

Frequency of hypocalcemia after thyroid surgery

Sheikh Atiq-ur-Rehman, Fayyaz Ahmad, Muhammad Khizer Hayat, Usman Rizvi, Rashid Mahmood, Sajida Naseem

Abstract

Introduction: Hypocalcaemia is the feared complication after total or near-total thyroidectomy. Symptoms like numbness, tingling and carpopedal spasm occurs in early post-operative period due to primary parathyroid deficiency or due to transient ischemia.

Objectives: To determine the frequency of hypocalcemia after thyroid surgery.

Study design: Descriptive, case series.

Settings: Department of General Surgery, Bahawal Victoria Hospital, Bahawalpur.

Study duration: 1st November 2018 to 31st October 2020

Material & Methods: Total 113 patients with benign goiter of duration < 5 years undergoing surgery, 20-60 years of age of both genders were selected. Patients with pre-operative hypocalcaemia, recurrent goiter, sub-acute thyroiditis and CRF were excluded. All patients were undergone near-total or total thyroidectomy. All patients were followed by the researcher himself and in all patients, 5 ml of venous blood was collected from ante-cubital vein under aseptic precaution and serum calcium was determined by colorimetric method. Outcome variable i.e. hypocalcemia (present/absent) were noted in each patient at 7th day post-operatively.

Results: Age range in this study was from 20 to 60 years with mean age of 42.84 ± 8.83 years. Majority of the patients 70 (61.95%) were between 41 to 60 years of age. Out of the 113 patients, 44 (38.94%) were male and 69 (61.06%) were females with male to female ratio of 1:1.6. Hypocalcemia after thyroid surgery was found in 14 (12.39%) patients, whereas there was no hypocalcemia in 99 (87.61%) patients.

Conclusion: This study concluded that percentage of hypocalcemia after thyroid surgery was found in 12.39% patients.

Keywords: Thyroidectomy, benign thyroid goiter, hypocalcemia, post-operative complications

Introduction:

Thyroidectomy is one of the major and frequent operations performed in general surgical units. The most notable thyroid surgeon was Kocher 1841–1917. Kocher collected data on 268 thyroid operations and identified recurrent laryngeal nerve injury, myxoedema and tetany as serious post-operative complications.¹ The total calcium concentration in plasma is 2.25-2.55mmol/L. 50 percent is ionized, 40% is bound to proteins (90% binds to albumin), and 10% circulates bound to anions (phosphate, carbonate, citrate, lactate, and sulphate).² Ionized calcium is the

necessary plasma fraction for normal physiologic processes. The levels of ionized calcium are rigidly controlled by parathyroid hormone (PTH), vitamin D and calcitonin through complex feedback mechanisms. The absence or deficiency of PTH (hypoparathyroidism) results in hypocalcaemia.^{3,4}

Hypocalcaemia is the feared complication after total thyroidectomy. Common symptoms of hypocalcaemia like numbness, tingling and carpopedal spasm occurs in the post-operative period due to primary parathyroid deficiency or

Received

date: 13th November, 2020

Accepted

date: 23rd March, 2021

Quaid-e-Azam Medical College, Bahawal Victoria Hospital, (QAMC/BVH) Bahawalpur
SA Rehman

Bahawal Victoria Hospital, Bahawalpur
F Ahmad
MK Hayat
U Rizvi
R Mahmood
S Naseem

Correspondence:

Dr. Sheikh Atiq-ur-Rehman, Associate Professor Surgery, Quaid-e-Azam Medical College/ Bahawal Victoria Hospital, Bahawalpur
Address: House no 9/A, Block 'X' model town C, Bahawalpur
Cell No: 0300-6808500
email: dratiq2002@gmail.com

due to relative causes like dehydration or transient ischemia.⁵ Parathyroid glands control the amount of calcium in the blood and within the bones. At surgery, it is harder to differentiate between thyroid, fat and parathyroid gland and inadvertent damage can occur to the gland. This can result in hypoparathyroidism and hence hypocalcaemia.^{6,7}

As the blood supply to the parathyroid glands had become better understood, total thyroidectomy (TT) is now routinely performed with division of the vascular supply as it directly enters the capsule of the gland.³ How to prevent and reduce the incidence of post-operative hypocalcaemia remains obscure. Intra-operative identification of the parathyroid glands can be a challenge even for experienced surgeons and unintentional parathyroidectomy may be as high as 9%.⁴ In addition to surgical technique modifications, there are a variety of clinical practices to try to prevent symptomatic hypocalcemia, including selective calcium and vitamin-D supplementation based on post-operative parathyroid hormone levels, and routine supplementation for all patients without evaluation of parathyroid hormone levels in the post-operative period.³ In several series the incidence of hypocalcaemia varied from 10.6% to 50% but may be as high as 83%.⁸ In a study, hypocalcemia was found in 12% patients after thyroid surgery.⁹ In another study, it was found in 21.6% patients following thyroid surgery.¹⁰ One more study has shown this prevalence as 39.0%.¹¹

As previous studies, they have found hypocalcemia as a common complication following thyroid surgery and shows variable incidence of hypocalcemia after thyroid surgery from population to population, so we have decided to conduct this study to determine the frequency of hypocalcemia after thyroid surgery in local population. The results of this study will not only help to resolve the previous controversy but will also be a useful addition in the existing literature. Although previously local studies are available on this but all these studies have shown different results so we have decided to conduct this study to re-evaluate the frequency of hypo-

calcemia after thyroid surgery in Bahawal Victoria hospital, Bahawalpur. This study will also encourage our clinicians to prescribe their patients calcium supplements post-operatively in order to prevent the hypocalcemia and its complications. Also public awareness programs can be arranged and general public can be educated for proper screening and management of hypocalcemia after thyroid surgery in order to reduce the morbidity of these patients.

The purpose of the study was to determine the frequency of hypocalcemia after thyroid surgery in Bahawal Victoria Hospital Bahawalpur.

Operational Definitions:

Benign Goitre presence of diffuse or nodular enlargement of thyroid on clinical examination along raised or decreased free T3 (normal values=3.5-6.5 pmol/L), free T4 (normal values=10-23 pmol/L) and thyroid stimulating hormone (TSH) (normal values=0.5-4.70 mIU/L) was deemed as positive.

Near-total thyroidectomy: is a surgical procedure, in which small thyroid remnant will leave in situ.

Total thyroidectomy is a surgical procedure, in which thyroid gland will be removed completely.

Hypocalcaemia: serum calcium levels <8.5 mg/dl at 7th day post-operatively was taken as positive.

BMI: was calculated by following formula;

BMI = weight in kilograms (measured by weight machine) / height in meters x2 (measured by measuring tape) and >27 was taken as obese and ≤27 as non-obese.

Material & Methods:

This is the descriptive case series, carried out at department of General Surgery, Bahawal Victoria Hospital, Bahawalpur from 1st November 2018 to 31st October 2020.

Sample size will be 113 with 95% confidence

Table 1: Age distribution of patients (n=113)

Age (in years)	No. of Patients	%age
20-40	43	38.05
41-60	70	61.95
Total	113	100.0

• Mean \pm SD = 42.84 \pm 8.83 years

Table 2: Distribution of patients according to duration of disease (n=113)

Duration (years)	No. of Patients	%age
1-2	75	66.37
3-4	38	33.63
Total	113	100.0

• Mean \pm SD = 2.15 \pm 0.97 years

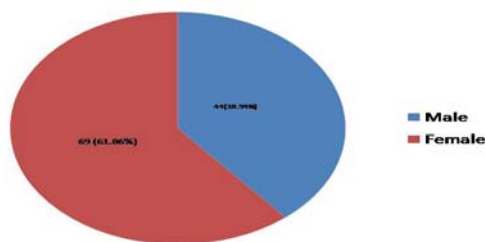


Figure 1: Distribution of patients according to gender (n=113)

level, 6% margin of error and taking percentage of hypocalcaemia after thyroid surgery as 12.0%.¹¹

Sample technique: Non-random, consecutive sampling.

Sample selection:

Inclusion Criteria: All patients with benign goiter (as per-operational definition) of duration < 5 years undergoing surgery. Age 20-60 years. Both genders.

Exclusion Criteria: Patients with recurrent goiter (assessed on history). Patients with pre-operative hypocalcaemia (serum calcium levels <8.5 mg/dl). Patients with sub-acute thyroiditis (presence of fever >100 F and tenderness over thyroid). Patients with chronic renal failure (assessed on history and s/creatinine >1.5 mg/dl).

Data collection procedure: Total number of 113 patients who were admitted to the Department of General surgery of Bahawal Victoria Hospital, Bahawalpur, fulfilling the inclusion criteria was selected. After taking informed written consent, all patients were undergone near-total or total thyroidectomy by one consultant surgeon (with at least 5 years of post-fellowship experience). All patients were followed by the researchers themselves and in all patients 5 ml of venous blood was collected from ante-cubital vein under aseptic precaution and serum calcium was determined by colorimetric method. Outcome variable i.e. hypocalcemia (present/absent) were noted in each patient at 7th day post-operatively. This all data was recorded on a specially designed proforma (Annexure-I).

Statistical analysis was performed using SPSS version 20.0. Results were presented as mean and standard deviation for quantitative variables i.e. age, duration of disease, height, weight, BMI and calcium levels. Frequency and percentage were calculated for gender, type of operation (near-total/total), education level (illiterate/primary/middle/matric/graduation), monthly income (<20000/20001-40000/>40000), place of living (rural/urban) and hypocalcemia (present/absent).

Effect modifiers like age, gender, duration of disease, BMI, type of operation (near-total/total), education level (illiterate/primary/middle/matric/graduation), monthly income (<20000/20001-40000/>40000) and place of living (rural/urban) were controlled through stratification and post-stratification chi square was applied to see their effect on hypocalcaemia. P-value \leq 0.05 was considered as significant.

Results:

Age range in this study was from 20 to 60 years with mean age of 42.84 \pm 8.83 years. Majority of the patients 70 (61.95%) were between 41 to 60 years of age as shown in Table I. Out of the 113 patients, 44 (38.94%) were male and 69 (61.06%) were females with male to female ratio of 1:1.6 (figure I). Distribution of patients according to type of thyroidectomy is

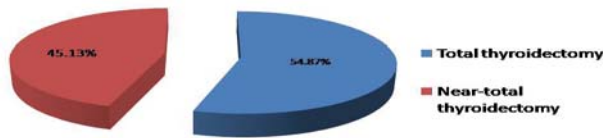


Figure 2: Distribution of patients according to type of thyroidectomy (n=113)

Table 3: Distribution of patients with other confounding variables (n=113)

Confounding variables		Frequency	%age
Place of living	Rural	51	45.13
	Urban	62	54.87
BMI (kg/m ²)	≤27	36	31.88
	>27	77	68.14
Monthly income	<20000	47	41.59
	20001-40000	31	27.43
	>40000	35	30.97
Education level	Illiterate	15	13.27
	Primary	20	17.70
	Middle	31	27.43
	Matric	28	24.78
	Graduate	19	16.81

Table 4: Stratification of hypocalcemia with respect to age groups

Age (years)	Hypocalcemia		p-value
	Present	Absent	
20-40	06	37	0.692
41-60	08	62	

Table 5: Stratification of hypocalcemia with respect to gender

Gender	Hypocalcemia		p-value
	Present	Absent	
Male	05	39	0.792
Female	09	60	

Table 6: Stratification of hypocalcemia with respect to gender

Duration (years)	Hypocalcemia		p-value
	Present	Absent	
1-2	10	65	0.669
3-4	04	34	

shown in figure II. Mean duration of disease was 2.15±0.97 years is shown in table II. Mean BMI was 29.40±2.56 kg/m². Distribution of patients

with other confounding variables is shown in table III.

Hypocalcemia after thyroid surgery was found in 14 (12.39%) patients, whereas there was no hypocalcemia in 99 (87.61%) patients. When Stratification of hypocalcemia was done on age groups, it was found that there was no significant difference between different age groups as shown in Table IV while the stratification of hypocalcemia with respect to gender is shown in Table V which also showed no significant difference between male and female. Table VI & VII have shown the stratification of hypocalcemia with respect to duration of disease and BMI respectively. Stratification of hypocalcemia with respect to type of thyroid surgery, place of living, monthly income and education level is shown in table VIII, IX, XI and XI respectively.

Discussion:

Post-operative hypocalcemia is a common complication following thyroidectomy. Decreased serum calcium, secondary to hypo-parathyroidism, may present clinically with muscle cramps, perioral and peripheral paresthesias, carpopedal spasm or tetany, and/or confusion. Symptomatic patients often require extended hospitalizations following thyroid surgery, leading to increased healthcare costs.¹² Depending on the extent of parathyroid gland damage, hypocalcemia may be transient, resolving within a few months, or permanent, requiring lifelong oral calcium and vitamin D supplementation.

Particularly with ambulatory thyroid surgery, which allows for early discharge of patients, post-operative hypocalcemia is an important consideration. In fact, some surgeons advocate in discriminate post-operative calcium supplementation, though this approach has been contested.¹³ The interest in outpatient and short-stay thyroid surgery makes it especially helpful for surgeons to be able to identify patients at risk of developing hypocalcemia.^{14,15} Therefore, accurate and standardized outcomes data following thyroidectomy are essential.^{16,17}

Unfortunately, although hypocalcemia is well

Table 7: Stratification of hypocalcemia with respect to BMI

BMI (kg/m ²)	Hypocalcemia		p-value
	Present	Absent	
≤27	07	29	0.120
>27	07	70	

Table 8: Stratification of hypocalcemia with respect to BMI

Type	Hypocalcemia		p-value
	Present	Absent	
Total	10	52	0.183
Near-total	04	47	

Table 9: Stratification of hypocalcemia with respect to place of living

Place of living	Hypocalcemia		p-value
	Present	Absent	
Rural	06	45	0.855
Urban	08	54	

Table 10: Stratification of hypocalcemia with respect to monthly income

Monthly income	Hypocalcemia		p-value
	Present	Absent	
<20000	06	41	0.855
20001-40000	04	27	
>40000	04	31	

Table 11: Stratification of hypocalcemia with respect to education level

Monthly income	Hypocalcemia		p-value
	Present	Absent	
Illiterate	01	14	0.704
Primary	03	17	
Middle	03	28	
Matric	03	25	
Graduate	04	15	

documented in the thyroid surgery literature, there are significant limitations to the results of previous studies. Perhaps most noteworthy, the reported hypocalcemia incidence rates range widely; studies report that anywhere from 0.3%–66.2% of patients develop hypocalcemia after thyroid surgery.¹⁸ Part of this variation in incidence is likely related to the fact that reports differ in the thyroid surgery procedure assessed. Some studies, for example, include patients who underwent not only total thyroidectomy, but also less extensive procedures with relatively

low risk of hypocalcemia, such as thyroid lobectomy.¹⁹ Such reporting can underestimate the incidence of hypocalcemia and may lead to misinterpretation.

Much of the variability among results may also be attributed to the numerous clinical definitions of hypocalcemia used at different institutions. For instance, some authors consider hypocalcemia to be the clinical presentation of symptoms, whereas others document hypocalcemia on the basis of serum thresholds alone.^{20,21} To demonstrate the effect of relying on the literature to compare outcomes, the authors of one recent study showed that their thyroidectomy patient cohort had a post-operative hypocalcemia rate ranging from 0–46%, depending on 10 different definitions of hypocalcemia adopted by previous studies.²²

Age range in my study was from 20 to 60 years with mean age of 42.84 ± 8.83 years. Majority of the patients 70 (61.95%) were between 41 to 60 years of age. Out of the 113 patients, 44 (38.94%) were male and 69 (61.06%) were females with male to female ratio of 1:1.6. Hypocalcemia after thyroid surgery was found in 14 (12.39%) patients, whereas there was no hypocalcemia in 99 (87.61%) patients. In several series the incidence of hypocalcaemia varied from 10.6% to 50% but may be as high as 83%.⁸ In a study, hypocalcemia was found in 12.0% patients after thyroid surgery.⁹ In another study, it was found in 21.6% patients following thyroid surgery.¹⁰ One more study has shown this prevalence as 39.0%.¹¹

Post-operative hypocalcemia is a common and most often transient event after extensive thyroid surgery. It may reveal iatrogenic injury to the parathyroid glands and permanent hypoparathyroidism. In a study²³ has prospectively evaluated the incidence of hypocalcemia and permanent hypoparathyroidism following total or subtotal thyroidectomy in 1071 consecutive patients. Postoperative serum calcium level under 2 mmol/l was observed in 58 patients (5.4%). In 40 patients hypocalcemia was considered severe (confirmed for more than 2 days,

symptomatic or both). At 1 year after surgery five patients (0.5%) had persistent hypocalcemia. The author found that patients carried a high risk for permanent hypoparathyroidism if fewer than three parathyroid glands were preserved in situ during surgery or the early serum parathyroid hormone level was ≤ 12 pg/ml, the delayed serum calcium levels ≤ 8 mg/dl, or the delayed serum phosphorus level ≥ 4 mg/dl under oral calcium therapy. When one or more of these criteria are present, long-term follow-up should be enforced to check for chronic hypocalcemia and to avoid its severe complications by appropriate supplement therapy.²³

In another prospective study²⁴ including 2,631 patients has found that the incidence of hypoparathyroidism was 28.8 % (757 patients), including transient hypocalcemia (27.9 %-734 patients) and permanent hypocalcemia (0.9 %-23 patients). The rate of asymptomatic hypocalcemia was 70.80%. The incidence of permanent hypocalcemia was higher in the symptomatic hypocalcemia group (7.5 %) than in asymptomatic one (1.5 %). Female patients experienced a transient post-operative hypocalcemia more frequently than male patients (29.7 and 21.2 %, respectively; $p < 0.0001$). The percentage developing hypocalcemia in patients in which parathyroid glands were intra-operatively identified and preserved was higher than in the patients in which the identification of parathyroid glands was not achieved (29.2 vs. 18.7 %, $p < 0.01$). This prospective study confirmed the main risk factors for post-operative hypocalcemia: thyroid cancer, nodal dissection, and female gender. It further showed that identifying parathyroid glands has an important role to prevent permanent hypocalcemia though with a higher risk of transient hypocalcemia.²⁴

In a study,²⁵ overall incidence of hypocalcaemia was 23.6% (n=190) and that of permanent hypocalcaemia was 1.61% (n=13). Onset was delayed up to 3rd post-operative day in 13 patients. Hypocalcaemia was significantly associated with thyroidectomy for Grave's Disease ($P = 0.001$), Hashimoto's thyroiditis ($P = 0.003$), and with incidental parathyroidectomy ($P =$

0.006). The intra-operative assay of parathyroid hormone showed low sensitivity (0.5) and satisfactory specificity (0.9) in predicting hypocalcemia.²⁵ In another study conducted by Sakouti et al²⁶ regarding the incidence of transient and permanent hypocalcemia after total thyroidectomy for thyroid cancer reveals higher incidence of hypocalcemia after total thyroidectomy in malignant diseases of the thyroid. The incidence increases more with thyroidectomy combined with radical neck dissection. The incidence of post-thyroidectomy hypocalcemia is more in the toxic thyroid diseases than non-toxic diseases; this also attributes to the extensive surgical dissection in the toxic disorders to avoid recurrence of the disease.²⁶

Conclusion:

This study concluded that the percentage of hypocalcemia after thyroid surgery was found in 12.39% patients. So, we recommend that clinicians should prescribe their patients calcium supplements post-operatively in order to prevent the hypocalcemia and its complications. Also public awareness programs can be arranged and general public can be educated for proper screening and management of hypocalcemia after thyroid surgery in order to reduce the morbidity of these patients.

Conflict of interest: None

Funding source: None

Role and contribution of authors:

Dr. Sheikh Atiq-ur-Rehman, collected the data, references and did the write up.

Dr. Fayyaz Ahmad, collected the data, referenes and helped in introduction writing.

Dr. Muhammad Khizer Hayat, collected the references and helped in discussion writing.

Dr. Usman Rizvi, critically review the article and advised useful changes.

Dr. Rashid Mahmmod, collected the data and helped in interpretation of the data

Dr. Sajida Naseem, collected the references and helped in result writing.

References:

- Chandrasekhar S, Randolph G, Seidman M. Clinical Practice Guideline: Improving Voice Outcomes after Thyroid Surgery. *Otolaryngol Head Neck Surg.* 2013; 148(6):S1-S37.
- Sajana VN, Atul PC. Post-thyroidectomy early serum ionic calcium level: predictor of prolonged hypocalcaemia. *ENT J.* 2013;92(8):382-90.
- Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. *Br J Surg.* 2014;101(4):307-20.
- Landry CS, Grubbs EG. Predictable criteria for selective, rather than routine, calcium supplementation following thyroidectomy. *Arch Surg.* 2012;147(4):338-44.
- Viswanathan KV, Jithunath MR, Viswanathan M. Incidence of post-operative hypocalcaemia after thyroidectomy: a case control study. *Int J Adv Health Sci.* 2014;1(5):1-9.
- Nair CG, Babu MJ, Menon R, Jacob P. Hypocalcaemia following total thyroidectomy: an analysis of 806 patients. *Indian J EndocrinolMetab.* 2013;17(2):298.
- Pradeep P, Ramalingam K, Jayashree B. Post total thyroidectomy hypocalcemia: a novel multi-factorial scoring system to enable its prediction to facilitate an early discharge. *J Postgrad Med.* 2013;59(1):4.
- Abboud B, Sargi Z, Akkam M, Sleilaty F. Risk Factors for post thyroidectomy hypocalcaemia. *J Am Coll Surg.* 2002;195:456-61.
- Shashikala CK, Manjunath BD, Nischal N. A clinical prospective study of hypocalcaemia following thyroid surgery. *Ann Int Med Den Res.* 2016; 2(5):9-13.
- Iqbal M, Subhan A, Baig MS, Shah MS. Frequency of hypocalcaemia in total thyroidectomy. *J Surg Pak.* 2010;15(2):87-91.
- Rajput A, Samad A, Channa GA, Khanzada TW, Ujjan I. Hypocalcemia; a genuine threat after thyroidectomy. *Pak J Surg.* 2009;25:6-9.
- Shaha AR, Jaffe BM. Parathyroid preservation during thyroid surgery. *American Journal of Otolaryngology.* 1998;19(2):113-117.
- Schwartz AE, Clark OH, Ituarte P, Lo Gerfo P. Thyroid surgery—the choice. *Journal of Clinical Endocrinology and Metabolism.* 1998;83(4):1097-1105.
- McHenry CR, Speroff T, Wentworth D, et al. Risk factors for postthyroidectomyhypocalcemia. *Surgery.* 1994;116(4):641-648.
- Mowschenson PM, Hodin RA, Siperstein A, et al. Outpatient thyroid and parathyroid surgery: a prospective study of feasibility, safety, and costs. *Surgery.* 1995;118(6):1051-1054.
- Barakate MS, Agarwal G, Reeve TS, Barraclough B, Robinson B, Delbridge LW. Total thyroidectomy is now the preferred option for the surgical management of Graves' disease. *ANZ Journal of Surgery.* 2002;72(5):321-324.
- Delbridge L. Total thyroidectomy: the evolution of surgical technique. *ANZ Journal of Surgery.* 2003;73(9):761-768.
- Wilhelm SM, McHenry CR. Total thyroidectomy is superior to subtotal thyroidectomy for management of Graves' disease in the United States. *World Journal of Surgery.* 2010;34(6):1261-1264.
- Thomusch O, Machens A, Sekulla C. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. *World Journal of Surgery.* 2000;24(11):1335-1341.
- Menegaux F, Turpin G, Dahman M. Secondary thyroidectomy in patients with prior thyroid surgery for benign disease: a study of 203 cases. *Surgery.* 1999;126(3):479-483.
- Pradeep PV, Agarwal A, Baxi M, Agarwal G, Gupta SK, Mishra SK. Safety and efficacy of surgical management of hyperthyroidism: 15-Year experience from a tertiary care center in a developing country. *World Journal of Surgery.* 2007;31(2):306-312.
- Mehanna HM, Jain A, Randeve H, Watkinson J, Shaha A. Post-operative hypocalcemia—the difference a definition makes. *Head and Neck.* 2010;32(3):279-283.
- Pattou F, Combemale F, Fabre S, Carnaille B, Decoulx M, Wemeau JL, Racadot A, et al. Hypocalcemia following thyroid surgery: incidence and prediction of outcome. *World J Surg.* 1998;22(7):718-24.
- Puzziello A, Rosato L, Innaro N, Orlando G, Avenia N, Perigli G, et al. Hypocalcemia following thyroid surgery: incidence and risk factors. A longitudinal multicenter study comprising 2,631 patients. *Endocrine.* 2014;47(2):537-42.
- Nair CG, Babu MJ, Menon R, Jacob P. Hypocalcaemia following total thyroidectomy: An analysis of 806 patients. *Indian J EndocrMetab.* 2013;17:298-303.
- Sakouti M, Montazeri V, Golzari S. The incidence of transient and permanent hypocalcemia after total thyroidectomy for thyroid cancer. *Int J Endocrinal Metab.* 2010;1;7-12.