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Research Article

ASSESSING THE NEED OF DOSAGE ADJUSTMENTS OF THYROXINE AMONG PREGNANT WOMEN WITH HYPOTHYROIDISM

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Hypothyroidism, dosage adjustment, levothyroxine

A B S T R A C T

Aim & objective: The aim of the study is to assess the need of dosage adjustments of thyroxine among pregnant women with hypothyroidism.
Methodology: To evaluate the effects of pregnancy on thyroxine requirements, we prospectively reviewed the thyroid function of 86 women receiving treatment for hypothyroidism in pregnancy. **Study design:** Prospective observational study
Results and findings: Out of 86 subjects, 44 subjects are having pre pregnancy hypothyroidism and 42 subjects are having gestational hypothyroidism. Age at presentation (yrs) was 23.78+ 4.17; Weight (kgs) was 61.11+13.27. Among 44(51.16%) subjects in pre pregnancy hypothyroidism, 9(20.45%) subjects required increase in levothyroxine dose; 10(22.7%) required decrease in levothyroxine dose. Among 42(48.83%) subjects in gestational hypothyroidism, 5(11.9%) subjects required increase in levothyroxine dose; 2(4.76%) subjects required decrease in dose; (P=0.032). Remaining 60 subjects in both pre pregnancy and gestational hypothyroidism required no change due to sufficient dose.
Conclusion: Based on our prospective observational study we finally conclude that Levothyroxine requirements was more in all trimesters but mostly in first trimester followed by third trimester. Levothyroxine requirement was more in Gestational hypothyroidism (19.76%) compared to Pre pregnancy hypothyroidism (16.27%).

INTRODUCTION

Background

Women with hypothyroidism have been thought not to require an increase in thyroxine replacement during pregnancy. In our clinical practice, we observed an apparent increase in the thyroxine requirement in a number of pregnant women with hypothyroidism.

Need of the Study

- Hypothyroidism is most common in pregnant women. As thyroid hormone requirements increase during pregnancy often leading to the need to increase the levothyroxine dose.
- It is necessary to assess TSH levels and adjust the dose of levothyroxine.
- Women who don't receive enough thyroid hormone during pregnancy are at greater risk of complications like miscarriage, low birth weight, neuro- psychological problems, respiratory problems, premature birth, post partum hemorrhage, abruptio placentae, pre-eclampsia, anemia.

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Aim

To study the need of dosage adjustments of thyroxine among pregnant women with hypothyroidism.

Objective

To monitor the thyroxine requirements in pregnancy with hypothyroidism based on TSH levels.

METHODOLOGY

***Study design*:** Prospective observational study.

***Study site*:** Department of Obstetrics and Gynaecology, Government general hospital, Guntur.

Study period: October 2017 to March 2018 (6 months).

***Sample size*:** Out of 137 subjects, 86 subjects were included in our study based on study criteria.

***Materials*:** Lab reports, data collection form, prescriptions, case records.

***Inclusion criteria*:** Pregnant women with hypothyroidism of age group more than 18 years.

***Exclusion criteria*:** Pregnant women with hypothyroidism who are chronically ill.

RESULTS

Table 1 Distribution of subjects among pre pregnant and gestational hypothyroidism

Distribution of hypothyroidism	Number of subjects
Pre pregnancy Hypothyroidism	44(51.16%)
Gestational Hypothyroidism	42(48.83%)

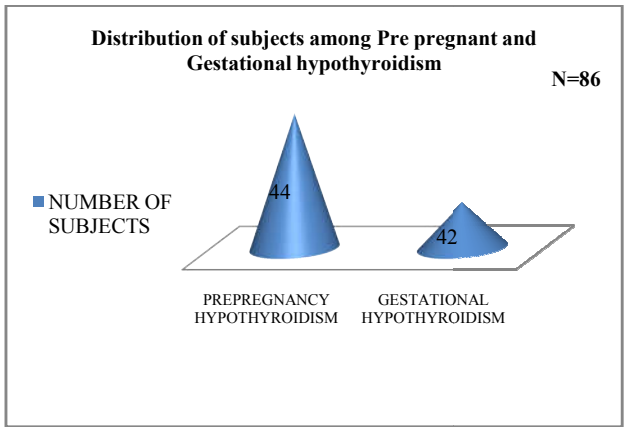

Figure 1 By the above figure 1; it shows that 44 subjects were included in pre-pregnancy hypothyroidism and 42 subjects were in gestational hypothyroidism. Finally, subjects were equally distributed between Pre pregnancy and Gestational hypothyroidism.

Table 2 Distribution of subjects based on trimester among Pre pregnant and Gestational hypothyroidism at the time of presentation

Trimester	Pre pregnancy Hypothyroidism	Gestational Hypothyroidism	Total(N=86)
First	5(11.36%)	0	5(5.81%)
Second	13(29.54%)	16(38.09%)	29(33.72%)
Third	26(59.09%)	26(61.90%)	52(60.46%)
Total	44	42	**86**

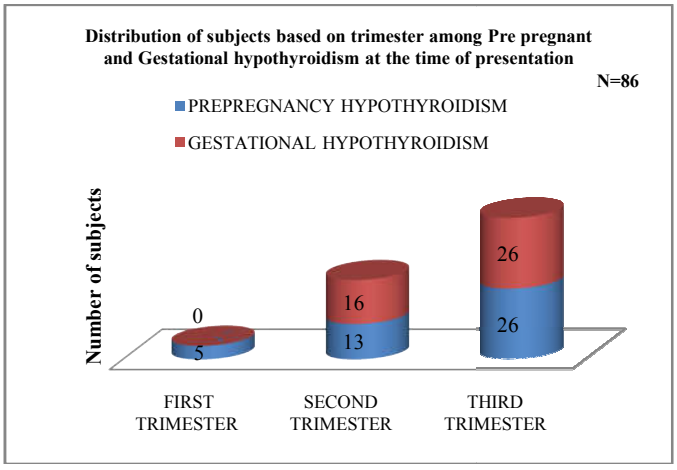

Figure 2 From the above figure 2; it shows that most of the sample were in third trimester with the number of 52 then followed by 29 subjects in third trimester and 5 subjects in first trimester. Finally, subjects were more in third trimester.

Table 3 Dose adjustment of Levothyroxine in gestational hypothyroidism subjects as per guidelines based on their trimester requirements

Dose	TSH Level(2.5-10iu/L) Dose 25ug	TSH Level(>10iu/L) Dose 50ug	Total (N=42)
Given	19(51.35%)	2(28.57%)	21
Not Given	18(48.64%)	3(42.85%)	21
Total	37	5	**42**

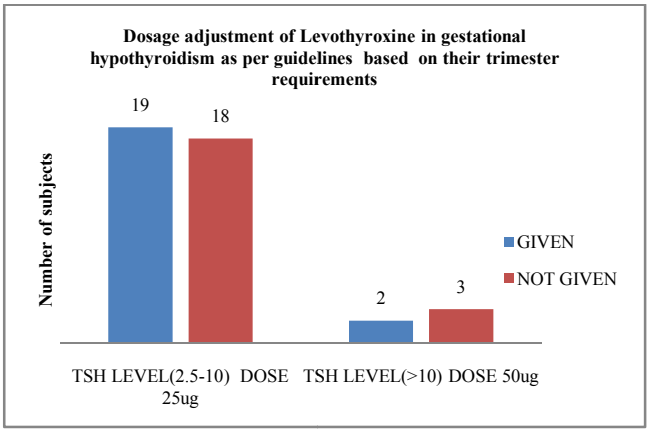

Figure 3 From the above figure 3, it shows that 19 subjects were given the dose of 25 µg with TSH level between 2.5-10IU/L and 18 subjects were not given according to guidelines. 2 subjects were given the dose 0f 50 µg with TSH level >10IU/L and 3 subjects were not given. Finally, dose given and not given were equal as per guidelines.

Table 4 Distribution of subjects based on TSH level in pre pregnancy and gestational hypothyroidism at the time of presentation.

TSH level (µIU/L)	Pre pregnancy hypothyroidism			Gestational hypothyroidism			Total (N=86)
	First trimester	Second trimester	Third trimester	First trimester	Second trimester	Third trimester	
<2.5	1(20%)	5(41.6%)	4(14.8%)	0	3(21.42%)	0	13(15.11%)
2.5-5	3(60%)	5(41.6%)	8(29.6%)	0	5(35.71%)	14(50%)	35(40.69%)
5-7.5	1(20%)	1(8.3%)	5(18.5%)	0	2(14.28%)	9(32.14%)	18(20.93%)
7.5-10	0	0	3(11.1%)	0	2(14.28%)	2(7.14%)	7(8.13%)
>10	0	1(8.3%)	7(25.1%)	0	2(14.28%)	3(10.7%)	13(15.11%)
Total	5	12	27	0	14	28	**86**

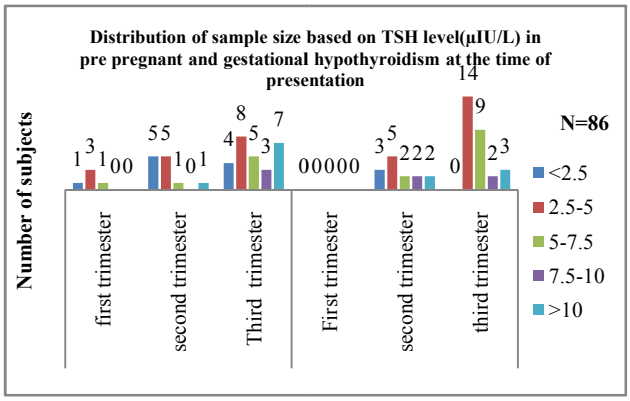

Figure 4 From the above figure 4; it depicts that out of 86 subjects, 13 subjects were having TSH level <2.5, 35 subjects were having TSH level between 2.5-5, 18 subjects were having TSH level between 5-7.5, 7 were having TSH level between 7.5-10 and 13 subjects were having TSH level between >10. Finally, subjects with TSH level between 2.5-5 were more in gestational hypothyroidism in third trimester.

Table 5 Dosage adjustment and subjects in pre pregnancy and gestational hypothyroidism

Levothyroxine dosage adjustment	Pre pregnancy hypothyroidism			Gestational hypothyroidism			Total (N=86)
	First trimester	Second trimester	Third trimester	First trimester	Second trimester	Third trimester	
No change	4(80%)	6(46.1%)	15(57.6%)	0	12(80%)	23(85.2%)	60
Decreased	1(20%)	4(30.7%)	5(19.2%)	0	1(6.6%)	1(3.7%)	12
Increased	0	3(23.07%)	6(23.1%)	0	2(13.3%)	3(11.1%)	14
Total	5	13	26	0	15	27	**86**

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	6.882[a]	2	.032
Likelihood Ratio	7.263	2	.026
Linear-by-Linear Association	3.983	1	.046
N of Valid Cases	86		

0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.37.

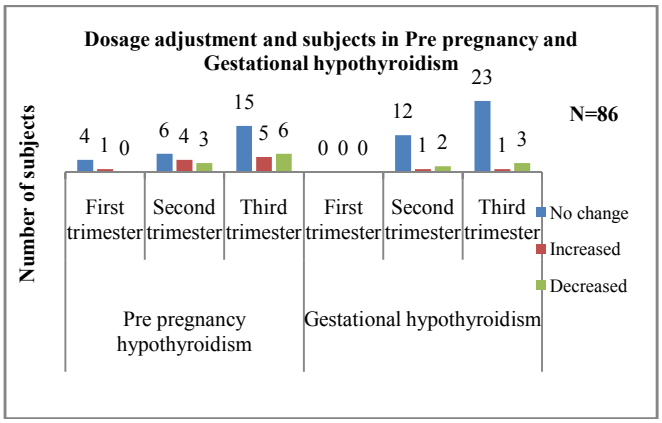

Figure 5 From the above figure 5; it depicts that out of 86 subjects, 60 subjects required no change in levothyroxine dose, 12 subjects required decrease in levothyroxine dose and 14 subjects required increase in levothyroxine dose. Finally, pre pregnanct women required increase in dose when compared to gestational hypothyroid women.

Table 6 Levothyroxine dosage requirements as per guidelines

Trimester	Pre pregnancy hypothyroidism		Gestational hypothyroidism		Total (N=86)
	LT4 dosage adjustment required	LT4 dosage adjustment not required	LT4 dosage adjustment required	LT4 dosage adjustment not required	
First trimester	1(9.09%)	4(12.12%)	0	0	5(5.81%)
Second trimester	3(27.27%)	10(30.30%)	8(50%)	7(26.92%)	28(32.57%)
Third trimester	7(63.6%)	19(57.52%)	8(50%)	19(73.07%)	53(61.12%)
Total	11	33	16	26	**86**

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.711[a]	1	.191		
Continuity Correction[b]	1.157	1	.282		
Likelihood Ratio	1.717	1	.190		
Fisher's Exact Test				.247	.141
Linear-by-Linear Association	1.691	1	.193		
N of Valid Cases	86				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 13.19.

b. Computed only for a 2x2 table

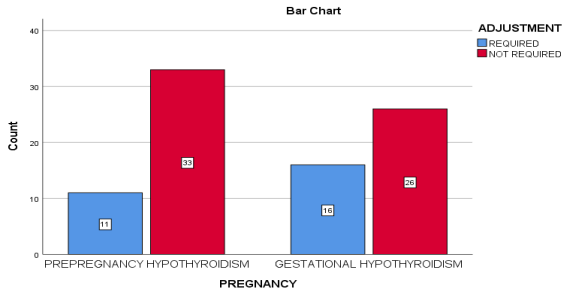

Figure 6 From the above figure 6; it shows that in pre pregnancy hypothyroidism 11 subjects required levothyroxine dosage adjustment and 33 subjects required no adjustment; while in gestational hypothyroidism 16 subjects required dosage adjustment and 26 subjects required no adjustment. Finally, levothyroxine requirement was more in gestational hypothyroid women.

DISCUSSION

The mother is the only source of T4 for the fetus during the first trimester, and it is the predominant source during the first half of gestation, at the time when key structures develop in the fetal brain. The aim is to provide mothers with an LT4 dose leading to euthyroidism as soon as possible.

TSH measurement is not a part of routine screening guidelines in pregnancy. In Government general hospital, TSH is not measured routinely in all pregnant women. Haddow JE *et al* have found that routine TSH testing is performed in 48% of all prenatal care practices and 76% of urban obstetric practices. Furthermore percentage of number of hypothyroid women at our center was higher (10%) compared to that study.

This prospective study indicates that frequent testing in association with frequent adjustments in the dose of levothyroxine can be used to estimate when levothyroxine requirements increase and decrease during pregnancy, and by how much.

A total of 86 subjects were recruited into the study population based on inclusion and exclusion criteria. In our study 44 prepregancy hypothyroidism subjects (51.17%) and 42 gestational hypothyroidism subjects (48.83%) were using levothyroixine therapy for hypothyroidism.

In normal pregnancy, there is a physiologic increase in free thyroxine and a decrease in thyrotropin, and these changes are maximal at the time the human chorionic gonadotropin concentration peaks. In our subjects we did not observe hCG concentrations. The temporary chorionic gonadotropin-induced increase of the thyroxine production rate in normal gestation can provide largely this increment (Mandel *et al*., 1990). Because thyroid glands in hypothyroid women are not able to respond either to thyrotropin or to chorionic gonadotropin, the incremented requirement for thyroxine is not achieved and the serum thyrotropin concentration increases. Our results that these women required higher dose of levothyroxine throughout gestation, rather than transiently, also suggest that there is a constant increase in thyroxine production throughout pregnancy.

Our study indicates that the need for a strict and early follow up in pregnancy of women with treated hypothyroidism. Close monitoring of treatment will allow detecting the need for increase and decrease in the LT4 dose in most patients during pregnancy.

Out of 86 subjects age group between 8-24 years were 55(63.95%) reflecting early marriage and early conception in India. Out of 86 subjects weights between 51-60 kgs were 28 (32.5%). Out of 86 subjects, 14 subjects are having the family history of hypothyroidism. By this we can say that despite of family history, hypothyroidism occurs in pregnancy.

Out of 86 subjects 35(40.69%) subjects were having TSH level between 2.5-5µIU/L mostly in third trimester. By this we can say that many of subjects were not in euthyroid state requiring of levothyroxine replacement therapy.

In our study Levothyroxine requirement was increased in 16.28% and decreased in 12.79% out of 86 subjects. Levothyroxine requirements increase in early during pregnancy in most women with hypothyroidism. In our study thyroxine requirements was more in all trimesters but mostly in first trimester followed by third trimester.

There are several possible explanations for an increased need for thyroxine during pregnancy. Since the rise in serum thyrotropin concentrations was associated with a decrease in serum free thyroxine indexes we can eliminate an alteration in hypothalamic – pituitary thyroid relations as a cause. The absorption and distribution of thyroxine may be altered by the gravid uterus, changes in distribution of cardiac output, and the effect of mass of fetal placental unit. Because the increased need for thyroxine occurs relatively early in gestation, it is unlikely that these physiological changes cause it. Thyroxine metabolism by fetal placental unit could contribute to an increased need for thyroxine in later phases of pregnancy.

Levothyroxine requirement was more in Gestational hypothyroidism (19.76%) compared to Prepregnancy hypothyroidism (16.27%).

CONCLUSION

Based on the findings of our prospective observational study we finally conclude that Levothyroxine requirement was more in all trimesters but mostly in first trimester followed by third trimester. Levothyroxine requirement was more in Gestational hypothyroidism (19.76%) compared to Prepregnancy hypothyroidism (16.27%). There is significant need for dosage adjustments based on TSH levels. Hence we also suggest that TSH should be performed for every trimester and levothyroxine levels must be monitored to improve the feto–maternal outcome.

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