

Sociodemographic and Clinical Pattern of Thyroid Nodules in Sindh, Pakistan: A Retrospective Analysis from a Tertiary Care Centre

Abstract

Objectives: To study the sociodemographic and clinical patterns of thyroid lesions in Sindh, Pakistan

Methodology: A prospective observational study was conducted at the department of Surgery, Ward - 26, Jinnah Postgraduate Medical Centre, Karachi between March 2018 to 2020. All patients presenting with complaints of thyroid nodule as diagnosed clinically and by ultrasound imaging were included in the study. Patients with deranged thyroid hormone levels were excluded. Sociodemographics, clinical, and pathological parameters were recorded in a predefined pro forma. Statistical Package of Social Sciences v.26 (SPSS) was used for data analysis.

Results: A total of 116 patients were evaluated for thyroid lesions. Out of these, only 82 patients were diagnosed with thyroid nodules. A mean age of 35.14 ± 12.28 years was observed. We had 13 patients (11.2%) with a diagnosis of thyroid carcinoma. This included papillary and follicular carcinoma majorly. Out of these, 11 (84.6%) malignant cases were found among female patients.

Conclusion: We presented a significantly higher rate of thyroid carcinoma on histopathology in our centre as compared to previous studies. The majority of the lesions were diagnosed among females. This highlights the increasing incidence of thyroid carcinoma in our population.

Keywords: grave's disease, hashimoto's, follicular carcinoma, FNAC, thyroiditis, papillary carcinoma

Introduction

Thyroid gland is located in front of the neck just below the larynx. It is an endocrine gland and is responsible for several bodily functions. Enlargement of the thyroid gland is a common problem resulting in inability to maintain normal physiological functions of the body.^{1,2} Thyroid nodules can be a manifestation of a wide array of disorders and require thorough investigations. Thyroid nodules are one of the common endocrine disorders, 3%-7% of which are discovered on palpation.¹ While among randomly selected individuals 19%-67% of TNs are detected on high-resolution ultrasonography.^{1,2} The prevalence of TNs is increasing globally per annum. Moreover, thyroid carcinoma, which has become the fastest growing cancer, constitutes 5%-15% of the TNs.³ In numerous parts of the world endemic goiter, which is hypothesized as a precursor lesion to thyroid carcinoma, is a serious concern.⁴ Additionally, iodine deficiency has a well-understood causal association with increased incidence of thyroid lesions.⁵ If left untreated, thyroid disease may develop some serious life threatening complications including Graves' disease, Hashimoto's thyroiditis or even carcinoma.^{6,7} Previous literature has highlighted the association between geographical location, age, and sex with the increasing incidence of thyroid lesions.^{4,6-8} Furthermore, exposure to radiation is among the major predisposing factors. It is estimated that one in every eight women will eventually suffer from thyroid related issues during her life.⁹

Thyroid lesions can present as solitary nodules, multinodular, or diffuse goiter and are diagnosed on clinical examination and non-invasive investigations such as ultrasonographic imaging.^{10,11} The prevalence of thyroid lesions differs in various reports both locally and globally. In Pakistan, the incidence of thyroid lesions is on the rise. A recent study by Afra et al., reported that out of a total of 1465 cases of thyroid nodules presented in their centre, 1169 cases were established as simple goiter, ten percent were diagnosed as adenoma while 6 percent were diagnosed as thyroid carcinoma.¹⁰ It is alarming to observe such a high percentage of thyroid carcinoma arising from only one city of the country. Therefore, the present study aimed to find out the sociodemographic and clinicopathological pattern of thyroid lesions detected on ultrasonography and histopathological examinations in Sindh, Pakistan.

Methodology

A prospective observational study was conducted at the Department of Surgery, Jinnah Postgraduate Medical Centre, Karachi between March 2018 to March 2020. Ethical approval was obtained prior to the data collection. All patients presenting to the outpatients department with thyroid-related concerns and prominent lesions were eligible to partake in the study. Patients with deranged levels of thyroid profile i.e. thyroid stimulating hormone (TSH), free thyroxine (FT₄), and free triiodothyronine (FT₃) were excluded from the study. Patients with abnormally high or low levels of thyroid profile tests were referred to the Medicine Department for pharmacological intervention.

All data regarding socio demographics and clinicopathological parameters were documented in a predefined proforma. A thorough clinical examination was done in the outpatients department in the examination room by the consultant while the ultrasound imaging of the thyroid lesion was performed by radiologists with an experience of over five years.

The final diagnosis was established on the findings of ultrasound imaging, followed by the FNAC of the nodule correlated with clinical and histopathological analysis. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was used in all the cases.¹²

For data analysis, Statistical Package for Social Sciences (SPSS) version 26 was used. The continuous variables including the age of the patient were presented as mean and standard deviation while for the categorical variables, frequency and percentages were determined. Chi square tests were applied to explore the associations between age groups and type of lesions. A p value of < 0.05 was set as the cut-off value for significance.

Results

A total of 116 patients were evaluated for thyroid lesions. Out of these, only 82 patients were diagnosed with thyroid nodules. A mean age of 35.14 ± 12.28 years was observed with a minimum age of 14 years and maximum age of 75 years. The mean age with standard deviation for men was 33.18 ± 8.43 years and for female patients, 35.63 ± 13.07 years. The majority of the patients were female i.e. 65 (80.2%). Table 1 demonstrates the distribution of patients according to the age groups and location of the thyroid nodules.

Table 1. Distribution of Patients according to their age groups and Location of the Thyroid Nodule

	Bilatera l	Isthm us	Left	Midline	Diffuse	Only LN	Right	P-value
--	---------------	-------------	------	---------	---------	---------	-------	---------

<18	0 (0.00%)	0 (0.00%)	1 (4.50%)	0 (0.00%)	1 (7.70%)	0 (0.00%)	0 (0.00%)	0.985
18-25	1 (16.70%)	0 (0.00%)	6 (27.30%)	0 (0.00%)	3 (23.10%)	0 (0.00%)	7 (18.90%)	
26-35	4 (66.70%)	1 (100.00%)	6 (27.30%)	1 (100.00%)	3 (23.10%)	1 (100.00%)	15 (40.50%)	
36-45	0 (0.00%)	0 (0.00%)	6 (27.30%)	0 (0.00%)	3 (23.10%)	0 (0.00%)	6 (16.20%)	
46-55	1 (16.70%)	0 (0.00%)	3 (13.60%)	0 (0.00%)	2 (15.40%)	0 (0.00%)	6 (16.20%)	
>55	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.70%)	0 (0.00%)	3 (8.10%)	

There was no significant association between the age groups and the location of the thyroid nodule as detected by ultrasound imaging ($P = 0.985$) (Table 1). However, 31 (37.8%) were in the age group between 26 and 35 years. 13 (16%) patients were diagnosed as multi nodular goiter on Ultrasonography.

Furthermore, the site of thyroid lesion was not significantly associated with the gender (Table 2).

Table 2. Distribution of Patients according to the gender and Location of the Thyroid Nodule

Gender	Bilateral	Isthmus	Left	Midline	Diffuse	LN Only	Right	P-value
Male	2 (33.30%)	0 (0.00%)	5 (77.00%)	1 (10.00%)	2 (15.40%)	1 (10.00%)	5 (13.50%)	0.114
Female	4 (66.70%)	1 (10.00%)	17 (77.00%)	0 (0.00%)	11 (84.00%)	0 (0.00%)	32 (86.50%)	

Table 3 shows the frequency and percentages of patients who presented with thyroid nodules. The most common of thyroid nodules were Benign Nodular Hyperplasia with a frequency of 27 (33.3%), followed by Papillary Carcinoma 19 (23.5%), and Follicular Carcinoma 15 (18.50%).

Table 3. Frequency and Percentage of Diagnosis of Thyroid Disease on Histopathology

Diagnosis	Frequency	Percent
-----------	-----------	---------

Benign Cyst	1	1.20%
Benign Nodular Hyperplasia	27	33.30%
Follicular Adenoma	9	11.10%
Follicular Carcinoma	15	18.50%
Hashimoto's Thyroiditis	1	1.20%
Medullary Carcinoma	3	3.70%
Non-diagnostic	4	4.90%
Papillary Carcinoma	19	23.50%
Suspicious of Malignancy (SOM)	1	1.20%
Thyroglossal Cyst	1	1.20%
Total	81	100%

Table 4 shows the distribution of patients according to the gender and diagnosis as established by histopathology.

Table 4. Distribution of Patients according to the Gender and Diagnosis

Diagnosis	Male	Female	Total	P-value
Adenoma	3 (33.30%)	6 (66.70%)	9 (100.00%)	0.861
Benign	6 (20.70%)	23 (79.30%)	29 (100.00%)	
Lymphocytic (Hashimotos)	0 (0.00%)	1 (100.00%)	1 (100.00%)	
Malignant	6 (16.20%)	31 (83.80%)	37 (100.00%)	
Non-diagnostic	1 (25.00%)	3 (75.00%)	4 (100.00%)	

Suspicious of Malignancy (SOM)	0 (0.00%)	1 (100.00%)	1 (100.00%)	
--------------------------------	--------------	----------------	----------------	--

We had 13 patients (11.2%) with a diagnosis of thyroid carcinoma. This included papillary and follicular carcinoma majorly. Out of these, 11 (84.6%) malignant cases were found among female patients while around fifteen percent of patients were male (Table 4).

Table 5. Distribution of Patients according to the Age Groups and Diagnosis

Age Groups	Ade nom a	Beni gn	Lym phoc ytic (Has him otos)	Mali gnan t	Non- diag nostic	Suspi cion of Malig nancy (SOM)	P- valu e
<18	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0.658
18-25	2 (11.80%)	4 (23.50%)	0 (0.00%)	11 (64.70%)	0 (0.00%)	0 (0.00%)	
26-35	4 (12.90%)	13 (41.90%)	0 (0.00%)	11 (35.50%)	3 (9.70%)	0 (0.00%)	
36-45	3 (20.00%)	6 (40.00%)	0 (0.00%)	5 (33.30%)	0 (0.00%)	1 (6.70%)	
46-55	0 (0.00%)	4 (33.30%)	1 (8.30%)	6 (50.00%)	1 (8.30%)	0 (0.00%)	
>55	0 (0.00%)	1 (25.00%)	0 (0.00%)	3 (75.00%)	0 (0.00%)	0 (0.00%)	

Table 5 presents the distribution of patients according to the final diagnosis in different age groups. It was found that 75% of the patients in the age group > 55 years were malignant lesions while 64.7% cases in the age group between 18-25 years were malignant lesions. The majority of the lesions in the age group between 26 and 35 years and 36 to 45 years were benign with a frequency of 13 (41.90%) and 6 (40.00%), respectively (Table 5).

Discussion

The prevalence of TNs in the general population is heavily dependent upon the screening modality used. The incidence of TNs discovered rose from a mere 4-7% on routine clinical examination to a staggering 20-76% on Ultrasonography.¹³⁻¹⁵ With incidence of thyroid cancer on the rise, it's pertinent to evaluate the clinical pattern of the TNs.

The patterns of TNs noticed in our current study are in concordance with the available world literature. Our study observes that the majority of patient's who presented with TNs were younger (age group of 26-35 years) and had a mean age of 35.14 ± 12.28 years, which is lesser than Handa et al. where the patient's mean age was found to be 37.69 ± 14.93 years.¹⁶ Some studies conducted in Pakistan and India, reveal the highest incidence in the age group 30-40 years, while those in Saudi Arabia report an even older population (age group 41-50).¹⁶⁻²⁰ Moreover, our investigation found a higher prevalence of TNs in women (80.2%) and a female to male ratio of 4:1. This finding is comparable with various researches worldwide that reveal a gender disparity and the female to male ratio between 2-9: 1.^{14,16, 24-26} Conditions like menstruation, pregnancy and breastfeeding where the demand of thyroid hormones is increased or the effects of estrogen could account for the female predisposition found in our study.²⁷

Furthermore, the nodules were predominantly located in the right lobe of the thyroid gland in both the genders, which could be due to the large size of the right lobe and its increased vascularity.²⁸ The most common of the TNs observed in our study were Benign Nodular Hyperplasia (33.3%), followed by papillary carcinoma (23.5%), and follicular carcinoma (18.50%). This finding is unlike a study conducted in western Algeria, where most of the cases were benign dystrophic lesions (25.93%), followed by benign nodular hyperplasia (22.56%) and suspicion of malignancy (14.14%).²⁹

Even though more than half of the TNs were benign lesions, an alarmingly high incidence of thyroid carcinoma (45.1%) was observed with papillary carcinoma constituting the majority of the cases. These results are slightly higher than the study conducted in China where 44.7% of the cases were found to be malignant.³⁰

Other retrospective studies conducted in India, Pakistan and Saudi Arabia report a lower prevalence in the range 4.63%-12.65%.^{17,20,21} Similarly, papillary carcinoma was reported to be the most common subtype in sengupta et al.¹⁷

Thyroid carcinoma is ranked the fifth most common cancer in women.³¹ The gender stratification of TNs based on histopathology in our study revealed that women (83.8%) presented with five times more malignant lesions than men (16.2%) which is higher than the female to male ratio of 3:1 for thyroid cancer.³² Moreover, majorly the malignancies (75%) were found in the older participants in the age group >55 years followed by the younger participants in the age group 18-25 years (64.7%). However, a study conducted by Kwong et al. reported a decreasing trend in the likelihood of thyroid malignancy with advancing age.³³

Conclusion

We presented a significantly higher rate of thyroid carcinoma on histopathology in our centre as compared to previous studies. The majority of the lesions were diagnosed among females. This highlights the increasing incidence of thyroid carcinoma. Further epidemiological studies are required to explore the various risk factors and socio-demographic patterns associated with thyroid nodules in our population.

References

1. Dean DS, Gharib H. Epidemiology of thyroid nodules. Best practice & research Clinical endocrinology & metabolism. 2008 Dec 1;22(6):901-11.
2. Forkin KT, Huffmyer JL, Nemergut EC. Endocrine Physiology. Pharmacology and Physiology for Anesthesia. 2019 Jan 1:6693-707.
3. DeLellis RA, Williams ED. Pathology of the thyroid and parathyroid. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C (eds), Pathology and genetics of tumours of endocrine organs, World Health Organization Classification of Tu- mours, IARC Press, Lyon, 2004; p. 57-66.
4. Lawal O, Agbakwuru A, Olayinka OS, Adelusola K. Thyroid malignancy in endemic nodular goitres: prevalence, pattern and treatment. European Journal of Surgical Oncology (EJSO). 2001 Mar 1;27(2):157-61.
5. LKim D, Kim W, Joo SK, Bae JM, Kim JH, Ahmed A. Subclinical hypothyroidism and low-normal thyroid function are associated with nonalcoholic steatohepatitis and fibrosis. Clinical gastroenterology and hepatology. 2018 Jan 1;16(1):123-31.
6. Regalbuto C, Le Moli R, Muscia V, Russo M, Vigneri R, Pezzino V. Severe graves' ophthalmopathy after percutaneous ethanol injection in a nontoxic thyroid nodule. Thyroid. 2012 Feb 1;22(2):210-3.
7. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmunity reviews. 2014 Apr 1;13(4-5):391-7.
8. Al-Awadhi N, Al-Kandari N, Al-Hasan T, AlMurjan D, Ali S, Al-Taiar A. Age at menarche and its relationship to body mass index among adolescent girls in Kuwait. BMC public health. 2013 Dec;13(1):1-7.
9. Sanabria A, Kowalski LP, Shah JP, Nixon IJ, Angelos P, Williams MD, Rinaldo A, Ferlito A. Growing incidence of thyroid carcinoma in recent years: factors underlying overdiagnosis. Head & neck. 2018 Apr;40(4):855-66.
10. Samad A, Ali KS, Fayyaz N, Akhtar N, Mahmood N, Kashif M. Histopathological audit of thyroid lesions: A retrospective study in a Tertiary Care Hospital. International Journal of Medical Research & Health Sciences. 2019;8(5):173-6.
11. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L. Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract. 2006;12(1):63-102.
12. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. Thyroid. 2017 Nov 1;27(11):1341-6.
13. Mazzaferri EL. Management of a solitary thyroid nodule. New England Journal of Medicine. 1993 Feb 25;328(8):553-9.
14. Ezzat S, Sarti DA, Cain DR, Braunstein GD. Thyroid incidentalomas: prevalence by palpation and ultrasonography. Archives of internal medicine. 1994 Aug .
15. Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. Annals of internal medicine. 1997 Feb 1;126(3):226-31.
16. Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients. Journal of cytology. 2008 Jan 1;25(1):13.

17. Sengupta S, Tuli I, Baruah B, Kesari S, Ilapakurty B, Gupta A. Spectrum of goitrous lesions in patients at a tertiary care center of Sikkim. *Sahel Medical Journal*. 2014 Jul 1;17(3):112-.
18. Qureshi IA, Khabaz MN, Baig M, Begum B, Abdelrehaman AS, Hussain MB. Histopathological findings in goiter: A review of 624 thyroidectomies. *Neuroendocrinology Letters*. 2015 Jan 1;36(1):48-52
19. Refeidi A, Al Shehri G, Al Ahmary A, Tahtouh M, AlSetei S, Al Ghamdi A, Mahfouz A, Abu Eshy S. Patterns of thyroid cancer in Southwestern Saudi Arabia. *Saudi Med J*. 2010 Nov 20;31(11):1238-41.
20. Saeed MI, Hassan AA, Butt ME, Baniyaseen KA, Siddiqui MI, Bogari NM, Al-Allaf FA, Taher MM. Pattern of thyroid lesions in western region of Saudi Arabia: A retrospective analysis and literature review. *Journal of clinical medicine research*. 2018 Feb;10(2):106.
21. Musani AM, Khan AF, Ashrafi KS, Jawaid I, Mugeru N, Malik S. Spectrum of thyroid disease presenting in ENT dept. Evaluation by FNAC *Pak J Otolaryngol*. 2010;26:74-5.
22. Hurtado-López LM, Basurto-Kuba E, de Oca-Durán ER, Pulido-Cejudo A, Vázquez-Ortega R, Athié-Gutiérrez C. Prevalence of thyroid nodules in the Valley of Mexico. *Cirugia y cirujanos*. 2011;79(2):114-7.
23. Ogbera AO, Kuku SF. Epidemiology of thyroid diseases in Africa. *Indian journal of endocrinology and metabolism*. 2011 Jul;15(Suppl2):S82.
24. Mansoor R, Rizvi SR, Huda ST, Khan C. Spectrum of thyroid diseases, an experience in the tertiary care and teaching hospital. *Ann Pak Inst Med Sci*. 2010;6:101-6.
25. Gamboa-Domínguez A, Lino-Silva S, Candanedo-González F, Medina-López E, Acuña-González D, Jacinto-Cortés I, González-Treviño O. Trends of thyroid pathology in a referral center: Steady prevalence of papillary thyroid carcinoma but goiter increase in thyroidectomies. *Revista de Investigación Clínica*. 2011;63(2):148-54.
26. Htwe TT, Hamdi MM, Swethadri GK, Wong JO, Soe MM, Abdullah MS. Incidence of thyroid malignancy among goitrous thyroid lesions from the Sarawak General Hospital 2000-2004
27. Wang K, Yang Y, Wu Y, Chen J, Zhang D, Liu C. The association of menstrual and reproductive factors with thyroid nodules in Chinese women older than 40 years of age. *Endocrine*. 2015 Mar;48(2):603-14
28. Larsen PR. , *Thyroid physiology and diagnostic evaluation of patients with thyroid disorders*. Williams textbook of endocrinology. 2003.
29. Bendouida AF, Harir N, Diaf M, Belhandouze L, Sellam F, Moulessehoul S, Rih A. Clinical cytohistopathological study of benign thyroid disease in Sidi Bel Abbes region, Western Algeria. *The Egyptian Journal of Internal Medicine*. 2016 Mar;28(1):5-8.
30. Yan HX, Pang P, Wang FL, Tian W, Luo YK, Huang W, Yang GQ, Jin N, Zang L, Du J, Ba JM. Dynamic profile of differentiated thyroid cancer in male and female patients with thyroidectomy during 2000–2013 in China: a retrospective study. *Scientific reports*. 2017 Nov 20;7(1):1-8.
31. Cerfolio RJ, Bryant AS, Scott E, Sharma M, Robert F, Spencer SA, Garver RI. Women with pathologic stage I, II, and III non-small cell lung cancer have better survival than men. *Chest*. 2006 Dec 1;130(6):1796-802.

32. Ortega J, Sala C, Flor B, Lledo S. Efficacy and cost-effectiveness of the UltraCision® harmonic scalpel in thyroid surgery: an analysis of 200 cases in a randomized trial. *Journal of Laparoendoscopic & Advanced Surgical Techniques*. 2004 Feb 1;14(1):9-12
33. Kwong N, Medici M, Angell TE, Liu X, Marqusee E, Cibas ES, Krane JF, Barletta JA, Kim MI, Larsen PR, Alexander EK. The influence of patient age on thyroid nodule formation, multinodularity, and thyroid cancer risk. *The Journal of Clinical Endocrinology & Metabolism*. 2015 Dec 1;100(12):4434-40.

UNDER PEER REVIEW