0.001$) decrease in serum zinc levels and not significantly decrease in serum magnesium levels in subclinical hypothyroidism patients.

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Introduction:-

Disorders of endocrine glands is quite common in India [1]. Hypothalamus released TRHto stimulatethe release of TSH from anterior pituitary, which help in control of thyroid gland to produceT3, T4, MIT&DIT [2]. SCH according to the American Thyroid Association, is defined as an elevated TSH levels when T3, T4 are within normal range. SCH is more common in the elderly people than in those younger than 65 years of age [3]. According to the endocrine Web, SCH is defined as a TSH level of 4.6 to 10.0 m I U/L [4]. In the cases of full-blown hypothyroidism, the TSH level is 10 m I U /L or higher [5]. In general population SCH occurs in 3% to 8%. It is seen thatwomen have greater occurrenceof SCH[6]. Increase in prevalenceis observed with age. In SCH the most common implication is highprobability of progress to clinical hypothyroidism. The cardiovascular disease is an important subject debate risk factor of SCH [7].Mg2+ is an essential macro-mineral, required for300 or more enzymesas a cofactorto regulate a lot ofbiochemical processes in human body [8].Mg2+ is involved in energy-dependent reactions or ATP generation reactions. The role of Mg2+ in thyroid hormone synthesis could be indirect, by affecting the iodine uptake step. Mg2+ also influences the deiodination process in which the iodothyronine and iodotyrosine deiodinase enzymes require FMN as a coenzyme and Mg^{2+} help in the reduction process of FMN involving electron transport chain. Studiesin experimental animals releaved that free Mg^{2+} ions in the intercellular space are important as a second messenger in the activation of immune system. $Mg^{2+}$is related to the immune responsein human body and associated with cellular oxidative stress [9]. Zn^{2+} acts as "master of hormone" with numerousZn^{2+} metalloenzymes and transcription factors, particularly in relation to cell division and growth [10]. For thyroid hormone homeostasis, Zn^{2+} is required for conversion of T4 toT3 by activation of 5'-deiodinase [11]. Zn^{2+} is important for TRH in which it acts as a cofactor. Transcriptionfactors are essential for modulating of gene expression of thyroid hormone contain Zn^{2+} bound to cysteine residues [12]. Due to paucity of information regarding the serumMg^{2+} and serum Zn^{2+} levels in SCH cases, it becomes more relevant to carry out this study.

Materials And Methods:-

The study was conducted in the Department of Biochemistry, School of Medical Sciences and Research, Sharda University and the Department of Medicine, Sharda Hospital, Greater Noida, UP..The study was approved from Institutional Ethical Committee. This study was a cross sectional study which included 88 individuals with SCH.

Inclusion criteria:

Known cases of SCH (TSH value 4.6-10 mIU/ L, and T3, T4 in normal range) in age of more than 18 years.

Exclusion Criteria:

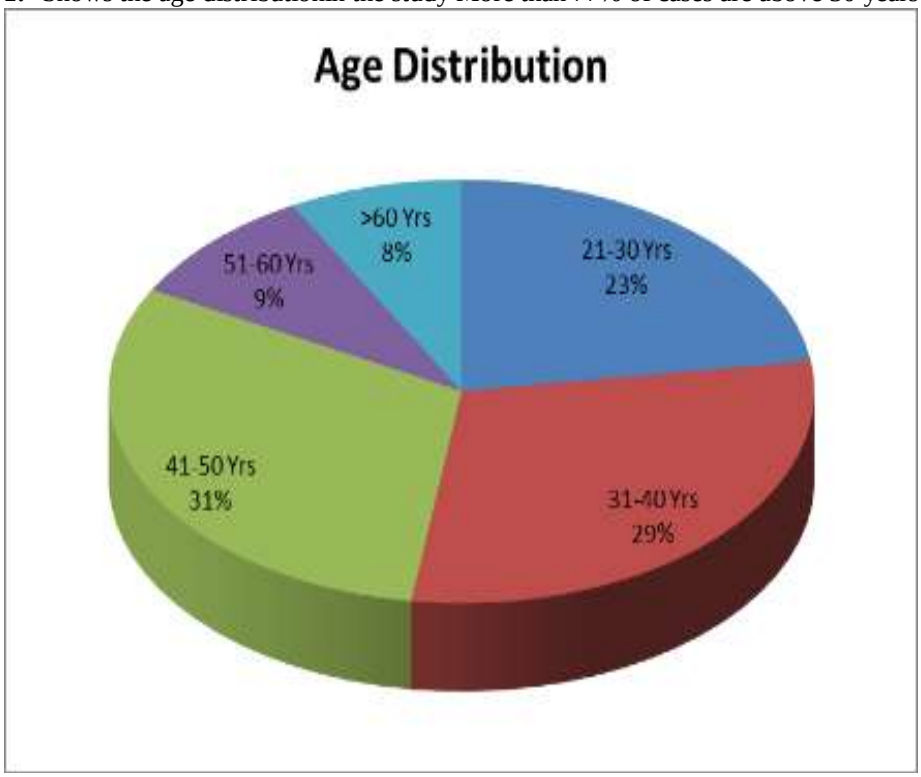
Patients of SCH below the age of 18 years, Pregnancy, known cases of other endocrine disorders ,Women on contraceptive pills, Patients with overt hypothyroidism-morbid conditions like Diabetes mellitus, heart diseases, high blood pressure (hypertension), psychiatric disorders or substance abuse etc.,Patients with malignancy on Chemotherapy /radiotherapy and Patients on medication (diuretics, proton pump inhibitors, amino glycoside antibiotics, amibidole and fluroquinolone antibiotics). The serum samples of patients suspected with hypothyroidism were collected and stored in -20 ^{0}C to be tested for TSH, T3, T4 by ELISA to diagnose the subclinical hypothyroidism patients. Serum zinc levels were measured by Vitros 5600.The obtained data was analyzed statistically.

Observation And Results:-

Serum T3, T4 and TSH measured to diagnose the group study. In SCH both T3, T4 with the normal range and TSH is between 4.6 – 10.0 mU/L.

Age distribution among the study group:

FIgure 1:- Shows the age distributionin the study More than 77% of cases are above 30 years of age.



Gender distribution among the study group:

Figure 2:- Depicts the gender distribution in the study group.

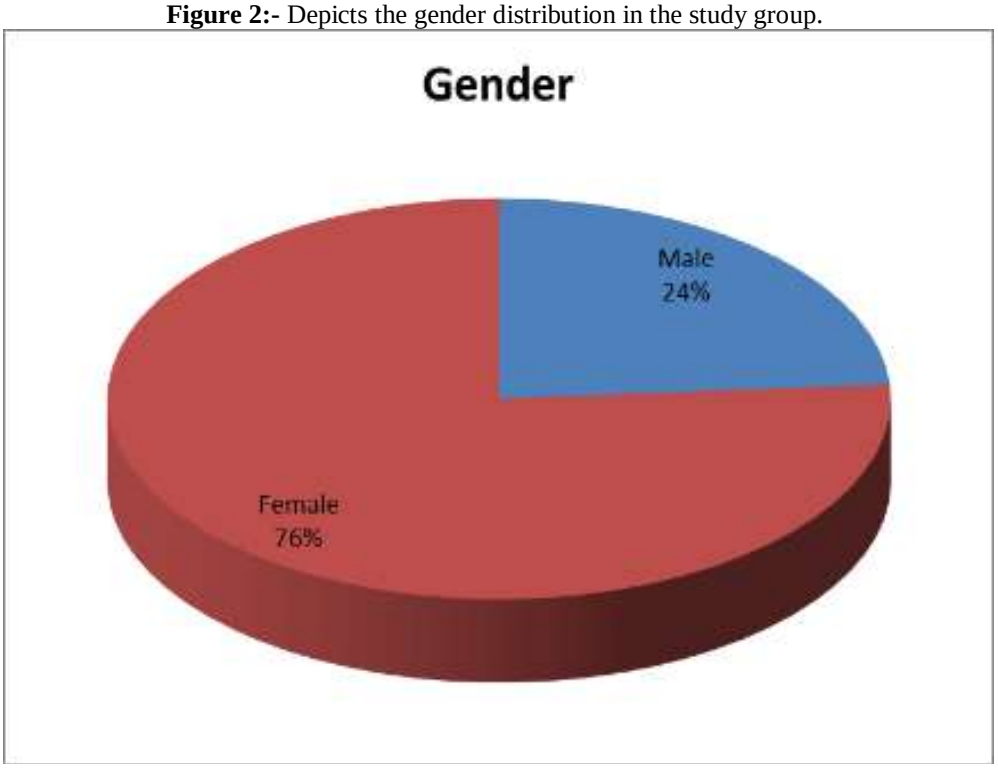


Table 1:- TSH in SCH.

One-Sample Statistics						
	N	Mean	Std. Deviation	Std. Error Mean		
TSH(m I U/l)	88	6.898	1.395	0.149		
One-Sample Test						
	Test Value = 4.5					
	t	Df	p-value	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
TSH(m I U/l)	13.431	87	<0.001	1.99784	1.7022	2.2935

Table 2:- Magnesium in serum of SCH.

T-Test						
One-Sample Statistics						
	N	Mean	Std. Deviation	Std. Error Mean		
Mg(mg/dl)	88	2.1773	0.53963	0.05752		
One-Sample Test						
	Test Value = 1.6					
	t	df	p-value	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Mg(mg/dl)	10.035	87	0.036	0.57727	0.4629	0.6916

Table 3:- Zinc in serum of SCH.

One-Sample Statistics						
	N	Mean	Std. Deviation	Std. Error Mean		
Zn(µg/dl)	88	35.5831	17.39297	1.85410		
One-Sample Test						
	Test Value = 70					
	t	df	p-value	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Zn(µg/dl)	-18.563	87	<0.001	-34.41693	-38.1021	-30.7317

Discussion:-

Hypothyroidism is a deficiency of thyroid hormone secretion and action. Both sexes are affected more frequently with increasing age and more women are suffering from hypothyroidism than men. Hypothyroidism is considered as a big health problem in India and worldwide [(1)]. SCH is considered as one type of hypothyroidism disease which occurs in the clinical setting with a serum TSH level between 4.5 to 10 m I U /L, despite T3, T4 within normal range. Progression to overt hypothyroidism is the most important implication due to SCH, cardiovascular risk factor may be the most likely possibility [(7)]. For normal thyroid hormone metabolism, mineralsand trace elements are required and their deficiencies may directly or indirectly affect their activity [(8)]. Low serum Mg^{2+} is the main clinical manifestation due to Mg^{2+}nutrition imbalance. In our study, serum Mg^{2+} normalrange is 1.6 -3.0 mg /dl, and the value less than 1.6 mg /dl is considered as low. In this study, serum levels of Mg^{2+} in early diagnosed SCH patients are not significantly affected. A previous study releaved that if oxidative phosphorylation in mitochondria is inhibited, this led to decrease intake of iodine by thyroid cells, because the uptake of iodine is achieved by sodium iodide co-transporter which is required for mitochondrial energy supply [(14)]. Mg^{2+} is very important for synthesis and production of ATP, and its deficiency can affectiodine uptake by thyroid cell and decrease the thyroid hormones. In a study conducted in Tianjin in China, showed that severely low serumMg^{2+}accompanied with increased risk of anti-thyroglobulin antibody in serum and hypothyroidism. Decreased in or abnormal activation of immune system might occur inlow serum Mg^{2+}. Inthe same study it is mentionedthat moderatelow serum Mg^{2+} is not associated with anti-thyroglobulin antibodylevels [(8)]. Therefore, in this study, we found that the level of serum Mg^{2+} is not significantly

affecting (p value = 0.338) in the early diagnosed SCH. Vitro experiments showed that mild to moderate magnesium deficiency may causeinflammatory response could be compensated by other factors oraggravated [15]. This indicated that the effect of Mg^{2+}deficiency is variable; therefore, different results may be obtainedby studies on different population. The results also can be different based on thedifference in definitions of low serum Mg^{2+} levels and different cut-off values. Zn^{2+} affects thyroid hormones at different levels, it can inhibit TRH synthesis and depress T3, T4. Zn^{2+} is also essential forformation of T3 in extrathyroidal tissues, by acting as a cofactor for 5'-deiodinase enzymes. It also plays a role in the binding of the receptors to DNA. InZn^{2+}defiecency alteration in thyroid gland function has been reported. Both, hypothyroidism causeZn^{2+} deficiency and Zn^{2+}deficiency cause hypothyroidism [1]. In this study, we found significantly decrease in the levels of serum Zn^{2+} in SCH patients when compared with cut-off value of 70 µg/dl. According to study conducted in South Asia Population including India, it showed the cut-off value of zinc as 70 µg/dl [16]. The mechanism which may cause decrease in the level of serum Zn^{2+}in patients with hypothyroidism is severe impairment in the gastrointestinal absorption of Zn^{2+}. Variation in the concentrations of iodine, selenium and $Zn^{2+}$is significantly influenced by TSH level inthyroid tissue. Also, the tubular excretion of Zn^{2+} leads to decreased serum Zn^{2+}level [1].

Conclusion:-

It is concluded that serum Zn^{2+}levels were decreased inSCH patients, which indicates abnormal metabolism of Zn^{2+} thosepatients. This may exaggerate the progression to clinical hypothyroidism and possibility as a risk for cardiovascular disease. Hence, diet rich in trace elements should be given to the SCH patients to maintain the normal function of thyroid hormone. Larger well -designed studies are required to explicate the effects of minerals and trace elements on SCH limits.

Limitations of study:-

1. Limitation of this study to specific area requires several longitudinal studies in larger geographical area for more reliable results.
2. Using only T3, T4, TSH to diagnose subclinical hypothyroidism, it would be worthwhile to estimate f T3, f T4 also.

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3. Data analysis and plagiarism check university software: Dr. Rajesh Kumar Thakur.
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5. Data acquisition:Dr. V.P.S Punia.
6. Data review; Dr. B.C. Kabi

Conflict Of Interest:-

The authors declare that there is no conflict of interest.

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