GENDER AND AGE-RELATED DIFFERENCES IN THE DISTRIBUTION OF NEOPLASTIC AND NON-NEOPLASTIC THYROID LESIONS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Many thyroid disorders respond well to both medical and surgical interventions. Research indicates that around 1-10% of adults in the United States exhibit solitary nodules in their thyroid glands. These nodules are more prevalent among females, with benign growths outnumbering malignant ones. Thyroid carcinomas, while relatively rare, comprise less than 1% of solitary nodules. Various thyroid gland lesions occur, highlighting the critical role of accurate and timely diagnosis in patient care.

Objective: To determine age and gender-wise distribution of the benign and malignant thyroid lesions.

Methodology: This cross-sectional study was conducted between September 2021 to August 2022, and a total of 100 participants were enrolled in the investigation. Data was collected from the surgical department of Nasser Teaching Hospital Peshawar, encompassing both men and women individuals who had undergone thyroidectomy. Study data was extracted from the department records.

Results: Our study involved 100 post-thyroidectomy patients, ages ranging from 20 to 70 years, comprising 15 males and 85 females. Most of the patients had non-neoplastic lesions.

The most prevalent non-neoplastic lesions were hyperplastic and inflammatory lesions with a higher incidence among females (60.0%). Within the neoplastic group, most of the cases were benign followed by malignant lesions upon microscopic examination.

Conclusion: This study highlights a significant gender and age-related disparity in thyroid lesions. Non-neoplastic conditions, such as hyperplastic thyroid nodules, were more common in females, particularly aged 30 to 50. In contrast, males had a slightly higher occurrence of neoplastic lesions, including malignancies in younger individuals. These findings emphasize the need for early detection and gender-specific strategies in managing thyroid diseases. Further research is required to understand this disparity for preventive and therapeutic purposes.

Keywords: Thyroid lesions, Thyroidectomy, Benign thyroid nodules, Malignant thyroid nodules, Goiter

INTRODUCTION

Thyroid disorders are among the most prevalent endocrine diseases in the world with a prevalence in people of all ages.[1] These disorders are further divided into neoplastic, which means tumor-related and non-neoplastic or primarily non-tumor-related lesions.[2]

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Thyroid diseases that are not neoplastic are goiter, hyperplastic nodules, and thyroiditis which mostly arise from derangement in hormonal secretion or inflammation while neoplastic thyroid diseases including benign thyroid adenomas, malignant thyroid cancers, and other pathological conditions that may be clinically significant.[3, 4]

The frequency of the thyroid lesions and nodules is well-known to be related to gender.[5, 6] In conducting literature research on thyroid disorders some evidence has revealed that thyroid disorders are more prevalent among females than males.[7, 8] Females are predisposed to non-neoplastic disorders including goiter and thyroiditis and also benign thyroid neoplasm. It has been argued that hormonal factors may play a role particularly estrogen which is expected to make female patients more vulnerable to thyroid disorders,

particularly when of childbearing age.[9, 10] In contrast, thyroid cancer represents a relatively rare pathology that affects male and female patients more or less equally; nevertheless, men appear to develop malignancies more often, which in turn points to certain gender-related factors in thyroid disease.[11, 12] Another factor that affects the distribution of thyroid lesions is age.[13, 14] Research shows that the prevalence of neoplastic and non-neoplastic thyroid disease is more common in the middle age group which is between 30 and 50 years.[15, 16] Non-neoplastic diseases, affecting the thyroid gland are dominated by hyperplastic thyroid nodules and goiters and such diseases preferentially affect the younger population.[17] While benign neoplastic lesions are seen in elder people; both the malignant and benign neoplastic lesions can be found in young to middle-aged groups of people.[18] Nevertheless, malignancies in general are slightly more often found in patients younger than 50 years of age, therefore any screening and early diagnostics initiatives should be focused on these age groups.[19] Inspite of a vast literature on thyroid disorders, there is a lack of evidence regarding the distribution of neoplastic and non-neoplastic lesions in various population groups. The majority of the published articles present regional or hospital-specific data and there is lack of sufficient study regarding the interaction between gender and age in these diseases. Furthermore, it is becoming apparent that such diagnostic and therapeutic approaches may be required in women and/or male individuals because of the differences in hormonal levels and risks factors. Obtaining additional information regarding gender and age distribution will help in early detection, prevention and treatment.

Our study will determine the prevalence of thyroid lesions regarding social, gender and age wise distribution both male and female participants in our population for improving clinical care of patients affected with thyroid disorders.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Pathology Dept, Kabir Medical College over a period of one year i.e. from September 2021 to August 2022. The sample size was 100 calculated through Open Epi software with a prevalence of 10%[20] and a confidence level of 95% with a 5% margin of error. About 100 individuals having undergone thyroid surgeries for thyroid abnormalities were included in this study.

The Naseer Teaching Hospital provided all the resources and biopsy specimens that were referred for histopathological evaluation. Other relevant information was taken from departmental archives. Each participant included in the study had been clinically evaluated and diagnosed with thyroid pathology. The study population comprised both males and females, ranging in age from 20 to 70 years.

Tissue Collection

The specimens from the test population labeled with patient name and medical registration number were already fixed in 10% formalin. Sections were taken from interest- related pathological areas and further processed, undergoing alcoholization dealcohlization, waxing, embedding, sectioning, dewaxing, staining (Hematoxylin and eosin), labeling and then examination under the microscope to assess the histopathological features of the tissue.

There are some major limitations in this research due to which it failed to address biases properly. Possible bias in data collection may also have arisen due to selection bias where samples were restricted to patients who had undergone surgery and those referred for histopathological analysis, not including non-surgical cases or diseases across the spectrum of thyroid disorders. Information bias can be an issue when database information is collected from departmental archives and therefore may include missing data or are not entirely accurate. Moreover, external bias is a problem of generalization in the study as the results will only be relevant to a population of a particular hospital in a particular country.

The collected data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Descriptive statistics were employed to summarize the data, with categorical variables presented as frequencies and percentages, and continuous variables expressed as means and standard deviations. The Chi-square test was used to assess the association between categorical variables such as gender and types of thyroid lesions. A p-value of less than 0.05 was considered statistically significant. Results were presented in the form of tables and charts to facilitate clear

interpretation and comparison.

RESULTS

The present study comprised 100 participants aged between 20 and 70 years with a mean age 45±2.5 years. Most cases were observed in the 20 to 40-year age group indicating a significant disease burden in this age range. Regarding gender distribution of the participants, most of the cases were females (n=85) while few of the cases were males (n=15) resulting in a male-to-female ratio of 1:6.2. (Figure 1) (Table 1)

In the non-neoplastic group (n=58), hyperplastic thyroid nodules were the most common lesion with goiter being the most predominant type with the majority of the cases occurring in females of 30 to 50 years. Inflammatory lesions were reported in a few cases (n=8) with thyroiditis being the most common type with the highest incidence observed in females aged 20 to 60 years.(Figure 2) In the neoplastic group, most of the cases were non-cancerous (n=27) with adenomas being the most common type. Most cases of benign neoplasms occurred in individuals aged 20 to 50 years. Malignancy was diagnosed in a few cases (n=15), with the majority occurring in the 20 to 45 years of age.(Figure 3)

The distribution of non-neoplastic and neoplastic thyroid lesions between male and female participants revealed a higher proportion of non-neoplastic lesions among females, while males have a slightly higher occurrence of neoplastic lesions. There was a statistically significant association between the genders and the distribution of these thyroid lesions. (Table 1)

Table 1: The Distribution of Non-Neoplastic and Neoplastic Thyroid Lesions among Male and Female Participants

Gender	Non-Neoplastic Lesions (n=58)	Neoplastic Lesions (n=42%)	p-value
Females (n = 85)	51 (60.0%)	34 (40.0%)	0.032
Males (n = 15)	7 (46.6%)	8 (53.3%)	

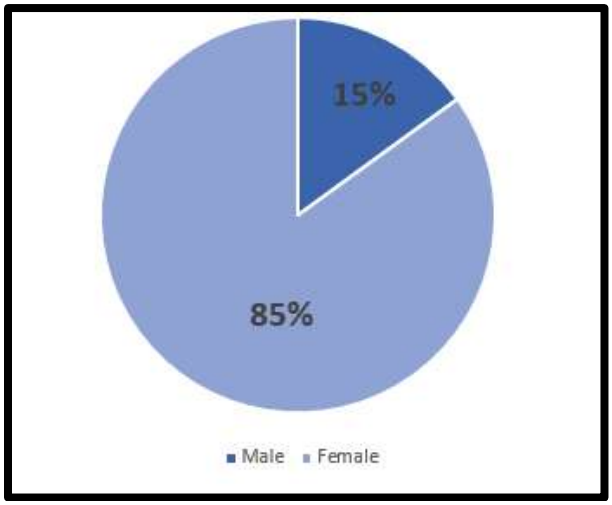

Figure 1: Gender-Wise Distribution of the Thyroid Lesions

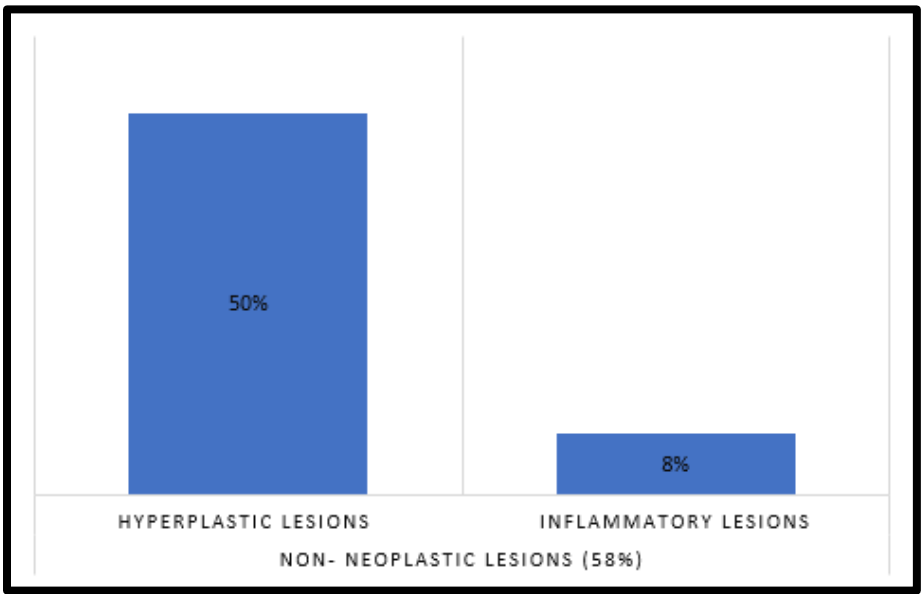

Figure 2: Figure 2: Distribution of Non-Neoplastic Thyroid Lesions

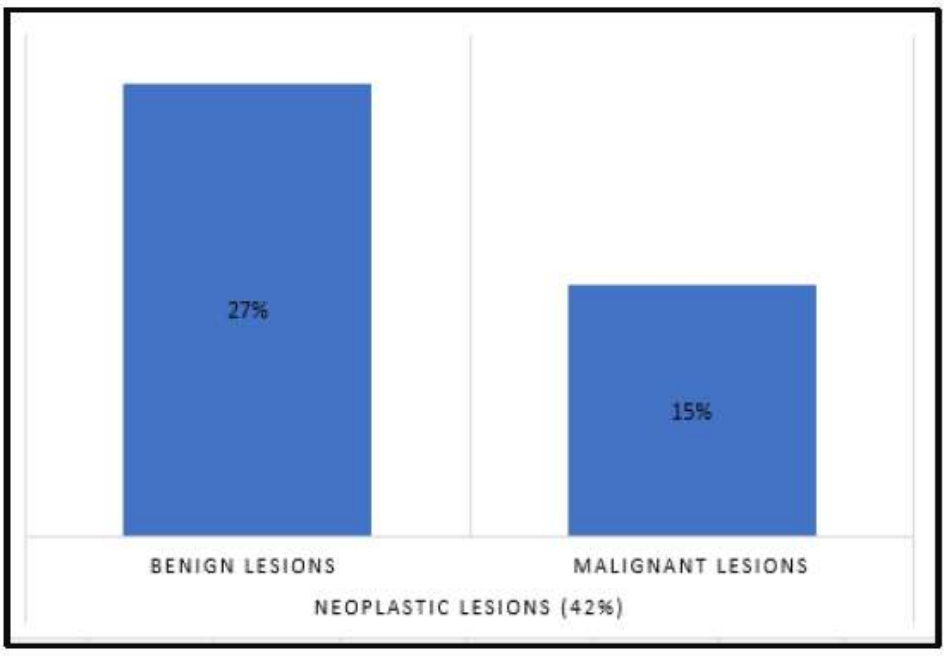

Figure 3: Distribution of Neoplastic Thyroid Lesions

DISCUSSION

The current study aims to assess the distribution of thyroid lesions among male and female participants, focusing on both neoplastic and non-neoplastic conditions. The findings highlight a higher prevalence of non-neoplastic lesions, particularly in females aged 30 to 50, with hyperplastic thyroid nodules and goiter being the most common types. In contrast, neoplastic lesions were more frequent among males, with adenomas being the predominant benign neoplasm, and malignancy largely confined to individuals aged 20 to 45. The overall male-to-female ratio of thyroid disorders was 1:6.2, with a mean participant age of 45 years, indicating a significant gender and age- related disparity in the burden of thyroid diseases.

Our findings align with several previous studies

that have also observed a greater incidence of thyroid disorders, particularly non-neoplastic lesions, among females. A study by Burkan N et al. (2021) confirmed that women are more likely to develop thyroid nodules and goiter, suggesting a potential link between female hormonal factors and thyroid disease development.[21] Similarly, Poppe K et al. (2021) reported a higher prevalence of thyroid lesions, especially goiters, in women due to fluctuations in estrogen and progesterone levels.[22] These studies support the gender disparity observed in our findings, where as the majority of non-neoplastic cases were seen in females.

Furthermore, our study showed that most cases occurred within the 20 to 40-year age group, emphasizing that thyroid disorders commonly manifest during midlife. This is consistent with the findings of Alyahya A et al (2021), who also reported that the peak incidence of thyroid disorders occurs between the ages of 18 and 60.[23] A study by Shimura H et al. (2021) noted that thyroid nodules and related disorders are frequently diagnosed in adults under 45 years.[24] The higher disease burden in this age group may be due to several factors, including hormonal changes, increased metabolic demands, and autoimmune processes that are more prevalent in this demographic.

In terms of neoplastic lesions, our study identified adenomas as the most frequent benign neoplasm, with malignancies accounting for a smaller portion of cases. Similar trends were observed by Ghartimagar D et al. (2020), who found that benign neoplasms, particularly adenomas, were the most common thyroid neoplastic lesions.[2] Moreover, malignancies, though less frequent, were predominantly seen in younger individuals, particularly those between 20 and 45 years of age. This pattern aligns with other studies, such as that by Wu J et al. (2024), which reported a higher incidence of thyroid cancer in younger populations, especially in females.[25] Vaccarella S et al. (2021) have pointed out that thyroid cancer can be seen in patients comparatively of a younger age.26

The male-to-female ratio of 1:6.2 in our study is noteworthy and mirrors previous studies. Several studies found that women are more likely to develop thyroid disorders than men, underscoring the significant gender disparity in the incidence of both non- neoplastic and neoplastic thyroid lesions.[7, 27, 28] This may be explained by genetic, hormonal, and environmental factors that differentially affect males and females. For instance, women are more susceptible to autoimmune thyroiditis, which can lead to both hypothyroidism and hyperthyroidism, further increasing their risk of developing thyroid nodules.

Additionally, the statistically significant difference between the distribution of neoplastic and non-neoplastic lesions among males and females in our study (p-value
= 0.032) suggests that gender plays a critical role in the type of thyroid pathology. This finding is supported by Lei R. et al. (2021) and Zahedi A. et al. (2020), who noted that women are more prone to benign thyroid lesions.[29], whereas men are at slightly higher risk for malignant neoplasms.[30] This differential distribution may have clinical implications for diagnostic and treatment strategies, necessitating gender-specific approaches to the management of thyroid diseases.

Though less common in our study (n=8), inflammatory lesions were primarily observed in females aged 20 to 60, with thyroiditis being the most frequently reported type. These findings are consistent with other studies, such as that by Samsami A et al. (2020), which also found a higher prevalence of autoimmune thyroiditis in women, especially during their reproductive years.[31] Autoimmune conditions, such as Hashimoto's thyroiditis, are known to affect females disproportionately, further explaining the higher incidence of inflammatory thyroid lesions among women in our study.[32]

CONCLUSION

This study highlights a significant gender and age-related disparity in thyroid lesions. Non-neoplastic conditions, such as hyperplastic thyroid nodules, were more common in females, particularly aged 30 to 50. In contrast, males had a slightly higher occurrence of neoplastic lesions, including malignancies in younger individuals. These findings emphasize the need for early detection and gender-specific strategies in managing thyroid diseases. Further research is required to understand these disparities and improve p

REFERENCES

1. Crafa A, Calogero AE, Cannarella R, Mongioi' LM, Condorelli RA, Greco EA, et al. The burden of hormonal disorders:

a worldwide overview with a particular look in Italy. Frontiers in Endocrinology. 2021;12:694325.
2. Ghartimagar D, Ghosh A, Shrestha MK, Thapa S, Talwar OP. Histopathological spectrum of non-neoplastic and neoplastic lesions of thyroid: A descriptive cross- sectional study. JNMA: Journal of the Nepal Medical Association. 2020;58(231):856.
3. Niedziela M. Hyperthyroidism in adolescents. Endocrine connections. 2021;10(11):R279-R92.
4. Marotta V, Bifulco M, Vitale M. Significance of RAS mutations in thyroid benign nodules and non-medullary thyroid cancer. Cancers. 2021;13(15):3785.
5. Ameer SS, Shahbaz S. Sonographic Incidence and Characteristics of Thyroid Nodules in Various Age Groups and Gender. 2020.
6. Demetriou E, Fokou M, Frangos S, Papageorgis P, Economides PA, Economides A. Thyroid nodules and obesity. Life. 2023;13(6):1292.
7. Sharma P, Magar NT, Mahesh B. Prevalence of thyroid disorder in residents of the Western region of Nepal. International Journal of Applied Sciences and Biotechnology. 2021;9(3):169-75.
8. Alqahtani SAM. Prevalence and characteristics of thyroid abnormalities and its association with anemia in ASIR region of Saudi Arabia: a cross-sectional study. Clinics and practice. 2021;11(3):494-504.
9. 9. Ren B, Zhu Y. A new perspective on thyroid hormones: crosstalk with reproductive hormones in females. International journal of molecular sciences. 2022;23(5):2708.
10. Palomba S, Colombo C, Busnelli A, Caserta D, Vitale G. Polycystic ovary syndrome and thyroid disorder: a comprehensive narrative review of the literature. Frontiers in Endocrinology. 2023;14:1251866.
11. Suteau V, Munier M, Briet C, Rodien P. Sex bias in differentiated thyroid cancer. International Journal of Molecular Sciences. 2021;22(23):12992.
12. Nosé V. Familial thyroid cancer: a review. Modern Pathology. 2011;24:S19-S33.
13. Grønlund MP, Jensen JS, Hahn CH, Grønhøj C, Buchwald Cv. Risk factors for recurrence of follicular thyroid cancer: a systematic review. Thyroid. 2021;31(10):1523-30.
14. Li Y, Jin C, Li J, Tong M, Wang M, Huang J, et al. Prevalence of thyroid nodules in China: a health examination cohort-based study. Frontiers in Endocrinology. 2021;12:676144.
15. Beigh A, Amin J, Junaid S, Wani LA, Farooq S, Farooq S. Histopathological study of thyroid neoplastic lesions in a tertiary care hospital-a 5-year study. International Journal of Contemporary Medical Research. 2018;5(4):D4-D7.
16. RIMS R. Histopathological study of neoplastic lesions of thyroid in a tertiary care centre–. Indian Journal of Pathology and Oncology. 2020;7(1):113-7..
17. Athey JM, Vieson MD, Bailey K, Rudmann D, Baumgartner WA, Selting KA. Canine thyroid carcinomas: A review with emphasis on comparing the compact subtype of follicular thyroid carcinomas and medullary thyroid carcinomas. Veterinary pathology. 2024 Jan;61(1):7-19.Ndukwe CO, Ndukwe CC, Uzoigwe JC, Eni AO, Nnamani CS, Nwokoro OC, et al. Histopathological spectrum of skin lesions in the elderly: Experience from a tertiary hospital in Southeast Nigeria. Journal of Applied Sciences and Clinical Practice. 2022;3(1):14-9.
18. Chen DW, Lang BH, McLeod DS, Newbold K, Haymart MR. Thyroid cancer. The Lancet. 2023;401(10387):1531-44.
19. Afridi M, Ghaffar T, Hayat I, Khan M, Ahmad W. Thyroid Disease Prevalence. 2023.
20. Burkan N, Qubati M, Qubati S. The Risk of Thyroid Carcinoma in Multinodular Goiter Compared to Solitary Thyroid Nodules: A Prospective Analysis of 207 Patients. Journal of Surgical Endocrinology. 2021;3:81-8.
21. Poppe K. Management of endocrine disease: thyroid and female infertility: more questions than answers?! European journal of endocrinology. 2021;184(4):R123- R35.
22. Alyahya A, AlNaim A, AlBahr AW, Almansour F, Elshebiny A. Knowledge of thyroid disease manifestations and risk factors among residents of the Eastern

Province, Saudi Arabia. Cureus. 2021;13(1).
23. Shimura H, Matsumoto Y, Murakami T, Fukunari N, Kitaoka M, Suzuki S. Diagnostic strategies for thyroid nodules based on ultrasonographic findings in Japan. Cancers. 2021;13(18):4629.
24. Wu J-Y, Shyu Y-K, Lee Y-K, Wang Y-C, Chiang C-J, You S-L, et al. Secular Increasing Trends in Female Thyroid Cancer Incidence in Taiwan. Life. 2024;14(7):809.
25. Vaccarella S, Lortet-Tieulent J, Colombet M, Davies L, Stiller CA, Schüz J, et al. Global patterns and trends in incidence and mortality of thyroid cancer in children and adolescents: a population-based study. The lancet Diabetes & endocrinology. 2021;9(3):144-52.
26. Vanderpump MP. Epidemiology of thyroid disorders. The thyroid and its diseases: A comprehensive guide for the clinician: Springer; 2019. p. 75-85.
27. Mammen JS, Cappola AR. Autoimmune thyroid disease in women. Jama. 2021;325(23):2392-3.
28. Lei R, Wang Z, Qian L. Ultrasonic characteristics of medullary thyroid carcinoma: differential from papillary thyroid carcinoma and benign thyroid nodule. Ultrasound quarterly. 2021 Dec 1;37(4):329-35.Zahedi A, Bondaz L, Rajaraman M, Leslie WD, Jefford C, Young JE, et al. The risk for thyroid cancer recurrence is higher in men than in women independent of the disease stage at presentation. Thyroid. 2020;30(6):871-7.
29. Samsami A, Ghasmpour L, Alamdarloo SM, Davoodi S, Rahmati J, Karimian A, et al. Do women with autoimmune thyroiditis have a lower reproductive life span or not? A cross-sectional study. International Journal of Community Based Nursing and Midwifery. 2020;8(4):305.
30. Shukla AK, Yadav VK, Yadav VP, Mishra MK, Maurya R, Mishra RK, et al. Autoimmune Diseases in Women and Treatment Options. Women's Health: A Comprehensive Guide to Common Health Issues in Women. 2024:247.