J Surg Res 2022; 5 (1): 80-91 *DOI: 10.26502/jsr.10020203*

Research Article

Clinico Pathological Analysis of Nodular Goiter: A Retrospective Study

Md. Iqbal Hossain Talukder[1*], Nisfun Naher[2], Shah Md. Rezaul Karim[3], Khandoker Moynul Hasan[4], Saiful Islam Khan[5], A.K.M Shahidur Rahman[6]

[1]Department of Surgery, Sheikh Hasina Medical College Hospital, Tangail, Bangladesh

[2]Department of Gynaecology and Obstetrics, 250 Bedded General Hospital Tangail, Bangladesh

[3]Department of Surgery, Sheikh Hasina Medical College, Habiganj, Bangladesh,

[4]Department of Pediatric Surgery, Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh

[5]Department of Surgery, Bangabandhu Sheikh Mujib Medical College, Faridpur, Bangladesh

[6]Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

[*]Corresponding Author: Md. Iqbal Hossain Talukder, Assistant professor, Department of Surgery, Sheikh Hasina Medical College Hospital, Tangail, Bangladesh, E-mail: nicrhiqbal@gmail.com

Received: 10 Febraury 2022; **Accepted:** 17 Febraury 2022; **Published:** 25 Febraury 2022

Citation: Talukder MIH, Naher N, Karim SMR, Hasan KM, Khan SI, Rahman AKMS. Clinico Pathological Analysis of Nodular Goiter: A Retrospective Study. Journal of Surgery and Research 5 (2022): 80-91.

Abstract

This retrospective study was conducted to evaluate the clinico-pathological pattern of nodular goiter among patients who underwent thyroidectomy. This study included 50 patients following selection criteria. All patients were properly evaluated by history, clinical examination along with blood chemistry, ultrasonography, nuclear scanning and histopathology [fine needle aspiration cytology (FNAC)]. Out of 50 patients 38 were females and 12 were males, the male to female ratio was 1:3.12. Majority of the patients belonged to the age group of 25-40 years. Most of them were in euthyroid state. Among the study patients; tiredness, palpitation, breathing difficulties, swallowing problem, altered appetite and cold preference were the major presenting features. Solitary nodules (60%) were more frequent than multi-nodular goiter (40%). Among the 20 patients having multi-nodular goiter; 18 were nontoxic goiter and 2 cases were diagnosed as carcinoma. On the other hand in 30 patients with solitary nodule; 27 cases were simple

nodule and rest 3 cases were carcinoma. Among total study patients 46 were cold nodules and 4 were warm nodules. Histopathological reports of excised tissues revealed that 45 cases were papillary adenoma, 3 cases were papillary carcinoma and 2 cases were follicular carcinoma. The study concluded that solitary thyroid nodules are frequent at the middle age and predominant among females. Most of the patients of thyroid goiter are in euthyroid state and majority of nodules are benign lesions. Papillary adenoma is the most frequent benign nodular tumor followed by papillary carcinoma and then follicular carcinoma.

Keywords: Clinico Pathological Analysis; Nodular Goiter; Thyroid Gland; Thyroidectomy

1. Introduction

Disorders of thyroid gland may or may not cause enlargement of the gland [1]. But when there is enlargement, it may be diffuse or nodular in nature [1]. A nodule is a swelling that can be solid mass or liquid filled cyst, most of which are benign (95%) but a few (5%) can be cancerous [2]. Thyroid nodules are not uncommon among adult population; about 2% of men and 4% of women have a palpable thyroid nodule [3]. Nodule may either be solitary or multiple, in all this sort of enlargement thyroid gland may retain its normal functional activity (euthyroid) or may be hypoactive (hypothyroidism) or hyperactive (hyperthyroidism) [1-3]. Isolated solitary nodules that are firm in consistency, rapid growing and nonfunctional on scans are important for their malignant potential [2]. However solitary thyroid nodule may be due to various benign conditions and malignancy is a relatively uncommon cause [2,4]. There are various causes of nodular goiter; among these iodine deficiency goiter is the commonest one [4]. The thyroid nodules (goiter) that are hypoactive (hypothyroidism) appear as a swelling at the base of the neck may associated with fatigue, weight gain, decrease appetite, depression, hoarse voice, dry/coarse skin, puffy face, felling cold, increased cholesterol, slower digestion and constipation [2]. On the other hand weight loss, hair loss, nervousness with irritability, arrhythmia, feeling hot, muscle weakness and tremor are the features of hyperactive (hyperthyroidism) thyroid nodules (goiter) [2]. During nodular (goiter) surgery, for a surgeon the only way to be certain is to subject the nodule to microscopic analysis. Routine surgery for all solitary thyroid nodules had been advocated by some surgeons in 1950s and 1960s following reports of high incidence of cancer. But in recent years trends in management of solitary thyroid nodule have been changed a lot due to the marked improvement in diagnostic facilities especially aspiration biopsy cytology (ABC) [5]. Although the aspiration biopsy cytology is not always conclusive, moreover for interpretation it requires expertise [5], so for solitary thyroid nodule there is still only one certain diagnostic procedure and that is excision biopsy. In the low-income countries, still less available scope of ABC and frozen section facilities are not always feasible, with technical difficulties and higher risk of re-operation, the ideal procedure in management of solitary nodule is still to perform lobectomy with removal of isthmus and submit the specimen for confirmation by histopathological examination. As the mainstay in the diagnostic evaluation of a nodular goiter includes; clinical, functional and morphological characterization along with histopathological evidence like- fine needle aspiration cytology (FNAC). Therefore the aim of this retrospective study was to evaluate the clinico-pathological pattern of nodular goiter among patients who underwent thyroid surgery.

2. Methodology

This retrospective study was conducted in the Department of surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2018 to June 2020. This study included 50 patients who underwent thyroid surgery, the approach of which was different according to underlying pathology, extent of enlargement and involvement of lymph nodes if any. In all cases detailed history was taken, thorough clinical examination with evaluation on the basis of Wayne's clinical diagnostic index (Table- 1) [6] was done and essential investigations along with their results were collected from patient's record file. Histopathological study of excised tissue was done in every case. Persons with physiological goiter and diffuse parenchymatous goiter were not included in this series. Only nodular goiter both solitary and multinodular was included.

Symptoms of recent onset and/or increased severity	Present Score	Absent Score	Signs	Present Score	Absent Score
Dyspnoea on effort	1		Palpable thyroid	3	-3
Palpitations	2		Bruit over thyroid	2	-2
Tiredness	2		Exophthalmos	2	
Preference for heat (irrespective or duration)		-5	Lid retraction	2	
Preference for cold	5		Lid Lag	1	
Indifferent to temperature	0		Hyperkinetic movement	+3	-2
Excessive sweating	3		Fine finger tremor	1	
Nervousness	2		Hands		
Appetite Decreased		-3	Hot Moist	2	-2
				1	-1
Appetite Increased	3				
Weight increased		-3	Causual pulse rate:		
Weight decreased	3		Atrial fibrillation	+3	
			Regular rates:		
			80 per minute		-3
			80 to 90 per minute	0	
			90 per minute	3	

Symptom score + Sign score = Diagnostic Index

INDEX - Under 11 = Non – Toxic: 11-19 = Equivocal: Over 19 = Toxic

Table 1: Wayne's clinical diagnostic index

Routine investigations like- hemoglobin level, urine for routine microscopic examination (R/M/E), stool for routine examination, fasting blood sugar, blood urea, serum creatinine, x-ray chest and electrocardiogram (ECG) were done in all cases. Necessary measures were taken to correct the abnormalities that were found clinically and in other investigations. Among the special investigations- radioiodine uptake study, isotope scanning, ultra sonogram (USG) of thyroid gland and fine needle aspiration cytology (FNAC) were done in all cases. Serum triiodothyronine (T_3), thyroxine (T_4) and thyroid stimulation hormone (TSH) level were measured in all cases accordingly. Confirmatory evident of diagnosis was histopathological finding of excised tissue.

3. Results and observation

This retrospective study was intended to evaluate the clinico-pathological pattern of nodular goiter among fifty (50) patients who underwent thyroid surgery. Out of 50 patients 38 were females and 12 were males, the male to female ratio was 1:3.12 (Table 2). In this study age of the patients ranged from 11 years to 70 years. The patients in different age groups were distributed in table 3. Majority of the patients belonged to the age group of 25-40 years (Table 3). Biochemical analysis of the study patients showed that 35(70%) patients were in euthyroid state, 12(24%) patients were hyperthyroid and 3(6%) patients were hypothyroid state (Table 4). About occupation, it was found that majority of the patients were housewife (50%) followed by service holder (20%), business man (10%) and retired person (10%) (Table 5).

Gender	Number of patients (n)	Percentage (%)	Ratio
Male	12	24%	**Male:Female** = 1:3.12
Female	38	76%	

Table 2: Gender distribution of the study patient (N= 50)

Age (years)	Total Number of Cases (n)	Percentage (%)
1-10		
11-15	1	2
16-20	3	6
21-25	4	8
26-30	12	24
31-35	7	14
36-40	6	12
41-45	5	10
46-50	3	6
51-55	2	4
56-60	3	6
69-65	3	6
66-70	1	2
Total	50	100

Table 3: Age distribution of the study patients (N= 50)

Types	Number of patients (n)	Percentage (%)
Euthyroid	35	70
Hyperthyroidism	12	24
Hypothyroidism	3	6
Total	50	100

Table 4: Biochemical analysis of the study patients (N= 50)

Occupation	Number of patients (n)	Percentage (%)
Service holder	10	20
House-wife	25	50
Business man	5	10
Cultivator	2	4
Student	3	6
Retired person	5	10

Table 5: Occupational analysis of the study population (N= 50)

Regarding presenting symptoms; it was observed that apart from neck swelling, majority of the patients complained of tiredness (30%) and palpitation (20%). Breathing difficulty was present in 10 cases due to enormous size of the thyroid gland. Gross tracheal shifting was present in 2 cases and 8 patients had deglutition difficulty. Appetite was lost in 8 cases; of them weight loss was found in 4 cases. Seven patients had cold preference and 5 patients had increased sweating. Two patients had recent increase in size of their neck swelling; one of them later proved to be malignant thyroid and other one was due to intra-glandular hemorrhage. Recent voice changes were present in three cases and occasional pain in the swelling was present in 2 cases. All of these were proved to be benign on subsequent histopathology and were probably due to pressure over the nerve by the enlarged gland. Cervical lymph node enlargement was present in 2 young girls with thyroid enlargement and was diagnosed as carcinoma thyroid with cervical lymph node metastases. Engorged neck vein was found in 3 cases and gross tracheal shifting was found in 2 cases which were probably due to pressure of the enlarged gland. On clinical examination of the thyroid gland, the number of nodules was extremely variable from solitary to multiple and in many cases having clinically solitary nodule found to have many nodules during operation. Similarly consistency of nodules was also variable from soft cystic swelling to firm and even hard. Many of the soft cystic swellings were found to be solid at operation (Table 6). In the context of duration of symptoms; maximum numbers of patients (15) were presented with 2-3 years duration of symptoms, the next large number of cases (10) was presented with 3-4 years duration of symptoms and nine (9) cases was presented with 4-5 years duration of symptoms. The shortest duration of symptoms was 6 months and the longest duration was 9 years (Table 7).

It was observed that among the study patients maximum numbers of nodules were found in the right lobe of the thyroid gland [22] followed by left lobe of the thyroid gland [17] and then both sides [10] (Table 8). During the study period none of the patient with thyroid enlargement presented any toxic manifestation. Solitary nodules [30] were more than multi-nodular goiter [20]. Among the patients having multi-nodular goiter; 18 were nontoxic goiter and 2 cases were diagnosed as carcinoma. On the other hand in 30 patients with solitary nodule; 27 cases were simple nodule and rest 3 cases were carcinoma (Table 9). Radioactive-iodine (1311) uptake was estimated at 2 hours and 24 hours in all cases. Radioactive-iodine uptakes of all of the patients were within normal limit. The results of uptake at 2 hours and 24 hours are shown in table 10.

Presenting Features*	Number of patient (n)	Percentage (%)
Neck Swelling	50	100
Palpitation	10	20
Tiredness	15	30
Breathing difficulty	10	20
Swallowing difficulty	8	16
Loss of appetite	8	16
Loss of weight	4	8
Increased liking for cold	7	14
Increased sweating	5	10
Voice change	3	6
Occasional pain in the swelling	2	4
Engorged neck vein	3	6
Enlarged neck glands	2	4
Gross tracheal shifting	2	4

*Multiple responses

Table 6: Various clinical presentations of the study patients (N= 50)

Duration of symptoms	Number of patients (n)	Percentage (%)
Less than one year	5	10
1- 2 years	7	14
2- 3 years	15	30
3-4 years	10	20
4- 5 years	9	18
More than 5 years	4	8

Table 7: Duration of symptoms among the study patients (N= 50)

Sites of nodules	Number of patients (n)	Percentage (%)
Left lobe of the thyroid gland	17	34
Right lobe of the thyroid gland	22	44
Isthmus	1	2
Both lobes	10	20

Table 8: Different sites of nodules in thyroid gland among the study patients (N= 50)

Type of thyroid nodules diagnosed clinically	Number of patient (n)	Percentage (%)
Multi-nodular Goiter	20	40
a) Nontoxic Goiter	18	36
b) Toxic Goiter	-	-
c) Carcinoma	2	4
Solitary Nodule	30	60
a) Toxic Nodule	-	-
b) Simple Nodule	27	54
c) Carcinoma	3	6

Table 9: Different types of thyroid on clinical basis among the study patients (N=50)

Uptake at 2 hours in percentage	Number of patients (n)	Uptake at 24 hours in percentage	Number of patients (n)
01-20	40	01-20	5
21-40	6	21-40	30
41-60	2	41-60	10
61- 70	2	61- 70	5

Table 10: Radioactive-iodine uptake results of all of the patients (N= 50)

A nodule is refer as "Cold nodule" when the uptake of isotope is nil or less. A “Warm nodule” takes up isotope as does the normal thyroid tissue about it and a "Hot nodule" is one which takes up more isotope than the rest of the gland [7]. In this series 46 study patients had diminished concentration of isotopes and 4 patients had normal concentration of isotopes in the nodules as shown in table 11. In this study subtotal thyroidectomy was done in 28 cases, hemithyroidectomy was done in 17 cases and total thyroidectomy was done in 5 cases (Table 12). Histopathological reports of the excised tissues revealed that 45 cases were papillary adenoma, 3 cases were papillary carcinoma and 2 cases were follicular carcinoma (Table 13).

Type of nodule on scanning	Number of patients (n)	Percentage (%)
Hot Nodule	-	-
Cold Nodule	46	92
Warm Nodule	4	8

Table 11: Different types of nodule on scanning (N=50)

Surgical procedures	Number of patients (n)	Percentage (%)
Subtotal thyroidectomy	28	56
Hemithyroidectomy	17	34
Total thyroidectomy	5	10
Total	50	100

Table 12: Surgical procedures among the study cases (N= 50)

Histopathological varieties	Number of patients (n)	Percentage (%)
Follicular adenoma	45	90
Papillary carcinoma	3	6
Follicular carcinoma	2	4
Total	50	100

Table 13: Histopathological variety of the study cases (N= 50)

4. Discussion

The term thyroid goiter refers to an abnormal growth of the thyroid gland. A goiter can be diffuse or nodular; depends on the cause and could be associated with normal, increased or decreased thyroid hormone production [8]. Clinical manifestations of a goiter may vary with thyroid function along with the size and location of the goiter [8]. The optimum diagnostic and therapeutic strategy of a thyroid nodule is still continues to be a controversial topic [9,10]. This is mainly because virtually any thyroid disease can manifest itself as thyroid nodule either solitary or multiple [9]. Moreover, the diagnostic techniques, which are available to distinguish benign from malignant lesion, vary in reliability [10]. In this study a total of 50 patients with thyroid nodule (multiple or solitary) who underwent thyroid surgery were evaluated retrospectively during a period of two years. Thyroid diseases as a whole is more common in female and the actual ratio varies from time to time and place to place and according to specific disease entity [11]. In this study it was found that all types of nodular involvement of thyroid gland is more common among females than males, the male to female ratio was 1 :3.12, which was consistent with other studies [2, 11-13]. Why thyroid nodule is more common in female is yet to be ascertained. The current view suggests that at the time of puberty and pregnancy, the estrogen increases the synthesis of more thyroxine binding globulin (TBG) which in turn binds more free T_4 and T_3, decreasing their blood level. Due to decrease in the serum T_3 and T_4, there is increased production of TSH which is responsible for hyperplasia and hypertrophy of the glandular epithelium of the thyroid. It is of interest that recently estrogen receptors have been identified in normal thyroid tissue and also in nodular goiter [14], but its role is yet to be investigated. In this study majority of the patients belonged to the age group of 25-40 years and biochemical analysis of this study population showed that 70% patients were in euthyroid state, 24% patients were hyperthyroid and 6% patients were in hypothyroid state. These findings were consistent with a similar previous study [2]. In the United States approximately 4% of the adult population has clinically palpable nodules [10] and prevalence increases in the later decades of life [2,11]. Occupational analysis showed that majority of the study patients (50%) were house wives as the disease is more common in females. Toxic manifestations were not found in any of our study patients which may be a coincidence and also probably indicates very low incidence of toxic nodular goiter. It was reported that the overall prevalence of autonomous functioning of toxic nodule is 2.8% [15]. In this study all patients presented with visible and/or palpable neck swelling of wide range of duration. About 50% of the patients had their neck swelling of 2-4 years duration. On the other hand 10% of the patient had their neck swelling for less than 1 year. Out of 50 cases, clinically solitary nodule was 60% and rest 40% was clinically multinodular goiter. These findings were comparable with the findings of other studies [2,4,16-17]. In this study it was observed that right lobe was affected more than the left lobe, although not significant but still it was nearer to one previous study [4]. In this study out of 46 cold nodules; only 10.86% was proved to be malignant, thus majority (89.24%) of the cold nodules were benign. This finding was supported by a couple of related study [2,4]. The aim of surgery (subtotal thyroidectomy/ hemithyroidectomy/ total thyroidectomy) is to reduce the transformation of benign thyroid swelling to malignant one [11]. In this study; highest number (92%) of patients having single cold nodular goiter which were diagnosed by history,

clinical examination, scanning and FNAC, which determined the indication of surgery [18-20]. In this series; subtotal thyroidectomy was done in 28 cases, hemithyroidectomy was done in 17 cases and total thyroidectomy with cervical lymph node clearance was done in 5 cases having correlation with other studies [20-22]. After excision histopathological reports of the excised tissues showed; 45 cases were papillary adenoma, 3 cases were papillary carcinoma and 2 cases were follicular carcinoma, this finding was consistent with similar previous studies [4,16,17]. In this study subtotal thyroidectomy was done for 28 (56%) cases of multinodular goiter. In surgical practice this type of surgery for multinodular goiter is done predominantly throughout the world [21]. In this study we found that, total thyroidectomy was done for papillary carcinoma of thyroid in 3 cases and follicular carcinoma in 2 cases; which were in an agreement with related previous studies [21,22]. The cases of total thyroidectomy with papillary carcinoma of thyroid were treated by radio-iodine ablation at the end of 4 weeks following surgery in accordance with related previous studies [12,17]. In this study, radioisotope scanning was performed in all cases. Reports revealed that 46 patients had cold nodules and 4 patients had warm nodules. None of the nodules were found to be toxic. Out of 46 cold nodules, 5 cases were proved to be malignant, thus majority (89.24%) of the cold nodules were benign. These findings were supported by a couple of previous study [23,24]. The main limitation of radio-isotope scanning is that it cannot distinguish benign from malignant nodules and can be used only to assign probability of malignant diseases on the basis of functional status of the nodule [24]. Radionuclide scanning is the most beneficial in evaluating the functional status of thyroid nodules [24]. When fine needle aspiration cytology is unavailable or unreliable, radionuclide scanning becomes a first line diagnostic tool [24]. Ultrasonography (USG) should be used primarily for identifying a solid component or a cystic nodule with a reported accuracy of 95 to 100%, determining the size of nodules on thyroxine suppression that are not easily palpable, or for performing guided fine needle aspiration [25]. Accurate localization and measurement of lesion, discrimination between diffuse and local disease, between solitary and multiple nodules can be made at the time of USG examination. It can also provide a guide for percutaneous needle aspiration biopsy. But it is not possible to distinguish benign from malignant lesion by ultrasound scan [25]. Ultrasound scanning was performed in all our study cases. Among total 50 study patients, 3 cases were cystic and rest 47 cases were solid lesions. Thus cysts comprise 6.66% of cold nodule and these were benign. Fine needle aspiration cytology (FNAC) has emerged as the best initial diagnostic step for the evaluation of nodular thyroid, when the technique is performed by an experienced physician and interpreted by an experienced cytopathologist. It was reported that in the hands of an experienced cytologist, aspiration cytology is a safe and the best diagnostic tool in the evaluation of nodular thyroid lesion [26]. The efficacy of FNAC has been evaluated in multiple series [24-28]. It was reported that the specificity of FNAC is 70-90%, while sensitivity is 83-99% and only 0-2.1% false negative result of FNAC [27,28]. In comparison with imaging procedures, including those giving information of functional activity, the combined sensitivity and specificity rates of aspiration cytology come closest to the ideal discriminatory situation [27]. In combination with case history and careful clinical examination, fine needle aspiration cytology is the best guidance for an optimal selection of patients for therapeutic or

diagnostic surgery [29,30]. Fine needle aspiration cytology (FNAC) of the excised tissue was performed in all cases in this study, reports revealed that 45 cases were papillary adenoma, 3 cases were papillary carcinoma and 2 cases were follicular carcinoma. In this study 30 cases were diagnosed to have clinically solitary thyroid nodule, and most common histopathological diagnosis was adenoma, accounting to 60%. These findings were somewhat different from previous studies as observed by Hoffmann *et al.;* according to their report, most common histopathologic diagnosis was benign colloid nodule, accounting to 47.50% [31], while Altae *et al*. reported 69.3 % colloid nodular goiter in their study population [2]. On the other hand among 50 study cases, 40% proved to be multinodular goiter. This finding was relatively less than that of other series where incidence of multinodular goiter was 54.94% [32]. Benign neoplasm (Adenoma) was found in 16 cases comprising 32%, This result was supported by a couple of related studies [13,15,32]. In this study, 3 cases were benign cyst-adenoma. This finding was in line of a previous study as reported that the incidence of malignancy in cystic lesion is about 1-2% [10]. In this study, 5 cases proved to be malignant on microscopic examination of excised tissue, the percentage was 10.86%. However in a report it was observed that, out of 986 thyroid nodules 152 were carcinoma, which was about 15.41 % [31]. In this study out of 5 malignant neoplasm's 3 were papillary carcinoma which was 60% and rest 2 cases were follicular carcinoma (40%). This finding was comparable with similar previous studies [30-32].

Conclusion

This study concluded that solitary thyroid nodules are more frequent in 3rd to 4th decade of life and predominant in females. Most of the patients of thyroid goiter are in euthyroid state and majorities are benign lesions. Papillary adenoma is the most frequent benign nodular tumor followed by papillary carcinoma and then follicular carcinoma. A longer duration of symptoms does not preclude the diagnosis of malignancy. To reach a reasonably correct preoperative diagnosis; careful clinical evaluation, thyroid scintiscan, ultrasonographic study and FNAC should carried out.

Limitations of the study

It was a single center study with a relatively small sample size.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this article.

References

1. Van Herle AJ, Rich P, Ljung BM, et al. The thyroid nodule. Annals of Internal Medicine 96 (1982): 221-232.
2. Altae MA, Al Mosaui HM, Alkhafaji MM. Clinical and pathological evaluation of patients with nodular goitre. Med J Babylon 6 (2009): 494-500.
3. Hermus AR, Huysmans DA. Treatment of benign nodular thyroid disease. New England Journal of Medicine 338 (1998):1438-1447.
4. Das AB, Alam MN, Haq SA, et al. Solitary thyroid nodule: a study of 100 cases. Bangladesh Medical Research Council bulletin 22(1996): 12-18.
5. Hamberger B, Gharib H, Melton III LJ, et al. Fine-needle aspiration biopsy of thyroid nodules: impact on thyroid practice and cost

of care. The American journal of medicine (1982): 381-384.

6. Kalra S, Khandelwal SK, Goyal A. Clinical scoring scales in thyroidology: A compendium. Indian journal of endocrinology and metabolism 15 (2011): S89.
7. Ross DS, Cooper DS. Diagnostic approach to and treatment of thyroid nodules. UpToDate. Wellesley, MA: UpToDate (2008).
8. Ross DS. Clinical presentation and evaluation of goiter in adults. UpToDate, Waltham, MA (2020).
9. Bennedbæk FN, Perrild H, Hegedüs L. Diagnosis and treatment of the solitary thyroid nodule. Results of a European survey. Clinical endocrinology 50 (1999): 357-63.
10. Rojeski MT, Gharib H. Nodular thyroid disease: evaluation and management. New England Journal of Medicine (1985): 428-436.
11. Doherty GM, Way LW. Thyroid and Parathuyroid: Current surgical diagnosis & treatment. In Current surgical diagnosis & treatment, 11th ed, (2006) 298-318.
12. Hashemian H, Keyhani A. Carcinoma of the thyroid gland in Iran. Journal of British Surgery 64 (1977): 457-459.
13. Taneri FE, Kurukahvecioglu OS, Ege B, et al. Prospective analysis of 518 cases with thyroidectomy in Turkey. Endocrine regulations 39 (2005): 85-90.
14. Guyton AC, Hall JE. Textbook of medical physiology. WB Sounders Company, Philadelphia (2006): 858-868.
15. Belfiore A, La Rosa GL, La Porta GA, et al. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. The American journal of medicine 93 (1992): 363-369.
16. Hossain MM, Haque MR, Rashid A, et al. Surgical management of thyroid diseases- a study on 78 cases. Mymensingh medical journal 11 (2002): 6-8.
17. Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules: final report of a 15-year study of the incidence of thyroid malignancy. Annals of internal medicine 69 (1968): 537-540.
18. Lansford CD, Teknos TN. Evaluation of the thyroid nodule. Cancer control (2006): 89-98.
19. Rojeski MT, Gharib H. Nodular thyroid disease: evaluation and management. New England Journal of Medicine 313 (1985): 428-36.
20. Friedrich J, Krause U, Schmidt U, et al. Is hemithyroidectomy as standard intervention of suspicious puncture cytology justified?. InLangenbecks Archiv fur Chirurgie. Supplement. Kongressband. Deutsche Gesellschaft fur Chirurgie. Kongress 113 (1996): 189-191.
21. Steinert M, Friedrich T, Keitel R, et al. Indications and surgical therapy of thyroid gland diseases- analysis of 725 operated patients. Zentralblatt fur Chirurgie 123 (1998):30-33.
22. Niepomniszcze H, Garcia A, Faure E, et al. Long-term follow-up of contralateral lobe in patients hemithyroidectomized for solitary follicular adenoma. Clinical endocrinology 55 (2001): 509-513.
23. Kapur MM, Sarda AK, Bal S, et al. Carcinoma of the thyroid: differential behaviour in solitary and multinodular

tumours. Journal of British Surgery 73 (1986): 894-895.

24. Krenning EP, Ausema L, Bruining HA, et al. Clinical and radio-diagnostic aspects in the evaluation of thyroid nodules with respect to thyroid cancer. European Journal of Cancer and Clinical Oncology 24 (1988): 299-304.
25. McLaughlin SJ, Gray JG, Marshall T. Aspiration cytology and ultrasonography of cold thyroid nodules. Australian and New Zealand Journal of Surgery 56 (1986): 331-334.
26. Hamming JF, Goslings BM, Van Steenis GJ, et al. The value of fine-needle aspiration biopsy in patients with nodular thyroid disease divided into groups of suspicion of malignant neoplasms on clinical grounds. Archives of internal medicine 150 (1990): 113-116.
27. Ashcraft MW, Van Herle AJ. Management of thyroid nodules II: Scanning techniques, thyroid suppressive therapy, and fine needle aspiration. Head & neck surgery 3 (1981): 297-322.
28. Reeve TS, Delbridge L, Sloan D, Crummer P. The impact of fine-needle aspiration biopsy on surgery for single thyroid nodules. Medical journal of Australia. 1986 Oct;145(7):308-11.
29. Block MA, Dalley GE, Robb JA. Thyroid nodules indeterminate by needle biopsy. The American Journal of Surgery 146 (1983): 72-78.
30. Bennedbæk FN, Perrild H, Hegedüs L. Diagnosis and treatment of the solitary thyroid nodule. Results of a European survey. Clinical endocrinology 50 (1999): 357-363.
31. Hoffmann GL, Thompson NW, Heffron C. The solitary thyroid nodule: a reassessment. Archives of Surgery (Chicago, Ill.: 1960) 105 (1972): 379-385.
32. Pendse AK, Gupta SP. A clinicopathological analysis of one hundred operated cases of goitre. Journal of the Indian Medical Association 80 (1983): 172-175.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license 4.0