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Characterization of benign papillary thyroid carcinoma (PTC) in the Iraqi women

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Abstract---*Papillary thyroid carcinoma (PTC) is a tumor malignancy observed commonly in the endocrine gland, comprises 75-85% of thyroid cancers. It predominately found in female, it is almost 2-3 fold higher than in male. The tumors in PTC are biologically lethargic and have exceptional prognosis. PTC is largely characterized by the presence of small or large thyroid nodules approximately having a maximum diameter of 10mm and detected in patients with benign thyroid goiter. Total thyroidectomy was preferred to treat PTC as it allows the correct risk assessment of the present tumor, depend on its size and provide safety to remove complete tissue with malignancy. The aim of the study is to characterize the benign PTC in Iraqi women. The study population consisted 6 patients with pathologically confirmed having papillary carcinoma (PTC). This study conducted in Al - Shafa hospital, Diyala, Iraq between January 2018 to January 2020. Seven female patients were recruited in the study aged between 20 to 60 years. Total thyroidectomy was performed after taking written consent for excision of lymph node. Present study was conducted on patients having palpable nodular swelling on their neck, while all the cases shown big thyroid nodule at the anterior side. women were included in the study, having minimum age of 20 years and maximum of 50 years. Total mean age recorded was 35 years. It suggests that, PTC was incident mainly in the middle age of adult life in women. Abnormal levels of thyroid hormones were detected. Total thyroidectomy was performed as a first line of treatment where benign single thyroid nodules were observed in histopathology analysis. Thus, Despite the increase in incidences of PTC, total thyroidectomy increases the survival rate and decrease the recurrence rate in studied cases. While, its etiopathology is complex, further investigation is required so that it can be translated in clinical applications for diagnosis and treatment of cancer.*

Keywords---*Papillary thyroid carcinoma, thyroid cancer, Malignancy, Thyroidectomy.*

1. Introduction

Papillary thyroid carcinoma (PTC) is a tumor malignancy observed commonly in the endocrine gland, comprises 75-85% of thyroid cancers. Global burden of disease is 1% of all malignancies and accounts for the 0.2% of cancer deaths (Jemal et al., 2008, Enewold et al., 2009). Thyroid cancers ascend mainly from thyroid follicular cells, which is of four types, 85% are Papillary, 11% follicular, 3% Hurthle cells and 1% Anaplastic (Zhu et al., 2003, Chowdhury et al., 2016). The incidence of PTC is high comparatively and it increases day by day in the countries from East Asia and West as well (Heminkki et al., 2005). It predominately found in females. It was observed that out of 26000 cases of PTC was found in

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the US in the year of 2006, 75% were women (Al-Brahim et al., 2006). This disease is mostly found in the countries having iodine excess diets in routine (LiVolsi, 2011, Mazzaferri and Masoll, 2002).

The tumors in PTC are biologically lethargic and have exceptional prognosis. Though it has a high prevalence, mortality rate is low, as most of the patients responds to targeted therapy like radioactive iodine and surgeries (Al-Brahim et al., 2006). There are several risk factors are associated with PTC which are nodular diseases, exposure to radiations, and even genetic factors. PTC is largely characterized by the presence of small or large thyroid nodules approximately having a maximum diameter of 10 mm and detected in patients with benign thyroid goiter (Gu et al., 2015). In PTC, damaged thyroid follicles cause hyperthyroidism which, leads to increase in the secretion of thyrotropin (TSH) a pituitary hormone. This damage to the TSH stimulation causes neoplastic transformation of thyroid cells (LiVolsi, 2011).

These follicles were detected parenthetically while physical examination or ultrasonography. Their investigation commonly includes nuclear scan, FNAC biopsy and ultrasound imaging (Yoon et al., 2011, Al-Brahim et al., 2006). Generally, the predictable incidence of thyroid nodule is as high as 20-70% and chances of finding malignancy in the thyroid nodule is 5 to 15%. Nowadays, malignant tumors were determined by using FNAC or surgical biopsy (Datta et al., 2006, Eng et al., 2010, Hoang et al., 2007). But due to complications associated with these techniques, ultrasound is more preferred method over them as it has been used to diagnose, to distinguish between benign and malignant thyroid nodules and to identify calcifications (Al-Brahim et al., 2006). PTC appears to be variable. These nodules are solid, firm usually gray white in color, but there are maximum chances these nodules may be cystic (Lloyd and Buehler, 2011). It is very common to have solid tumor having cystic metastasis to lymph node. Basically, PTC has a papillary structure with branching, and they are covered by eosinophils and have enlarged nuclei. Cytologic features showed nuclear enlargement which may be useful in the diagnosis of PTC (Zhu et al., 2003).

As PTC is highly incident among the thyroid cancer with female predominance, our aim is to apply surgical intervention helps to removal of the cancer. About 1% of the solid malignant tumors are thyroid carcinomas and they are cured by surgical management (Davies and Welch, 2006). In the light of the complications found in other type of surgeries and treatment total thyroidectomy was preferred method over the other to get rid from the tumor (Gharib et al., 2010). It significantly improves the recurrence as well as survival rate. In the present study, we would like to analyze the clinicopathological characterization of benign papillary thyroid carcinoma (PTC) in the Iraqi women undergone to total thyroidectomy.

2. Methodology

The ethical committee of Al - Shafa hospital, approved this clinicopathological characterization study. This study was to analyze the thyroid swelling operated in the Al - Shafa hospital, Diyala, Iraq during January 2018 to January 2020. Female patients were recruited in this study as prevalence of PTC was found mostly on them. The outcome of this study was diagnosed as papillary thyroid carcinoma after histopathological analysis. Patients were recruited on the basis of thyroid swelling, swallowing difficulties, thyroid function abnormality, lymphadenopathy. Early detection of PTC was carried out using USG and FNAC. Thyroid function test was necessary before and after the surgery. Consent was taken from each recruited patients and prior idea for the surgery was elaborated to each.

Total thyroidectomy was performed after taking written consent for excision of lymph node. All surgeries were done under general anesthesia by using an Endo tracheal tube. Reverse tredlenberg position (head up) with the extended neck position were given to the patients. The collar incision was used. Upper and lower flaps was placed to retractinstead of

Joll's retractor. This was done by using cautery (coagulation diathermy). Ligations of middle thyroid veins was done by 3 0 vicryl followed by ligations of superior thyroid artery and veins. Inferior thyroid vessels were also ligated. During the surgery, redivac drains were used and removed after 2 to 3 days. Second generation cephalosporins antibiotics were given after surgery. After 1 week after surgery, thyroxine was given.

Statistical Analysis

The data were represented as the mean± standard error (SE). The biochemical estimation was performed in triplicate.

3. Results

The present study was conducted on patients having palpable nodular swelling on their neck, while all the cases shown big thyroid nodule at the anterior side. Patients were confirmed by using techniques like ultrasound, with or without lymphadenopathy and with FNAC in which patients were suspected for thyroid carcinoma.

In the present study, women were included in the study, having a minimum age of 20 years and maximum of 50 years. Total mean age recorded was 35 years. In this study 7 patients were recruited, in which maximum patients were found in the age range of 20-40 years having percentage of 71.43, suggesting PTC was incident mainly in the middle age of adult life in women.

Table 1. Age distribution in PTC patients

No.	Age in years	No. of patients (n)	Percentage (%)
1	20-40	5	71.43
2	41-60	2	28.57

All the 7 women, enrolled in the study have shown abnormal levels of TSH, T3 and T4. Average values obtained in the patients were 74.24 mU/L, 1.45 ng/dl and 63.41 ng/dl respectively (Table 2). On the basis of physical examination, biochemical tests, USG and FNAC tests patients were recruited to the total thyroidectomy (Figure 1). As surgery is stated to be a first line of treatment for the management of thyroid cancers.

Table 2. Thyroid function test of distribution of the study patients (n=6).

Parameters	Average Values (n=6)
TSH	74.24 mU/L
T3	1.45 ng/dl
T4	63.41ng/dl

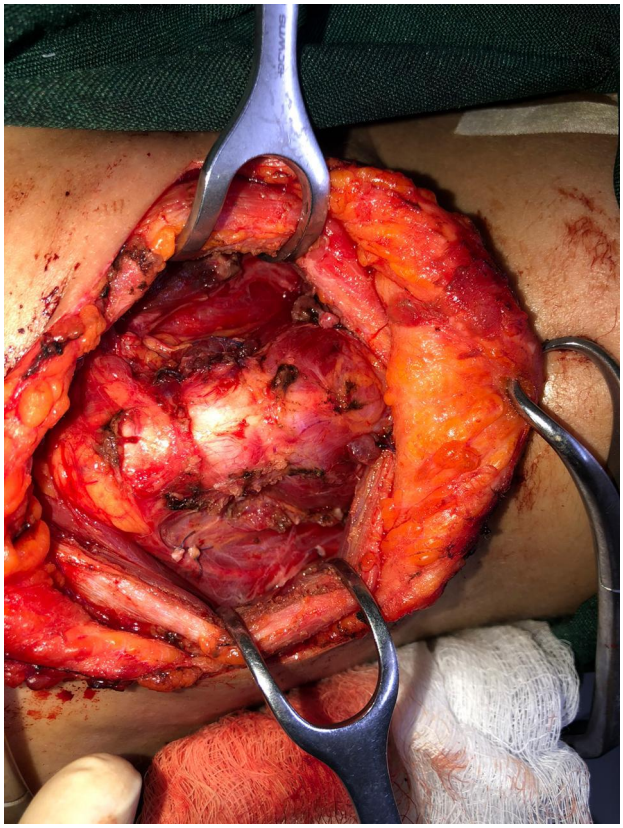

Figure 1. An exposed multinodular gland

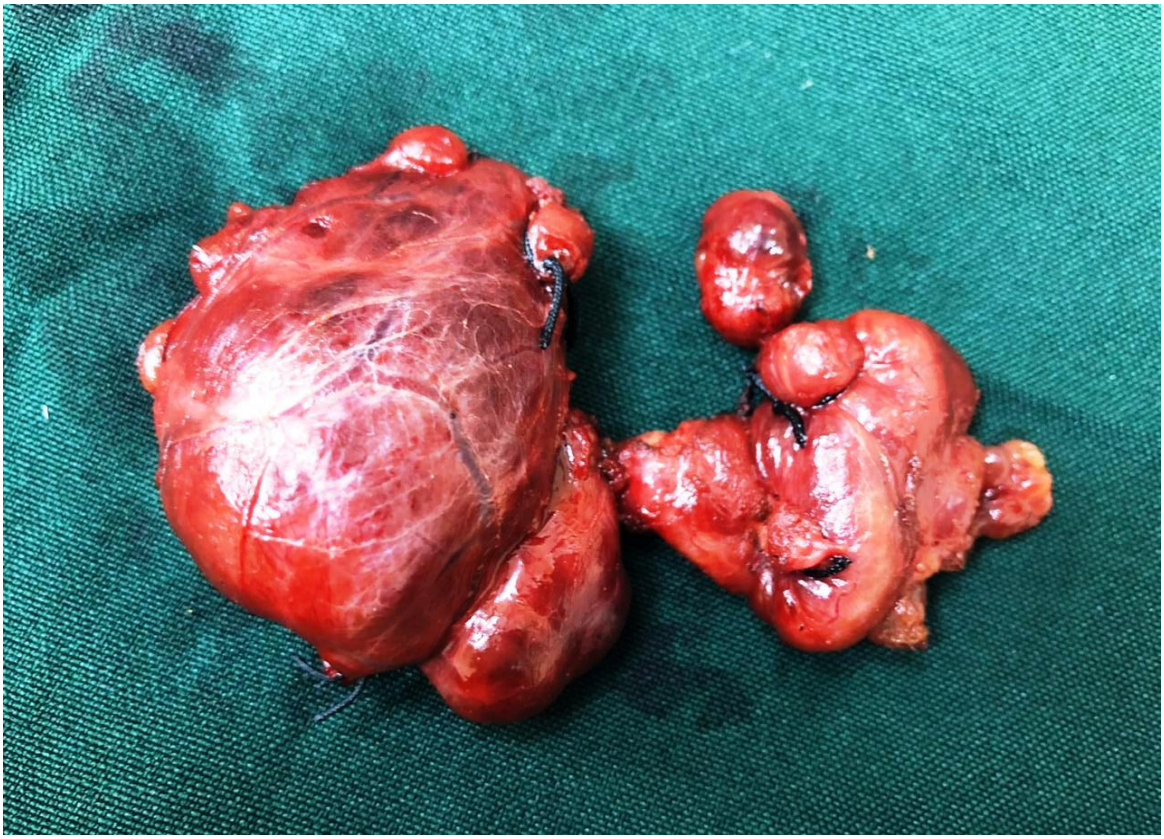

Figure 2. Macroscopic giant nodular goiter

Figure 3. Immediate postoperative incisions

4. Discussion

Thyroid cancer is most common malignancy observed in the endocrine system and its prevalence is more in women. It ranks seventh common cancers found in females, while it's not common in men (Ortega et al., 2004). Aggressive types of cancers like anaplastic or medullary thyroid cancers were found in similar rates in both men and women, but follicular and papillary thyroid cancers are the most common cancers incident in women (Liu et al., 2016, Rahbari et al., 2010). It is almost 2-3-fold higher than in male, approximately 80% of the female cases were observed, while the factors responsible are still unknown than the established factors (Chen et al., 2009, Ortega et al., 2004).

Few studies hypothesized that this disparity was due to reproductive, environmental and menstrual factors, but very less molecular factors were known (Brindel et al., 2008). Some studies proved that at the beginning of the reproductive years, the age specific incident rate of PTC was rises in females and it reaches at its peak at the age of 40-49 years than in men in which peak was observed at the age of 60-69 years (Rahbari et al., 2010). The incidence of PTC rate was equalized at the age of 85 years (Kilfoy et al., 2009, Ortega et al., 2004). It has been stated that onset of PTC was at the early age in females than in men due to which mortality rate was lower in females while male gender was found associated with lower disease-free survival (Gilliland et al., 1997, Kilfoy et al., 2009). Thus, in our study we have decided to enroll Iraqi women diagnosed with PTC.

Thyroid carcinoma has high prevalence among the malignant diseases, its incidences continues to rise. It became a sixth most diagnosed cancer in women in 2008, while it was estimated that about 44670 cases were diagnosed in US in the year of 2010 (Brown et al., 2011). Among all thyroid cancer PTC accounts for the higher burden, almost 80% than other mainly in the countries having iodine excess or iodine deficient diets (Mazzaferri, 2000). It can cause at any age of life. Third to fifth decade is the most common phase of human life to detect PTC with mean age at 40 years (Mazzaferri, 2000, Mazzaferri and Masoll, 2002). This data well compared with our studied data where we have found mean age was 35 years.

PTC was detected mostly in the patients diagnosed with the benign thyroid goiter (Abdullah et al., 2019). Other than previous history of exposure to radiation other risk factors like preexisting benign thyroid disease and having PTC in the family history is also affect to the progression of PTC. (Constantinides and Pallazzo., 2013, Lee et la., 2016). An earlier study reported that chances of incidence to detect PTC is 50% in older patients having history of nodular goiter (Alevizaki et al., 2009). Almost 0.5 to 18% of the patients having PTC, have been observed variation in the thyroid cancer which causes Graves' disease (Pazaitou-Panayiotou et al., 2012).

Nowadays, depending on the stage and type of the thyroid cancer, treatment or therapy options are available. These treatment options are surgery, molecular targeted therapy mostly with tyrosine kinase inhibitors and radioactive iodine therapy. (Nguyen et al., 2015). Among these treatments' surgery is the preferable and first line of option for thyroid cancers. There are several options available in surgeries includes hemithyroidectomy, near total thyroidectomy and total thyroidectomy. Total thyroidectomy was mostly recommended for the thyroid cancers having tumor size ≥1.0 cm to 2.0 cm. (Cooper et al., 2010).

Many patients have low morbidity from their cancers, thus better tool having lower risk are recommended in order to avoid overtreatment. (Brown et al., 2011). Thyroid cancer has high percentage of (42.7%) of multifocal distribution in the gland, to avoid the chances of malignancy in the residual parenchyma, removal of all neoplastic tissue in the neck is preferred which we achieved in total thyroidectomy (Schlumberger, 2004). It also allows the correct risk assessment of the

present tumor depend on its size and provide safety to remove complete tissue with malignancy (Lucchini et al., 2013). It also helps to reduce recurrence rate as papillary carcinomas are generally multifocal and bilateral (Schlumberger, 2004). In the present study all the recruited patients diagnosed with the swelling on the neck by physical examination and nodular thyroid gland by FNAC and USG examination. All the patients underwent to the Total thyroidectomy procedure as a first line of treatment.

In our study, single thyroid nodule was observed in all the cases, while all the female detected with the PTC after the histopathological analysis of removed thyroid gland. There is being much controversy in the malignancy of single verses multiple thyroid nodules. But earlier studies showed no difference in the cancer prevalence in any of this type of nodules. (Belfiore et al., 1992). Further some studies have proved that there is high risk associated with the single thyroid nodule than multinodular goiter. However, some studies have reported the equal risk of PTC in the cases diagnosed with the multiple thyroid nodules. (Barroeta et al., 2006).

In our study, elevated levels of thyroid hormones were recorded, as literature credited the fact that hyperthyroidism was observed due to radiation exposure on neck which causes damage to the thyroid follicles which leads to increase secretion of pituitary thyrotropin. It was ventured that this stimulation from damaged epithelium will lead to neoplastic transformation of thyroid cells creating the possibility of malignant nodules (LiVolsi, 2011). This may be due to expression of genes up or down regulated by TSH. Some earlier studies found that increased expression was observed of Id1 gene in PTC which was increased by TSH. (Finley et al., 2004). TSH controls the growth of thyroid tumor cells and its inhibition with thyroxin improves the recurrence and survival rate (Schlumberger, 2004). Thus, suitability of this therapy was monitored by measuring levels of TSH, T3 and T4 in serum.

5. Conclusion

PTC has proved to be highest incident form of thyroid malignancy found at any stage of human life. Prevalence is found high in women. While, its etiopathology is complex, further investigation is required so that it can be translated in clinical applications for diagnosis and treatment of cancer. Despite the increase in incidence of PTC, total thyroidectomy increases the survival rate and decrease the recurrence rate in studied cases. Further studies are required in gene expression profiling, which will lead us to understand the molecular basis lay behind the tumor growth and eventually to carcinoma.

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