

Pattern of Thyroid Disorders in a Tertiary Care Centre of a High-Altitude Region of Nepal: A hospital-based retrospective study

Tirtha Narayan Shah,¹ Anuraj Anu,¹ Binamra Bista²

¹Department of Clinical Biochemistry, Karnali Academy of Health Sciences, Jumla, Nepal

²Department of Forensic Medicine and Toxicology, Karnali Academy of Health Sciences, Jumla, Nepal

Corresponding Author: Dr. Tirtha Narayan Shah, Email: tirthabiochemist15@gmail.com,

ORCID: <http://orcid.org/0000-0002-1981-1298>

ABSTRACT

Background: Millions of people globally suffer from thyroid disorders, with over half of them are unaware of their conditions. Untreated, these disorders can lead to severe health complications such as heart problems, pregnancy complications, goiter, bone health issues, etc. Jumla, a high-altitude Himalayan region in Nepal, includes iodine-deficient areas, making it prone to thyroid disorders. This study aimed to identify the prevalence and pattern of thyroid disorders in this region.

Methods: A retrospective hospital-based cross-sectional study was conducted using data from the Karnali Academy of Health Sciences, Jumla, spanning from 1st January–31st December 2023. Participants of all ages with complete thyroid function test results (fT3, fT4, and TSH assessed via chemiluminescence immunoassay) were included. Data were extracted from Bahmni EMR, cleaned in MS-Excel, and analyzed in R software, with a significance threshold of $p < 0.05$.

Results: Among 816 participants (mean age: 35.66 ± 14.60 years), 660 (80.8%) were female, and 156 (19.1%) were male. The most represented age group was 25–34 years. Subclinical hypothyroidism was the most prevalent disorder, affecting 33 males (21.15%) and 143 females (21.66%). Primary hyperthyroidism was the least common, found in 1 male (0.64%) and 7 females (1.06%). Other disorders included secondary hypothyroidism, secondary hyperthyroidism, primary hypothyroidism, and subclinical hyperthyroidism.

Conclusion: Subclinical hypothyroidism was the most common thyroid disorder, with females disproportionately affected. Wider population screening for early detection and management is essential to mitigate health risks.

Keywords: Thyroid Disorders, Subclinical Hypothyroidism, Primary Hyperthyroidism, High Altitude

Article Information

Received: 14 October 2024

Accepted: 24 December 2024

Published online: 26 December 2024

Copyright © 2024 by the author(s), wherein the author(s) are the only owners of the copyright of the published content

Licensing: This published content is distributed under the terms of the [Creative Commons Attribution International License \(CC BY 4.0\)](https://creativecommons.org/licenses/by/4.0/) license, and is free to access on the Journal's website. The author(s) retain ownership of the copyrights and publishing rights without limitations for their content, and they grant others permission to copy, use, print, share, modify, and distribute the article's content even for commercial purposes.

Disclaimer: This publication's claims, opinions, and information are the sole creations of the specific author(s) and contributor(s). Errors in the contents and any repercussions resulting from the use of the information included within are not the responsibility of the publisher, editor, or reviewers. Regarding any jurisdictional assertions in any published articles, their contents, and the author's institutional affiliations, the Journal and its publisher maintain their objectivity.

INTRODUCTION

The term "thyroid disorder" refers to the combination of normal or abnormal thyroid hormones, free tri-iodothyronine (FT3), and free tetra-iodothyronine (FT4), as well as abnormal thyroid stimulating hormone (TSH). More than 300 million people worldwide are afflicted with this most prevalent endocrine illness, and over half of them are thought to be unaware of their condition [1]. A thyroid problem affects 20 million Americans alone, and at least 12% will develop a thyroid condition during their lifetime, according to the American Thyroid Association [2]. In poor nations in Asia, Africa, and Latin America, the majority of thyroid problems still exist [3]. The prevalence and pattern of thyroid disorders depend on ethnicity, gender, diet and nutrition, geographic, environmental factors and iodine intake status [4,5].

Jumla is the centre of Chandannath Municipality in Jumla District of Karnali Province of Nepal. It is located at 2514 metres elevation from the sea level. Jumla has a highland oceanic climate that is cooled down by its elevation. The highest temperature ever recorded in Jumla was 33.3 °C (91.9 °F) on 24 May 1998, while the lowest temperature ever recorded was -15.0 °C (5.0 °F) on 2 February 1975 [6]. The increase in FT4 is occurring due to cold weather associated with high altitude area [7]. The anterior pituitary's production of thyroid stimulating hormone is not necessary for the increase in free thyroid hormone at high elevations. Higher altitudes are associated with an increase in free thyroxine, but populations tested at high elevations show no change in FT₃ levels [8]. FT4 was significantly elevated at 3750 m, but not FT3 and TSH. Results were not clear for FT3 and TSH, but overall, the thyroid axis was activated. As the thyroid gland releases mainly FT4, which is metabolized to FT3, and as T4 has a much longer half-life than FT3, it can be speculated that the altitude adaptations of thyroid function are easier to be detected using FT4 levels [9]. In Nepal's Himalayan, sub-

Himalayan, and Terai regions, iodine deficiency is common [10]. In fact, iodine deficiency is thought to be the primary cause of thyroid problems globally [11-13]. Congenital conditions, genetic predispositions, pregnancy, radiation therapy, viral infections, surgery, underlying illnesses including infiltrative disorders, or even autoimmune can all be additional causes of thyroid disorders [14,15]. While thyroid disorders were detected in all age groups, the age groups of 31–45 years old exhibited a greater number of patients [16]. There has been some research indicating that the prevalence of hypothyroidism rises with age [17]. In a study conducted at a high altitude, Alhazmi et al. discovered elevated thyroid hormone levels [18]. In order to determine the prevalence of pattern of thyroid problem patterns in the people living in Nepal's high-altitude regions, this study was conducted.

METHODS

This is a descriptive and cross-sectional retrospective study about the pattern of thyroid disorders of the participants who visited the tertiary care centre and got their thyroid function tests (TFT, FT3, FT4 and TSH) estimated in the hospital laboratory from 1st January 2023 to 31st December 2023 were included and the participants having incomplete TFT were excluded from the study. After approval from Institutional Review Committee of Karnali Academy of Health Sciences, Jumla, (reference no. 081/081/31), the data were obtained from the records review of the hospital laboratory. Assessment of TFT was done by fully automated CLIA (Maglumi X3) following its protocol. The reference values of FT3, FT4 and TSH were 2 – 4.2 pg/mL, 0.89 – 1.72 ng/dL and 0.3 – 4.5 mIU/L respectively in the laboratory. Further, thyroid disorders were set as euthyroidism for normal TSH and FT4 irrespective of FT3, primary hyperthyroidism for low TSH with high FT4, subclinical hyperthyroidism for low TSH with normal FT4, primary hypothyroidism for high TSH with low FT4, subclinical hypothyroidism for high TSH with normal FT4, secondary hyperthyroidism

for low or normal TSH with high fT4 and secondary hypothyroidism for low or normal TSH with low fT4 which mostly aligns with content given in Harrison's Manual of Medicine, 19th edition [19]. Initially the data were extracted from Bahmni open source EMR and Hospital Information System, cleaned in MS-Excel 2010 and the statistical analysis was done in R. $P < 0.05$ was set for statistical significance with 95% confidence interval.

RESULTS

The total of 816 participants in the study got their TFT done within one year. The participants were from newly born to 88 years with the mean age of 35.66 ± 14.60 years. Out of the total 816 participants, 660 (80.8%) were female and the remaining 156 (19.9%) were male. Of the total male, 92 (58.97%) had normal thyroid function test whereas 408 (61.81%) female had the same. In the thyroid disorders, the subclinical hypothyroidism was the most prevalent in both the male [i.e. 33 (21.15%)] and female [i.e. 143 (21.66%)] and the least prevalent was primary hyperthyroidism i.e. 1 (0.64%) in male and 7 (1.06%) in female. The other thyroid disorders prevalence in male were secondary hyperthyroidism in 10 (6.41%), secondary hypothyroidism in 9 (5.76%), primary hypothyroidism in 7 (4.48%) and subclinical hyperthyroidism in 4 (2.56%). In female, the

prevalence of pattern of thyroid disorders were secondary hypothyroidism in 39 (5.90%), secondary hyperthyroidism in 33 (5.0%), primary hypothyroidism in 21 (3.18%) and subclinical hyperthyroidism in 9 (1.36%). However, in all the thyroid disorders among the gender, the p-value was >0.05 , hence it was statistically insignificant (Table 1).

The maximum and the minimum participants were in the age groups of 25-34 years and less than 25 years respectively. In total 816 participants, 500 (61.27%) had euthyroidism, followed by subclinical hypothyroidism in 176 (21.56%), secondary hypothyroidism in 48 (5.88%), secondary hyperthyroidism in 43 (5.26%), primary hypothyroidism in 28 (3.06%), subclinical hyperthyroidism in 13 (1.59%) and primary hyperthyroidism in 8 (0.98%) participants. Among the different age groups, subclinical hypothyroidism was the most prevalent in all the age groups. Primary hyperthyroidism and primary hypothyroidism were least prevalent [i.e. 2 (1.11%) each] in the age group of less than 25 years where as the subclinical hyperthyroidism was the least prevalent i.e. 3 (1.29%) in age group 25-34 years. In the age groups of 35-45 years and above 45 years the primary hyperthyroidism was the least prevalent i.e. 1 (0.53%) and 1 (0.45%) respectively (Table 2).

Table 1: Pattern of thyroid disorders in gender

Thyroid disorders	Male	Female	Statistic	P-value
Euthyroidism	92 (58.97%)	408 (61.81%)	$\chi^2 = 0.318$	0.572
Subclinical hypothyroidism	33 (21.15%)	143 (21.66%)	$\chi^2 = 0.001$	0.974
Subclinical hyperthyroidism	4 (2.56%)	9 (1.36%)		0.286*
Primary hyperthyroidism	1 (0.64%)	7 (1.06%)		1*
Secondary hyperthyroidism	10 (6.41%)	33 (5.0%)	$\chi^2 = 0.259$	0.610
Primary hypothyroidism	7 (4.48%)	21 (3.18%)	$\chi^2 = 0.314$	0.574
Secondary hypothyroidism	9 (5.76%)	39 (5.90%)	$\chi^2 < 0.001$	1
Total [816]	156	660		
*Fischer's exact test				

Table 2: Pattern of thyroid disorders in different age groups

Thyroid disorders	Age group <25 years	Age group 25-34 years	Age group 35-45 years	Age group >45 years	Total
Euthyroidism	114 (63.68%)	153 (66.23%)	104 (55.61%)	129 (58.90%)	500 (61.27%)
Subclinical hypothyroidism	35 (19.55%)	43 (18.61%)	46 (24.59%)	52 (23.74%)	176 (21.56%)
Subclinical hyperthyroidism	3 (1.67%)	3 (1.29%)	2 (1.06%)	5 (2.28%)	13 (1.59%)
Primary hyperthyroidism	2 (1.11%)	4 (1.73%)	1 (0.53%)	1 (0.45%)	8 (0.98%)
Secondary hyperthyroidism	12 (6.70%)	9 (3.89%)	13 (6.95%)	9 (4.10%)	43 (5.26%)
Primary hypothyroidism	2 (1.11%)	8 (3.46%)	10 (5.34%)	8 (3.65%)	28 (3.06%)
Secondary hypothyroidism	11 (6.14%)	11 (4.76%)	11 (5.88%)	15 (6.84%)	48 (5.88%)
Total	179	231	187	219	816

DISCUSSION

In this hospital-based retrospective study in Jumla, Nepal, a total of 816 participants were present. Most of the participants i.e. 231 (28.3%) were in the age group 25 – 34 years which is biologically active and reproductive age group. In a study conducted by Baral et al. in 2002, the majority of the study population belonged to the active age group (21-40 years) [20]. Additionally, Sharma et al. discovered that the highest number of participants were in the reproductive age range. This could be attributed to the possibility of fertility problems among the participants, which may have intensified the screening for thyroid profiles [21]. In total 816 participants, 61.27% had euthyroidism, followed by subclinical hypothyroidism in 21.56%, secondary hypothyroidism in 5.88%, secondary hyperthyroidism in 5.26%, primary hypothyroidism in 3.06%, subclinical hyperthyroidism in 1.59% and primary hyperthyroidism in 0.98% participants. In a study done by Saroj Khatiwada et al. in 2015, euthyroidism was 64%, subclinical

hypothyroidism was 26.5%, overt hypothyroidism was 5.5%, and subclinical hyperthyroidism was 4.1% among the study population [22].

The prevalence of clinical and subclinical hypothyroidism was 3% and 7.4%, respectively, while the prevalence of clinical and subclinical hyperthyroidism was 0.2% and 1.1%, respectively [23].

The largest thyroid function study conducted in the US, NHANES III, estimated that the prevalence of hypothyroidism was 4.6% (0.3% clinical and 4.3% subclinical), while the prevalence of hyperthyroidism was 1.3% (0.5% clinical and 0.7% subclinical) [24]. Subclinical hypothyroidism (21.66%), primary hyperthyroidism (1.06%), secondary hypothyroidism (5.90%) showed higher prevalence in female than in male 21.15%, 0.64% and 5.76% respectively. This result aligns with the conclusions of several studies conducted by Meng et al., Bauer et al., and McGrogan et al., which assert that females have a greater prevalence of some thyroid disorders. [25–27]. Our finding showed 6.41% male and 5.0% female have secondary hyperthyroidism whereas 5.76%

male and 5.90% female have secondary hypothyroidism with all the age groups affected. It can be due to hypothalamo-pituitary-dependent adaptations in endocrine regulation due to extreme altitude conditions. The changes in dynamical response to extreme altitude were the highly significant changes in the burst-like mode of intermittent fT4 and TSH secretion over time [28].

CONCLUSIONS

The pattern of thyroid disorders was 48.5% in our study with subclinical hypothyroidism being the most common and primary hyperthyroidism being the least common. Females were more likely to have over all abnormal thyroid function tests as compared to the male population, however statistically insignificant. Secondary thyroid disorders are also found in all the ages of male and female. Screening of thyroid disorders by measuring TSH level alone may not give the complete picture of thyroid disorders, so complete assessment of fT3, fT4 and TSH is recommended. Further it will help to educate and aware the public about the importance of healthy thyroid functions.

Study Limitations: This study has shown that thyroid disorders can affect almost all age groups and present with various patterns of thyroid disorders. However, because this study was hospital-based and because the study population constituted of subjects who came to the institute seeking TFTs, the results may not be applicable to the general population. Other important factors like medical conditions, drugs history, iodine level, pregnancy, ethnicity, etc. may influence the thyroid hormones level that are limited in this study. To short out these limitations, the different

factors like medical conditions, drug history, iodine concentration in the environment, etc which can influence the prevalence of thyroid disorders can be included to make the study more significant in the future.

Author Contributions:

TNS conceptualized and designed the research; TNS and AA performed data collection; TNS and BB helped in data interpretation and drafted the manuscript; and all authors reviewed the manuscript and approved the final version of the manuscript. All authors agreed to be accountable for all aspects of the research work.

Acknowledgement: The authors are very thankful to Dr. Lokraj Joshi who gave his valuable time for data analysis and critical reviews.

Conflict of Interest: The authors do not have any conflicts of interest regarding this publication.

Ethical Approval: Ethical approval was obtained from Institutional review board of Karnali Academy of Health Sciences, Jumla, Nepal (Ref. No 081/081/31).

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon request.

Source of Funding/Support: The research was funded by researchers themselves.

Layman summary: Thyroid disorders are very common and which vary from asymptomatic to symptomatic conditions. The consequences of the thyroid disorders are usually awful. This study was done to identify the pattern of thyroid disorders with their prevalence in a high altitude region as the regulation of thyroid function tests also depend on iodine level, altitude, temperature, etc.

REFERENCES

1. Asmelash D, Tesfa K, Biadgo B. Thyroid dysfunction and cytological patterns among patients requested for thyroid function test in an endemic goiter area of Gondar, North West Ethiopia. *International Journal of Endocrinology*. 2019;2019(1):9106767. <https://doi.org/10.1155/2019/9106767>
2. General Information/ Press Room (Internet). American Thyroid Association. (cited 2020 Apr 7).

3. Ogbera AO, Kuku SF. Epidemiology of thyroid diseases in Africa. *Indian J Endocrinol Metab.* 2011;15(Suppl 2):S82-8. <https://doi.org/10.4103/2230-8210.83331>
4. de Escobar GM, Obregon MJ, del Rey FE. Iodine deficiency and brain development in the first half of pregnancy. *Public Health Nutr.* 2007;10(12A):1554-70. <https://doi.org/10.1017/S1368980007360928>
5. Paudyal N, Chitekwe S, Rijal S, Parajuli K, Pandav C, Maharjan M, et al. The evolution, progress, and future direction of Nepal's universal salt iodization program. *Matern Child Nutr.* 2020:e12945. <https://doi.org/10.1111/mcn.12945>
6. Jumla (town) [Internet]. Wikipedia: The Free Encyclopedia. 2011 July 13 [updated 2024 Dec 16 1; cited 2024 Dec 17]. Available from: [https://en.wikipedia.org/wiki/Jumla_\(town\)](https://en.wikipedia.org/wiki/Jumla_(town))
7. Kimberly E., et al. "Endocrine responses to acute and chronic high-altitude exposure (4,300 meters): modulating effects of caloric restriction". *American Journal of Physiology-Endocrinology and Metabolism* 290 (2006): E1078 -E1088. <https://doi.org/10.1152/ajpendo.00449.2005>
8. Nepal O, Pokhrel BR, Khanal K, Gyawali P, Malik SL, Koju R, Kapoor BK. Thyroid hormone levels in highlanders- a comparison between residents of two altitudes in Nepal. *Kathmandu Univ Med J (KUMJ).* 2013 Jan-Mar;11(41):18-21. <https://doi.org/10.3126/kumj.v11i1.11017>
9. von Wolff M, Nakas CT, Tobler M, Merz TM, Hilty MP, Veldhuis JD, Huber AR, Pichler Hefti J. Adrenal, thyroid and gonadal axes are affected at high altitude. *Endocr Connect.* 2018 Oct 1;7(10):1081-1089. <https://doi.org/10.1530/EC-18-0242>
10. Regmi A, Shah B, Rai BR, Pandeya A. Serum lipid profile in patients with thyroid disorders in central Nepal. *Nepal Medical College journal: NMCJ.* 2010 Dec 1;12(4):253-6. PMID: 21744769
11. Vanderpump MPJ, Tunbridge WMG. The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, editors. *Werner and Ingbar's the thyroid.* Philadelphia: Lippincott-Raven. 1996; 474-82. DOI: [10.1093/bmb/ldr030](https://doi.org/10.1093/bmb/ldr030)
12. Dunn JT, Pretell EA, Daza CH, Viteri FE. Towards the eradication of endemic goiter, cretinism, and iodine deficiency. In: *Towards the eradication of endemic goiter, cretinism, and iodine deficiency* 1986; 419.
13. Delange F. The disorders induced by iodine deficiency. *Thyroid.* 1994;4(1):107-28. <https://doi.org/10.1089/thy.1994.4.107>
14. Brownlie BE, Wells JE. The epidemiology of thyrotoxicosis in New Zealand: incidence and geographical distribution in north Canterbury, 1983-1985. *Clinical endocrinology.* 1990 Aug;33(2):249-59. <https://doi.org/10.1111/j.1365-2265.1990.tb00489.x>
15. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. *Thyroid.* 2002;12(10):839-47. <https://doi.org/10.1089/105072502761016458>
16. Mahato RV, Jha B, Singh KP, Yadav BK, Shah SK, Lamsal M. Status of Thyroid disorders in Central Nepal: A Tertiary care Hospital based study. *International Journal of Applied Sciences and Biotechnology.* 2015 Mar 25;3(1):119-22. <https://doi.org/10.3126/ijasbt.v3i1.12218>
17. Shaw CK, Thapalia A, Nanda S, Shaw P. Thyroid dysfunction in Down syndrome. *Kathmandu Univ Med J.* 2006; 4: 182-6.
18. Alhazmi AS, Alomey A, Almalki H, Almehmadi M, Albshri M, Algarni N, Almutiri S. Effect of high altitude on thyroid and thyroid stimulating hormones levels in Taif city. *Acta Scientific Nutritional Health.* 2018;2(12):11-3.
19. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson J, Loscalzo J, editors. *Thyroid gland disorders.* In: *Harrison's Manual of Medicine.* 19th ed. New York: McGraw-Hill Education; 2016.
20. Baral N, Lamsal M, Koner BC, Koirala S. Thyroid dysfunction in eastern Nepal. *Southeast Asian journal of tropical medicine and public health.* 2002 Sep 16;33(3):638-41.

21. Sharma VK, Niraula A, Tuladhar ET *et al.* Autoimmune thyroid status in subclinical thyroid disorders in patients attending a tertiary care center in Nepal: a hospital-based cross-sectional study. *BMC Endocr Disord* **23**, 221 (2023). <https://doi.org/10.1186/s12902-023-01480-6>
22. Khatiwada S, Kc R, Sah SK, Khan SA, Chaudhari RK, Baral N, et al. Thyroid Dysfunction and Associated Risk Factors among Nepalese Diabetes Mellitus Patients. *Int J Endocrinol.* 2015. <https://doi.org/10.1155/2015/570198>
23. Strikić Đula I, Pleić N, Babić Leko M, Gunjača I, Torlak V, Brdar D, Punda A, Polašek O, Hayward C, Zemunik T. Epidemiology of hypothyroidism, hyperthyroidism and positive thyroid antibodies in the Croatian population. *Biology.* 2022 Mar 2;11(3):394. <https://doi.org/10.3390/biology11030394>
24. Hollowell J.G., Staehling N.W., Flanders W.D., Hannon W.H., Gunter E.W., Spencer C.A., Braverman L.E. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III) *J. Clin. Endocrinol. Metab.* 2002;87:489–99. <https://doi.org/10.1210/jcem.87.2.8182>
25. Meng Z, Liu M, Zhang Q, Liu L, Song K, Tan J, et al. Gender and age impacts on the Association between thyroid function and metabolic syndrome in chinese. *Med (Baltim).* 2015;94(50):e2193. <https://doi.org/10.1097/MD.0000000000002193>
26. Bauer M, Glenn T, Pilhatsch M, Pfennig A, Whybrow PC. Gender differences in thyroid system function: relevance to bipolar disorder and its treatment. *Bipolar Disord.* 2014;16(1):58–71. <https://doi.org/10.1111/bdi.12150>
27. McGrogan A, Seaman HE, Wright JW, De Vries CS. The incidence of autoimmune thyroid disease: a systematic review of the literature. *Clin Endocrinol (Oxf).* 2008;69(5):687–96. <https://doi.org/10.1111/j.1365-2265.2008.03338.x>
28. Keenan DM, Pichler Hefti J, Veldhuis JD, and Von Wolff M. Regulation and adaptation of endocrine axes at high altitude. *American journal of physiology Endocrinology and metabolism* 318: E297-e309, 2020. <https://doi.org/10.1152/ajpendo.00243.2019>