Original article

The Estimation of the Pervasiveness of Thyroid Dysfunction among Pregnant Women

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Abstract:

Introduction: This study is design to determine the common types of thyroid dysfunctions among pregnant ladies and to determine trimester-specific reference ranges for free Tri-Iodothyronine (FT3), Free Thyroxine (FT4) and Thyrotropin (TSH) among healthy pregnant women.

Materials and Methods: This was a cross sectional hospital based study. All pregnant ladies- aged 20 to 50 years- who attended antenatal clinics in Department of Obstetrics and Gynaecology, KPC Medical College Jadavpur, Calcutta, West Bengal, India. The participants who agreed in the study were included. According to these criteria the total number of patients attended the antenatal clinics during the period of the study were 500. $P < 0.05$ was considered significant.

Result: mean age, duration of marriage and parity was (27.7 ± 9.1) year, (4.91 ± 8.2) year and (2.1 ± 01.14) respectively. The vast majority had completed university education (67.5%), most of the women were housewives (86.57%). Significant medical history and co-morbidity was found in 10 patients as follow: 1.5% patients with diabetes mellitus and 3% patients with hypertension

Conclusion: Thyroid dysfunction is highly prevalent among Indian pregnant women. There is slight fluctuation of thyroid hormones during pregnancy in euthyroid women and thyroid dysfunction is affected by rural residence and history of auto-immune disorder.

Keywords: Thyroid dysfunction, Tri-Iodothyronine (FT3), Free Thyroxine (FT4), Thyrotropin (TSH).

INTRODUCTION

Thyroid disorders commonly affect women of reproductive age group, so it is more common disorder during pregnancy. Inadequate maternal thyroid hormone production, particularly during the first stages of gestation when the foetus is reliant on maternal thyroxine, has been associated with multiple obstetric and neonatal adverse outcomes,[1-3] including inadequate neuropsychological development in the offspring.[3,4] In a study of 48 women treated for hypothyroidism with a normal prepregnancy serum TSH level, increasing levothyroxine by two doses per week prevented maternal TSH elevation above 2.5 mIU per L and above 5 mIU per L in 85% and 100% of patients, respectively, with only two patients requiring a subsequent dose reduction.[5] Preconception counseling for women with known hyperthyroidism should include discussion of available treatments and potential adverse effects, as well as the impact on future pregnancies. Standard treatments include long-term antithyroid medication, radioactive

iodine ablation, and near-total thyroidectomy. Potential adverse fetal effects of antithyroid medications include congenital abnormalities and neonatal hypothyroidism caused by transplacental transfer. Although radioactive iodine ablation is not associated with long-term consequences on gonadal function, fertility, or pregnancy outcomes, it is customary to wait six months after the therapeutic dose is administered before attempting conception.[6]

The most frequent thyroid disorder in pregnancy is maternal hypothyroidism. It is associated with fetal loss, placental abruptions, preeclampsia, preterm delivery and reduced intellectual function in the offspring.[7] There is a wide geographic variation in prevalence of hypothyroidism during pregnancy. It varies from 2.5% from the west to 11% from India.[8,9]

The prevalence of overt hyperthyroidism complicating pregnancy has been reported to range between 0.4 and 1.7 % and an estimated 2–3 % of women are hypothyroid during pregnancy .[10,11] Overt hyperthyroidism occurs in 0.4–1.7 % of pregnant women.[12] Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labor, placental abruption, and postpartum hemorrhage. Fetal complications include low-birth-weight babies, firsttrimester spontaneous abortions, preterm delivery, fetal or neonatal hyperthyroidism, intrauterine growth retardation, high rates of still birth and neonatal deaths, neonatal hyperbilirubinemia, higher incidence of neonatal hypothyroidism, and increased perinatal mortality .[13]

The investigation and management of thyroid dysfunctions are not considered in routine screening protocols of pregnant women, or of those planning to get pregnant, even though missing the diagnosis and the delay in managing the thyroid dysfunctions has been proved to have a deleterious effect on the wellbeing of mother and offspring.[14] However, in many developing countries routine assessment of thyroid status is not being done in all pregnant women. Furthermore, the incidence of subclinical hypothyroidism or autoimmune status in this population of women, especially women in India is not known as we do not have any published data. Hence this study has been undertaken among pregnant women attending Department of Obstetrics and Gynaecology, KPC Medical College Jadavpur, Calcutta, West Bengal, India. Thus this study was designed to determine the common types of thyroid dysfunctions among pregnant ladies and to determine trimester-specific reference ranges for free Tri-Iodothyronine (FT3), Free Thyroxine (FT4) and Thyrotropin (TSH) among healthy pregnant women.

MATERIAL AND METHODS

This was a cross sectional hospital based study. All pregnant ladies- aged 20 to 50 years- who attended antenatal clinics in KPC Medical College Jadavpur, Calcutta, West Bengal, India. The participants who agreed in the study were included. According to these criteria the total number of patients attended the antenatal clinics during the period of the study were 500. After we obtained signed informed consent the data has been collected by direct interview with patients, by four trained data collectors, using a detailed structured questionnaire, covering socio-demographic information (age, residence, education, and occupation), history of thyroid disease and past medical history (diabetes mellitus, auto-immune disease, hypertension). Also the questionnaire included the obstetric (parity, history of miscarriage, stillbirth delivery, preterm birth.) and gynaecological (delay of conception, irregular menstrual period) data. This was followed by, systemic clinical examination and examination of the thyroid gland. 5 ml of venous blood sample were collected from each participant to evaluate the thyroid function; serum was

separated immediately by a fine centrifugation machine and sent for thyroid function test. TSH, free T3 and free T4 were quantitatively determined using Microparticle Enzyme Immunoassay (MEIA). We compared the obstetric and gynaecological data and socio-demographic characteristics between the women who were suffering from thyroid dysfunction and those who were euthyroid. All participants were under multidisciplinary care and were treated according to their diagnosis. The different variables were compared between the women with thyroid dysfunction and euthyroid women. Proportions were compared between the two groups of the study using chi-square test. Univariate and multivariate analyses were performed. Thyroid dysfunction was the dependent variable; socio-demographic characteristics, obstetric and gynaecological data were independent variables. This study was designed to investigate the prevalence and spectrum of thyroid dysfunctions among pregnant females aged 20-50 years, to determine the common types of thyroid dysfunctions among pregnant ladies and to determine trimester-specific reference ranges for free Tri-Iodothyronine (FT3), Free Thyroxine (FT4) and Thyrotropin (TSH) among healthy pregnant indian women.

Statistical Analysis

We used SPSS 16 for entire calculation. Confidence intervals of 95% were calculated and $P < 0.05$ was considered significant. In case of discrepancy between the results of the univariate and the results of multivariate analyses, the later was taken as final.

RESULTS

Table 1: Thyroid hormone levels among pregnant females with normal thyroid function

Level of thyroid hormones in all Euthyroid females		**Test**	**Mean ±SD**	**Minimum**	**Maximum**
		TSH	1.84±0.79	0.08	4.76
		T3	3.78 ±0.56	0.35	5.21
		T4	0.57±0.83	0.17	4.96
Level of thyroid hormones in Euthyroid females per trimester	**Ist**	TSH	1.734 ±0.96	0.32	4.26
		T3	3.892± 0.79	0.43	4.91
		T4	0.765±0.9	0.51	4.68
	IInd	TSH	1.4629±1.2	0.09	4.83
		T3	3.7219±0.3	0.67	4.11
		T4	1.07±0.79	0.14	5.01
	IIIrd	TSH	1.2963 ±1.09	0.06	8.83
		T3	3.62±0.94	0.86	5.11
		T4	0.9201± 0.58	0.28	4.74

Table 2: Comparison showing the obstetric outcome and gynecological data between pregnant women with thyroid dysfunctions and euthroid women

Variable	With thyroid dysfunction(n=66)	Euthroid (n=434)	P value
Miscarriage	27 (40.9%)	72 (16.6%)	0.006*
Preterm birth	9 (13.6%)	29(6.7%)	0.218
Stillbirth delivery	6 (9.1%)	9 (2.1%)	0.421
Mentally retarded baby	2 (3.0%)	2 (0.5%)	0.234
Delay of conception	10 (15.2)	39 (8.10%)	0.134
Irregular cycle	12 (18.1%)	2 (0.5%)	0.002*

*Significant (P < 0.05)

Figure 1: Comparison showing the obstetric outcome and gynecological data between pregnant women with thyroid dysfunctions and euthroid women

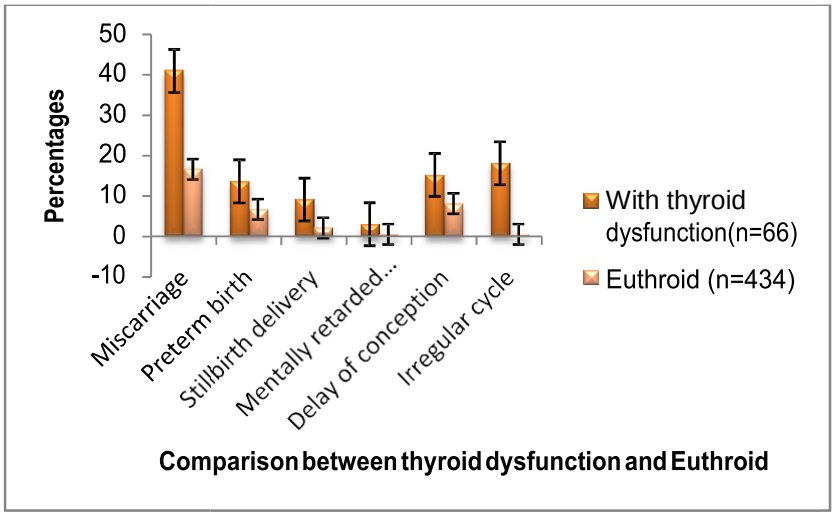

Table 3: Risk factors for thyroid dysfunction among pregnant women

Variable	Univariate analyses			Multivariate analyses		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Age ≥ 35	1.3	1.0-1.2	0.023	1.9	1.2-1.4	0.09
Parity ≥ 5	1.6	1.1-1.6	0.261	0.5	0.4-1.1	0.325
Rural residence	5,9	3.1-18	0.007*	12.6	4.9-47	0.006*
Comorbidity	1.1	0.1-2.1	0.675	1.2	1.1-3.6	0.271
Family history of AID	7.1	1.9-28.3	0.06	9.2	1.5-76.3	0.09

*Significant

During the study period a total of 500 pregnant women were included, their mean age, duration of marriage and parity was (27.7 ± 9.1) year, (4.91 ± 8.2) year and (2.1 ± 01.14) respectively. The vast majority had completed university education (67.5%), most of the women were housewives (86.57%). Significant medical history and co-morbidity was found in 10 patients as follow: 1.5% patients with diabetes mellitus and 3% patients with hypertension. 4% women gave family history of auto-immune disease.

From the study, we found that the prevalence of thyroid dysfunctions among Indian pregnant females evaluated for thyroid dysfunction was 12.2% (66/500). On further analysis and with regard to thyroid dysfunctions 4.8% of the women were found having hyperthyroidism, 4.4% having hypothyroid, 2.9% having simple goitre and 1.6% were diagnosed and treated as thyroiditis. Table 1 shows the Thyroid hormone levels among pregnant females with normal thyroid function, and Comparison showing the obstetric outcome and gynecological data between pregnant women with thyroid dysfunctions and euthroid women were shown in table 2, Figure 1. Risk factors for thyroid dysfunction among pregnant women were shown in table 3.

DISCUSSION

It is highly recommended that all females with pre-existing thyroid diseases should have their thyroid function rechecked and normalized prior to conception, and thyroid functions monitored throughout pregnancy, especially during the first 12 gestational weeks when the maternal thyroid is solely responsible for delivering thyroid hormone to the growing fetus, which is crucial for its normal brain development.[15] During normal pregnancy, significant but reversible changes in thyroid function might occur as a result of the normal physiological and hormonal changes, such as the influence of the Human Chorionic Gonadotropin (HCG) as a weak stimulus of thyroid hormones production resulting in subclinical hyperthyroidism. Also, the high estrogen level increases serum thyroid hormone binding proteins, with a consequent increase of the total level of thyroid hormones. These possible changes should be considered when interpreting the thyroid function test during pregnancy.[16] In agreement with our results Stricker et al. (Switzerland) and Soldin et al. (USA) observed similar fluctuation in the trimester specific levels of thyroid hormones.[17,18]

Possible reasons for higher prevalence of hypothyroidism, both overt and sub‐clinical, in Asian Countries include: increased iodine intake in diet as suggested by a Chinese study, presence of goitrogens in diet as reported from India and micronutrient deficiency such as selenium or iron deficiency that may cause hypothyroidism and goiter.[19] Thus, it is expected that the prevalence of hypothyroidism during pregnancy is higher in India and Asia. Moreover, prevalence of hypothyroidism in India is variable.

Hyperthyroidism is much less common than hypothyroidism. The frequency of the disorder is relatively low, occurring in only 0.5–2/1000 pregnancies.[20] Untreated hyperthyroidism is associated with a significantly higher frequency of obstetric complications such as preeclampsia, premature labor, low birth weight, fetal and perinatal loss.[21]

Although there is still no strong evidence concerning the effect of the thyroid disease on pregnancy there are clear data confirmed that with thyroid dysfunction there is increase risk of miscarriage, premature delivery, preeclampsia, low birth weight.[22] Our study demonstrated significant association between thyroid dysfunction and history of

miscarriage. This fact might be changed if the patients were adherent to the follow up and preconception management. Interestingly thirteen women with thyroid dysfunction gave family history of auto-immune disease and there were 4 cases claimed that their menstrual period was irregular. The immune system may produce antibodies against the ovarian tissue, harming the egg-containing follicles and damaging the egg.[23] What triggers the immune response is unclear, but may be explained by being a multiple endocrinological dysfunction. Among the different socio-demographic and risk factors rural residence was found significantly associated with thyroid disorders among the investigated pregnant women. This might be attributed to change in diet and iodine intake; however more research is needed to conclude an evidence for this factor.

CONCLUSION

Thyroid dysfunction is highly prevalent among Indian pregnant women. There is slight fluctuation of thyroid hormones during pregnancy in euthyroid women and thyroid dysfunction is affected by rural residence and history of auto-immune disorder, Thus, universal screening of pregnant women for thyroid dysfunction should be considered especially in a country like India due to the high prevalence of undiagnosed thyroid dysfunction. We recommend investigation for thyroid function test during pregnancy and in preconception clinics

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