PREVALENCE OF THYROID DISORDERS AMONG PREGNANT AND NON-PREGNANT WOMEN ATTENDING A TERTIARY CARE CENTER IN KATHMANDU

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ABSTRACT

Thyroid hormones are crucial for the overall development of the fetus, and their impact on the pregnancy outcomes needs to be considered seriously. Hence, universal screening for thyroid disorders is recommended in the first trimester of pregnancy. One hundred pregnant women in their first trimester and 100 non-pregnant women of the reproductive age group were screened for thyroid function test. The prevalence of thyroid disorders among the total participants was 32.0% of which 23.5% were hypothyroid and 8.5% were hyperthyroid. Pregnant females had a significantly higher prevalence of thyroid disorders (46.0%) than non-pregnant counterparts (18.0%; P <0.001). Pregnant females had significantly higher odds of hypothyroid disorders than non-pregnant females (OR 3.95; P <0.001). The prevalence of subclinical hypothyroidism among pregnant and non-pregnant was 34.0% and 12.0% respectively which makes it the most common thyroid disorder in both study groups. The median values of FT3, FT4, and TSH levels were, however, not significantly different between the study groups. After adjusting for the confounding effect of age, the odds of thyroid disorders were still significantly higher in pregnant women than in non-pregnant (p =0.001). The prevalence of thyroid disorders, specifically hypothyroidism, is higher in pregnant women compared to non-pregnant counterparts. And this emphasizes on the need of antenatal thyroid screening to be made mandatory in the health policy.

KEYWORDS

Hypothyroidism, hyperthyroidism, subclinical, overt, pregnant and non-pregnant women

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INTRODUCTION

Thyroid hormones are crucial for the overall development of the fetus, and their impact on the pregnancy outcomes needs to be considered seriously.[1,2] Various physiological changes like increased thyroid hormone-binding globulin concentration, increased iodine clearance in the kidneys, and thyrotropic effect of human chorionic gonadotropin etc. happening during pregnancy might lead to alteration in thyroid functions which are associated with an increased risk of miscarriage, placental abruption, preterm delivery, preeclampsia, and physical and mental growth restriction in fetus, if timely treatment is not sought.[3] Assessment of thyroid function during pregnancy is essential for both maternal and fetal health outcomes. Hence, universal screening for thyroid disorders is recommended in the first trimester of pregnancy.[4] Data shows at least 2.0% - 3.0% of women of the reproductive age group are affected by thyroid problem,[5] making it the second most common endocrine disorders seen in pregnant women.[6]

A thyroid screening or thyroid function test (TFT) is a blood test that includes thyroid stimulating hormone (TSH), free thyroxine (FT_4), and free triiodothyronine (FT_3). Thyroid antibody tests like anti-thyroid peroxidase may also be done if required.[7] Thyroid disorders can be categorized into hypothyroidism and hyperthyroidism.[8] Several studies show the prevalence of thyroid disorders to range from 2.8% to 18.7% amongst the Indian pregnant population.[9,10] The prevalence of 24.0%, 29.0% and 39.5% were reported by different studies conducted in Kathmandu.[11-13] Also, one study from Western Nepal has reported the prevalence of hypothyroidism to be 44.0%.[14] These data show the higher prevalence of thyroid disorders among pregnant women in Nepal compared to India. However, such studies, especially comparative studies, from Nepal are not available. Also, the data on the burden of thyroid disorders among the Nepalese pregnant women is not well established. This study aims to study the prevalence of thyroid disorders in pregnant women as compared to non-pregnant females of reproductive age-group.

MATERIALS AND METHODS

Ethical approval (Ref. No.: 16-079/080) was obtained from the Institutional Review Committee at Nepal Medical College (NMC-IRC) for this hospital-based observational cross-sectional study. The study was conducted in the Department of Obstetrics and Gynecology, Nepal Medical College Teaching Hospital (NMCTH) from September 2022 to May 2023. Study participants were divided into two groups: pregnant and non-pregnant. One hundred pregnant women of 18-49 years, in their first trimester coming for antenatal check-ups were selected irrespective of their gravida status (primigravida or multigravida) and parity. Apparently healthy 100 non-pregnant women of the similar age group visiting NMCTH laboratory for routine examination were counseled for TFT. Informed verbal and written consent was taken from both the groups prior to the study. Socio-demographic and medical history were recorded, and those with previous history of thyroid dysfunction and or under medication for it were excluded. A convenience sampling technique was used for selection of participants and the sample size was calculated using following formula: $N = z^2pq/d^2$

All the participants were screened for TFT which was done using enhanced chemiluminescence immunoassay (ECLIA) in the laboratory of NMCTH. The reference range used in the study was based on the guidelines of the American Thyroid Association (ATA) 2017 according to which the upper limit of TSH should be 2.5 µIU/L in the first trimester, and 3.0 µIU/L in the second and third trimesters.[15] The reference range for TFT parameters used for the non-pregnant women according to the laboratory of NMCTH was: FT_3: 2.77-5.27 pg/ml, FT_4: 0.78-2.19 ng/dl and TSH: 0.465-4.68 µIU/ml.

According to the ATA guidelines, pregnant women will be classified into five groups:[15]

1. Subclinical hypothyroidism (SCH): High serum TSH level with normal FT_4, FT_3 level.
2. Overt hypothyroidism (OH): High serum TSH level with FT_4, FT_3 level less than the normal range.
3. Normal (Euthyroid).
4. Subclinical hyperthyroidism: Low serum TSH level with normal FT_3, FT_4 level.
5. Overt hyperthyroidism: Low serum TSH level with FT_3 and FT_4 more than the normal range.

Data was analyzed using SPSS-16. Normality distribution of the variables were tested. Accordingly, continuous data were expressed as median (IQR) and categorical data as counts (percentages). Prevalence of thyroid disorders along with their 95.0% confidence interval (CI) were calculated. Odds ratio for hypothyroidism,

hyperthyroidism, and thyroid disorders were calculated. Mann-Whitney U test, Chi-square analysis, and binary logistic regression analysis were performed. P value of less than 0.05 was considered as statistically significant at 95.0% confidence intervals.

RESULTS

A total of 200 participants within 18-49 years were recruited in the study of which 100 were pregnant and 100 were non-pregnant. The median age of the participants was 30 years. The prevalence of thyroid disorders among the total participants was 32.0% of which 23.5% were hypothyroid and 8.5% were hyperthyroid. Pregnant females had significantly higher prevalence of thyroid disorders (46.0%) than non-pregnant females (18.0%; P <0.001). Pregnant females had significantly high odds of hypothyroid disorders than non-pregnant females (OR 3.95; P <0.001). The distribution of thyroid disorders among total participants and study groups are presented in table 1 and table 2. The prevalence of SCH among pregnant and non-pregnant women was 34% and 12 % respectively. The sub-group wise distribution of thyroid disorders is shown in figure 1. The median values of FT_3, FT_4, and TSH levels were, however, not significantly different between the study groups (table 3). Pregnant females had significantly lower age than non-pregnant females (P < 0.001). After adjusting for the confounding effect of age, the odds of thyroid disorders were still significantly higher in pregnant women than non-pregnant (p = 0.001) as shown in table 4.

DISCUSSION

Thyroid disorders represent a prevalent clinical issue in females of childbearing age, with an even higher incidence among pregnant women due to the significant alterations in thyroid gland functions during pregnancy. Most of the studies about the thyroid disorders are done among pregnant women only. To the best of our knowledge, this is the first study in Nepal

Table 1: Prevalence of thyroid disorders among the total participants and the study groups

	Thyroid disorders		Euthyroid		
	Prevalence % (95.0% CI)	n	Prevalence % (95.0% CI)	n	P value
Total participants (N = 200)	32 (25.5 – 38.5)	64	68 (61.5 – 74.5)	136	
Pregnant (N = 100)	46 (36.1 – 55.9)	46	54 (44.1-63.9)	54	**<0.001**
Non- pregnant (N = 100)	18 (10.3 – 25.7)	18	82 (74.3 -89.7)	82	

P- value obtained from chi-square analysis. p <0.05 considered statistically significant.

Table 2: Prevalence of hypothyroid and hyperthyroid disorders along with their OR

	Thyroid Disorder		Odds Ratio (Hypothyroidism)		Odds Ratio (Hyperthyroidism)	
	Hypothyroidism (prevalence % with 95.0% CI)	Hyperthyroidism (prevalence % with 95.0% CI)	OR	P- value	OR	P-Value
Total participants (N = 200)	23.5 (17.6 – 29.4)	8.5 (4.6 – 12.4)	N/A		N/A	
Pregnant (N = 100)	35 (25.5 – 44.5)	11 (4.8 – 17.2)	3.95	**0.0002**	1.94	0.211
Non- pregnant (N = 100)	12 (5.5 – 18.5)	6 (1.3 – 10.7)				

N/A = Not applicable. P <0.05 considered statistically significant

Table 3: Median values of thyroid function parameters and age between the study groups			
Thyroid Hormones	**Pregnant Median (IQR)**	**Non - Pregnant Median (IQR)**	**P value**
FT_3 (pg/ml)	3.58 (3.24 - 3.89)	3.75 (3.20 – 4.22)	0.153
FT_4 (ng/dl)	1.06 (0.87 - 1.23)	1.10 (0.94 – 1.27)	0.208
TSH (IU/ml)	1.72 (1.11 – 3.95)	2.24 (1.20 – 3.47)	0.360
Age (years)	27 (24-31.75)	34 (27- 40)	**< 0.001**

P-values obtained from Mann-Whitney U test. P <0.05 considered statistically significant.

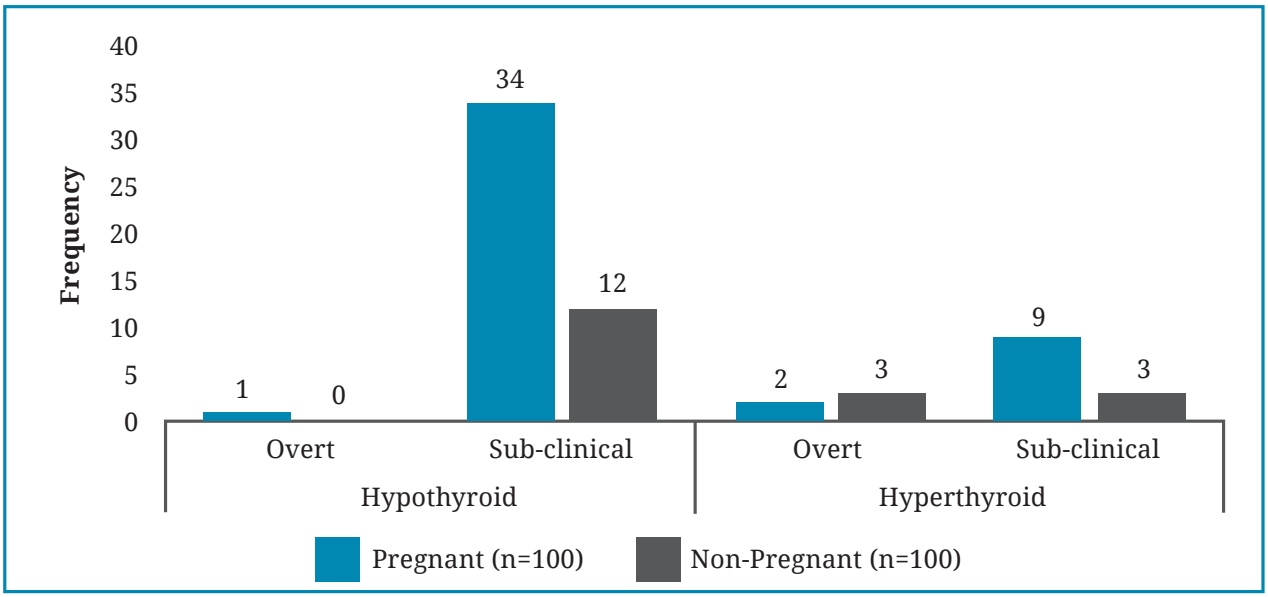

Fig. 1: Frequency distribution of sub-clinical and overt thyroid disorders

Table 4: Unadjusted and adjusted odds ratio of thyroid disorders between study groups					
	Coefficient (β)	**Unadjusted Odds Ratio**		**Adjusted Odds Ratio**	
		OR	**P -value**	**OR (exp β)**	**P - value**
Pregnancy status (Pregnant)	1.168	3.88	**<0.001**	3.21	**0.001**

Adjusted OR and P-values from binary logistic regression analysis. Dependent variable = Thyroid status (Euthyroid/ Thyroid disorder); Independent Variable = Pregnancy status (Pregnant/non-pregnant). OR and P-value adjusted for age as participants ages were significantly different between the study group (See table 3).

which compares the prevalence of thyroid disorders among pregnant and non-pregnant women of the reproductive age group.

The current investigation reveals a notable prevalence of undetected thyroid disorders, standing at 46% among pregnant women in their first trimester and 18% among their non-pregnant counterparts. This prevalence is even higher than the previously reported prevalence of 39.48% in a study conducted in Obstetrics and Gynaecology department of Tribhuvan University Teaching Hospital, Kathmandu from 2020 to 2021 among the pregnant women in their first trimester.[13] Other studies conducted by Shrestha *et al*[11] and Khakurel *et al.*[12] in tertiary care centers in Kathmandu reported a slightly lower prevalence of 29% and 24.62% for thyroid disorders respectively.[11,12] Additional studies by Upadhyaya *et al*[14] conducted in western Nepal

and Chaudhary *et al*[16] conducted in eastern Nepal, documented prevalence rates of 44.0% and 20.6%, respectively. Possible explanations for these variations include geographical distinctions between central, western, and eastern Nepal, also the dietary differences and the implementation of different upper limit cutoff values for TSH. The notable difference in thyroid disorder rates between pregnant and non-pregnant females in our study may also be attributed to the utilization of trimester-specific TSH cutoff values for pregnant women and laboratory-specific TSH cutoff values for non-pregnant women.

In India too, numerous studies have affirmed the significant geographic variability in the prevalence of hypothyroidism during pregnancy. Gayathri *et al*[9] found a 2.8% prevalence of hypothyroidism among pregnant women in Chennai, whereas Sahu *et al*[17] reported that 11.0% of pregnant women had hypothyroidism (6.5% SCH and 4.6% OH). Nambiar *et al*[18] documented a 4.8% prevalence of hypothyroidism in the pregnant women during their first trimester, much lower than observation by Dhanwal *et al*[19] at 14.3%. An alarming prevalence of 18.7% of antenatal thyroid dysfunction was reported by Bandela *et al*[10] from Andhra Pradesh and majority (10.0% SCH, 2.9% OH) of them had hypothyroidism. Various possible reasons for higher prevalence of hypothyroidism in Asian population have been suggested which include increased iodine intake, presence of goitrogens in diet, deficiency of selenium, iron in the diet.[20,21]

Normal upper limit of TSH in pregnancy has been a topic of ongoing debate. In the current study, we utilized trimester-specific cut-offs based on the recent ATA guidelines for diagnosis. This approach revealed a substantial 46% prevalence of thyroid dysfunction in pregnant women, contrasting with various studies in different regions of Nepal where higher cut-offs, based on non-pregnant kit reference values, were employed. For instance, Khakurel *et al*[11] used a TSH range of 0.3 - 4.5 mIU/L in her Kathmandu study, while Upadhyaya *et al*[14] in his study in the western Nepal employed a TSH cut-off of 6 mIU/L as the cut-off. Similarly, in eastern Nepal, Chaudhary *et al*[16] used a cut-off value of 0.39-6.16 mIU/L for TSH in interpreting the TFT results among the pregnant population. Notably, the prevalence of SCH surged to over 50.0% in a study by Dhanwal *et al*,[17] who utilized a first-trimester-specific TSH cut-off of 2.5 mIU/L, deviating from the non-pregnant TSH cut-off of 4.5 mIU/L. These variations underscore the importance of considering TSH cut-off values in pregnant women before evaluating and interpreting the prevalence rates of thyroid dysfunctions.

Hypothyroidism is more common than hyperthyroidism in the general population and this pattern extends to pregnant women as well. In the present study, 35.0% had hypothyroidism of which only 1.0% had OH, while the majority exhibited the SCH (34.0%). Approximately close prevalence of 28.8% of SCH were reported in the study of Sharma *et al*.[13] Additionally, 9.0% of pregnant women in this study were identified with subclinical hyperthyroidism, indicating a relatively high prevalence compared to other researches. For instance, Shrestha *et al*[12] reported a 2.6% prevalence of subclinical hyperthyroidism in a study conducted at a tertiary hospital in Kathmandu. Furthermore, Pahwa *et al*[22], Mahadik *et al*,[23] and Gupta *et al*[24] observed prevalence rates of 2.0%, 1.5%, and 3.1%, respectively, for subclinical hyperthyroidism among the pregnant Indian population in their respective studies. The observed discrepancies may also be attributed to the diverse cut-off values for TSH in diagnosing hyperthyroidism, as previously mentioned. Presently, there is no established association between subclinical hyperthyroidism and pregnancy outcomes, and therefore, the identification and treatment of this condition during pregnancy are not considered necessary.[25]

In our study, the odds of thyroid disorders were significantly high in pregnant females compared to non-pregnant counterparts (adjusted OR 3.21; p =0.001). This was especially evident for hypothyroid disorders (OR =3.95; P =0.0002). These results strongly support and advocate for the importance of screening for thyroid dysfunction during early pregnancy. However, thyroid disease can equally affect women either before, during, or immediately after pregnancy. Moreover, careful consideration of TSH cut-off levels seems to be essential in the analysis and interpretation of the data.

This remarkably high prevalence of thyroid disorders among the Nepalese pregnant women compared to the previous studies and worldwide prevalence points towards the

urgent need of TFT screening policies to be made mandatory during antenatal visits in all the health care set ups of Nepal. Also, the need to establish nationwide or region-specific TSH cut-off ranges, especially for pregnant women cannot be underscored. This could be an area that requires further investigation.

LIMITATIONS: As this is a single center hospital based study conducted in a small sample, it may not represent the general population.

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REFERENCES

1. Davis LE, Leveno KJ, Cunningham FG. Hypothyroidism complicating pregnancy. *Obs Gynecol* 1988; 72: 108-12.
2. Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. Perinatal outcome in hypothyroid pregnancies. *Obs Gynecol* 1993; 81: 349-53.
3. Glinoer D, Nayer P, Bourdoux P *et al*. Regulation of maternal thyroid during pregnancy. *J Clin Endocrinol Metab* 1990; 71: 276-87. doi: 10.1210/jcem-71-2-276.
4. Dave A, Maru L, Tripathi M. Importance of universal screening for thyroid disorders in the first trimester of pregnancy. *Indian J Endocrinol Metab* 2014; 18: 735-8. doi: 104103/2230-8210139221.
5. Negro R, Mestman JH. Thyroid disease in pregnancy. *Best Pract Res Clin Endocrinol Metab* 2011; 25: 927-43.
6. Carney LA, Quinlan JD, West JM. Thyroid disease in pregnancy. *Am Fam Physician* 2014; 89: 273-8.
7. National Institute for Health and Care Excellence (NICE). Thyroid disease: assessment and management NICE Guideline, No. 145. London: National Guideline Centre (UK) 2019. ISBN-13 978-1-4731-3595-6.
8. Monaco F. Classification of thyroid diseases: Suggestions for a Revision. *J Clin Endocrinol Metab* 2003; 88: 1428-32. DOI: 10.1210/jc.2002-021260.
9. Gayathri R, Lavanya S, Raghavan K. Subclinical hypothyroidism and autoimmune thyroiditis in pregnancy-a study in south Indian subjects. *J Assoc Physicians India* 2009; 57: 691-3.
10. Bandela PV, Havilah P, Hindumathi M, Prasad KD. Antenatal thyroid dysfunction in Rayalaseema region: a preliminary cross sectional study based on circulating serum thyrotropin levels. *Int J Appl Biol Pharm Technol* 2013; 4: 74-8.
11. Khakurel G, Karki C, Chalise S. Prevalence of thyroid disorder in pregnant women visiting a tertiary care teaching hospital: a descriptive cross-sectional study. *J Nepal Med Assoc* 2021; 59: 51-4. DOI: 10.31729/jnma.5529.
12. Shrestha B, Adhikari P. Screening of thyroid disorder among pregnant ladies in a tertiary hospital of Nepal. *Nepal Med Coll J* 2019; 21: 235-9. DOI: https://doi.org/10.3126/nmcj.v2i3.26470.
13. Sharma SK, Gurung G, Katuwal N, Joshi PR, Chaurasia H, Lamsal S. Prevalence of thyroid dysfunction during first trimester of pregnancy: A descriptive cross-sectional study. *Reproductive Female Child Health* 2023; 2: 203-7.
14. Upadhyaya TL, KC A, Paudel S. Prevalence and complications of hypothyroidism during pregnancy in western Nepal. *Nepal J Med Sci* 2014; 3: 48-50. DOI: 103126/njms.v3i110358.
15. Alexander EK, Pearce EN, Brent GA *et al*. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017; 27: 315–89.
16. Chaudhary LN, Khatiwada S, Gelal B *et al*. Iodine and thyroid function status, and anti-thyroid peroxidase antibody among pregnant women in eastern Nepal. *J Nepal Health Res Counc* 2017; 15: 114-9. DOI: 10.3126/jnhrc.v15i2.18182.
17. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch Gynecol Obs* 2010; 281: 215-20. DOI: 10.1007/s00404-009-1105-1.
18. 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; 2011: 429097. DOI: 10.4061/2011/429097.
19. Dhanwal DK, Prasad S, Agarwal AK, Dixit V, Banerjee AK. High prevalence of subclinical hypothyroidism during first trimester of pregnancy in North India. *Indian J Endocrinol Metab* 2013; 17: 281-4. DOI: 104103/2230-8210109712.
20. Teng X, Shan Z, Chen Y *et al*. More than adequate iodine intake may increase subclinical hypothyroidism and autoimmune thyroiditis: a cross-sectional study based on two Chinese communities with different iodine intake levels. *Eur J Endocrinol* 2011; 164: 943-50. DOI: 10.1530/EJE-10-1041.
21. Das S, Bhansali A, Dutta P *et al*. Persistence of goitre in the post-iodization phase: Micronutrient

deficiency or thyroid autoimmunity? *Indian J Med Res* 2011; 133: 103-9.

22. Pahwa S, Mangat S. Prevalence of thyroid disorders in pregnancy. *Int J Reprod Contracept Obs Gynecol* 2018; 7: 3493-6. DOI: https://doi.org/10.18203/2320-1770.ijrcog20183401.
23. Mahadik K, Choudhary P, Roy PK. Study of thyroid function in pregnancy, its feto-maternal outcome; a prospective observational study. B*MC Pregnancy Childbirth* 2020; 20: 769. DOI: 10.1186/s12884-020-03448-z.
24. Gupta P, Jain M, Verma V, Gupta NK. The study of prevalence and pattern of thyroid disorder in pregnant women: a prospective study. *Cureus* 2021; 13: e16457. DOI: 10.7759/cureus.16457.
25. Casey BM, Dashe JS, Wells CE, McIntire DD, Leveno KJ, Cunningham FG. Subclinical hyperthyroidism and pregnancy outcomes. *Obs Gynecol* 2006; 107: 337-41. DOI: 101097/01AOG0000197991642469a.