

Comparative study of Thyroid hormone in different trimester of normal pregnancy: A Jharkhand Population Based study.

Dr Avnish Kumar Tarwey¹, Dr Santosh Kumar²
Junior resident¹ Professor and Head of department², Department Of Biochemistry
Rajendra Institute of Medical Science, Ranchi, Jharkhand

Abstract: The interpretation of changes in thyroid hormones concentration during normal pregnancy should be based on an understanding of the normal physiological changes during pregnancy, the iodine adequacy, medication and ambient goitrogens in different geographical region⁽¹⁻⁵⁾ It also depends upon topography, nutrition intake, socioeconomic status and cultural practices. Indian thyroid society has taken recommendation of American thyroid association strongly recommends population defined, trimester-wise and region specific reference range for the diagnosis^{6,7} **Aim and Objectives** To evaluate the variation in thyroid status in different trimester of normal pregnancy. **Material And Method** Total of 150 normal pregnant women (50 in each trimester) enrolled for study. Their FT3, FT4 and TSH were estimated. **Observation And Result** Range of FT3 is 1.76-4.08 pg/ml in first trimester, 1.54-4.83 pg/ml in second trimester and 1.24-4.91 pg/ml in third trimester. Range of FT4 is 0.74-4.03 ng/dl in the first trimester, 0.70-3.86 ng/dl in second trimester and 0.60-4.67 ng/dl in third trimester. Range of TSH in the first, second and third trimesters were 0.46-5.72 mIU/ml, 0.60-5.10 mIU/ml, 0.39-6.68 mIU/ml, respectively. **Conclusion** Free T3 and Free T4 level increases subsequently from first to third trimester and TSH level decreases from first to third trimester

Keywords: Pregnancy, Trimester, FT3, FT4, TSH

Date of Submission: 06-05-2020

Date of Acceptance: 19-05-2020

I. Introduction

Pregnancy is very important stage in the life of a couple. Baby is precious for the family. The ultimate aim is to have a healthy baby and a healthy mother at the end of pregnancy. There is a constant interplay of hormones among fetus, mother and placenta during development.

The interpretation of changes in thyroid hormones concentration during normal pregnancy should be based on an understanding of the normal physiological changes during pregnancy, the iodine adequacy, medical consideration, medication and ambient goitrogens in different geographical region⁽¹⁻⁵⁾ Physiological changes in pregnancy such as haemodilution, increased serum thyroxine binding globulin under influence of oestrogen on the liver, increased hCG particularly in 1st trimester, increase in type 5 deiodinase due to increase in placental mass, increase in thyroglobulin production and increase in iodine clearance due to increase in renal blood flow could affect functioning of thyroid gland and interpretation of thyroid function. These variations during pregnancy necessitate the formation of trimester related reference intervals from pregnant population. Understanding the normal physiological adaptation of the pituitary-thyroid axis in pregnancy enables management of cases of thyroid dysfunction.

Gestational age dependent reference intervals for thyroid hormones for local population should help to avoid underdiagnosis of hyperthyroidism as well as the over diagnosis of hypothyroidism. It also depends upon topography, nutrition intake, socioeconomic status and cultural practices. Indian thyroid society has taken recommendation of American thyroid association regarding diagnosis and management of thyroid disease during pregnancy but there are significant ethnic differences in serum thyroid hormone concentration, so American thyroid association strongly recommends population defined, trimester-wise and region specific reference range for the diagnosis^{6,7}. It has been suggested that even in one country, different regions should have their own reference range interval and thus there is a need of multicentric study to define this range in India. Some studies have reported this reference range in southern and a few in northern states, but there has been no data from Jharkhand population yet. The importance of this study lies here.

II. Aims and Objectives

To evaluate the variation in thyroid status in different trimester of normal pregnancy.

III. Materials and Methods

The study was undertaken in the Department of Biochemistry, RIMS Ranchi Jharkhand as per the standard protocol followed in the institute and with prior approval from ethical committee and proper consent of patient was taken. It is a cross sectional study. Study population consists of 150 healthy pregnant women attending Ante Natal check up(ANC) from Feb 2018 to October 2019.

Inclusion criteria : Cases having no known thyroid problem and Patients with adequate diet and iodine in adequate amount .

Exclusion criteria

- Patients having other endocrinopathies like Diabetes Mellitus, thyroid disorder, polycystic ovary disease.
- Pre-eclampsia & eclampsia.
- History of hepatitis and liver dysfunction
- Patient suffering from HIV, cancer or severe illness.

Parameters studied : Serum free T₃, Serum free T₄ and Serum TSH was estimated by chemiluminescent microparticle immunoassay(CMIA) method on ABBOT ARCHITECT i1000SR IMMUNOASSAY machine(A Fully Automated Hormone Analyser).

Observations and Results:

In this study(chart No 1) 55% were primigravida, while 45% were multigravida. Total patients were divided in different age groups(chart No 2).. Maximum patients were in the age group 20-25yrs.

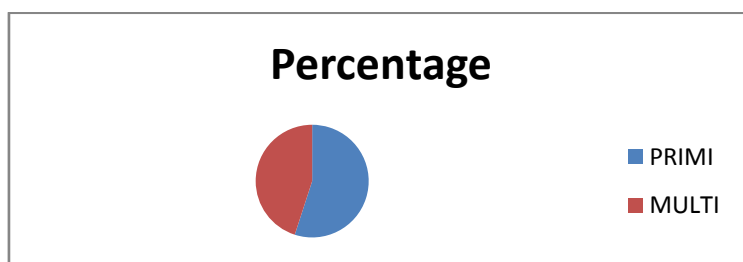


Chart no 1. Parity wise distribution in the study

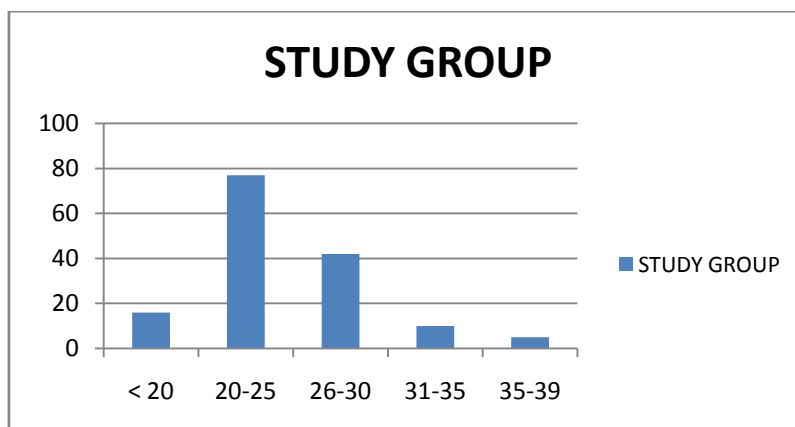


Chart no2. Age wise distribution in the study

GROUP	TSH (microIU/ml)	FT3 (pg/ml)	FT4 (ng/dl)
1 st Trimester	0.46-5.72	1.76-4.08	0.74-4.03
2 nd Trimester	0.60-5.10	1.54-4.83	0.70-3.86
3 rd Trimester	0.39-6.68	1.24-4.91	0.60-4.67

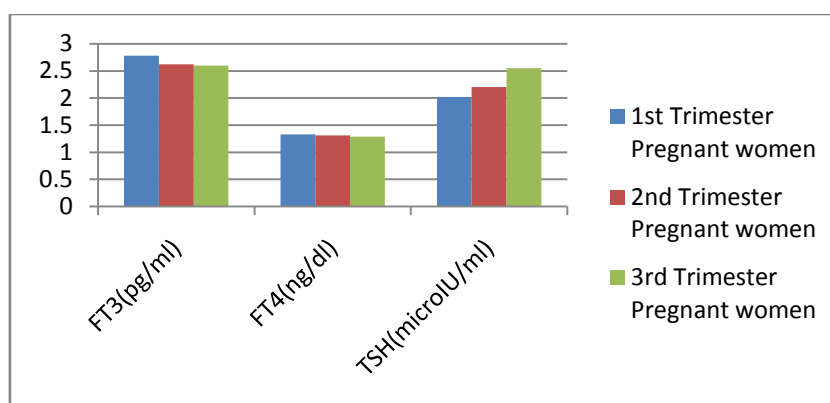
Table no.1 Range of FT3, FT4 ,TSH level

Table No.1 shows Range of FT3 is 1.76-4.08 pg/ml in first trimester, 1.54-4.83 pg/ ml in second trimester and 1.24-4.91 pg/ml in third trimester. Range of FT4 is 0.74-4.03ng/dl in the first trimester, 0.70-3.86 ng/dl in second trimester and 0.60-4.67 ng/dl in third trimester. Range of TSH in the first, second and third trimesters were 0.46-5.72mIU/ml, 0.60-5.10 mIU/ml, 0.39-6.68mIU/ml, respectively.

Parameter(mean	FT3(pg/ml)	FT4(ng/dl)	TSH(microiu/ml)
1st trimester pregnant women	2.78±0.45	1.33±0.83	2.02±1.11
2nd trimester pregnant women	2.62±0.58	1.31±0.83	2.20±0.97
3rd trimester pregnant women	2.60±0.69	1.29±0.90	2.55±1.22

Table no.2 Thyroid hormone in Different Trimester

Table No.2 shows mean value of TSH is highest in 3rd trimester and lowest in 1st trimester, mean value of FT3 is highest in 1st trimester and lowest in 3rd trimester and mean value of FT4 is lowest in 3rd trimester and highest in 1st trimester in all the age groups.



IV. Discussion

This study provides further documentation that average TSH levels are lower more during the first trimester and also provides trimester specific reference range of thyroid hormone for Jharkhand population.

There is a constant interplay of hormones among fetus, mother and placenta during development. The neuroendocrine development of fetus is dependent on the thyroid hormones.^{8,9,10,11} The fetal thyroid acquires the capacity to concentrate and organify iodine at about 10-12 weeks of gestation and T₄ and TSH gradually increases in fetal blood from then onwards. Till then thyroid hormones are supplied exclusively by the mother. Maternal TRH crosses the placenta and may play a major role in the maturity of fetal pituitary thyroid axis. Fetus remains dependent on the mother for ingestion of adequate amount of iodine, which is essential to make thyroid hormones. The WHO recommended iodine intake of 200µg/day during pregnancy to maintain adequate thyroid hormone production, and 150µg/day for non pregnant healthy women.^{12,13}

Estrogen and hCG influences thyroid function test.¹⁴ hCG is produced in large quantities during pregnancy particularly at the end of the 1st trimester. Because of its molecular similarity with TSH, hCG acts as a weak thyrotropic hormone and stimulates the maternal thyroid gland to enlarge and increase its hormone production.^{15,16,17} The peak rise in hCG and serum TSH occur together at about 10-12 weeks of gestation. Most cases of hCG-induced increase in thyroid hormone level usually return to normal by 2nd trimester without treatment. As a result of stimulatory effect of estrogen on liver, TBG (thyroid binding globulin) synthesis increases and its plasma clearance decreases.^{18,19} The concentration of TBG, become twice by 16th-20th week of gestation.

According to RK Marwaha, the range of TSH is (0.6–5.0, 0.44–5.78 and 0.74–5.7 microIU/ml) in three consecutive trimesters²⁰. Rajput R et al Haryana study showed range of TSH as 0.37-3.69, 0.54-4.47, 0.70-4.64 microIU/ml²¹. Jebasing et al Manipur study has 0.21-1.82, 0.72-1.71, 0.69-1.93 micro IU/ml²³. Sekhri et al study found the range as 0.09-6.65 ,0.51-6.61 ,0.91-4.86 microIU/ml in consecutive trimester²². In our study range of TSH in the first, second and third trimesters were 0.46-5.72 microIU/ml, 0.60-5.10 microIU/ml, 0.39-6.68 microIU/ml, respectively. Our study also showed this increase through the trimester.

Rajput R et al the range of FT3 in the first trimester is 2.53–4.54, 2.01–4.73 in second trimester and 2.01–4.01 pg/ml in third trimester²¹, Sekhri et al range of serum FT3 as 3.1-6.35 ,2.39-5.12, 2.57-5.68 pg/l in different trimester²².

In our study, the range of serum FT3 in the first trimester is 1.76-4.08, 1.54-4.83 in second trimester and 1.24-4.9 pg/ml in third trimester.

According to Rajput R et al the range of FT4 in the first trimester is 0.88-1.78, 0.91-1.78 in second trimester and 0.83-1.70 ng/dl in third trimester²¹, Sekhri et al range of serum FT4 as 9.81-18.53, 8.52-19.43, 7.39-18.28 pg/l in different trimester²².

In our study, the range of serum FT4 in the first trimester is 0.74-4.03, 0.70-3.86 in second trimester and 0.60-4.67 ng/dl in third trimester. Mankar et al showed 1.0-2.2 ng/dl in first, 0.45-2.24 ng/dl in second trimester and 0.47-5.10 ng/dl in third trimester²⁴ and Maji R et al 0.64-2.00 ng/dl, 0.53-2.02 ng/dl in second trimester and 0.64-1.99 ng/dl in third trimester²⁵.

Our study also matches the findings of these surveys. The major difference between these studies and our study is that they have estimated Total T3 and Total T4 as well while we have done Free T3 and FreeT4.

Indian thyroid society recommends screening of all pregnant females at first antenatal visits by measuring TSH level.

V. Conclusion

Free T3 and FreeT4 level increases subsequently from first to third trimester and TSH level decreases from first to third trimester.

Reference

- [1]. Glinoe D : The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. *Endocr Rev* 1997 ; 18 : 404–433.
- [2]. Brent GA : Maternal thyroid function: Interpretation of thyroid function tests in pregnancy. *Clin Obstet Gyn* 1997 ; 40 : 3–15.
- [3]. Kol S, Karnieli E, Kraiem Z, Itskovitz-Eldor J, Lightman A, Ish-Shalom S Thyroid function in early normal pregnancy: Transient suppression of thyroid-stimulating hormone and stimulation of triiodothyronine . *Gynecol Obstet Invest* 1996 ; 42 : 227–229.
- [4]. Glinoe D : Maternal thyroid function in pregnancy. *J Endocrinol Invest* 1993 ; 16 : 374–378.
- [5]. Burrow GN, Fisher DA, Larsen PR : Maternal and fetal function. *N Engl J Med* 1994 ; 331 : 1072–81.
- [6]. Strucker RT, Perez V, Quinn and Stricker Rn. evaluation of maternal thyroid function during pregnancy: the importance of using gestational age specific reference interval. *European journal of endocrinology*, 2007, 157, 509-514.
- [7]. Laulu LS and Robert WI. Second trimester reference interval for thyroid test; The role of ethnicity. *clinical chem* 2007; 53: 658-664.
- [8]. Man EB, Jones WS. Thyroid function in human pregnancy. V. Incidence of maternal serum low butanol-extractable iodine and of normal gestational TBG and TBPA capacities; retardation of 8-month-old infants. *Am J Obstet Gynecol* 1969 ; 104: 898–908.
- [9]. Davis LE, Leveno KJ, Cunningham FG. Hypothyroidism complicating pregnancy. *Obstet Gynecol* 1988 ; 72 : 108–12.
- [10]. Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. Perinatal outcome in hypothyroid pregnancies. *Obstet Gynecol* 1993 ; 81 : 349–53.
- [11]. Allen WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, et al.: Maternal thyroid deficiency and pregnancy complications: implications for population screening. *J Med Screen* 2000 ; 7 : 127–30.
- [12]. Delange F, Burgi H : Iodine deficiency disorders in Europe. *Bull WHO* 1989 ; 67 : 317–325.
- [13]. Delange F, Dunn JT, Glinoe D : 1993 General comments, conclusions and final recommendations. In : Delange F, Dunn JT, Glinoe D (eds) *Iodine Deficiency in Europe : A Continuing Concern*. NATO ASI Series (Vol 241) . Plenum Press, New York, pp 473–478.
- [14]. Williams obstetrics 22nd ed. Maternal Physiology, 121-50.
- [15]. Glinoe D, De Nayar P et al : Regulation Of Maternal Thyroid During Pregnancy, *J Clin Endocrinol metab* 1990 ; 71 : 276.
- [16]. Laurell CB, Rannevik G: A comparison of plasma protein changes induced by danazol, pregnancy, and estrogens. *J Clin Endocrinol Metab* 1979 ; 49 : 719-725.
- [17]. Skjoldebrand L, Brundin J, Carlstrom A, Pettersson T : Thyroid associated components in serum during normal pregnancy. *Acta Endocrinol (Copenh)* 1982 ; 100 : 504–511.
- [18]. Sparre LS, Brundin J, Carlstrom K, Carlstrom A : Oestrogen and thyroxine-binding globulin levels in early normal pregnancy. *Acta Endocrinol (Copenh)* 1987 ; 114 : 298–304.
- [19]. Brent GA : Maternal thyroid function: interpretation of thyroid function tests in pregnancy. *Clin Obstet Gynecol* 1997 ; 40 : 3–15.
- [20]. Marwah RK, Chopra S, Gopalakrishna Set Al Establishment of normal range of thyroid hormone in normal pregnant Indian women *BJOG* 2008; 115: 602-6.
- [21]. Rajput R, Goel V, Nanda S, Rajput M. Prevalence of thyroid dysfunction among women during the first trimester of pregnancy in a tertiary care hospital in Haryana. *Indian Journal of Endocrinol metabolism* 2015; 19: 416-9.
- [22]. Sekhri T, Juhi JA, Wilfred R, Kanwar RS, Sethi J et al Trimester Specific reference interval for thyroid function tests in normal Indian pregnant women. *Indian Journal of Endocrinol metabolism* 2016; 20: 101-7.
- [23]. Jebasingh FK, Salam R Reference interval in evaluation of maternal thyroid function test of Manipuri women. *Indian Journal of Endocrinol metabolism* 2016; 20: 167-70.
- [24]. Mankar J, Sahasrabudhe A, Pitale S. Trimester specific reference range for Thyroid hormones in normal pregnancy. *Thyroid Res Pract* 2016; 13: 106-9.
- [25]. Maji R, Nath S, Lahiri S, Saha Das M: Establishment of Trimester Specific reference interval for serum TSH and FT4 in pregnant Indian population

Dr Avnish Kumar Tarwey, et. al. "Comparative study of Thyroid hormone in different trimester of normal pregnancy: A Jharkhand Population Based study." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(5), 2020, pp. 28-31.