

# Thyroid Profile in Infertile Women

Rojina Manandhar,<sup>1</sup> Bekha Laxmi Manandhar,<sup>2</sup> Jyoti Sharma<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Nepal Police Hospital, Kathmandu, Nepal, <sup>2</sup>Department of obstetrics and Gynaecology, T.U. Teaching Hospital, Maharajgunj, Kathmandu, Nepal.

## ABSTRACT

**Introduction:** Infertility is defined as inability to conceive after one year of regular unprotected intercourse. Thyroid disorders can lead to infertility arising from different pathophysiological mechanisms. The aim of this study is to determine the prevalence and type of thyroid disorder in infertile women and to compare the prevalence of thyroid disorder in primary and secondary infertility.

**Methods:** A hospital-based descriptive cross-sectional study conducted in the Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

**Results:** Among 156 infertile women enrolled and analyzed in the present study, thyroid disorder was found in 12 women giving the prevalence of thyroid disorder in infertile women as 7.7%. Hypothyroidism was more common comprising 6.4% of all infertile women, out of which subclinical hypothyroidism was 3.8% and clinical hypothyroidism was 2.6%. Hyperthyroidism was seen in 1.3% of all infertile women of which subclinical hyperthyroidism was 0.64% and clinical hyperthyroidism was 0.64%. Prevalence of thyroid disorder in primary infertility was 9.8% and in secondary infertility it was 3.7%. Among the 12 infertile women with thyroid disorder, four infertile women (33%) conceived. Three cases of hypothyroidism conceived after treatment and one case of subclinical hyperthyroidism conceived without any treatment.

**Conclusions:** This study shows that thyroid dysfunction shows a significant role in infertility. Proper management of the thyroid dysfunction can result regain of fertility. Therefore, routine screening is required to all cases of infertility for possible thyroid disorders.

**Keywords:** hypothyroidism; hyperthyroidism; infertility; thyroid disorder.

## INTRODUCTION

Infertility is defined as inability to conceive after one year of regular unprotected intercourse.<sup>1</sup> Infertility is a global health issue, affecting approximately 8-10% of couples worldwide.<sup>2</sup> Infertility, though not a life threatening condition, it has been a serious social problem.<sup>3</sup> It can be classified as primary infertility, in which no previous pregnancies have occurred, and secondary infertility,

in which a prior pregnancy, although not necessarily a live birth has occurred.<sup>1</sup>

Thyroid disorders can lead to infertility arising from different pathophysiological mechanisms. The exact mechanism of infertility in thyroid disorder is still ill-defined. It is assumed that hypothyroidism causes infertility by causing anovulation and by luteal phase defect.<sup>4</sup> Similarly, it is thought that hyperthyroidism also causes infertility by causing anovulation as there is increase in estrogen and gonadotrophins in hyperthyroidism.<sup>5,6</sup> Hence thyroid disorders reduce the likelihood of pregnancy. In addition, they also adversely affect pregnancy outcome and hamper fetal neuropsychological development. But good point is that thyroid disorders have reversible or preventable

## Correspondence:

Dr. Rojina Manandhar,  
Department of Obstetrics and Gynaecology,  
Nepal Police Hospital,  
Kathmandu, Nepal.  
Email: rosy\_mdr@hotmail.com  
Phone: +977-9851281586

effect on fertility. Proper management of such thyroid disorder results in improvement in health status, normalization of menstrual abnormalities and restoration of normal fertility. Thus, estimation of thyroid function is an integral part of infertility work-up.

Thus, the aim of this study is to determine the prevalence and type of thyroid disorder in infertile women presenting to the infertility clinic of Tribhuvan University Teaching Hospital and to compare the prevalence of thyroid disorder in primary and secondary infertility.

## METHODS

This was a cross-sectional descriptive study conducted in the Infertility care center of the Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. This study was undertaken over a period of 12 months from 14<sup>th</sup> April 2011 to 12<sup>th</sup> April 2012.

Initially, all the staffs of the Infertility care center were informed about the study. Infertile women, who attended to the infertility clinic for the first time during study period, who were married for more than one year, and agreed to be a part of this study were enrolled in this study. An informed consent was taken prior to carrying out the study. Those women with duration of marriage less than one year, refused to be enrolled in the study and with any history of thyroid disease or previous thyroid surgery or being on thyroid medications were excluded from study.

A detail history was taken and general, systemic, thyroid, breast and pelvic examination were carried out. Routine investigations for infertility work-up like hemoglobin (Hb), random blood sugar (RBS), thyroid function test (FT3, FT4 and TSH), premenstrual endometrial biopsy, hysterosalpingography (HSG) and semen analysis were sent. Prolactin, FSH, LH, USG Abdomen/pelvis was done only when indicated.

Five milliliters of fasting venous sample was obtained in a glass tube irrespective of phase of menstrual cycle. Serum was separated and stored for further analysis. Quantitative

determination of serum FT3, FT4 and TSH was done using Chemiluminescence immunoassay (CLIA) using EKONCLIA FT3 kit, FT4 Kit and TSH kit respectively. The reference range of our laboratory for FT3:1.2-4.2 pg/ml, FT4:7.2-17 pg/ml, TSH:0.6-4.5  $\mu$ U/ml.

Depending on thyroid function test values, the women were classified as hypo and hyperthyroidism and were further subdivided into clinical/subclinical hypo and hyperthyroidism.

Infertile women with thyroid disorder were consulted with endocrinologist for further management. Data analysis was done using a computer-based program, statistical package for social sciences (SPSS) version 16. The statistical tools used were frequency, percentage, mean, range and Chi-square test to calculate P-value. The P-value less than 0.05 were considered significant.

## RESULTS

During one year study period, 171 infertile women presented for the first time in infertility care center. Among them, 15 women were excluded from study as 12 women refused to be enrolled and 3 women had duration of marriage less than one year. So, the remaining 156 infertile women were enrolled and analyzed in this study.

The ages of infertile women ranged from 18-41 years. The maximum number of infertile women was 101 (64.7%) and they fell in age group of 20-29 years. The mean age of infertile women was 26.62 years. Twelve infertile women had thyroid disorder giving the prevalence rate of thyroid disorder in infertile women as 7.7%. Hypothyroidism was found in 10 (6.4%) cases whereas hyperthyroidism in two (1.3%) cases. Different sub-classification of thyroid disorder was shown (Table 1).

**Table 1. Sub-classification of thyroid disorder.**

Thyroid disorders	n (%)
Subclinical Hypothyroidism	6 (3.8%)
Clinical Hypothyroidism	4 (2.6%)
Subclinical Hyperthyroidism	1 (0.64%)
Clinical hyperthyroidism	1 (0.64%)

Maximum number of infertile women that is 102(65=4%) has primary infertility and 54(35.6%) had secondary infertility.

**Table 2. Thyroid disorder and types of infertility.**

	NORMO THYROIDISM	CLINICAL HYPO THYROIDISM	SUBCLINICAL HYPO THYROIDISM	CLINICAL HYPER THYROIDISM	SUBCLINICAL HYPER THYROIDISM
PRIMARY INFERTILITY (n=102)	92 (90.2%)	4 (3.9%)	4 (3.9%)	1 (1%)	1 (1%)
SECONDARY INFERTILITY (n=54)	52 (96.3%)	-	2 (3.7%)	-	-

Among 12 cases of thyroid disorder, four cases i.e. 33% conceived. Three cases who conceived were hypothyroid (two subclinical and one clinical hypothyroid) and one case was hyperthyroid (subclinical hyperthyroid). Two women with hypothyroidism was on thyroxin 50 µg once daily and one was on 25 µg once daily dose. They conceived within six weeks before they had repeated TFT.

## DISCUSSION

It is generally accepted that increase in age decreases fertility. Contradictory to this general concept, 64.7% of infertile women in this study were of age group 20-29 years. Similar finding was seen in a study done by Akhter et al.<sup>7</sup> in Bangladesh from January 2003 to August 2004 who reported that majority i.e. 78% of infertile women were of age group 21-30 years. Likewise, a study done by Biradar et al.<sup>8</sup> in India revealed that most of the infertile were of age group 24-28 years.

In the present study, mean age of infertile women was 26.62 years. This result was compatible to the study conducted by Rijal et

al.<sup>9</sup> in 735 primary infertile women in Nepal from March 2009 to 2011 who reported mean age of infertile women as 26.3 years. However, the mean age of infertile women was 30 years in the study conducted by Arjoki et al.<sup>10</sup> in Finland and Abalovich et al.<sup>11</sup> in Argentina. Likewise, a study performed by Grassi et al.<sup>12</sup> and Raber et al.<sup>13</sup> showed mean age of infertile women was 32 years which was higher than the present study. The cause of less mean age of infertile women in this study might be because of early marriage of the Nepalese population and when they failed to conceive after a couple of months of marriage they seek treatment earlier.

The majority of infertile women i.e. 65.4% were of primary infertility and remaining 34.6% were of secondary infertility in this study. Similar report of high prevalence of primary infertility compared to secondary infertility was seen in a study performed by Farhi et al.<sup>14</sup> in Israel who reported 65% of infertile women had primary infertility and 35% had secondary infertility. Likewise in a study done by Grassi et al.<sup>12</sup> and Raber et al.<sup>13</sup> 72% of infertile women had primary infertility and 28% had secondary infertility showing the prevalence of primary infertility was more than secondary infertility. A study carried out by Rania WM<sup>15</sup> in 2011 in 1392 couple in Razan centers in Nablus found 83.3% of infertile women had primary infertility and 16.7% had secondary infertility. Similarly, a study conducted by Emma BO et al.<sup>16</sup> in northern Nigeria showed 96% had primary infertility and only 4% had secondary infertility. The higher prevalence of primary infertility might be because they seek for treatment more seriously rather than secondary infertility group who already had children.

The prevalence of thyroid disorder in general population was 5.9% according to the study done by NHANES (National Health and Nutrition Examination Survey) from 1988 to 1994 in United States.<sup>17</sup> In present study among 156 infertile women studied, 12 women had thyroid disorder giving the prevalence rate of thyroid disorder in infertile women as 7.7%. Thus the prevalence of thyroid disorder in infertile women was more than in general population. This finding was also compatible to a study carried out by Elahi et al.<sup>18</sup> in Lahore among 140 infertile women from July 2003 to December 2006 who found thyroid disorder in 10.7% of infertile women.

Whereas this finding was less compared to the prevalence of 25.6% noted in a study performed by Rijal et al.<sup>9</sup> in Nepal over a period of two years from March 2009 to 2011 among 735 women. This could be because Rijal et al.<sup>9</sup> had included only primary infertile women and had excluded infertility due to male factor and the female factors with any congenital anomaly of urogenital tract, or any obvious organic lesion. Similarly, a study conducted by Verma et al.<sup>19</sup> from 2007 to 2010 in Delhi on 394 infertile women reported prevalence of thyroid disorder in infertile women as 23.8%. This high prevalence could be because infertile women having tubular blockage, pelvic inflammatory disease, endometriosis on diagnostic laparoscopy or hysteroscopy, with genital TB (PCR-positive), with liver, renal or cardiac diseases, those already on treatment for thyroid disorders or hyperprolactinemia or cases where abnormality was found in husband's semen analysis also were excluded from their study. Likewise, Rahaman et al.<sup>20</sup> conducted a case control study in 30 infertile women and 30 fertile women in 2007 in Bangladesh excluding the women with organic lesion in uterus or ovary and with history of previous abdominal surgery. They reported the prevalence of thyroid disorder as 33.3% which was higher than the present study.

But a study conducted by Lincoln et al.<sup>21</sup> in 1999 in USA among 704 infertile women and Arjoki et al.<sup>10</sup> from 1992 to 1994 in Finland among 299 infertile women showed the prevalence of thyroid disorder in infertile women as 2.3% and 4% respectively which was less than this study.

This difference in prevalence of thyroid disorder could be because of difference in iodine deficient status in different countries. Higher prevalence of thyroid disorder was seen in iodine deficient countries of Asia compared to countries like United States, Finland where iodine status has remained generally adequate in the last two decades.

Majority of thyroid disorder in this study was hypothyroidism which comprises 6.4% compared to hyperthyroidism found in 1.3% of infertile women. Relatively high prevalence rate of hypothyroidism than hyperthyroidism found in this study could be due to high prevalence of iodine deficiency in Nepal (13.6%) as it lies in iodine deficient range.<sup>22,23</sup> This result was compatible with the result of other studies conducted in Nepal and its neighborhood countries. Study performed by Rijal et al.<sup>9</sup> in Nepal reported that 20.1% of thyroid dysfunction was hypothyroidism and only 5.5% was hyperthyroidism. Sharma et al.<sup>24</sup> in their study in India reported hypothyroidism in 20% and hyperthyroidism in 3% of primary infertile women. Similarly, a study done in 2007 in Bangladesh by Rahaman et al.<sup>20</sup> showed hypothyroidism in 33.3% of infertile women and hyperthyroidism in none. Goswami et al.<sup>25</sup> performed a study in Delhi in 2007 and found hypothyroidism in 8% infertile women and hyperthyroidism in 5%.

Among all thyroid disorders, subclinical hypothyroidism was the most common and was found in 3.8% of all infertile women in this study. Whereas subclinical hypothyroidism was found in 1.8% of infertile women by Bohnet et al.<sup>26</sup>, in 4.6% by Grassi et al.<sup>12</sup>, in 12% by Biradar et al.<sup>8</sup>, in 13.9% by Abalovich et al.<sup>11</sup>, in 25% by Bals Pratsch et al.<sup>27</sup> and 62.7% by Verma et al.<sup>19</sup>

The prevalence of thyroid disorder in primary infertility in this study was 9.8%. This finding was less compared to the study conducted by Goswami et al.<sup>25</sup> in Bangladesh, Rijal et al.<sup>9</sup> in Nepal and Biradar et al.<sup>8</sup> in India who had reported the prevalence of thyroid disorder in primary infertility to be 13%, 25.6% and 42% respectively. They had excluded infertility due to male factor and the female with tubal factor infertility, any congenital anomaly of urogenital tract or any obvious organic lesion, pelvic inflammatory disease,

endometriosis, genital TB. This might be the reason that prevalence of thyroid disorder in primary infertility in the present study was less compared to their study.

The prevalence of thyroid disorder in primary infertility was 9.8% which was more compared to that in secondary infertility which was 3.7%. But the study done by Akhter et al.<sup>7</sup> in Bangladesh and Emokpae et al.<sup>28</sup> in Nigeria had shown contradictory result. They had reported that sub-clinical thyroid disorder (both hypothyroidism and hyperthyroidism) was more in secondary infertility than in primary infertility. The cause of contradictory report might be because they had included only subclinical thyroid disorder.

## CONCLUSIONS

This study shows that thyroid dysfunction shows a significant role in infertility. Proper management of the thyroid dysfunction can result regain of fertility. Therefore, routine screening is required to all cases of infertility for possible thyroid disorders.

## ACKNOWLEDGEMENTS

I would like to thank Dr. Nabin K. Rauniyar and Mr. Jeevan Manandhar.

**CONFLICTS OF INTEREST:** None.

## REFERENCES

1. Richard OB, Daniel JS, Myelene WY. Berek and Novak's gynecology. 14th ed. Philadelphia: Lippincot Williams and Wilkins; 2007. Chapter 30, Infertility; 1185-275 p.
2. Inhorn MC. Global infertility and the globalization of new reproductive technologies: illustrations from Egypt. Soc Sci Med. 2003 May;56(9):1837-51. PubMed PMID: 12650724.
3. Insler V, Lunefeld B. Infertility: the dimension of problem. In: Insler V, Lunefeld B, editors. Infertility: Male and Female. 2nd ed. Edinburgh: Churchill Livingstone; 1993. 3-10 p.
4. Keye WR, Chang RJ, Rebar RW, Soules MR. Infertility: Evaluation and Treatment. 1st ed. Philadelphia: W.B. Saunders; 1995. Chapter 10, Practical Evaluation of Amenorrhea and Abnormal Uterine Bleeding; 98-106 p.
5. Insler V, Lunefeld B. Medical conditions leading to infertility. In: Insler V, Lunefeld B, editors. Infertility: Male and Female. 2nd ed. Edinburgh: Churchill Livingstone; 1993. 703-38 p.
6. Cecconi S, Rucci N, Scaldaferrì ML, Masciulli MP, Rossi G, Moretti C, D'Armiento M, Ulisse S. Thyroid hormone effects on mouse oocyte maturation and granulosa cell aromatase activity. Endocrinology. 1999;140:1783-88.
7. Akhter N, Hassan SA. Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination. Internet J Endocrinol. 2009;5(1):1540-2606.
8. Biradar M, Poornima RT, Sonagra A, Murthy J. Thyroid Dysfunction in infertile women. International Journal of Pharmacy and Biological Sciences. 2012;3:53-8.
9. Rijal B, Shrestha R, Jha B. Association of thyroid dysfunction among infertile women visiting infertility center of Om Hospital, Kathmandu, Nepal. Nepal Med Coll J. 2011;13(4):247-9.
10. Arjoki M, Jokimaa V, Juuti A, Koskinen P, Irjaka K, Anttila L. Hypothyroidism among infertile women in Finland. Gynecological endocrinology. 2000;14:127-13.
11. Avalovich M, Metelberg L, Allami C, Gitterrez S, Alcaraz G, Otero P, Levaloe O. Subclinical hypothyroidism and thyroid autoimmunity in women with Infertility. Gynaecological Endocrinology. 2007 May;23(5):279-83.
12. Grassi G, Balsamo A, Ansaldi C, Balbo A, Massobrio M, Benedetto C. Thyroid autoimmunity and infertility. Gynecological Endocrinology. 2001;15:389-96.
13. Raber W, Nowotny P, Vytiska-Binstorfer E, Vierhapper H. Thyroxine treatment modified in infertile women according to thyroxine-releasing hormone testing: 5 year follow-up of 283 women referred after exclusion of absolute cause infertility. Hum Reprod. 2003;18:707-14.
14. Farhi J, Ben-Haroush A. Distribution of Causes of Infertility in Patients Attending Primary Fertility Clinics in Israel. IMAJ. 2011;13:51-54.
15. Rania WA. Main Causes of Infertility among Men Treated at Razan Centers in West Bank: Retrospective study [dissertation]. [Palestine]: An-Najah National University Faculty of Graduate Studies; 2011. 89 p.

16. Emma BO, Fasubaa OB, Togun RA, Fakunle JB, Aderemi A, Adediran T. Semen Profile in Ile- Ife, Nigeria. *Journal of Medicine and Medical Science*. 2011;2(5):879-s84.
17. Joseph G, Norman W, Flanders W, Hannon W, Elaine W, Carole A, Lewis E. Serum TSH, T4 and Thyroid Antibodies in the United States Population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *The Journal of Clinical Endocrinology & Metabolism*. 2002;87:2489-99.
18. Elahi S, Tasneem A, Nazir I, Nagra SA, Hyder SW. Thyroid dysfunction in infertile women. *J Coll Physicians Surg Pak*. 2007;17(4):191-4.
19. Verma I, Sood R, Juneja S, Kaur S. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. *Int J App Basic Med Res*. 2012;2:17-9.
20. Rahaman D, Fatima P, Banu J. Thyroid disorder in female subfertility. *JCMCTA*. 2008;19(2):46-50.
21. Lincoln SR, Ke RW & Kutteh WH. Screening for hypothyroidism in infertile women. *Journal of Reproductive Medicine*. 1999;44:455-7.
22. Pandav CS. IDD in Southeast Asia. In: Hetzel BS, Pandav CS, eds. *SOS for a billion, the conquest of iodine deficiency disorders*. Delhi: Oxford University Press; 1994. 213-31 p.
23. Baral N, Ramprasad C, Lamsal M, Koner BC, Koirala S. Assay of iodine deficiency status in three ecological regions of Nepal by a microdigestion method. *Southeast Asian J Trop Med Public Health*. 1999;30:527-31.
24. Sharma UR, Parmar C. Thyroid profile in infertile women and menstrual dysfunction. *Source Indian Medical Gazette*, updated 2007.
25. Goswami B, Patel S, Chatterjee M, Koner BC, Saxena A. Correlation of Prolactin and Thyroid Hormone Concentration with Menstrual Patterns in Infertile Women. *Journal of Reproduction and Infertility*. 2009;10(3):207-213.
26. Bohnet HG, Fiedler K, Leidenberger FA. Subclinical hypothyroidism and infertility. *The Lancet*. 1981;5:1278.
27. Bals-Pratsch M, Schober O, Hanker JP, Geyter C, Schneider HP. Disorders of thyroid function and sterility in the woman. *Zentralbl Gynakol*. 1993;115(1):18-23.
28. Emokpae M, Osadolor H, Omole Ohonsi A. Sub-clinical hypothyroidism in infertile Nigerian women with hyperprolactinaemia. *Nigerian Journal of Physiological Sciences*. 2011;6(1):27.