Original Research Article

A study of clinicopathological and etiological profile of goiter at tertiary cate centre in Kumaon region of Uttarakhand

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Abstract

Background: Goiter is one of the common manifestations in Uttarakhand region because of iodine deficiency.**Objective:** This study was undertaken to illustrate the clinicopathological and etiological profile of patients presenting with Goiter at Tertiary Care Hospital in Kumaon Region of Uttarakhand. **Materials & methods**: This hospital based cross sectional study was done in 121 patients aged >16 years presenting with goiter in Medicine, ENT OPD/ IPD, Dr. Sushila Tiwari Hospital, Haldwani District Nainital between January 2020- September 2021. Clinical features of goiter were observed, relevant investigations were done, and most probable diagnosis was made as to the reason of goiter. **Results**: In majority (94.21%) of patients, WHO Goiter grade 2 was observed. Majority (69.42%) of patients had hypothyroidism. Only 2.48% patients had hyperthyroidism. On FNAC majority (95.04%) of patients had Bethesda grade II. In 43.80% of patients, fine needle aspiration finding was suggestive of nodular colloid goiter followed by chronic Lymphocytic thyroiditis (27.27%) and simple colloid goiter (16.53%). Most of the cases of benign category had euthyroid or hypothyroid levels. Both cases of malignancy had euthyroid levels. Both cases of follicular neoplasms of thyroid and adenomatoid nodular thyroiditis also had euthyroid levels. (P=0.012). In majority (60.33%) of patients, probable etiology was iodine deficiency followed by Autoimmune/ Hashimoto's Thyroiditis (27.27%). **Conclusion**: Iodine deficiency is common in the Kumaon region of Uttarakhand leading to most cases of palpable goiter (WHO grade 2). Goiter was more common among females and in third decade of life. Benign nodules were commonest on FNAC with more proportion of hypothyroid levels followed by euthyroid levels.

Keywords: Autoimmune Thyroiditis, Hashimoto's Thyroiditis, FNAC, Iodine deficiency, thyroid swellings.

Introduction

Common clinical presentation of thyroid disease is a thyroid nodule (TN) since it is subjected to various pathological and physiological disturbances like developmental, hyperplastic, inflammatory, and neoplastic. [1] Thyroid nodules are among the common diseases of the endocrine system, with 3%– 7% prevalence by palpation. The prevalence of thyroid nodules in the general population is high, the percentages vary depending on the mode of discovery: 2–6 % (palpation), 19–35 % (ultrasound) and 8–65% (autopsy data). The prevalence by high-resolution ultrasonography among randomly selected individuals is 19%–67%, with annual increasing trends worldwide. 5% to 15% of TNs is thyroid cancer. [2,3] Clinically, thyroid diseases have been functionally categorized into hypothyroidism and hyperthyroidism. Hypothyroidism is common throughout the world. [4] In iodine-sufficient countries, the prevalence of hypothyroidism ranges from 1% to 2%, rising to 7% in individuals aged between 85 and 89 years. [5] The prevalence of overt hyperthyroidism ranges from 0.2–1.3% in iodine-sufficient parts of the world. [6] The clinical presentation of hyperthyroidism ranges from asymptomatic to thyroid storm. Patients with long-standing untreated hyperthyroidism may develop atrial fibrillation or heart failure (5.8% of patients). [7] On examination, thyroid nodules may be solitary or multinodular. This distinction is essential because solitary nodules are more likely to be malignant than a multinodular goiter. A proper demographic and personal history along with a complete local and systemic examination is very crucial towards a proper diagnosis and management of the thyroid nodules. Most of the thyroid nodules being benign; and only 5-10% nodules being malignant, [8, 9] the display of a wide range of lesions differing in biological behaviour are a source of concern for the patient and a diagnostic dilemma for physicians. A multitude of diagnostic tests are available to evaluate goiter. The functional nature of the nodule can be established by chemical hormonal analysis (thyroid profile: mainly Serum TSH) and nuclear imaging method. [8,9] The measurement of thyroid hormones in the blood (serum T3, T4 and TSH) is most helpful for evaluation of hypo and hyperthyroidism, among which the most sensitive one is TSH levels. Grave's disease and Hashimoto's thyroiditis are Autoimmune thyroid diseases with the diagnostic hallmark being anti-thyroglobulin antibody and anti-thyroid peroxidase antibody for Hashimoto's thyroiditis and antibody to TSH receptor for Graves's disease (TRAB). [9] Thyroid ultrasonography (US) is pivotal in the evaluation of thyroid nodules: in seeing the features suspicious for malignancy. Some of the US features suggestive of malignancy include calcifications (microcalcifications called as psammoma bodies), local invasion & direct lymph node metastasis, marked intrinsic hypervascularity and hypoechoic solid nodule; however, its sensitivity and specificity are not very high. FNAC remains a well-accepted and established OPD procedure used in the primary diagnosis of palpable thyroid swelling with high sensitivity and specificity. We aimed to study clinicopathological and etiological profile of patients presenting with Goiter at Tertiary Care Hospital in Kumaon Region of Uttarakhand.

Material and methods

This study was a hospital based cross- sectional study carried out in Medicine, ENT OPD/ IPD of Dr. Sushila Tiwari hospital, Haldwani District Nainital. The study duration was January 2020- September 2021. All patients aged > 16 years presenting with goiter in Medicine,

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ENT OPD/ IPD of Dr. Sushila Tiwari Hospital giving informed written consent during study period (n=121) were included in study. Patients aged <16 years, pregnant females, having other chronic systemic illness such as chronic renal disorder, hepatic disorders, cardiac disorders, patients using drugs such as amiodarone, lithium and other thyrotoxic drugs, pubertal goiter, not giving informed written consent were excluded from study. The socio-demographic information regarding age and gender was collected from all patients, based on predesigned data sheet. Full clinical examination was done for presence of goiter, and it was graded as per WHO grading. Thyroid profile (TFT: T3, T4, TSH) were measured by drawing 4 ml of blood in the plain red topped vacutainer and sent to laboratory for investigation in the fasting state of the patients. The cut-offs for thyroid function test were T3 (0.85-2.02 ng/ml), T4 (5.13-14.06 µg/ml) and TSH (0.27-4.20 µIU/ml). Fine needle aspiration cytology was done. FNAC was done with hypodermic needle of 21-24 gauge needle attached to 10-cc disposable syringe. The evaluation of cytological features was done. Reporting was done as per the 2017 Bethesda system of reporting thyroid cytology. Ultrasonography of neck was performed and the report was obtained.

Ethical clearance was obtained from the Institutional Ethical Committee, prior to the start of the study. The written informed consent was taken from all study participants. Confidentiality and privacy were ensured at all stages. The presentation of the categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the mean±SD and as median. The association of the variables which were qualitative in nature were analyzed using Fisher's exact test. The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

Results

Most (28.93%) of patients belonged to age group 21-30 years followed by 31-40 years (25.62%), 41-50 years (20.66%), 18-20 years (10.74%) and 51-60 years (10.74%). The mean age was 36.79 ± 14 with median of 35 (26-46) years. There were 86.78% females and 13.22% males.

Table 1: Distribution of age and sex of study participants

		Frequency	Percentage
Sex	Female	105	86.78%
	Male	16	13.22%
Age (years)	18-20	13	10.74%
	21-30	35	28.93%
	31-40	31	25.62%
	41-50	25	20.66%
	51-60	13	10.74%
	>60	4	3.31%
	Mean ± SD	36.94 ± 13.75	
	Median (25th-75th percentile)	35 (26-46)	
	Range	18-80	

Table 2: Distribution of WHO Goiter grade of study participants

		Frequency	Percentage
WHO Goiter grade	Grade 1	7	5.79%
	Grade 2	114	94.21%
Thyroid profile	Euthyroid	34	28.10%
	Hyperthyroid	3	2.48%
	Hypothyroid	84	69.42%
Bethesda grading	Grade I	1	0.83%
	Grade II	115	95.04%
	Grade III	1	0.83%
	Grade IV	2	1.65%
	Grade VI	2	1.65%

In majority (94.21%) of patients, WHO Goiter grade was 2 with grade among 7 (5.79%). Majority (69.42%) of patients had hypothyroid followed by euthyroid (28.10%) and 2.48% were hyperthyroid. Majority (95.04%) of patients had Bethesda grade II followed by grade IV (1.65%) and grade VI (1.65%) and grade I and III in only 1 (0.83%) patient each.Among 43.80% of patients, fine needle aspiration finding was nodular colloid goiter followed by chronic Lymphocytic thyroiditis (27.27%), simple colloid goiter (16.53%), benign Hyperplastic nodule (5.79%), adenomatoid nodule with thyroiditis (1.65%) and follicular neoplasm of thyroid (1.65%).

Ultrasound findings showed that 43.80% patients, had hypoechoic nodule followed by hypoechoic micronodule with echogenic fibrous septae (27.27%), diffuse hypoechoic (18.18%), diffusely enlarged gland with hypoechogenicity (5.79%) and hyper to isoechoic (1.65%). Majority(60.33%) of patients, probable etiology was iodine deficiency followed by Autoimmune/Hashimoto's Thyroiditis (27.27%) Autoimmune/ Grave's disease (5.79%) and neoplastic (5.79%). Probable etiology was unknown in only 1 out of 121 patients (0.83%).

Table 3: Association of fine needle aspiration finding and ultrasound findings with thyroid profile

		Euthyroid (n=34)	Hyperthyroid (n=3)	Hypothyroid (n=84)	Total	p-value
Fine needle aspiration finding	Adenomatoid nodule with thyroiditis	2 (5.88%)	0 (0%)	0 (0%)	2 (1.65%)	0.012*
	Benign Hyperplastic nodule	4 (11.76%)	0 (0%)	3 (3.57%)	7 (5.79%)	
	Chronic Lymphocytic thyroiditis	4 (11.76%)	0 (0%)	29 (34.52%)	33 (27.27%)	
	Colloid cyst	0 (0%)	0 (0%)	1 (1.19%)	1 (0.83%)	

	Follicular neoplasm of thyroid	2 (5.88%)	0 (0%)	0 (0%)	2 (1.65%)	
	Follicular neoplasm of undetermined significance	0 (0%)	0 (0%)	1 (1.19%)	1 (0.83%)	
	Medullary carcinoma thyroid	1 (2.94%)	0 (0%)	0 (0%)	1 (0.83%)	
	Nodular colloid goiter	15 (44.12%)	1 (33.33%)	36 (42.86%)	53(43.8%)	
	Papillary carcinoma thyroid	1 (2.94%)	0 (0%)	0 (0%)	1 (0.83%)	
	Simple colloid goiter	5 (14.71%)	1 (33.33%)	14 (16.67%)	20 (16.5%)	
Ultrasound findings	Anechoic	0 (0%)	0 (0%)	1 (1.19%)	1 (0.83%)	0.033*
	Diffuse hypoechoic	7 (20.59%)	1 (33.33%)	14 (16.67%)	22 (18.18%)	
	Diffusely enlarged gland with hypo echogenicity	4 (11.76%)	0 (0%)	3 (3.57%)	7 (5.79%)	
	Hyper to isoechoic	2 (5.88%)	0 (0%)	0 (0%)	2 (1.65%)	
	Hypoechoic ill defined lesion	0 (0%)	0 (0%)	1 (1.19%)	1 (0.83%)	
	Hypoechoic micronodule with echogenic fibrous septae	4 (11.76%)	0 (0%)	29 (34.52%)	33 (27.27%)	
	Hypoechoic nodule	15 (44.12%)	2 (66.67%)	36 (42.86%)	53	
	Hypoechoic with coarse calcification	1 (2.94%)	0 (0%)	0 (0%)	1 (0.83%)	
	Punctate hyperechogenic foci	1 (2.94%)	0 (0%)	0 (0%)	1 (0.83%)	

The FNAC showed that benign Hyperplastic nodule was significantly higher in euthyroid and hypothyroid as compared to hyperthyroid. (Benign Hyperplastic nodule: - 11.76%, 3.57% vs 0% respectively). Proportion of patients with fine needle aspiration finding:- Nodular colloid goiter, simple colloid goiter was significantly higher in hyperthyroid as compared to euthyroid and hypothyroid. (Nodular Colloid goiter:- 66.67% vs 44.12%, 42.86% respectively, Simple colloid goiter:- 33.33% vs 14.71%, 16.67% respectively). Chronic Lymphocytic thyroiditis was significantly higher in hypothyroid as compared to euthyroid and hyperthyroid. (Chronic Lymphocytic thyroiditis:- 34.52% vs 11.76%, 0% respectively).As per ultrasound findings, diffusely enlarged gland with hypo echogenicity was significantly higher in euthyroid as compared to hypothyroid and hyperthyroid (Diffusely enlarged gland with hypo echogenicity 11.76% vs 3.57% and 0% respectively). Proportion of patients with ultrasound findings:- diffuse hypoechoic, hypoechoic nodule was significantly higher in hyperthyroid as compared to euthyroid and hypothyroid (Diffuse hypoechoic:- 33.33% vs 20.59%, 16.67% respectively, Hypoechoic nodule:- 66.67% vs 44.12%, 42.86% respectively). Hypoechoic micronodule with echogenic fibrous septae was significantly higher in hypothyroid as compared to euthyroid and hyperthyroid (Hypoechoic micronodule with echogenic fibrous septae:- 34.52% vs 11.76%, 0% respectively). (p value=0.033)

Discussion

In the present study, the mean age of the patients was 36.79 ± 14 years. This correlated with the findings by Basharat R et al. [10] and Kothari et al., [11] who reported that the mean age of the patients was 33.04 and 37.04 years, respectively. Chavan US et al. [12] reported that most of the patients with thyroid nodules were 28-37 years of age; median age was 40 years. Mandal N et al. [13] also reported that most of the patients were in 3rd and 5th decade. Similarly, Ranabhat S et al. [14] also reported mean age as 44.6 years. In the present study, majority (86.78%) of patients were females and 13.22% of patients were males. Kothari et al, [11] Thakor T et al, [15] and Ranabhat S et al. [14] also reported that predominant population of 76%, 84%, and 90% were females, respectively. We palpated the thyroid swelling where we found that only 7 patients (5.79%) had grade 1 goiter where the swelling was only palpable but not visible at rest. However, 114 patients (94.21%) patients had grade 2 goiter where the swelling was visible at rest even without palpation. In a South Indian study by Reddy et al., [16] 11.5% of the goiter were Grade 1 and 1.5% were Grade 2. Aminorroaya et al. [17] found that Grade I goiter was present in 12.4% and Grade II goiter in 6.6% patients. Mesele et al. [18] stated that grade 1 goiter was present in 28.50% and in grade 2 was 9.10%.In our study, there were 34 (28.1%) patients with euthyroid levels and 84 (69.42%) patients with hypothyroidism with only 3 patients (2.48%) having hyperthyroid levels. Among previous studies, Thakor T et al. [15] reported that in 125 patients, 21 cases of the patient's showed hyperthyroidism, 42 showed hypothyroidism, and rest were euthyroid. In another similar study, Ranabhat S et al. [14] reported that out of 50 patients, 12% of the patients had hyperthyroidism and 22% had hypothyroidism. Mandal N et al. [13] found 87% were in euthyroid state, 7% of the patients had hyperthyroidism and 6% had hypothyroidism. Kartha PP et al. [9] reported that 2.9% of the patient's showed hyperthyroidism and 33.4% showed hypothyroidism while 63.7% had normal thyroid profile.We used the Bethesda classification for FNAC where the most common diagnosis fell into Grade 2 Bethesda grading (95.04%). Bethesda grade 2 included all the benign categories of goiter, which included nodular colloid goiter (n=53, 43.80%), chronic lymphocytic thyroiditis (n=33, 27.27%), simple colloid goiter (n=20, 16.53%), benign hyperplastic nodule (n=7, 5.79%), and adenomatoid nodule with thyroiditis (n=2, 1.65%). In the study by Thakor T et al, [15] FNAC showed 6.4% Non-Diagnostic or Unsatisfactory (ND/UNS), 80% benign, 2.4% Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance (AUS/FLUS), 4% Follicular Neoplasm (FN), 4% Suspicious for Malignancy (SFM), and 3.2% Malignant." In another similar study, Devi B et al. [19] found that out of 243 thyroid nodules, FNAC showed colloid goiter in 54.7% cases, lymphocytic thyroiditis in 9.54% cases, follicular neoplasm in 7.05%, Hashimoto thyroiditis in 5.8%, benign thyroid lesions in 3.31%, and multinodular goiter in 2.9% cases. Chavan US et al. [12] reported that out of 138 thyroid nodules, FNAC demonstrated 60.1% benign cases, 13% inflammatory cases, 1.4% malignant cases, 20.3% indeterminate cases, and 5.1% inadequate cases. In benign cases, 44.9% were colloid goiter, colloid cyst (8.0%), Thyroglossal cyst (3.6%), and 2.2% cases of multinodular goiter. Khatib et al. [20] reported that out of 287 thyroid nodules, "0.68% were non-diagnostic, 88% were benign, 3.4% Atypia of undetermined significance (AUS) / Follicular lesion of undetermined of significance (FLUS), 4.5% Follicular neoplasm, 1.4% Suspicious for malignancy and 2.06% malignant". Athavale et al. [21] reported that out of 100 patients, FNAC showed that 62 patients had colloid goiter, 27 patients had multinodular goiter, 6 patients had neoplastic etiology, 3 patients had Hashimoto's Thyroiditis and 2 patients had Papillary Carcinoma Thyroid.Both cases of malignancy, i.e., medullary carcinoma thyroid and papillary carcinoma thyroid had euthyroid levels. Both cases of follicular neoplasms of thyroid and adenomatoid nodular thyroiditis also had euthyroid levels. Overall, statistically we found a significant association of TFT with FNAC diagnosis and grading. Among other studies, Thakor et al. [15] also reported that most of the cases with altered TFT were found in category II. In contrast, category V and VI had euthyroid levels as seen in our study. In category II, among the 16 cases of thyroiditis (14 of lymphocytic/Hashimoto's' thyroiditis, 2 of

granulomatous thyroiditis) majority were hypothyroid, while among 84 cases of benign thyroid lesion, majority were euthyroid. In the study by Khatib et al, [20] thyroid function tests were deranged in 42.06% among category 2 lesions, whereas only 1 case of category 4 presented with hypothyroidism. All cases of category 3, 5 and 6 were found to be euthyroid. Out of 68 patients of thyroiditis, 37 had hypothyroidism (54.4%) and 7 patients were hyperthyroid (10.29%). There was a significant association of thyroid functional status with both benign and neoplastic lesions ($p<0.05$).

In present study, in 43.80% of patients, ultrasound findings was hypoechoic nodule followed by hypoechoic micronodule with echogenic fibrous septae (27.27%), diffuse hypoechoic (18.18%), diffusely enlarged gland with hypoechogenicity (5.79%) and hyper to isoechoic (1.65%). Ultrasound finding was anechoic, hypoechoic ill-defined lesion, hypoechoic with coarse calcification and punctate hyperechogenic foci in only 1 out of 121 patients (0.83%) each. Arpana et al. [22] found that in benign and malignant thyroid nodules, hypogenicity was present in 11.8% and 40%, respectively; isoechoic in 5.9% and 6.7%, respectively; hyperechoic in 16.2% and 0%, respectively; and heteroechoic in 66.2% and 53.3%, respectively. Shen et al. [23] reported that on USG, compared with benign lesions, malignant lesions were more likely to be solid or almost solid (92.1% vs. 61.6%), hypoechoic (92.4% vs. 87.7%), Taller-than-wide in shape (42.9% vs. 4.3%), ill-defined margins (9.4% vs. 1.5%), and microcalcification (64.9% vs. 11.5%) ($P<0.05$). In our study we made a probable etiology of Autoimmune thyroiditis in 40 cases on FNAC. Iodine deficiency was labeled in 73 cases (60.33%), with patients showing simple colloid goiter and nodular colloid goiter on FNAC. One case remains unknown/undiagnosed on FNAC while 7 cases had neoplastic etiology and fell into grade 3, 4, 5 of the Bethesda classification. So, overall, in our study there were 7 cases (5.79%) malignant nodules, while rest of them were benign nodules. In a study conducted at Karnataka (South India), Reddy et al. [16] found that in 170 urine samples, the median urinary iodine level was 125 µg/L that indicated no iodine deficiency. In another study conducted in a South India state Kerala the prevalence of goiter was 12.20%.

Conclusion

Iodine deficiency is common in the Kumaon region of Uttarakhand leading to most cases of palpable goiter (WHO grade 2). The thyroid swellings were more common among females and most commonly affects individuals in third decade of life. Relating to iodine deficiency the study found benign nodules to be the commonest on FNAC with more proportion of hypothyroid levels followed by euthyroid levels. Only two cases of malignancy were identified which were euthyroid. Both FNAC and USG serves as good screening techniques for goiter, with significant association with thyroid profile of the patients allowing for us to make a probable diagnosis to start the treatment.

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