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Original Research Article

Thyroid Stimulating Hormone As A Biomarker and its Role in Predicting IUGR

Varsha Sinha[1], Swetabh Verma[2]

[1]Senior Resident, Department of Obstetrics and Gynaecology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

[2]Tutor, Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

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Corresponding author: Dr. Swetabh Verma
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Abstract

Aim: To Study Predictive value of thyroid stimulating hormone as a biomarker in IUGR.

Materials and Methods: This observational prospective study was carried out in the Department of Obstetrics and Gynaecology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India. A total of 98 consecutive clinically suspected cases of IUGR with singleton pregnancies at 34-40 weeks of gestation attending the hospital were enrolled in the study after taking an informed consent. The gestational age was determined on the basis of the date of last menstrual period or by first trimester ultrasound if available.

Results: The Body Mass Index (BMI) ranged from 15.2 kg/m2 to 26.6 kg/m2 with the average BMI being 20.93 kg/m2 The BMI of <19.6 kg/m2 was observed in 28 underweight antenatal mothers (28%) whereas only ten (10%) of the subjects evaluated was overweight with a BMI of 26.6 kg/m2. The average height of the subjects was 154.72 cm 4.08 SD and the average pre-pregnancy weight as recorded was 48.17kg 5.92 SD. The TSH levels below 0.3 mIU/L was recorded in three antenatal mothers in the age-group of 26-30 years. All three antenatal mothers were from rural background and vegetarian. In these, one was born dead while the other two babies were born alive. The antenatal mother with normal BMI delivered live babies. However, the mode of delivery in the two born alive was LSCS due to fetal distress. Both neonates had a very low birth weight; less than1.5 kgs and required admission to neonatal intensive care unit for 2-5 days.

Conclusion: Many studies indicate a possible effect of thyroid dysfunction and IUGR. However, the results between studies are variable, and drawing clear cut conclusions is difficult though it is widely accepted that overt hypothyroidism increases the risk for deleterious outcomes and the risk for IUGR.

Keywords: IUGR, thyroid dysfunction, TSH

Introduction

Thyroid dysfunction and gestational diabetes mellitus (GDM) are the two most com- mon endocrine disorders that can be registered during pregnancy. These conditions are at the root of several complications for both the mother and the fetus.[1–3] Therefore, adequate follow-up of pregnant women and timely diagnosis of thyroid and carbohydrate impairments is essential.

Although pregnancy is a physiological condition, it may change the way thyroid hormone production and glucose homeostasis are balanced. To some extent, this is associated with the development of the placenta and the secretion of a number of hormones, growth factors, and enzymes.[4]

In most pregnant women, the adaptation mechanisms of thyroid gland function and carbohydrate metabolism provide the necessary hormonal and metabolic terms for the normal course of pregnancy. In some pregnant women, however, the production of thyroid hormones does not lead to the necessary adaptation to the requirements of pregnancy. This could be related to the development of subclinical or overt hypothyroidism during pregnancy. Given the role of the normal levels of thyroid hormones in carbohydrate metabolism, this could be associated with possible disorders in the latter.[5]

Universal screening for thyroid dysfunction in early pregnancy has not been widely recommended by scientific societies. The ongoing debate towards universal screening is based on whether the treatment of women identified with thyroid disease, in particular subclinical hypothyroidism, is beneficial and cost-effective. Most of the current guidelines recommend targeted or selective screening. However, in this case, mainly women with risk factors for thyroid dysfunction are tested. Thyroid status is tested in pregnant women with concomitant thyroid disease or those with known risk factors such as a family history of thyroid disease, those living in an endemic area with iodine deficiency, goiters, positive antithyroid antibodies, dyslipidemia, type 1 diabetes, other autoimmune diseases, obesity, infertility, premature birth, etc.[6–9] This selective screening fails to detect thyroid dysfunction in women without risk factors. It is well known that thyroid hormones are essential for the normal course of pregnancy and the normal development of the fetus, in particular its nervous system. Therefore, early detection and elimination of abnormalities in thyroid hormone levels are of great importance.

Regarding carbohydrate metabolism, universal screening for GDM is recommended in the period between 24–28 weeks of gestation.[10–12] In many cases, this is a prerequisite for delaying the diagnosis, and it is often facilitated after complications have already occurred. The question arises whether biochemical markers of placentation, such as placental growth factor (PlGF), may have some predictive value in the early diagnosis of GDM and/or thyroid dysfunction.

During pregnancy, the main focus is on the placenta, which can be considered as a large temporary endocrine organ. The placenta produces a variety of hormones such as human placental lactogen, human chorionic gonadotropin (hCG), progesterone, estradiol, somatotropic hormone, cortisol, placental growth factor (PlGF), soluble FMS-like tyrosine kinase 1 (sflt-1), pregnancy-associated plasma protein-A (PAPP-A), prolactin, cytokines, and others.[5] Most of these hormones contribute to the occurrence of pregnancy-associated insulin resistance (IR).[13,14] Pre-existing overweight and obesity, as well as excessive weight gain

during pregnancy, are associated with the deepening of the IR.[15] It is well known that IR could become a prerequisite for the manifestation of carbohydrate impairments during pregnancy.[14] Placental hormones may also affect thyroid function. The effects of hCG on the thyroid gland have long been known.[16] In recent years, the effect that PlGF can have on maternal thyroid function was discussed.[17,18]

Taken separately, most placental products show attitudes towards changes in insulin sensitivity and carbohydrate metabolism, respectively, mainly due to their insulin-antagonistic effects. Each of them can have its prognostic value for the manifestation of GDM. The only factor that is associated not only with carbohydrate metabolism but also with thyroid function is PlGF.

Material and methods:

This observational prospective study was carried out in the Department of obstetrics and gynaecology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for 10 months

Methodology:

A total of 98 consecutive clinically suspected cases of IUGR with singleton pregnancies at 34-40 weeks of gestation attending the hospital were enrolled in the study after taking an informed consent. The gestational age was determined on the basis of the date of last menstrual period or by first trimester ultrasound if available.

The clinical diagnosis of IUGR was made on the basis of poor maternal weight gain and a non- correspondence with the period of gestation (fundal height less than the period of gestation). In all cases the serum TSH was done by automated chemiluminescence method and readings recorded.

Results:

Approximately 80.61% (n=79) were from the rural background and 19.39% (n=19) were from urban area. The mean age of the subjects was 21.8 years 3.1 SD. 37.76%of the antenatal mothers were in the age group of 20-25 years (n=37) followed by 35.71% in the age group of 26- 30 years as shown in Table 1 & 2.

Table 1: Age distribution in study population

Age	Number (n=98)	Percentage %
<20 years	12	12.24%
20-25 years	37	37.76%
25-30 years	35	35.71%
>30 years	10	10.2%

Table 2: Demographic characteristics of the study population

Demographic characteristics	Number (n=98)	Percentage (%)
Rural	79	80.61%
Urban	19	19.39%

The Body Mass Index (BMI) ranged from 15.2 kg/m2 to 26.6 kg/m2 with the average BMI being 20.93 kg/m2 The BMI of <19.6 kg/m2 was observed in 28 underweight antenatal mothers (28%) whereas only ten (10%) of the subjects evaluated was overweight with a BMI of 26.6 kg/m2 (Table 3).

Table 3: Body mass index of the study population

BMI (Wt/Ht2)	Reference	Number (n=100)	Percentage (%)
Underweight	<18.5	28	28%
Overweight	>25	10	10%
Normal weight	18.5-25	62	62%

The average height of the subjects was 154.72 cm 4.08 SD and the average pre-pregnancy weight as recorded was 48.17kg 5.92 SD. Out of 43 caesarean delivery, 22 caesareans were done due to fetal distress out of which 16 were conducted for non-reassuring fetal heart rate. Other causes were failed induction and poor Manning score. Forty-three neonates required admission to neonatal intensive care unit (NICU). The major cause was respiratory distress syndrome 40%. Other causes for admission included hypoglycaemia, neonatal jaundice, and meconium aspiration syndrome in decreasing order. The neonates were admitted to NICU for about 2 to 5 days.

The TSH levels below 0.3 mIU/L was recorded in three antenatal mothers in the age-group of 26-30 years. All three antenatal mothers were from rural background and vegetarian. In these, one was born dead while the other two babies were born alive. The antenatal mother with normal BMI delivered live babies. However, the mode of delivery in the two born alive was LSCS due to fetal distress. Both neonates had a very low birth weight; less than1.5 kgs and required admission to neonatal intensive care unit for 2-5 days.

Discussion:

The borderline hypothyroid women, who conceive can become subclinical or overt hypothyroid during pregnancy. About 2–3% of pregnant women are hypothyroid, of whom 0.3–0.5% have overt hypothyroidism and 2–2.5% present subclinical hypothyroidism.[19] In a study on the prevalence of thyroid diseases the authors report thyroid diseases greater in females as compared to males in the rural population though not statistically significant.[20,21] In our study all three antenatal mothers where from the rural areas as well as vegetarians.[21] Vegan diet tends to be associated with lower risk of hypothyroidism. Body Mass Index (BMI) significantly increases during pregnancy due to gain of weight with normal progression of pregnancy. In a study the BMI correlated positively with TSH level in first and second trimesters while it correlated negatively with FT4 level in second and third trimesters, but, failed to demonstrate significant association with FT3 level in any of trimesters in euthyroid pregnant women.[22] In our study one antenatal mother had a low BMI while the two with live births had a normal body weight.

Early diagnosis and treatment of hypothyroidism in pregnancy is very essential. The main test mainly used to diagnose thyroid dysfunction is TSH. It is generally reproducible, reliable and available. The evaluation of the results is important as it requires trimester specific reference ranges so as not to underestimate hypothyroidism and/or overestimate of hyperthyroidism. The TSH reference range is based on “Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum,” established in 2012. The upper limit for TSH is taken as 2.5 mIU/L in the first trimester, and 3.0 mIU/L in the second and third trimesters, while the lower physiological limit is considered to be 0.1 mIU/L in the first trimester, 0.2 mIU/L in the second, and 0.3

mIU/L in the third. [23,24] In a study on fetal outcome in hypothyroid women conducted by Ruchi Kishore et al reported that 13% were IUGR in hypothyroid patients 6.2% were IUD [25] Several authors have performed cordocentesis for fetal blood sampling in babies affected by severe IUGR and have reported a statistically significant reduction in circulating concentrations of free T4 and free T3. In our study we took TSH as the standard and in three the levels were below 0.3 mIU/L.[26,27] Out the three one was born dead. The two born live were delivered by LSCS because of fetal distress. In both neonates the birth weight was less than 1.5 kgs and required admission to neonatal intensive care unit.

Biomarkers as predictors of IUGR has been quite a research interest. IUGR results from multifactorial causes. Serum metabolites for prenatal screening of aneuploidy and open neural tube defects, either individually or in combination has been proposed but the predictive efficacy has not been adequately evaluated in a systematic manner. TSH as a biomarker for IUGR in combination could be of value. Overt hypothyroidism (TSH greater than 10 mIU/L and/or low FT4) is treated in pregnant women, but the approach to subclinical hypothyroidism is more complicated because the harms and benefits are not well established. These uncertainties have led to disagreement on whether women should be screened for thyroid disease in pregnancy or not.

Conclusion:

Many studies indicate a possible effect of thyroid dysfunction and IUGR. However, the results between studies are variable, and drawing clear cut conclusions is difficult though it is widely accepted that overt hypothyroidism increases the risk for deleterious outcomes and the risk for IUGR.

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