

Standard practice recommendations (SPR)

Hypothyroidism in Pregnancy



2022

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MESSAGE BY PRESIDENT AMOGS



Dear Members,

I am very much happy and proud to put forward these AMOGS - Standard Practice Recommendations on Hypothyroidism in pregnancy. This is an era of evidence based medicine. Keeping in this mind we have introduced AMOGS-SOPs and Guidelines committee from this year. I am very much happy that first chairperson of this committee, Dr. Gorakh G. Mandrupkar has started the work in a very magnificent manner. He has involved the members from all parts of Maharashtra as experts for making these SPR as- ...of AMOGS...by AMOGS and ...for AMOGS. These SPR are reviewed by the stalwarts and senior teachers in the subject. I hope these SPR will be useful to the obstetricians at all levels of healthcare facilities. I congratulate Dr. Gorakh G. Mandrupkar and his team for this collaborative scientific work.

Date: 23/09/2022

Dr. Rajendrasingh Pardeshi

President, AMOGS 2022

MESSAGE BY CHAIRPERSON



Respected colleagues,

First of all, I am thankful to AMOGS president, Dr. Rajendrasingh Pardeshi for his trust on me to work as chairperson of this newly introduced committee. Increasing evidence suggests that the timely screening, prevention and early intervention will reduce the maternal and perinatal morbidity and mortality caused by the medical disorders of pregnancy. We have tried to make a simplified document in a systematic and scientific manner on pregnancy hypothyroidism. I am very much thankful to all expert members and the stalwarts in review committee without whom this task was not possible. Thank you all.

Date: 23/09/2022

Dr. Gorakh G. Mandrupkar

Chairperson, SOPs and Guideline Committee,
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AMOGS: Standard Practice recommendations: Hypothyroidism in pregnancy

Introduction:

Thyroid disorders especially uncontrolled hypothyroidism during pregnancy has profound effects on gestation, the mother and even neonates like the occurrence of late intellectual problems.

Increasing evidence suggests that the early identification and intervention in the form of thyroid hormone supplementation in cases of thyroid hypofunction has reduced pregnancy complications much more.

Need for standard practice recommendations (SPR):

AMOGS -SOPs and Guidelines Committee, after making surveys and discussions with many members in almost all parts of Maharashtra has come to the conclusion that simplified and clear recommendations are needed to standardize and universalize the antenatal care.

Process of preparing SPRs:

Almost all Indian and western guidelines and recommendations regarding thyroid disorders in pregnancy were reviewed. National and international research papers were also studied.

After initial opinion building, the SPRs were reviewed by expert review committee.

Women from most rural area to women from metro cities of Maharashtra are accounted and considered for the SPR.

The motto behind preparing these recommendations is very honest and clear i.e. to reduce the maternal and neonatal morbidity and mortality due to the complications of hypothyroidism.

Review of SPRs:

The SOPs and Guidelines Committee, AMOGS 2022-24 recommends that after every 3 years these guidelines must be reviewed and necessary changes must be made.

DISCLAIMER

We do not claim that these recommendations are the last word. Medical science and clinical research are ongoing phenomenon. However all possible efforts were taken to prepare and depict these standard practice recommendations.

The recommendations given here do not guarantee any specific outcome and hence are not intended to dictate the treatment of a particular patient.

Obstetricians must rely on their own experience and knowledge to make diagnosis, determine dosages and the best treatment for each individual patient and at the same time take appropriate safety precautions and opinions.

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DEFINITIONS

For all practical purposes, the definitions are made simple and self explanatory.

Euthyroid means having normal functioning of thyroid gland with normal FT4 and TSH.

Subclinical Hypothyroidism (in pregnancy)-

It is biochemical representation of thyroid hormone deficiency.

Thyroid Stimulating Hormone (TSH) > 2.5 mIU to 10 mIU; with normal free Thyroxine (FT4) levels is called as subclinical hypothyroidism.

Overt Hypothyroidism (in pregnancy)-

It is actually the hypo-functioning of thyroid gland.

TSH > 2.5 mIU/L to 10 mIU/L; with low FT4 levels is called as overt hypothyroidism.

Also,

TSH > 10 mIU/L even with normal FT4 is considered as overt hypothyroidism.

Thyroid antibodies:

There are three types of antibodies those can be present in thyroid disease.

1. **Anti-TPO antibodies-** Thyroid peroxidase (TPO) is an important enzyme in the formation of thyroid hormones in thyroid gland. Antibodies developed against it are called as anti-TPO antibodies.
2. **Anti-Tg antibodies-** Thyroglobulin (Tg) also takes part in the formation of thyroid hormones. Antibodies developed against it are called as anti-Tg antibodies.
3. **Anti-Tr antibodies-** TSH bind the receptors on thyroid gland to make it release T3 and T4 hormones. Antibodies developed against receptor are called as anti-Tr antibodies.

SCREENING FOR THYROID DISORDERS IN PREGNANCY

After long debates, discussions and reviews, we at AMOGS recommend **Universal Screening** for thyroid disorders in pregnancy by measuring **serum TSH**.

Why universal screening?

Hypothyroidism has ill effects on pregnancy.

Undiagnosed and untreated hypothyroidism may lead to-

1. Miscarriages
 2. Preterm birth
 3. Intrauterine fetal death
 4. Increased incidence of Hypertensive disorders of pregnancy
 5. Increased incidence of postpartum hemorrhage
 6. Low birth weight baby
 7. Respiratory distress and neonatal hospitalization
 8. Possibility of birth defects and low IQ baby
- Maternal euthyroidism is essential throughout pregnancy for normal development of fetus, maintaining the fetoplacental communication and maternal well being as well.
 - Hypothyroidism is considered individually as moderate risk factor in the clinical risk factor assessment for hypertensive disorders of pregnancy.
 - Not only overt but subclinical hypothyroidism has similar ill effects.

How to screen?

AMOGS recommends the universal screening for thyroid disorders by measuring **serum TSH levels preferably in morning fasting status** and preferably in **each trimester**.

Assessment of T3 and T4 levels may mislead and is not recommended.

Screening for Thyroid antibodies during pregnancy-

AMOGS does not recommend screening for thyroid antibodies in pregnancy as routine. In hyperthyroid women these can be assessed for analyzing the cause and prognosis.

CLASSIFICATION OF HYPOTHYROIDISM IN PREGNANCY

How to classify?

Those pregnant women, who are screen positive, must be assessed clinically and with Free T4 levels to classify further as subclinical or overt variety.

Cut-off levels for TSH during pregnancy:

We have accepted following levels, as recommended in our Indian national guidelines.

First Trimester	:	0.1- 2.5 mIU/L
Second Trimester	:	0.2- 3.0 mIU/L
Third Trimester	:	0.3- 3.0 mIU/L

Frequency of TSH monitoring:

During treatment of hypothyroidism, only serum TSH is to be monitored and is maintained between trimester specific ranges.

Frequency recommended is at every 4-6 weeks.

Frequency of FT4 monitoring:

In screen positive women, assessment of FT4 is to be done for classification of hypothyroidism.

The increments or decrements of L-thyroxine doses will depend on TSH values and not on FT4.

MANAGEMENT OF HYPOTHYROIDISM IN PREGNANCY

Hormone replacement therapy using L-Thyroxine is the gold standard treatment.

Preparations with thyroid extract or other alternative medicines are not recommended.

Ideal timing to take L-thyroxine tablets:

It is a consensus opinion that L-Thyroxine tablet is to be taken in fasting status as first thing in morning at least an hour before eating or it can be taken 3-4 hours after dinner.

Calcium tablets or calcium rich food like milk, cheese should not be taken with L-thyroxine as it may reduce the absorption of L-thyroxine.

Newly diagnosed subclinical hypothyroidism:

The dosage recommended for newly diagnosed subclinical hypothyroid pregnant woman is Thyroxine 25-50 µg/day.

Known case of subclinical hypothyroidism and now has become pregnant:

The increment in the dosage of thyroxine for such pregnant woman may be required. TSH is to be done and now read as pregnancy cut off levels. Increment, if required is to be done with additional 25µg/day. For example, if she is already on 25µg/day before pregnancy, her dose of thyroxine after detection of pregnancy will be $25+25=50$ µg/day and so on.

Newly diagnosed overt hypothyroidism:

The dosage recommended for newly diagnosed overt hypothyroid pregnant woman is Thyroxine 75-100µg/day.

Known case of overt hypothyroidism and now has become pregnant:

The increment in the dosage of thyroxine for such pregnant woman may be required. TSH is to be seen and now read as pregnancy cut off levels. Increment, if required is to be done with additional 25µg/day. For example, if she is already on 75 µg before pregnancy, her dose of thyroxine after detection of pregnancy will be $75+25=100$ µg/day and so on.

Increments in dosages of Thyroxine during pregnancy:

TSH should be monitored every 4-6 weeks.

At all times, TSH >2.5 in first trimester and TSH >3.0 in second and third trimester is to be avoided. Such situation is handled by increasing the dose of thyroxine by $25\mu\text{g}/\text{day}$. For example, if she is already on $75\mu\text{g}/\text{day}$ and TSH is >2.5 in first trimester or >3.0 in second and third trimester then dose of thyroxine will be $75+25=100\mu\text{g}/\text{day}$.

Decrements in dosages of Thyroxine during pregnancy:

TSH should be monitored every 4-6 weeks.

At all times TSH <0.1 is to be avoided.

Such situation is handled by decreasing the dose of Thyroxine by $25\mu\text{g}$. For example, if she is already on $75\mu\text{g}$ and TSH <0.1 then dose of thyroxine will be $75-25=50\mu\text{g}/\text{day}$.

Postpartum period:

1. Those woman having subclinical hypothyroidism and were on Thyroxine $25\mu\text{g}/\text{day}$ during pregnancy, the treatment should be stopped from day of delivery.
2. Those woman having subclinical hypothyroidism and were on Thyroxine more than $25\mu\text{g}/\text{day}$, the dose of thyroxine should reduced by $25\mu\text{g}$ in postpartum period.
3. Those woman having overt hypothyroidism and were on Thyroxine more than or equal to $50\mu\text{g}/\text{day}$, the dose of thyroxine should be continued as it is.
4. Those women having pre pregnancy hypothyroidism and needed increments during pregnancy must be shifted back to pre pregnancy doses of Thyroxine.

TSH levels must be done after 6 weeks and treatment is decided as per non pregnant levels of TSH.

Other medications:

1. Recent evidence shows that hypothyroidism and vitamin D3 deficiency go hand in hand. Standard and safe doses of vitamin D3 recommended in pregnancy are to be continued.
2. Hypothyroidism in pregnancy is considered as moderate risk factor for development of hypertensive disease in pregnancy (HDP). If present with any other known mild, moderate or high risk clinical factor for HDP, we endorse prevention of HDP in the form of daily low dose aspirin 75 mg at bed time and calcium $1-1.5\text{ grams}$ daily in divided doses.

PRECONCEPTION CARE

1. Pre-pregnancy check up for thyroid disorders in all women who are planning pregnancy should be offered.
2. The women with hypothyroidism should plan the pregnancy when their TSH level is normal.
3. L-thyroxine treatment can improve embryo quality, implantation rate and live birth rate in infertile women even with subclinical hypothyroidism undergoing IVF/ICSI.

HYPOTHYROIDISM AND MEDICAL TERMINATION OF PREGNANCY

1. We re-emphasize the need of pre-pregnancy normalization of thyroid dysfunction.
2. We are of same opinion as all national and international guidelines that overt hypothyroidism cannot be the sole reason for recommending MTP.
3. The decision to continue or terminate pregnancy will vary from case to case based on multiple factors like severity of overt hypothyroidism, gestation at which overt hypothyroidism is diagnosed, age of woman, presence of other medical disorders like diabetes, iodine nutrition status, past history of infertility and miscarriages, past and family history of fetal congenital malformations. The shared decision of obstetrician and the pregnant woman is recommended.

REFERENCES AND FURTHER READINGS

1. Maternal health division, Ministry of health and family welfare, Government of India. 2014 National guidelines for screening of hypothyroidism during pregnancy.
2. Federation of Obstetric and Gynecological Associations of India and Indian Thyroid society, recommendations for management of thyroid dysfunction in pregnancy, 2019.
3. Practice committee of the American Society for Reproductive Medicine. Subclinical hypothyroidism in the infertile female population: A guideline. *Fertil and Steril* 2015; 104:545–53.
4. FIGO working group on good clinical practice in maternal-fetal medicine. Good clinical practice advice: Thyroid and pregnancy. *Int. J Gynecol Obstetr* 2019; 144(3):347-51.
5. Thyroid disease and pregnancy. The American Thyroid Association. <https://www.thyroid.org/wp-content/uploads/patients/brochures/ata-thyroid-disease-pregnancy-brochure.pdf>.
6. 2012 Indian Thyroid Society guidelines for management of thyroid dysfunction during pregnancy. Clinical practice guidelines. Elsevier. New Delhi.
7. Alex Stagnaro-Green, Abalovich M, Alexander E, *et al*. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. The American Thyroid Association taskforce on thyroid disease during pregnancy and postpartum. Available from: <http://thyroidguidelines.net/hyperthyroidism/results>.
8. Unnikrishnan AG, Kalra S, Baruah M, *et al*. Endocrine Society of India management guidelines for patients with thyroid nodules: A position statement. *Indian J Endocrinol Metab*. 2011; 15(1):2–8.
9. Banerjee S. Thyroid disorders in pregnancy. Special issue on Indian thyroid guidelines 2011. *JAPI*. 2011; 59 (Suppl):32-34.
10. Dhanwal DK, Bajaj S, Rajput R, *et.al*. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. *Indian J Endocrinol Metab*. 2016; 20(3):387–90.
11. Marwaha RK, Chopra S, Gopalakrishnan S, *et al*. Establishment of reference range for thyroid hormones in normal pregnant Indian women. *BJOG*. 2008; 115(5):602-06.
12. Kalra S, Agarwal S, Aggarwal R and Ranabir S. Trimester-specific thyroid-stimulating hormone: An Indian perspective. *Indian J Endocr Metab* 2018; 22:1-4.
13. Nambiar V, Jagtap VS, Sarathi V, *et al*. Prevalence and impact of thyroid disorders on maternal outcome in Asian-Indian Pregnant Women. *J Thyroid Res*. 2011; 429097.
14. Sahu MT, Das V, Mittal S, *et al*. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch Gynecol Obstet*. 2010; 281(2):215-20.
15. Vaidya B, Anthony S, Bilous M, *et al*. Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? *J Clin Endocrinol Metab*. 2007; 92(1):203-07.
16. Nuzhat A, Pranathi R, Evita F. Hypothyroidism in pregnancy: Is universal screening needed? *J Obstet Gynecol India*. 2006; 56(6):495-98.
17. Goel P, Radotra A, Devi K, *et al*. Maternal and perinatal outcome in pregnancy with hypothyroidism. *Indian J Med Sci*. 2005; 59 (3):116-17.

18. Tiwari BD, Godbole MM, Chattopadhyay N, *et al.* Learning disabilities and poor motivation to achieve due to prolonged iodine deficiency. *Am J Clin Nutr.* 1996; 63(5):782–86.
19. Gayathri R, Lavanya S, Raghavan K. Subclinical hypothyroidism and autoimmune thyroiditis in pregnancy - A study in south indian subjects. *JAPI.* 2009; 57:691-93.
20. Unnikrishnan AG. Maternal hypothyroidism. *KMJ.* 2008; 4:19-23.
21. Rajput R, Singh B, Goel V, *et al.* Trimester specific reference interval for thyroid hormones during pregnancy at a tertiary care hospital in Haryana, India. *Ind J Endocrinol and Metab* 2016; 20(6):810-15.
22. Vaidya B, Hubalewska-Dydejczyk A, Laurberg P, *et al.* Treatment and screening of hypothyroidism in Pregnancy: Results of a European survey. *Eur J Endocrinol.* 2011. doi: 10.1530/EJE-11-0729.
23. Unnikrishnan AG. Management of maternal hypothyroidism: A practical perspective. *Thyroid Res and Pract.* 2009; 6(1):6-11.
24. Sahay R, Kalra S, Magon N. Ensuring an intelligent India: Managing hypothyroidism in pregnancy. *Indian J Endocrinol Metab.* 2011; 15(Suppl 2):S76–S77.
25. Negro R, Formoso G, Mangieri T, *et al.* Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: Effects on obstetrical complications. *J Clin Endocrinol Metab.* 2006; 91(7):2587-91.
26. Mithal A, Kalra S. Vitamin D supplementation in pregnancy. *Indian J Endocrinol Metab.* 2014 Sep; 18(5):593-6. doi: 10.4103/2230-8210.139204. PMID: 25285272; PMCID: PMC4171878.
27. Kim CH, Ahn JW, Kang SP, *et al.* Effect of Levothyroxine treatment on *in vitro* fertilization and pregnancy outcome in infertile women with subclinical hypothyroidism undergoing *in vitro* fertilization/intracytoplasmic sperm injection. *Fertil Steril.* 2011; 95(5):1650-54.
28. Velkeniers B, Van Meerhaeghe A, Poppe K, *et al.* Levothyroxine treatment and pregnancy outcome in women with subclinical hypothyroidism undergoing assisted reproduction technologies: Systematic review and meta-analysis of RCTs. *Hum Reprod Update.* 2013; 19(3):251-58.
29. Kalra, Sanjay & Ganie, Mohd Ashraf & A G, Unnikrishnan. (2013). Overt hypothyroidism in pregnancy: Can we consider medical termination of pregnancy?. *Indian journal of endocrinology and metabolism.* 17. 197-9. 10.4103/2230-8210.109655.

