Original Research Article

To evaluate the influence of ferritin on thyroid hormones in second trimester antenatal cases in Perambalur District

Nageshwari A[1], G. Kavitha[2*]

[1]Final year Postgraduate student, [2]Associate Professor
Department of Biochemistry, Dhanalakshmi Srinivasan Medical College, Perambalur, India
[*]Corresponding author email: **rockervijay79@gmail.com**

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Abstract

Background: Hypothyroidism is the most common pregnancy-related thyroid disorder, affecting 3–5% of all pregnant women. Pregnant women are often iron deficient, and iron deficiency has adverse effects on thyroid metabolism. Impaired maternal thyroid function during pregnancy may cause neurodevelopmental delays in the offspring. Iron deficiency is frequent during the first trimester of pregnancy and associated with a higher prevalence of thyroid autoimmunity, higher serum TSH and lower fT4 levels. Anemia is a decrease in the number of red blood cells (RBC's) or less than the normal quantity of hemoglobin in the blood. Anemia can have several reasons, such as abnormality of the formation and reduction on the half-life of the red cells.

Aim of the study: To evaluate the thyroid status in second-trimester antenatal cases.

Materials and methods: Totally 60 female patients were included in the study. Group-1(30) pregnant women with hypothyroidism. Group -2(30) pregnant women without hypothyroidism. The study was conducted from July – November 2018 over a period of 6 months at OG Department of DSMCH, perambalur. Ferritin levels were estimated in 60 female patients newly diagnosed patients of hypothyroidism using chemiluminescence technique (advia centaur cp). Total T3 and T4 levels were estimated using radioimmunoassay. Free T3, T4, and thyroid-stimulating hormone (TSH) levels were estimated using chemiluminescence. These were then compared with age- and sex-matched healthy controls. Results were correlated statistically.

Results: Serum ferritin levels were found to be significantly reduced in pregnant women with hypothyroidism compared to normal pregnant women ($p < 0.001$).

Conclusion: Complications that may occur during pregnancy and delivery could be due to low thyroid function, but was not able to be clearly proven in this study. Although prior or early-

pregnancy testing for iodine level and thyroid function can help early identify iodine deficiency and thyroid disorder, justifying a general screening will require further studies with multicentre-recruitment and ante-natal clinics involvement.

Key words

Pregnancy, Thyroid Function, Ferritin Level, Hypothyroidism.

Introduction

Hypothyroidism during pregnancy is deleterious to both mother and her child. Children born to untreated or undertreated mothers have a profound effect on future intellectual development [1]. Pregnancy has a deep impact on the thyroid gland and thyroid function. During pregnancy, the thyroid gland may enlarge by 10% in countries where iodine sources are sufficient and to a greater extent in iodine-poor countries [2]. Production of thyroid hormones and iodine requirement each increases by approximately 50% during pregnancy. Pregnancy is a stress test for the thyroid, resulting in hypothyroidism in women with limited thyroidal reserve or iodine deficiency [3]. Hypothyroidism is the most common pregnancy-related thyroid disorder, affecting 3–5% of all pregnant women. Pregnant women are often iron deficient, and iron deficiency has adverse effects on thyroid metabolism. Impaired maternal thyroid function during pregnancy may cause neurodevelopmental delays in the offspring. In one of the studies conducted on a large population, it was estimated that 87% of the Indian pregnant women are anemic [4]. Iron deficiency anemia during early pregnancy has been linked to low birth weight, premature birth, and negative effects on children's neuropsychological development. Also, iodine deficiency is a common nutrient deficiency, globally affecting individuals, and which can lead to impaired thyroid endocrine function [5]. During pregnancy, iodine deficiency and impaired thyroid endocrine function implies a serious risk of mental retardation, low birth weight, increased infant mortality, as well as increased risk of health complications later in life such as metabolic syndrome and type-2 diabetes. Several studies showed that iron deficiency anemia affects thyroid function via several mechanisms [6]. Iron deficiency decreases serum total and free T3, T4 concentrations and TPO activity. Iron deficiency decreases pituitary TSH response to TRH [7]. Iron deficiency decreases the activity of hepatic T4 deiodination and T3 turnover rates, increases peripheral type III de-iodinase activity resulting in high T4 and T3 clearance rate. There was little impact of low Serum Ferritin level on obstetrical outcomes including miscarriage, birth weight and premature delivery [8]. Low serum Ferritin may be a risk factor for thyroid dysfunction during pregnancy although the occurrence of thyroid dysfunction in pregnant women is influenced by a lot of factors with complicated interaction. Thyroid function and Serum Ferritin status should be normalized rapidly in gestational women [9].

Materials and methods

Totally 60 female patients were included in the study. Group -1(30) pregnant women with hypothyroidism. Group -2(30) pregnant women without hypothyroidism. The study was conducted from July – November 2018 over a period of 6 months at OG Department of DSMCH, perambalur. Ferritin levels were estimated in 60 female patients newly diagnosed patients of hypothyroidism. Total T3 and T4 levels were estimated using radioimmunoassay. Free T3, T4, and thyroid-stimulating hormone (TSH) levels were estimated using chemiluminescence. These were then compared with age- and sex-matched healthy controls. Results were correlated statistically.

Inclusion criteria: Second-trimester antenatal cases.

Exclusion criteria: Patients with known thyroid history, Known anemic cases. Newly diagnosed

as hypothyroidism and anemia - in first-trimester Antenatal routine investigations. Blood (5 ml) was taken from the antecubital vein under all aseptic conditions in a red-capped plain vacutainer from the subjects and the serum was analyzed for ferritin, thyroid-stimulating hormone (TSH), and free T3 and T4 on chemiluminometer (Advia Centaur CP; Siemens, USA). Total T3 and T4 levels were assessed using radioimmunoassay.

Statistical analysis

Data were analyzed using SPSS software version 22 and MedCalc software version 15. Data were interpreted using descriptive and inferential statistics. The Chi-square test was used to test the statistical significance of the relationship between variables.

Results

Mean ± SD of age among cases and controls were 22.75 ± 10.36 and 24.69 ± 12.24 years with the range of 18–29 years and 19–27 years, respectively. There was no significant difference with respect to age distribution in cases and controls ($p > 0.05$) as per **Table – 1**.

Table – 1: Thyroid profile ferritin levels pregnant hypothyroidism women who are in II –trimester.

Parameters estimated	Group -1 N=(30) Pregnant women with hypothyroidism	Group -2 N= (30) Pregnant women without hypothyroidism	P-Value
Serum ferritin (ng/ml)	18.08 ± 7.18	51.89 ± 8.56	<0.001
FT3 (pg/ml)	2.34 ± 0.06	3.12 ± 0.89	<0.001
FT4 (ng/dl)	0.73 ± 0.03	1.07 ± 0.08	<0.001
TSH (µIU/ml)	6.86 ± 1.16	2.76 ± 0.42	<0.001
T3 (ng/dl)	88.76 ± 6.54	126.25 ± 8.53	<0.001
T4 (µg/dl)	5.17 ± 0.76	8.56 ± 1.57	<0.001

Discussion

The present study shows that there is a state of low ferritin concentration in patients with hypothyroidism. It is observed that the FT4 level was significantly lowered in cases as compared to controls ($p < 0.001$), suggesting that depletion of iron stores may decrease serum FT4 levels. FT3 levels were also significantly lower in individuals with hypothyroidism as compared to healthy controls. TPO is a membrane-bound glycosylated hemoprotein that has a key role in the biosynthesis of thyroid hormones. This enzyme is responsible for the oxidation of iodide and the binding of iodine to tyrosyl residue of thyroglobulin (organification). Two diiodotyrosine (DIT) molecules undergo an oxidative condensation for the formation of thyroxine (T4). Triiodothyronine (T3) is yielded from the coupling of one mono-iodotyrosine and one DIT [10]. A separate coupling enzyme has not been found, and as this is an oxidative process, it is assumed that same thyroperoxidase catalyzes this reaction. This hypothesis is supported by the observation that the same drug that inhibits iodide oxidation also inhibits coupling. Thyroid hormone has a central role in differentiation, development, and maintenance of body homeostasis [11]. It has been suggested in various studies that thyroid hormones regulate ferritin expression. The iron regulatory protein (IRP, previously known as the iron-responsive element-binding protein, IRE-BP, and iron-responsive factor, IRF) is a transacting RNA-binding protein that binds with high affinity to conserved stem-loop structures, iron-responsive elements (IREs), present in the ferritin, and transferrin receptor (TfR). The IRP has a key role in the regulation of iron (Fe) homeostasis. In the absence of iron, the IRP binds to the IRE in the 5′-untranslated region (5′-UTR) of ferritin and represses translation [12]. Binding of the IRP to IREs in the 3′-untranslated region (3′-UTR) of

TfR mRNA stabilizes the mRNA and prevents its degradation [13]. In iron-replete states, the reverse holds, which results in increased ferritin translation and decreased TfR mRNA stability. This reciprocal regulation is achieved at the post-translational level and is independent of new protein synthesis. The symptom-based risk score using commonly accepted indicators of thyroid dysfunction has some ability to differentiate low and normal thyroid status. There doesn't appear to be a clear rationale for the variables included in the risk score [14]. It may require orders of magnitude larger patient groups to reliably identify all the possible symptomatic expressions of low thyroid status. Also, the relatively small numbers of patients found with low thyroid status, as well as the relatively unstable estimates associated with nearby alternative thresholds, means that uncertainties around the usefulness of the risk score need to be considered [15]. The estimation of the coefficients to be included in the risk score, and the calculation of the patient risk scores for the purpose of evaluation of efficacy of differentiation were performed on the same patients, rather than on two separate groups, as would be preferable (due to insufficient numbers of patients with low thyroid status) [16]. A broader objection to this particular expression of an asymptomatic screening test for potential low thyroid status is that it was not conducted completely in a primary antenatal clinic where pregnant women undergo a routine check-up from early gestational age with consequent follow-up throughout all pregnancy period [17, 18].

Conclusion

Complications that may occur during pregnancy and delivery could be due to low thyroid function, but was not able to be clearly proven in this study. Although prior or early-pregnancy testing for iodine level and thyroid function can help early identify iodine deficiency and thyroid disorder, justifying a general screening will require further studies with multicentre-recruitment and ante-natal clinics involvement. Thus, Pregnancy may affect the course of thyroid disorders and, conversely, thyroid diseases may affect the course of pregnancy. Moreover, thyroid disorders and their improper management may affect both the pregnant woman and the developing fetus. In patients with hypothyroidism, it is important to recognize that therapeutic requirements for exogenous thyroxine are increased by 50% on average during pregnancy. This should be taken into account in the management of such patients.

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References

1. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol., 2005; 105: 239-245.
2. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, StagnaroGreen A. Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. J Clin Endocrinol Metab., 2010; 95: E44-E48.
3. Tudela CM, Casey BM, McIntire DD, Cunningham FG. Relationship of subclinical thyroid disease to the incidence of gestational diabetes. Obstet Gynecol., 2012; 119: 983–988.
4. Wilson KL, Casey BM, McIntire DD, Halvorson LM, Cunningham FG. Subclinical thyroid disease and the incidence of hypertension in pregnancy. Obstet Gynecol., 2012; 119: 315–320.
5. Cleary-Goldman J, Malone FD, Lambert-Messerlian G, et al. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol., 2008; 112: 85–92.

6. Männistö T, Vääräsmäki M, Pouta A, et al. Perinatal outcome of children born to mothers with thyroid dysfunction or antibodies: a prospective population-based cohort study. J Clin Endocrinol Metab., 2009; 94: 772–779.
7. Korevaar TI, Schalekamp-Timmermans S, de Rijke YB, et al. Hypothyroxinemia and TPO-antibody positivity are risk factors for premature delivery: the generation R study. J Clin Endocrinol Metab., 2013; 98: 4382-4390.
8. Henrichs J, Bongers-Schokking JJ, Schenk JJ, et al. Maternal thyroid function during early pregnancy and cognitive functioning in early childhood: the generation R study. J Clin Endocrinol Metab., 2010; 95: 4227-4234.
9. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med., 1999; 341: 549 – 555.
10. Pop VJ, Brouwers EP, Vader HL, Vulsma T, van Baar AL, de Vijlder JJ. Maternal hypothyroxinaemia during early pregnancy and subsequent child development: a 3-year follow-up study. Clin Endocrinol (Oxf)., 2003; 59: 282–288.
11. Finken MJ, van Eijsden M, Loomans EM, Vrijkotte TG, Rotteveel J. Maternal hypothyroxinemia in early pregnancy predicts reduced performance in reaction time tests in 5- to 6-year-old offspring. J Clin Endocrinol Metab., 2013; 98: 1417–1426.
12. Casey BM, Dashe JS, Spong CY, McIntire DD, Leveno KJ, Cunningham GF. The perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. Obstet Gynecol., 2007; 109: 1129 –1135.
13. Craig WY, Allan WC, Kloza EM, et al. Mid-gestational maternal free thyroxine concentration and offspring neurocognitive development at age two years. J Clin Endocrinol Metab., 2012; 97: E22–E28.
14. Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med., 2012; 366: 493–501.
15. Päkkilä F, Männistö T, Surcel HM, et al. Maternal thyroid dysfunction during pregnancy and thyroid function of her child in adolescence. J Clin Endocrinol Metab., 2013; 98: 965–972.
16. Hess SY, Zimmermann MB, Arnold M, Langhans W, Hurrell RF. Iron deficiency anemia reduces thyroid peroxidase activity in rats. J Nutr., 2002; 132: 1951–1955.
17. Beard JL, Borel MJ, Derr J. Impaired thermoregulation and thyroid function in iron-deficiency anemia. Am J Clin Nutr., 1990; 52: 813-819.
18. Hess SY, Zimmermann MB.The effect of micronutrient deficiencies on iodine nutrition and thyroid metabolism. Int J Vitam Nutr Res., 2004; 74: 103–115.