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Increased Prevalence of Auto Immunity among Pregnant Women in Kolkata, West Bengal - Is Hypovitaminosis D to Be Blamed For It?

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ABSTRACT

Aim: A cross-sectional study was conducted at Ramakrishna Mission Seva Pratishthan (RKM), Kolkata to evaluate the correlation between the vitamin D level and thyroid function among Bengalee women in the first trimester of their pregnancy.
Methods: The cross sectional study was conducted at the Dept. of Biochemistry, RKM among women who registered in the Obstetrics over a period of three months. Patients were screened based on the inclusion exclusion criteria. 506 patients were included in the study and their TSH, FT4, Vitamin D, Anti TPO levels were measured based on which they were classified as Gestational Hypothyroid and Euthyroid patients.
Results: A shocking 72% was found to be Gestational Hypothyroid (based on Indian Thyroid Association guidelines) and 141 were Euthyroids. Very high Vitamin D deficiency was observed in the entire study population but it was more prevalent among GHT mothers in comparison to euthyroids. Vitamin D and Anti TPO levels were found to be significantly negatively correlated (r= -0.4498, p <0.0001) among the Gestational Hypothyroid patients. Significant differences of serum TSH, Vitamin D and Anti TPO levels (put the results a vs b) were observed in gestationally hypothyroid mothers as compared to euthyroid women.
Conclusion: The study highlights the significant contribution of vitamin D in causing thyroid auto immunity among gestational mothers thus emphasizing the need of antenatal thyroid screening and vitamin D supplementation.

Keywords: Vitamin D deficiency, gestational hypothyroid, euthyroid, TSH

INTRODUCTION

Vitamin D plays a profound role in pregnancy due to its strong influence on the absorption of calcium in intestine as it is extremely required for optimum growth and development of foetal bones and regulation of bone mineral homeostasis of mother and the foetus. [(1)] Pregnancy poses a huge impact on vitamin D metabolism because of increased demand of calcium with the advancement of pregnancy. Vitamin D deficiency (VDD) is associated various adverse outcome of pregnancy including gestational hypothyroidism, intrauterine growth retardation, preeclampsia, low birth weight, gestational diabetes and neonatal sepsis. [(2)] Another important aspect of VDD in developing autoimmune hypothyroidism has already been demonstrated in numerous studies across the globe. [(3)] Our earlier studies also indicated a close association of VDD with Hashimoto Thyroiditis in the local inhabitants of West Bengal, India. [(4)] The immunomodulatory role of vitamin D is being appreciated in the underlying pathogenesis of multiple auto immune disorders in last few years. [(5)] A discernible change of thyroid function is noted in normal pregnancy to meet up the metabolic need of both mother and foetus which is reflected in the raised levels of thyroid hormones (T3 & T4). HCG (Human

chorionic gonadotropin), a key hormone in pregnancy elevates the level. Gestational hypothyroidism has a deleterious effect on pregnancy. The prevalence of gestational hypothyroidism is reported to be 4.8- 11% as compared to West (2.5%). [(6)] Auto immunity is found to be the commonest cause of gestational hypothyroidism (GHT) which bears a close association with Hypovitaminosis D. Apart from that iodine deficiency still remains a leading contributing factor for causing subclinical and overt hypothyroidism. Anti TPO positivity in pregnancy is of high concern as it is observed that 1 in 10 pregnant mothers develop anti TPO antibody in their first trimester of pregnancy due to low iodine uptake of thyroid gland caused by the deficiency of calcitriol. [(7)] Anti TPO ab positivity is reported to enhance the risk of miscarriage, recurrent pregnancy loss in early pregnancy and preterm birth. [(8)] Various other abnormalities including attention deficit disorders and hyperactivity syndromes are demonstrated in the children born to the untreated mothers with autoimmune/gestational hypothyroidism. There is a real dearth of studies indicating the role of VDD in autoimmunity responsible for a continual increase of GHT in pregnant women of Eastern India in spite of its immense role in developing autoimmunity. The aim of our study is to evaluate the role of VDD in gestational hypothyroidism in Kolkata, West Bengal which has not been much explored so far.

MATERIALS & METHODS

This is a prospective observational study carried out at Ramakrishna Mission Seva Pratishthan (RKMSP) Kolkata over a period of 3 months. A total of 686 pregnant women attending RKMSP in their first trimester for check-up were recruited for the study. 506 patients who satisfied all inclusion criteria were recruited for the study after an initial screening.

Inclusion Criteria:

- Pregnant Women who registered in the OPD
- Patients in first trimester of pregnancy
- Patients having no history of past or present serious illness.

Exclusion criteria:

- Patients with previous thyroid disorders
- Patients with complicated pregnancy
- Patients on medications affecting thyroid function or vitamin D metabolism, with calcium or vitamin D supplementation.

Ethics: Ethical clearance was obtained from institutional ethical committee. All the patients were consented for the study.

A detailed clinical history was obtained for each patient. The patients were classified as Gestational Hypothyroid (TSH >2.5 mIU/ml with normal FT4) & Euthyroid (TSH 0.1 - 2.5mIU/ml).Three hundred sixty five GHT and one hundred forty one Euthyroid patient samples were assayed for serum TSH, FT4, vitamin D and anti TPO. All the analytes were estimated in a full auto analyzer (Cobas 6000 series, Roche Diagnostic, Metodo: ECLIA)

RESULTS

The prevalence of GHT was observed to be 72% (365/506) among all included patients. Very high prevalence of VDD 86.4% (317/365) was observed in the GHT group whereas among Euthyroids it was 72.3% (102/141). The comparative study of the two groups are represented in the following table:

Table 1: Comparative study of the base line characters of the two groups:

Parameters	Gestational Hypothyroid	Euthyroid	T score	P value
Total Population	365	141	-	-
Vitamin D deficiency	317(86.4%)	102(72.3%)	-	-
Autoimmunity	111(28.7%)	2.12(3%)	-	-
Mean Vitamin D	10.33±6.81	18.27±4.68	0.7185	<0.001
Mean TSH	7.89±2.9	1.89±0.6	0.05095	<0.001
Mean Anti TPO	68.74±168.56	28±5.2	0.89385	<0.001

Prevalence of autoimmunity among GHT group was 28.7% (111/365) while in Euthyroid it was 2.12% (3/141). The mean age of GHT & Euthyroid groups were in accordance (26.3±4.1 vs 25.9±1.2). The Gestational ages for GHT & Euthyroid were 7.5±2.4 vs 6.9±1.8. The mean TSH varied significantly (p <0.001) among GHT & Euthyroid group (7.89±2.9 vs1.9±0.6).The vitamin D levels for GHT & Euthyroid groups showed significant difference (10.33±6.81 vs 18.27±4.68 ; p <0.001). Significantly high levels of Anti TPO was found to be present in GHT mothers compared to their Euthyroid counterparts (68.74±168.56 vs 28±5.2 ; p <0.001). The Vitamin D and Anti TPO levels were found to be negatively correlated in GHT mothers (r= - 0.4498, p <0.0001)

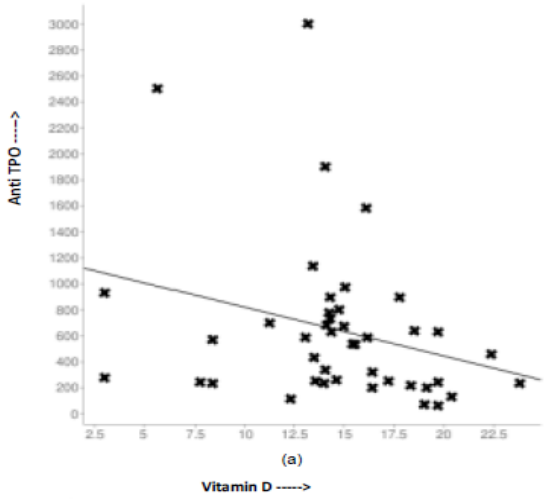

Fig 1: Vitamin D in x-axis and Anti TPO in y axis. The graph indicates a significant negative correlation between the plotted parameters.

DISCUSSION

Our study revealed a significantly high prevalence (72%) of gestational hypothyroidism (GHT) in Kolkata which was found to be much higher than it was earlier reported (11.76%) by Dhanwal et al. in 2016. [(9)] Even the prevalence in West Bengal has increased from 33.93% reported by Mandal et al. [(10)] to 72% in a period of last three years indicating the steep rise of the hypothyroidism in pregnancy. 28.7% of GHT group showed anti TPO positivity in their first trimester which might enhance the possibility of overt hypothyroidism in their late pregnancy. [(11)] Overall incidence of thyroid autoimmunity is significantly increased in past few decades as compared to Western countries. [(12)] According to a multicenter study conducted in various parts of India Kashmir showed much higher prevalence of GHT (39%) in comparison to Uttar Pradesh (15.6%), Haryana (16.2%), Maharashtra (17.85%) [(13)] and in North east India (32.94%). [(14)] Iodine deficiency in the hilly terrains might be cause of the higher prevalence of GHT in Kashmir and north ease India .Anti TPO positivity in GHT has been documented in some parts of India but it has not been seriously addressed despite its potential effects on adverse pregnancy outcomes. Autoimmunity in pregnancy accelerates the chances of miscarriage, premature delivery (31.4%) as compared to euthyroid (4%) which has been reflected in several studies. [(13,14)] The exact mechanism lying behind this still remains obscure. It is commonly perceived that anti TPO decreases the bio-availability of thyroid hormones required to fulfill the metabolic need of mother foetus duo in pregnancy leading to develop GHT Incidentally presence of autoantibody especially anti TPO antibody is quite often observed in reproductive aged women which might be responsible for various complications in their pregnancies. In addition to placental abruption, preterm labour, preeclampsia etc GHT also contributes to develop gestational hypertension and diabetes in later age. [(15)] Poor neurocognitive skill is also observed in the children of untreated hypothyroid mothers. Emerging studies indicated presence of anti TPO antibody in euthyroid mothers also. [(16)] 2.12% of euthyroid women showed raised levels of serum anti TPO antibody in this study. Increased iodine uptake might be a contributing factor for this growing incidence of autoimmunity as iodine supplementation is often required due to increased need of thyroid hormones especially in pregnancy. Iron deficiency and the goitrogenous food items are reported to aid in developing auto antibody in

pregnancy. [17] Vitamin D deficiency also poses a severe impact on pregnancy including gestational hypothyroidism, intrauterine growth retardation, recurrent miscarriage, gestational diabetes; preeclampsia etc. [18] Foetal graft rejection due to immunological imbalance caused by vitamin ad deficiency has also been documented. Association of growing incidence vitamin D deficiency with continual increase of autoimmunity has renewed global interest. Multifactorial causes including increase of the usage of sunscreens, decreased uptake of vitamin d enriched food like milk, sedentary lifestyle, prolonged indoor activities, increased BMI come in to play for the roaring up rise of Vitamin D deficiency among the young females. Significantly high percentage of vitamin d deficiency was observed in this study in the gestationally hypothyroid and euthyroid female 88% vs.80% which might be attributed to the shockingly high prevalence of autoimmunity in the present study. Vitamin D supplementation in pregnancy has been proved to be beneficial to combat with thyroid autoimmunity [19,20] but it is not in much use till today. Lack of proper awareness might drive clinical inertia towards vitamin D supplementation or routine screening of Vitamin D deficiency. On the other hand universal antenatal thyroid screening is still not implemented even after its recommendation from Indian Thyroid Society in 2014 despite its urgent need.

CONCLUSION

Our study highlights the significant contribution of vitamin D deficiency / insufficiency in pregnancy towards development of thyroid autoimmunity. In view of this vitamin D supplementation and antenatal thyroid screening s need to be emphasized to pre-empt the serious consequences caused by hypovitaminosis D in gestational hypothyroidism although both the issues remain the areas of key debate in obstetrics.

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