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The frequency of parathyroid insufficiency after total thyroidectomy

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Abstract
Background: Parathyroid insufficiency is an essential risk factor after total thyroidectomy. A significant amount of patients, especially females are suffering from thyroid disorders mostly. Severe disorder needs thyroidectomy which is associated with hypoparathyroidism.
Objective: This study revolves around the determination of the frequency of parathyroid insufficiency after total thyroidectomy with some secondary objectives. The secondary objective includes finding the demographic data of the patients and determining the total calcium level after thyroidectomy and serum intact parathyroid hormone (iPTH) level after total thyroid surgery.
Methodology: This is a yearlong prospective observational study. The study was centered at the Department of Otolaryngology at Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh. The patient presented with a history of thyroid disorders and scheduled for thyroid surgeries are the primary population in this study. With ethical considerations, a total of 50 patients were enrolled in this study in 2019.
Results: The demographic data represents the male-female ratio in this study was 1:3.14. The mean age of patients who underwent thyroidectomy is (39.40 ± 10.23), whereas, most of the study subjects belong to 31-40 age ranges. A significant 38% of patients are also noticed aged >41 years. Hypoparathyroidism (24%) and hypocalcemia (20%) affected the patients after total thyroidectomy. Total thyroidectomy with neck dissection was performed in a total of 20% of patients. Among them, 14% and 12% of patients reported about hypoparathyroidism and hypocalcemia. Serum iPTH level (pg/ml) in the 3rd POD also joins the likewise results to S. calcium and both of the investigations show normal results after 1 month of operations in most cases.
Conclusion: Total thyroidectomy and total thyroidectomy with neck dissections are medical procedures that come with several risk factors. Good surgical monitoring of patients is invaluable and helps in the early detection and management of such complications.

Keywords: Parathyroid insufficiency, hypoparathyroidism, hypocalcemia, thyroidectomy

Introduction
Thyroidectomy is a well-defined and common procedure in modern medicine. It involves excising thyroid glands to treat thyroid goitre, prevent sequelae of thyroid carcinoma, and achieve hormonal control of hyperthyroidism-like diseases [1]. Acute and Chronic parathyroid insufficiency is the most common complication after total thyroidectomy [2]. It imposes a medical burden on patients regarding changing lifestyles, medications, and visiting physicians regularly all their lifetime. Parathyroid insufficiency is prevalent in women subjects, and hardly men are affected by this [3]. The Spanish Ministry of Health recorded a sum of 12,903 patients with parathyroid disorders in Spain between year 2003 to 2017; whereas, 74.70% of patients were female [4]. Estimated parathyroid insufficiency after total thyroidectomy has been noted as 0-3% in recent research [5]. Parathyroid glands are located near the thyroid gland in the neck region. The third and fourth pharyngeal pouches develop the parathyroid glands. It releases a hormone named parathyroid hormone (PTH) that functions to regulate serum calcium, vitamin D, and phosphorus levels in blood and bone [6]. Parathyroid insufficiency can be referred to as hypoparathyroidism. It can be caused by injury to the parathyroid glands from ligation of the blood supply,

inadvertent or deliberate removal, and improper use of electrocauterization or destruction due to hematoma formation [7]. The main symptoms of hypoparathyroidism are a result of low serum calcium level, which interferes with normal muscle contraction and nerve conduction. As a result, people can experience paresthesia, an unpleasant tingling sensation around the mouth and the hands and feet, as well as muscle cramps and severe spasms known as tetany [8]. Calcium imbalance is considered an indicator of parathyroid insufficiency in the body [9]. Post-operative hypocalcemia is a common complaint of patients after thyroidectomy. It impacts negatively patients' Quality of life to the need for lifetime medication, regular visits, and significant long-term costs. $P<0.0001$ at the 3rd POD of thyroidectomy refers to a significant reduction of calcium level in serum after thyroidectomy.

Methodology

A prospective observational study on parathyroid insufficiency after total thyroidectomy at the Department of Otolaryngology at Sir Salimullah Medical College Mitford Hospital, Dhaka in the year 2019. 50 thyroid surgery scheduled patients were the study population. The primary objective of this study is to determine the frequency of parathyroid insufficiency after total thyroidectomy with some secondary objectives like finding the total calcium level after thyroidectomy and serum intact parathyroid hormone (iPTH) level after total thyroid surgery. The study was conducted with the ethical guidance of the Declaration of Helsinki and all subjects provided written consent before being included in this study. A purposive non-randomized sampling method was applied during sample collections and study subjects were selected based on some relevant inclusion and exclusion criteria.

Inclusion criteria

- Patients scheduled for total thyroid surgery with or without neck dissection.
- Normocalcaemic patient scheduled for total thyroid surgery.
- Both sexes of any age
- Patients willing to participate in the study.

Exclusion criteria

- Patients with Hemithyroidectomy
- Patients who received calcium and vitamin D supplementation before surgery.
- Patients who underwent parathyroid autotransplantation during surgery.

Data were collected using a preformed case report form. The relevant socio-demographic data of these patients were collected and recorded in accordance. Statistical analysis was performed by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22) (SPSS Inc, Chicago, IL, USA). A 95% confidence limit was taken. The summarized data was interpreted accordingly and was then presented in the form of tables.

Results

Table 1: Demographic profile of the study subjects, Age (N=50)

Age	Frequency (n)	Percentage (%)	Std. Deviation	Mean
≤30	10	20%	39.40 ± 10.23	39.40
31-40	21	42%		
>40	19	38%		
Total	50	100%		

Table 01 shows the demographic profile of the study subjects. The minimum age of study subjects was 18 years and the maximum age was 60.

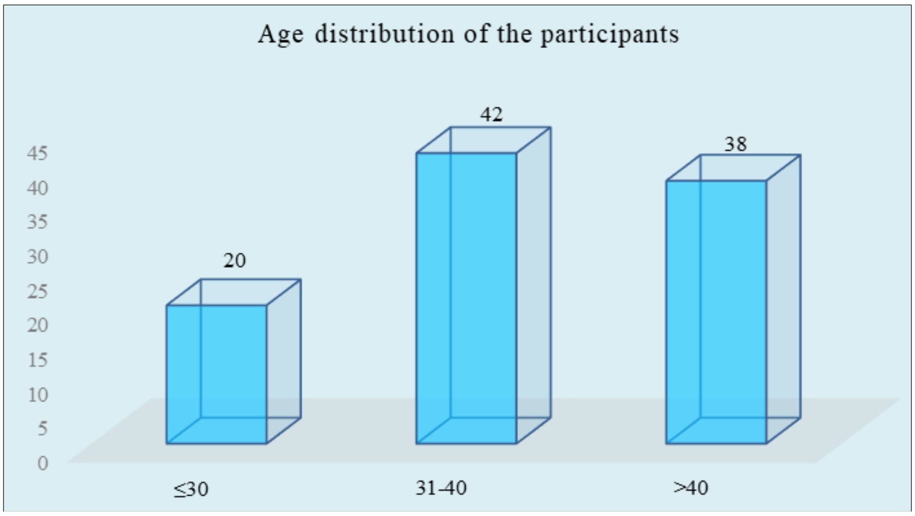

Fig I: Column chart showed age wise patients' distribution (N=50)

Table 2: Demographic profile of the study subjects, Sex (N=50)

Sex	Frequency (n)	Percentage (%)
Male	11	22%
Female	39	78%
Total	50	100%

Females are more affected by parathyroid deficiency. In this study, female subjects dominated male subjects with a ratio of 1:3.54.

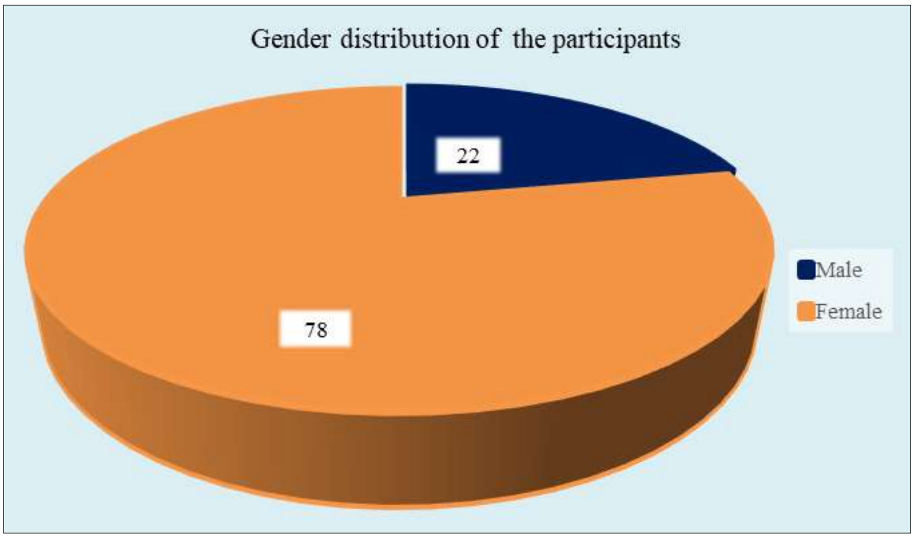

Fig 2: Pie chart showed gender wise patients' distribution (N=50)

Table 3: Clinical findings of the study subjects (N=50)

Clinical findings	Frequency (n)	Percentage (%)
Consistency		
Firm	43	86%
Hard	7	14%
Regional lymhnode		
Thyroid swelling only	41	82%
Thyroid swelling with nodal metastasis	9	18%

Table 03 shows clinical findings. 86% of the thyroid swelling was firm, and 14% was hard. 82% of the lymph nodes were not palpable, and 18% were palpable.

Table 04a: Frequency of hypoparathyroidism based on extent of thyroid surgery (N=50)

	Total n (%)	No hypoparathyroidism	Hypoparathyroidism
Total thyroidectomy	40 (80%)	27 (67.50%)	13 (32.50%)
Total thyroidectomy with neck dissection	10 (20%)	3 (30%)	7 (70%)

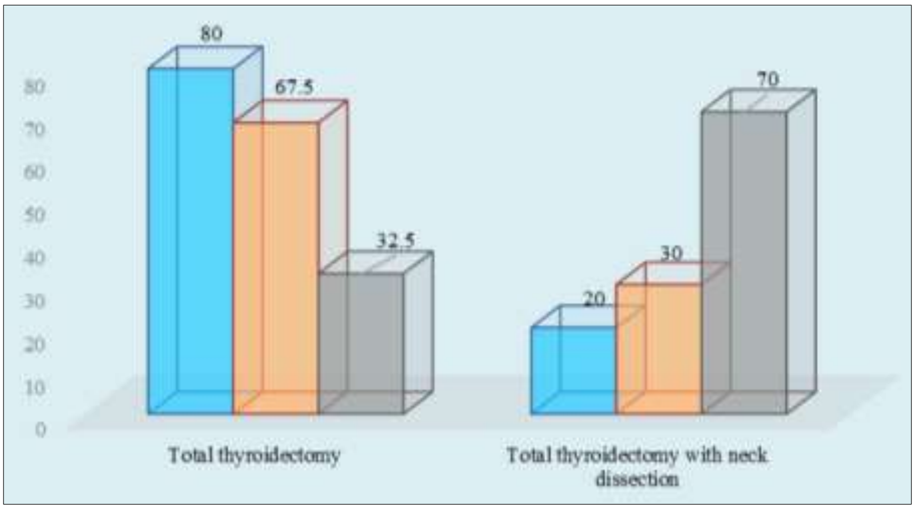

Fig 3: Line chart showed frequency of hypoparathyroidism based on extent of thyroid surgery (N=50)

Table 04b: Frequency of hypocalcemia based on the extent of thyroid surgery (N=50)

	Total n (%)	No hypocalcemia	Hypocalcaemia
Total thyroidectomy	40 (72%)	29 (72.50%)	11 (32.50%)
Total thyroidectomy with neck dissection	10 (20%)	4 (40%)	6 (60%)

Table 04a and table 04b show total thyroidectomy was done in 40 (80%) patients, total thyroidectomy with neck dissection was done in 10 (20%) patients, and completion thyroidectomy was done on 4 (8%) of patients and frequency of hypoparathyroidism and hypocalcemia was more in total thyroidectomy with neck dissection.

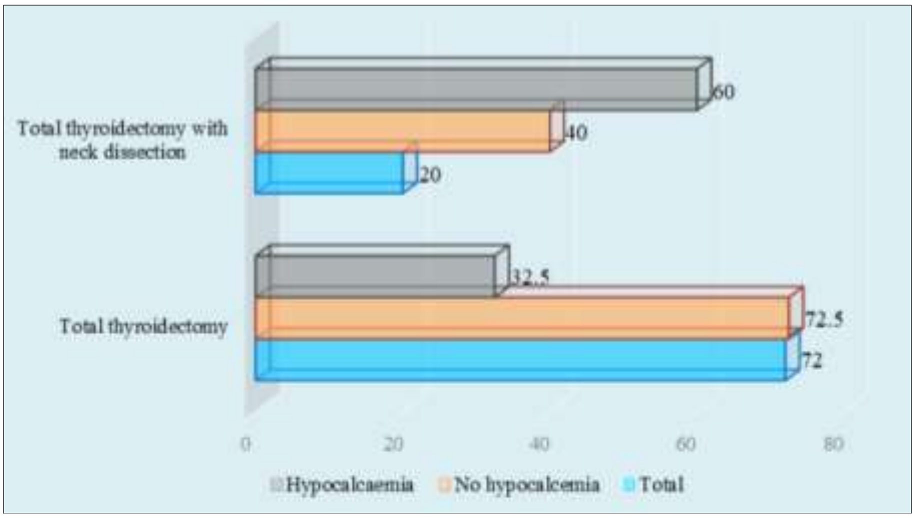

Fig 4: Bar chart showed frequency of hypocalcemia based on extent of thyroid surgery (N=50)

Table 5: Pre and post-operative day (POD) total serum calcium (mg/dl) (N=50)

Pre-operative	**Mean ± SD**	**Min-max**	**p-value**	
	8.87±0.28	**8.40 – 9.50**		
1st POD	8.098±0.41	7.0 – 9.12	<0.001	Pre vs 1st POD
3rd POD	8.4±0.46	7.5 – 10.10	<0.001	Pre vs 3rd POD
After 1 month	8.74±0.66	7.7 – 10.10	<0.50	Pre vs 1 month
After 6 month	8.96±0.66	7.4 – 10.2	<0.84	Pre vs 6 month

Table 05 shows pre-operative and post-operative serum total calcium. After the operation, serum total calcium was reduced at 1st POD & 3rd POD, and after 1 month it was increased. Pre-operative serum total calcium was 8.87 ± 0.28 (mg/dl).

Table 6: Post-operative Serum iPTH level (N=50)

	1st POD	**3rd POD**	**1 month**	**6 month**
Serum iPTH level (pg/ml)	13.5±10.39	21.61±14.33	29.707±12.69	33.99±9.79

Table 06 shows post-operative serum iPTH. After operation serum iPTH is reduced at 1st POD & 3rd POD and after 1 month it will be increased.

Table 7: Association of iPTH with serum calcium at 1st POD and at 1 month and 6 month (N=50)

iPHT	**Serum Calcium**			
	1st POD	**3rd POD**	**1 month**	**6 month**
<7	7.81±0.31	7.85±0.29	7.84±0.08	7.83±0.24
≥7	8.3±0.28	8.5±0.36	8.80±0.35	9.04±0.58
p-value	0.010	0.003	0.001	0.001

Table 07 shows there is significant association of iPHT with serum calcium. serum calcium level increased according to the increment of iPTH.

Table 8: Frequency of Parathyroid insufficiency and recovery within 6 month after total thyroidectomy pf the study subjects (N=50)

Parathyroid insufficiency	**1st POD**	**3rd POD**	**1 month**	**6 month**
Yes	20 (40%)	12 (24%)	5 (10%)	3 (6%)
No	30 (60%)	38 (78%)	45 (90%)	47 (94%)
Total	50	50	50	50

Table 08 shows Parathyroid insufficiency was found in 40% patients after total thyroidectomy at 1st POD and 24% at 3rd POD, 10% after 1 month and 6% after 6 month.

Discussion

Thyroid diseases are very common nowadays. Although the mortality rate is not that severe in thyroid disorders, permanent hypoparathyroidism, post-operative hypocalcemia, and bleeding are some associated risk factors with thyroid surgeries [10]. This article draws a linear relationship between the frequencies of patients who went through thyroidectomy and the frequencies of hypoparathyroidism, and hypocalcemia. This study is clearly female dominant with three and a half-fold higher female population. Due to physiological differences, women are more susceptible to thyroid disorders mostly during puberty, pregnancy, and menopause [11]. In 2011, another research proved that females are more tend to be affected by post-thyroidectomy hypocalcemia [12]. The mean age detected of these study subjects was 39.40±10.23, where most of the patients were 31-40 years of age ranges. 38% of patients detected who underwent thyroidectomy at the age greater than 41 years. The endocrine glands including thyroid and parathyroid glands undergo significant changes with aging, the frequencies of thyroid and parathyroid disorders thus increase with age. Diab. N. *et al*, 2019 conducted research and found the abnormal diagnosis of thyroidal tests in people aged ≥65 [13]. 86% and 14% of patients presented in the hospital with firm and hard thyroid glands. Among them, 82% of patients complained about thyroid gland swelling only, and 18% of patients complained about Thyroid swelling with nodal metastasis. The current study shows a tendency of their participants to develop hypoparathyroidism (24%) and hypocalcemia (20%) after total thyroidectomy in patients. The percentage of hypoparathyroidism (14%) and hypocalcemia (12%) declines when the thyroidectomy is done with neck dissection. Still, the complication of hypoparathyroidism (4%) and hypocalcemia (4%) lies with thyroidectomy. Several studies describe these two are the common complications of patients after thyroidectomy due to age, sex, increased gland size, type of thyroid disease, presence of fibrosis and inflammation, extent of thyroidectomy, and lymph node dissection [14, 15]. Previous studies resulted that the risk of hypoparathyroidism increases after total thyroidectomy with neck dissection surgeries than total thyroidectomy as total thyroidectomy removes only thyroid glands but thyroidectomy with neck dissection removes additional tissues along with lymph nodes in the neck [16]. The results of calcium levels of Pre and post-operative days shows significant changes. $p<0.0001$ reveals that calcium level decreases in the 1st and 3rd POD but it is manageable within 1 month of surgery. The 2021 study on Post-Thyroidectomy Hypocalcemia also shares similar results with us where 63.7% of patients developed hypocalcemia within 24 hours of total thyroidectomy [14]. Reduction of S. iPTH level defines the insufficiency of parathyroid in patients after thyroidectomy. A significant reduction is followed in the iPTH level on the 3rd operative day but the iPTH level increases after 1 month of the surgery. A 2021 clinical study in Rome also noted a reduction of iPTH level in 37.6% of study subjects within 3 hours of thyroidectomy [17].

Discussion

Parathyroid hormone insufficiency, along with hypocalcaemia and bleeding (Stoll *et al*., 2009), is a common complication associated with total thyroidectomy. This study was conducted to find out frequency of parathyroid insufficiency after total thyroid surgery. In this study, mean age of the patients was 39.40±10.23 years. Mean age of the patients was more than 40 years in the study of Ritter *et al*. (2015). Mean age was 43±15 years in the study of Suwannasarn *et al*. (2015). Females were predominant than males. Female to male ratio was 3.54:1. Similar female predominance was seen in the study of Ritter *et al*. (2015), Suwannasarn *et al*. (2015) and Nair *et al*. (2014).Regarding clinical presentation of the study population thyroid swelling present in all cases (100%). Out of them 18% patients were presented along with cervical lympadenopathy correspond with the other study which showed in thyroid swelling with cervical lympadeopathy is 24% (Mahmud *et al*., 2016). This study was carried out based on pre operative and post operative serum total calcium and post operative serum intact parathyroid hormone level who were undergone total and completion thyroidectomy.In this study total thyroidectomy was done of 40 patients, total thyroidectomy with neck dissection was done of 10 patients. We defined low PTH as a measurement of PTH <7 pg/ml (According to manufacturer's normative data, BIRDEM, the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder at Shahbag, Dhaka). In our study, 20(40%) of patients had a postoperative PTH <7 pg/ml at 1st POD, but the majority of these patients showed recovery of parathyroid gland function within 1 months of surgery. Only 5(10.0%) of the study subjects had remain PTH <7 pg/ml after 1 month of surgery. and 3 (6%) after-6 months. Hypocalcaemia is the most common complication of thyroidectomy in the literature. The more widespread proposal that postoperative hypocalcaemia be defined as s-Ca <8 mg/dl 24 hours after total thyroidectomy (Lorente-Potch *et al*., 2015). In our study frequency of hypocalcaemia (s- Ca <8 mg/dl) was 36.0% in 1st POD, but the majority of these patients showed recovery within 1 month. Only 5(10.0%) of the study subjects had remain serum total ca <8 mg/dl after 1 month of surgery. Kim *et al*. (2013) found 46% hypocalcaemia in their study. Many different studies show temporary hypocalcaemia occurs in 1 to more than 50% of patients undergoing total thyroidectomy or completion thyroidectomy (Cayo *et al*., 2013). Furthermore, different time points have been used to determine when postoperative hypoparathyroidism should be classified as permanent. Some consider postoperative hypoparathyroidism to be permanent if recovery of function has not occurred within 6 month (Chow *et al*., 2014; Thomusch *et al*., 2003; Karamankos *et al*., 2010; Pfleiderer *et al*., 2009; Earbil *et al*., 2007; Ozbas *et al*., 2005) while others define permanent at 1 year after surgery (Almquist *et al*., 2014; Nawrot *et al*., 2014). Chow *et al*. found that 2.8% of patients developed permanent hypoparathyroidism, as defined as 6 month of surgery. In our study permanent hypoparathyroidism was 6%. at 6 month after total thyroidectomy. Transient, protracted and permanent hypoparathyroidism is mildly high in our study due to surgeon factor. Junior surgeons had done 18 patients of total thyroidectomy out of 50 patients, where hypoparathyroidism was more.

Limitation

The small sample size, the limited time span, and single-centered data are the main limitations of this prospective observational study on parathyroid insufficiency after total thyroidectomy. Here, it may not represent the whole population of the country. It would be great if free Ca^{2+} could be measured to indicate clinically overt hypoparathyroidism. Moreover, it is an expensive study to perform.

Conclusion

The study represents the data of frequencies after thyroidectomy disorders. Females are more susceptible to thyroid disorders and to develop parathyroid insufficiency after thyroidectomy and the risk of parathyroid insufficiency rises in the midlife. Patients with total thyroidectomy with neck dissection developed hypoparathyroidism more than patients with total thyroidectomy. This can be because only 20% of study subjects performed total thyroidectomy with neck dissection whereas the study population of total thyroidectomy was 72%. The study can be concluded with a message that the chance of parathyroid insufficiency increases after thyroidectomy. The patient should be kept under observation after the operative procedure.

Conflict of Interest

Not available

Financial Support

Not available

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