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Original Article

# Thyroid Carcinoma: Prevalence and Associated Risk Factors.

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**Abstract:**

**Introduction:** Thyroid nodules are a prevalent condition all over the world. Majority of thyroid nodules are brought on by an expansion of healthy thyroid tissue. There is a substantial hereditary basis for this enlargement, however the reason is frequently unclear.

**Objective:** To identify the frequency and risk factors for thyroid cancer in patients attending JPMC Karachi, Pakistan.

**Methods:** A retrospective cross-section study was performed at JPMC, Karachi, Pakistan. Five years data (2016 to 2020) was retrieved from the electronic medical record. All adult patients 30 years of age and older, regardless of gender, had preoperative thyroid and cervical ultrasound imaging were enrolled. The condition of the thyroid nodule was noted. The final diagnosis was reached after a pathological study of the operation specimen.

**Results:** Of 520 patients, the mean age was 55.35 ±4.64 years. There were 320 (61.5%) males and 200 (38.5%) females. Thyroid cancer was observed in 149 (28.7%) patients. After adjustment of other covariates, thyroid cancer was 16.74 times significantly higher in single nodular goiter patients than with multinodular goiter patients (aOR: 16.74, 95% CI 9.70-28.88) and 8.11 times significantly higher among whom patients with positive thyroid cancer family history than with no positive family history (aOR: 8.11, 95% CI 4.35-15.11). Of 149 patients with thyroid cancer, papillary cancer was observed in majority 123 (23.7%), follicular cancer in 15 (10.1%), Hurthle Cancer observed in 11 (7.4%).

**Conclusion:** Thyroid cancer was observed in almost one third of patients. In particular, single nodular goiter and positive family history were the significant variables.

**Keywords:** Goiter, Nodules, Thyroid Cancer.

## Introduction:

Thyroid nodules are a prevalent condition all over the world.[1] Majority of thyroid nodules are brought on by an expansion of healthy thyroid tissue. There is a substantial hereditary basis for this enlargement, however the reason is frequently unclear.[2]

It is reported that nodules that are palpable found in approximately 5 percent and incidentally reported on ultrasonography in more than 70 percent of the individuals. Moreover, studies have also reported a high prevalence in elderly individuals.[3,4]

Thyroid nodules are significant because they must be evaluated for thyroid function, local neck symptoms, and cancer.[5,6] According to a recent estimate, thyroid cancer was

responsible for more than five hundred thousand new cases and more than forty thousand deaths.[7] In Pakistan, thyroid cancer is a very frequent type of cancer, accounting for 2% of all cancers, and it is more common in women.[8,9] On the idea that there is an equal danger of thyroid cancer in a single nodule as there in a multimodule goiter. Risk of thyroid cancer in people with single nodular goiter and multinodular goiter has been a source of debate in the literature. It is stated that patients with a single thyroid nodule had a bigger probability for developing thyroid cancer than those with toxic nodular goiter and multinodular goiter.[10] The rationale of the study is that the global burden of thyroid cancer, as well as the burden in our country, is growing substantially. It is crucial to assess the current scope of the problem and the related risk factors. The lack of data from Pakistan reporting the thyroid cancer risk in single versus multinodular goiter was particularly highlighted by a thorough literature search.

## Methodology:

At JPMC Karachi, Pakistan, a retrospective cross-sectional investigation analysis was carried out. Data from the electronic medical record were extracted over five years, from 2016 to 2020. Prior to conducting the study, institutional authorization was sought from the institute. The condition of consent was waived as the data were retrieved from the electronic medical record. All data were collected using non-probability consecutive sampling. Ultrasound imaging was performed on all adult 30 years of age and older, regardless of gender. The status of thyroid nodule was noted. Preoperative ultrasonography was used to diagnose multinodular goiter, which is characterized by thyroid gland enlargement and the prevalence of multi-nodules in the thyroid parenchyma. A single nodule in the thyroid parenchyma was considered a sign of single nodular goiter on preoperative ultrasonography, which was described as thyroid gland hypertrophy. Complete or almost total thyroidectomy was the surgical procedure carried out. A single pathologist with experience in thyroid cancer performed the pathological study of the surgical specimen to reach the final diagnosis. Histopathological findings such as papillary cancer, follicular cancer, and Hurthle cell cancer was observed. This information along with demographic characteristics such as age, gender, duration of disease, smoking status, positive thyroid cancer family history, functional thyroid status, and indication of surgery were recorded. Moreover, thyroid stimulating hormone and thyroglobulin were also noted. All those patients with any of the above mentioned missing data were excluded.

Statistical analysis using SPSS version 24 was under taken. Empirical variables like age, duration of disease, TSH, and Tg were expressed in mean ±standard deviation (SD), while rate of recurrence were calculated for sex, smoking status, positive family history of carcinoma of thyroid, functional thyroid status, type of surgical operation, thyroid cancer, and histological finding of cancer. The relation of thyroid cancer vis a vis histological type of cancer with independent variables were explored using Chi Square testing. The p value of ≤0.05 determined as significant. Binary logistic regression analysis was also applied. All those variables found significant at chi-square test were encompassed a binary logistic regression analysis.

## Results:

Of 520 patients, mean age was 55.35 ±4.64 years. Males were higher as compared to females, i.e., 320 (61.5%) and 200 (38.5%) respectively. There were 185 (35.6%) smokers. Positive household history of carcinoma of thyroid was observed in 112 (21.5%). Majority of the patients had euthyroid 311 (59.8%) followed by hyperthyroidism 175 (33.7%), while hypothyroidism was observed in 34 (6.5%) patients. Thyroid cancer was found in 149 (28.7%) of the patients. Thyroid nodule (p=0.001), disease duration (p=0.010), positive family history of carcinoma of thyroid (p=0.001), thyroid surgery type (p=0.007), TSH level (p=0.001), and thyroglobulin (p=0.001) were all substantially linked with thyroid cancer. (Table 1) The findings of univariate analysis revealed that thyroid cancer was 15.45 times higher in single nodular goiter than multinodular goiter (OR 15.45, 95% CI 9.67-24.69), 73% significantly higher in males than females (OR 1.73, 95% CI 1.15-2.60), 97% significantly in smokers than non-smokers (OR 1.73, 95% CI 1.15-2.60), 5.07 times significantly higher in positive family history patients than with no positive family history (aOR 5.07, 95% CI 3.25-7.89), while 76% significantly higher among whom total or near-total thyroidectomy surgery was performed as compared to those in whom hemithyroidectomy surgery was performed (OR 1.76, 95% CI 1.16-2.69). The results of the multivariable study revealed that, after controlling for other covariates, thyroid cancer was 16.74 times more common in single nodular goiter than in multinodular goiter (adjusted odd ration (aOR) 16.74, 95% CI 9.70-28.88) and 8.11 times more common in patients with a positive household history of carcinoma of thyroid than in cases with negative family history (aOR 8.11, 95% CI 4.35-15.11). (Table 2 In patients with single nodular goiter, positive family history (p value <0.001), TSH (p value <0.001), and thyroglobulin (p value <0.001) were the variables significantly associated with thyroid cancer. While among multinodular goiter patients, age (p value <0.001), family history (p value <0.001), TSH (p value <0.001), and thyroglobulin (p value .006) were the variables associated with thyroid cancer. (Table 4) Of 149 patients with thyroid cancer, papillary cancer was observed in majority 123 (23.7%), followed by follicular cancer 15 (10.1%), and Hurthle Cancer 11 (7.4%). The histological findings of can-

cer showed that age (p value <0.001), longevity of disease (p value 0.015), smoking (p value 0.001), functional thyroid cancer (p value <0.001), and type of thyroid surgery (p value <0.001) were the variables related with histological findings of thyroid cancer. (Table 5)

**Discussion:**

As the global burden of thyroid cancer is increasing remarkably all over the world, including Pakistan, finding out the burden and factors leading to the increasing prevalence is an ultimate requirement. It is critical to examine the present breadth of the problem and the risk factors associated with it. The current study was carried out among more than five hundred individuals with the aim to assess the thyroid cancer risk in single versus multinodular goiter. The results of the current investigation showed that 28.7% of people had thyroid carcinoma. A higher prevalence is reported by Apostolou et al in which the prevalence was reported to be 31.7%.[11] However, a lower prevalence was reported from studies conducted by various previous studies.[12-14] Somewhat similar prevalence was reported in a previous study conducted in North Pakistan.[15] These statistics highlighted the constantly prevalent issue of thyroid cancer in Pakistan. In this study, thyroid cancer was 16.74 times significantly higher among patients with single nodular goiter as compared to the patients with multinodular goiter. Similar findings were reported by other studies as well.[11] According to a study, the number of thyroid nodules within a multinodular goiter has no impact on the incidence of thyroid cancer, while the quantity of thyroid nodules overall has an effect on the likelihood of cancer within a nodule.[16] Another study reported lower cancer prevalence in multinodular goiter than those with single nodular goiter.[10] Further study that only include patients with single nodule goiter should be carried out to explore the risk factors and outcome in these at risk individuals. Current study reflected; patients with a positive family history had thyroid cancer risk that was 8.11 times higher than that of patients without a positive family history. According to a new meta-analysis, people with multinodular goiter are less exposed to suffer thyroid cancer as compared to people having single thyroid nodule.[11] According to a study done on Pakistani women, important factors for thyroid cancer involve marital status, domestic prevalence, dietary iodine intake, stress, junk food.[17] It is speculated that presence of positive family history particularly in parents, siblings or child for various disease including thyroid cancer is one of an important factors that make people vulnerable to caught that particular disease.

Furthermore, the current study finding also reported that among patients with single nodular goiter, positive family history, TSH, and thyroglobulin were the variables significantly associated with thyroid cancer. While among multinodular goiter patients, age, family history of carcinoma of thyroid, TSH, and thyroglobulin were the variables significantly associated with thyroid cancer. Moreover, papillary cancer was observed in majority of the patients, followed by follicular cancer, and Hurthle Cancer. A higher prevalence of papillary cancer was also reported in a previous study from Pakistan.[18]

In this study, the histological findings of cancer showed that age, duration of disease, smoking, functional thyroid cancer, and type of thyroid surgery were the variables significantly associated with histological findings of thyroid cancer.

Considering that this was a retrospective study that was done at a single centre, the results of the current study might be highlighted. Additionally, other crucial clinical factors as laboratory traits, radiation exposure, and the existence of comorbidities were left out. Despite these drawbacks, this study is important since it has presented data from one of Pakistan's major public healthcare institutions. It is advised to do more large-scale multicenter prospective trials that only contain the key predictive factors and undertake patient follow-up for the treatment's effectiveness and quality.

**Conclusion:**

The frequency of carcinoma of thyroid was observed in almost one third of the patients. In particular, single nodular goiter and positive family history were the significant variables. Furthermore, among those with thyroid cancer, papillary cancer was observed in majority of the patients.

| Table 1: Comparison of thyroid cancer with demographic and clinical characteristics of the patients (n=520) | | | | |
|---|---|---|---|---|
| | | Thyroid Cancer | | |
| | Total | Yes | No | p= |
| | n=520 | n=149 | n=371 | |
| **Thyroid Nodule** | | | | |
| Single Nodular Goiter | 188 | 117 (62.2) | 71 (37.8) | 0.001 |
| Multinodular Goiter | 332 | 32 (9.6) | 300 (90.4) | |
| **Age, years** | 55.35 ±4.64 | 55.89 ±5.17 | 55.13 ±4.39 | 0.092 |
| **Gender** | | | | |
| Male | 320 | 105 (32.8) | 215 (67.2) | 0.008 |
| Female | 200 | 44 (22.0) | 156 (78.0) | |
| **Duration of disease, years** | 7.60 ±1.16 | 7.39 ±1.25 | 7.68 ±1.11 | 0.010 |
| **Smoking Status** | | | | |
| Yes | 185 | 70 (37.8) | 115 (62.2) | 0.001 |
| No | 335 | 79 (23.6) | 256 (76.4) | |
| **Positive family history of thyroid cancer** | | | | |
| Yes | 112 | 64 (57.1) | 48 (42.9) | <0.001 |
| No | 408 | 85 (20.8) | 323 (79.2) | |
| **Functional thyroid status** | | | | |
| Hypothyroidism | 28 | 8 (28.6) | 20 (71.4) | 0.263 |
| Euthyroid | 317 | 83 (26.2) | 234 (73.8) | |
| Hyperthyroidism | 175 | 58 (33.1) | 117 (66.9) | |
| **Surgery** | | | | |
| Total or near-total thyroidectomy | 338 | 110 (32.5) | 228 (67.5) | 0.007 |
| Hemithyroidectomy | 182 | 39 (21.4) | 143 (78.6) | |
| **TSH, munits/l** | 1.25 ±0.39 | 1.60 ±0.44 | 1.11 ±0.25 | <0.001 |
| **Thyroglobulin, ng/ml** | 175.1 ±34.9 | 187.24 ±23.02 | 170.32 ±37.71 | <0.001 |
| Chi-square test, independent t-test applied, p= <0.05 considered as significance | | | | |

| Table 2: Regression analysis for variables associated with thyroid cancer | | | | |
|---|---|---|---|---|
| | OR (95% CI) | p= | aOR (95% CI) | p= |
| **Thyroid Nodule** | | | | |
| Single nodular goiter | 15.45 (9.67-24.69) | <0.001 | 16.74 (9.70-28.88) | <0.001 |
| Multinodular goiter | Ref | | Ref | |
| **Gender** | | | | |
| Male | 1.73 (1.15-2.60) | 0.008 | 1.48 (0.82-2.69) | 0.197 |
| Female | Ref | | Ref | |
| **Duration of disease** | 0.81 (0.69-0.95) | 0.011 | 0.89 (0.72-1.12) | 0.334 |
| **Smoking Status** | | | | |
| Yes | 1.97 (1.34-2.91) | 0.002 | 1.02 (0.59-1.77) | 0.95 |
| No | Ref | | Ref | |
| **Positive family history of thyroid cancer** | | | | |
| Yes | 5.07 (3.25-7.89) | <0.001 | 8.11 (4.35-15.11) | <0.001 |
| No | Ref | | Ref | |
| **Surgery** | | | | |
| Total or near-total thyroidectomy | 1.76 (1.16-2.69) | 0.008 | 1.60 (0.93-2.75) | 0.087 |
| Hemithyroidectomy | Ref | | Ref | |
| aOR: Adjusted Odds Ratio, CI: Confidence Interval, OR: Odds Ratio | | | | |

| Table 3: Stratification of thyroid nodules and comparison of thyroid cancer with associated risk factors (n=520) | | | | | | |
|---|---|---|---|---|---|---|
| | Single Nodular Goiter (n=188) | | | Multinodular Goiter (n=332) | | |
| | Thyroid Cancer | | | Thyroid Cancer | | |
| | Yes | No | p= | Yes | No | p= |
| | n=117 | n=71 | | n=32 | n=300 | |
| **Age, years** | 55.12 ±5.09 | 54.45 ±3.97 | 0.340 | 58.68 ±4.50 | 55.29 ±4.48 | <0.001 |
| **Gender** | | | | | | |
| Male | 82 (60.3) | 54 (39.7) | 0.375 | 23 (12.5) | 161 (87.5) | 0.049 |
| Female | 35 (67.3) | 17 (32.7) | | 9 (6.1) | 139 (93.9) | |
| **Duration of disease, years** | 7.51 ±1.24 | 7.40 ±1.28 | 0.582 | 6.96 ±1.23 | 7.75 ±0.25 | <0.001 |
| **Smoking Status** | | | | | | |
| Yes | 59 (60.2) | 39 (39.8) | 0.549 | 11 (12.6) | 76 (87.4) | 0.269 |
| No | 58 (64.4) | 32 (35.6) | | 21 (8.6) | 224 (91.4) | |
| **Positive family history of thyroid cancer** | | | | | | |
| Yes | 49 (92.5) | 4 (7.5) | <0.001 | 15 (25.4) | 44 (74.6) | <0.001 |
| No | 68 (50.4) | 67 (49.6) | | 17 (6.2) | 256 (93.8) | |
| **Functional thyroid status** | | | | | | |
| Hypothyroidism | 12 (66.7) | 6 (33.3) | 0.066 | 2 (12.5) | 14 (87.5) | 0.438 |
| Euthyroid | 61 (55.5) | 49 (44.5) | | 16 (8.0) | 185 (92.0) | |
| Hyperthyroidism | 44 (73.3) | 16 (26.7) | | 14 (12.2) | 101 (87.8) | |
| **Surgery** | | | | | | |
| Total or near-total thyroidectomy | 88 (64.2) | 49 (35.8) | 0.354 | 22 (10.9) | 179 (89.1) | 0.318 |
| Hemithyroidectomy | 29 (56.9) | 22 (43.1) | | 10 (7.6) | 121 (92.4) | |
| **TSH, munits/l** | 1.62 ±0.46 | 1.08 ±0.27 | <0.001 | 1.52 ±0.32 | 1.11 ±0.25 | <0.001 |
| **Thyroglobulin, ng/ml** | 186.28 ±22.54 | 161.96 ±40.84 | <0.001 | 190.78 ±24.75 | 172.30 ±36.72 | 0.006 |
| Chi-square test, independent t-test applied, p= <0.05 considered as significance | | | | | | |

| Table 5: Comparison of thyroid cancer with demographic and clinical characteristics of the patients (n=520) | | | | |
|---|---|---|---|---|
| | | Histological findings of Cancer | | |
| | Papillary Cancer | Follicular Cancer | Hurthle Cell Cancer | p= |
| | n=123 | n=15 | n=11 | |
| **Thyroid Nodule** | | | | |
| Single Nodular Goiter | 83 (79.0) | 11 (10.5) | 11 (10.5) | 0.074 |
| Multinodular Goiter | 40 (90.9) | 4 (9.1) | 0 (0) | |
| **Age, years** | 54.86 ±5.02 | 61.53 ±2.44 | 59.63 ±2.11 | <0.001 |
| **Gender** | | | | |
| Male | 83 (79.0) | 11 (10.5) | 11 (10.5) | 0.074 |
| Female | 40 (90.9) | 4 (9.1) | 0 (0) | |
| **Duration of disease, years** | 7.26 ±1.30 | 8.07 ±0.70 | 8.01 ±0.77 | 0.015 |
| **Smoking Status** | | | | |
| Yes | 52 (74.3) | 7 (10.0) | 11 (15.7) | 0.001 |
| No | 71 (89.9) | 8 (10.1) | 0 (0) | |
| **Positive family history of thyroid cancer** | | | | |
| Yes | 54 (84.4) | 8 (12.5) | 2 (3.1) | 0.177 |
| No | 69 (81.2) | 7 (8.2) | 9 (10.6) | |
| **Functional thyroid status** | | | | |
| Hypothyroidism | 8 (57.1) | 5 (35.7) | 1 (7.1) | <0.001 |
| Euthyroid | 57 (74.0) | 10 (13.0) | 10 (13.0) | |
| Hyperthyroidism | 58 (100.0) | 0 (0) | 0 (0) | |
| **Surgery** | | | | |
| Total or near-total thyroidectomy | 92 (83.6) | 15 (13.6) | 3 (2.7) | <0.001 |
| Hemithyroidectomy | 31 (79.5) | 0 (0) | 8 (20.5) | |
| **TSH, munits/l** | 1.58 ±0.47 | 1.57 ±0.28 | 1.87 ±0.18 | 0.107 |
| **Thyroglobulin, ng/ml** | 187.60 ±23.60 | 184.27 ±26.13 | 187.36 ±8.76 | 0.871 |
| Chi-square test, independent t-test applied, p= <0.05 considered as significance | | | | |

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