Original Article

TSH level in various age groups of pregnancy and its relation with serum magnesium concentration

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ABSTRACT

Background: Alteration of thyroid hormone profile is common in pregnancy. Very few studies have been done on the level of Thyroid Stimulating Hormone in different age group of pregnancy and its association with serum magnesium, especially at this geographical location. Thyroid hormones are one of the key factors for regulation of metabolism which has immense importance for fetal growth. Many factors interplay to regulate synthesis and secretion of them and maintain Thyroid Stimulating Hormone level thereby. Magnesium is an important factor in such regulation. It acts as a cofactor of ATPase and along with selenium also activates deiodenase. Both of these are required for thyroid hormone synthesis. Hence there might be a relation between serum TSH and magnesium.

Method: 90 pregnant study participants in their first trimester of gestation were distributed equally in three groups depending on their age distribution of pregnancy. The groups were Group A (upto 20 years), Group B (> 20 years to 30 years), Group C (> 30 years to 40 years) with 30 participants in each group. Serum TSH and magnesium were measure in 12 hours fasting venous blood sample.

Result: No significant difference in mean Thyroid Stimulating Hormone and magnesium were found in three age groups ($p=0.29$). But when all participants were taken together serum Thyroid Stimulating Hormone and magnesium showed a significant negative correlation ($r=-0.44$, $p<0.05$)

Conclusion: Serum Thyroid Stimulating Hormone does not alter significantly with increase age group of pregnancy. Serum Thyroid Stimulating Hormone level increases with decrease of serum magnesium.

Keywords: ATPase, deiodenase, magnesium, Thyroid Stimulating Hormone

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Introduction

Altered thyroid profile is quite common among pregnant women and pregnant mothers frequently suffer from subclinical hypothyroidism.[1] In fact, hypothyroidism has been described as the most common thyroid disorder in pregnancy.[2] Hypothyroidism is one of the common causes of spontaneous early and recurrent abortion.[3] Hypothyroidism may interfere with the fetal psychomotor development which significantly increases socio-economic burden. It is also associated with several other possible poor outcomes including labor abnormalities, fetal distress. This may further extend to postpartum complications including postpartum hemorrhage, thyroiditis and depression.[4] These factors indicate the utmost importance of thyroid profile assessment in pregnancy.

A number of physiological changes take place during pregnancy including thyroid and its secretions. The endocrine gland itself increases in size by about 10% and the hormone secretions increase by nearly 50%.[5] There is also significant increase in iodine requirement as well.[6] Nodular diseases of thyroid have also been reported in pregnancy.[7] In pregnancy thyroid hormones secretion is also influenced by several other factors of which human chorionic gonadotropin (hCG) and estrogen are most notable. While hCG has a stimulatory effect on the thyroid gland with consequent increased levels of triiodothyronine (T3) and tetraiodothyroinine (T4) but estrogen has inhibitory effect on the gland by inhibiting thyroid stimulating hormone (TSH) level. Thus reference ranges of TSH, T3 and T4 also differ in pregnancy from a non-pregnant adult individual. In so far as TSH is concerned accepted guidelines by American Thyroid Association and Endocrine Society clinical practice guideline both suggest TSH cutoffs 0 .1 to 2.5 mIU/L in first trimester, 0.2 to 3.0 mIU/L in second trimester and 0.3 to 3 mIU/L in third trimester.[8,9] Though other recommendations are also there but the same cut off values have been supported by 2014 National guidelines, Maternal Health division, Ministry of Health and Family Welfare, Govt. of India and also by The Federation of Obstetric and Gynaecological Societies of India (FOGSI).

Magnesium (Mg) a divalent trace element is the fourth most abundant cation in the body and second most common intracellular cation serving wide range of cellular functions. It is also the cofactor for more than 300 enzymes[10] including ATPase.[11] These enzymes are essential for iodination and deiodination for synthesis of T3 and T4. Thus it is evident that Mg has important roles in synthesis and further actions of thyroid hormones. Earlier studies have concluded with a direct correlation between degree of hypothyroidism and hypomagnesemia[12,13,14] but there are also studies with inconclusive or even contradictory results.[15,16,17,18]

Materials and Methods

The present hospital based, descriptive, cross sectional study was undertaken at the Department of Biochemistry, College of Medicine and JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal. Thirty (30) pregnant participants in each group namely Group A (upto 20 years), Group B (> 20 years to 30 years), Group C (> 30 years to 40 years) in their first trimester were selected randomly for the study. Pregnant with hypothyroidism, history of smoking, alcoholism, or receiving treatment for any other chronic illness were excluded.

The study was aimed to find out

1. The difference in serum TSH level during first trimester of pregnancy from different age group, if any.
2. The relation between serum TSH and serum Mg, if any.

After obtaining approval from Institutional Ethics Committee (Ref. No. F-24/PR/COMJNMH/IEC/20/333) and written consent from the study participants, only the first trimester pregnant women who fulfilled the inclusion criteria were considered for the study. 90 study participants were distributed equally in three groups depending on their age at the time of pregnancy. The groups were Group A (upto 20 years), Group B (> 20 years to 30 years), Group C (> 30 years to 40 years) with 30 participants in each group.

After 12 hrs. of fasting, 5 ml venous blood was collected from each of them. Samples were collected in vials without any preservative or anticoagulant and subjected to centrifugation. Isolated serum was used for assessment of TSH, and serum Mg. When analysis could not be done immediately, the separated serum was preserved in capped vials at 4°C in a freezer.

Biochemical analysis of serum TSH was done by Immuno-enzymometric assay (solid phase enzyme-linked immunosorbent assay) using 96 well microplate assay kits from Monobind Inc., California, USA and absorbance was measured by TECAN'S Magellan universal reader (Sunrise) at 450 nm.

Quantitative estimation of serum Mg was done by Calmagite Dye Method[19] and the absorbance of the supernatant was measured at 510 nm using UV-VIS Spectrophotometer 117 (Spectronics).

Results

TSH and serum Mg were measured and results are expressed in Mean ± Standard Error (SE) using SPSS statistical software version 20.

When all participants were considered together, serum TSH and Mg levels were found to be 1.71±0.05 μIU/L and 1.93±0.03 mg/dL respectively (Table 1). TSH was found 1.9±0.08 μIU/L, 1.62±0.08 μIU/L and 1.6±0.1 μIU/L in group A, B and C respectively. Whereas the corresponding figures in serum Mg levelwas found to be Serum Mg was found 1.9±0.05 mg/dL, 1.94±0.04 mg/dL and 1.91±0.06 mg/dL in group A, B and C respectively (Table 1, Figure 1).

Turkey HSD Test was performed among Group A, B and C for analysis of variance and in that no significant difference in mean TSH was observed ($p=0.29$).

However, when Pearson's correlation was performed between serum TSH and serum Mg, it showed a significant negative correlation ($r= - 0.44, p<0.05$) (Figure 2).

Discussion

During pregnancy several hormonal and metabolic changes take place which are

Table 1: Serum TSH (μIH/L) and Serum Magnesium (mg/dL) levels in Group A, B, C and total participants

Parameters	Total (n=90)	Group A (n=30)	Group B (n=30)	Group B (n=30)
Serum TSH (μIU/L) Mean±SE	1.71±0.05	1.9±0.08	1.62±0.08	1.6±0.1
Serum Magnesium (mg/dL) Mean±SE	1.93±0.03	1.9±0.05	1.94±0.04	1.91±0.06

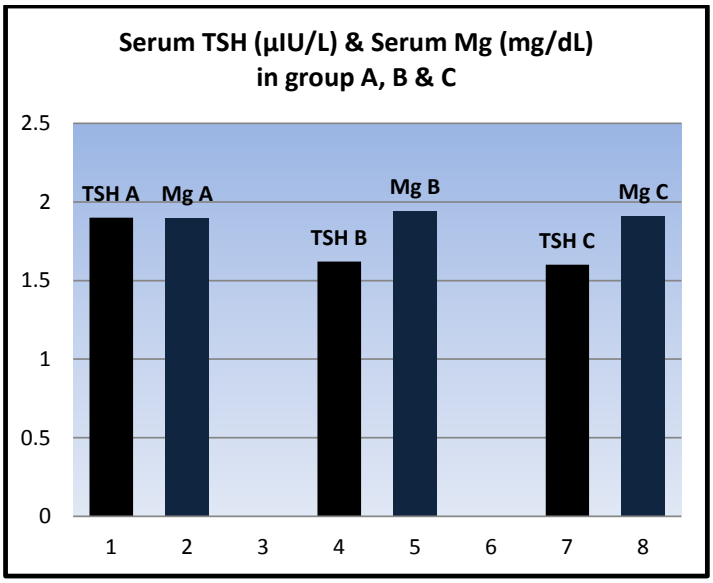

Figure 1: Serum TSH (µIH/L) and Serum Magnesium (mg/dL) levels in Group A, B, C

essential for maintenance of feto-maternal health. To support pregnancy progesterone level remains increased till about 10 weeks of gestation.[20] Estrogen also rises steadily throughout the pregnancy reaching highest at term.[21] Level of several other hormones like Human placental lactogen (hPL), Human chorionic gonadotropin (hCG), Adrenocorticotropic hormone (ACTH), Growth hormone (GH), Calcitonin, Relaxin, Inhibins Activins, Hypothalamic-like releasing and inhibiting hormones, Thyrotropin releasing hormone (TRH), Gonadotropin releasing hormone (GnRH), Corticotropin-releasing hormone (CRH), Somatostatin, Growth hormone-releasing hormone (GHRH) also are increased.

Thyroid hormones are the group of major hormones that control metabolic rate and thus growth and development of adult, child and the fetus as well.[23,24] Thyroid hormones have been well correlated with body weight and energy balance.[25] Several recent articles have highlighted importance of thyroid hormones in regulation of lipid metabolism,[26] interaction with nuclear receptors,[27] effects on cell membrane and membrane embedded channels and transporters[28] and also metabolic regulation of thyroid hormones.[29] But fetus can concentrate and synthesize thyroid hormones only after 10-12 weeks of gestation. Further fetal pituitary TSH can regulate such synthesis only around 20 weeks of gestation.[30] About 30% of T4 in cord blood at birth is of maternal origin.[31]

Serum TSH concentration varies from non pregnant to pregnant individuals. There are several factors which interplay during pregnancy which are responsible for such variation. Among them hCG and estrogen are two major factors.

hCG in serum is a mixture of several isoforms with variable amount of carbohydrate content in the form of oligosaccharide side chains. Studies with thyroid follicles have demonstrated that hCG acts as a weak stimulator of the thyroid gland.[32] Placenta produces hCG which binds to TSH receptors on thyroid gland and stimulates the same. This results in increased T3 and T4 production

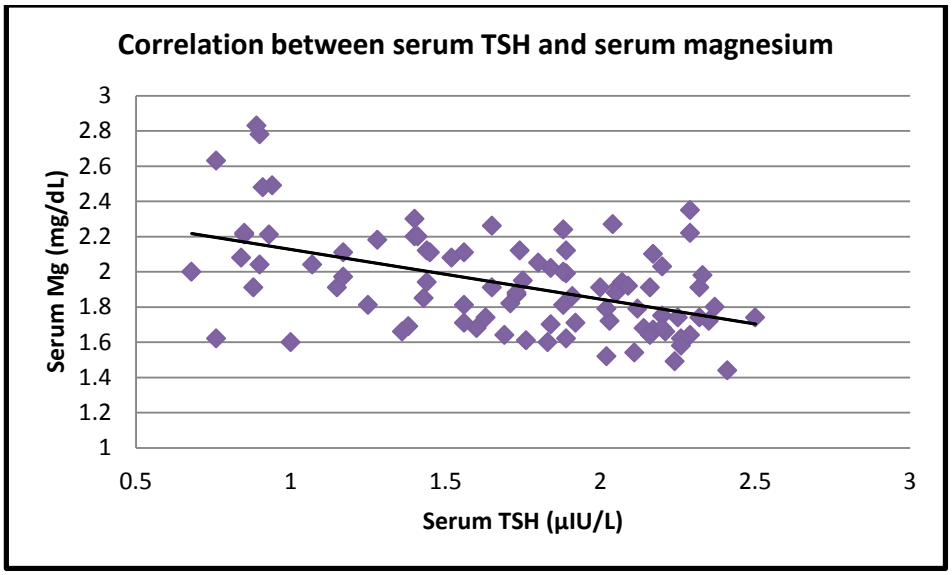

Figure 2: Correlation between serum TSH and serum magnesium

and consequent decrease in TSH secretion especially in the first trimester of gestation.[33] This overrides the physiological hypothalamo-pituitary-thyroid axis for regulation of thyroid hormone synthesis and secretion.[34] Thus hCG has been described as one of the major factors for decreased TSH concentration in early part of pregnancy.

Throughout the pregnancy estrogen level rises steadily which further stimulates synthesis of thyroid binding globulin (TBG). TBG has high T4 affinity and helps in Thyroid hormone transport in blood. That decreases circulating T4 level which further induces increased TSH secretion. Estrogen receptors have also been reported on thyroid tissue as early as 1981[35] which are associated with thyroid proliferation and further actions.[36] Balancing of thyroid hormones in pregnancy is thus complex and a result of interplay between several other hormones and metabolites.

Comparing different age groups namely A, B and C our study didn't find any significant difference in TSH level in their first trimester though it showed slightly lower concentration in higher age group.

For a normal adult total body Mg is approximately 25 gm and out of this 55% is distributed in skeletal system. About 1% - 3% of the total intracellular Mg remains in free ionized form which is about 0.5 to 1.0 mmol. Mg being cofactors of several enzymes has immense importance in metabolism. Low serum Mg level is associated with several pathologies which might result into cardiovascular diseases,[37] hypertension, type 2 diabetes mellitus,[38] metabolic syndrome[39] and many others. It has already been established that Mg is associated with immune system, inflammatory responses[40] and cellular oxidative stress.[41] Autoimmune thyroiditis is a quite common endocrine pathology that is associated with genetic, environmental factor and several trace elements too. Studies have already showed that Mg supplementation improves thyroid dysfunction.[12] It has also been suggested that patients with thyroiditis have lower serum Mg level and Mg is negatively related to the degree of lymphocyte activation.[42]

It has been found that with 150 µg/ day iodine intakes thyroid clears the iodide from 17 ml of plasma/ minute. For synthesis of thyroid hormones thyroid uptake and concentrate this iodide. Iodine uptake requires sodium iodide cotransporter or sodium/iodide symporter which is located on the thyrocyte membrane. This symport system is largely dependent on membrane ATPase; which further depends on mitochondrial oxidative phosphorylation for ATP.[43] Mg, being an enzyme cofactor of mitochondrial oxidative phosphorylation and ATP synthesis has immense importance. Hence in Mg deficient state mitochondrial energy supply is affected negatively which further results in decreased iodine uptake and thus decreased thyroid hormone synthesis.[13] In an animal model study it has been demonstrated that Mg supplementation increases uptake of radioactive iodine and the same is decreased in Mg deficient state.[44]

Deiodination is one of the major steps for thyroid hormone synthesis which is catalyzed by the enzyme deiodinase. Three subtypes of iodothyronine deiodenase enzymes have been isolated namely type 1 (D1), type 2 (D2) and type 3 (D3). While D1 and D2 convert the prohormone T4 to its bioactive form T3 and degrading rT3 to 3,3'-T2, D3 has inner ring deiodinase activity that degrades T4 to rT3 and T3 to 3,3'-T2. Study has demonstrated that there is increased deiodenase activity with increased Mg in a dose dependent manner. Selenium is an integral part of the deiodenase enzyme. As strong interaction and relationship has been established between selenium and Mg.[45] Hence increased deiodenase activity with increased Mg can be explained from this point of view, at least by part.[46]

This study had some limitations. Maximum Mg content in the body is in intracellular compartment and serum Mg status does not represent completely the nutritional status of Mg. However it has been established through a large-scale epidemiological investigation that serum Mg is still the most acceptable and representative index. Second, its limitation lies in its sample size. A greater number of samples could give a clearer picture.

Conclusion

Our study has demonstrated that mean serum TSH level doesn't vary significantly during pregnancy with increased age of the mother. Also it has shown that since serum TSH level in negatively related to serum Mg concentration, hypomagnesemia may render the pregnant mother vulnerable to hypothyroidism. However an interventional prospective study is required to confirm any cause effect relationship.

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Conflict of interest

There is no conflict of interest in the study.

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