

# Evaluating the Time Interval for Presenting the Signs of Hypocalcaemia after Thyroidectomy

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## ABSTRACT

**Introduction:** Thyroidectomy is one of the most prevalent treatments for thyroid malignancies. It has very low rate of complications except the hypocalcaemia. Only a small number of studies have evaluated the clinical signs of hypocalcaemia but no study have reported the time interval between the procedure and signs of hypocalcaemia.

**Aim:** The aim of this study was to determine that time interval in those patients.

**Materials and Methods:** Medical files of a group of patients who underwent thyroidectomy were reviewed. Demographic characteristics of the patients and the time interval to hypocalcaemia were recorded and analysed by SPSS software. p-value <0.05 was considered significant.

**Results:** One hundred and eight patients, 65 women (60.2%) and 43 men (39.8%) with a mean age of 42.6±12.2 years were included. Perioral numbness was reported in 30 (27.8%) patients while 29 (26.8%) patients had lip numbness. Numbness in extremities and muscle spasm were found in 19 (17.6%) and 13 (12%) patients respectively. Seizure was reported in 3 (2.8%) patients. The Trousseau and Chvostek signs were found in 17 (15.7%) and 9 (8.3%) patients respectively. Only the Trousseau sign was different between the two surgical groups. The mean time interval was 41.25±11.5 hours postoperatively. However the time interval was shorter for the total thyroidectomy.

**Conclusion:** Physical examination is useful for diagnosing hypocalcaemia due to the presentation of signs during the first 48 hours of thyroidectomy. Total thyroidectomy is associated with shorter time interval.

**Keywords:** Postoperative, Thyroid surgery, Parathyroid failure- occurrence

## INTRODUCTION

Hypocalcaemia is a common issue following the surgical removal of all or part of the thyroid gland. Nevertheless, the occurrence of postoperative hypocalcaemia varies widely in the medical literature and ranged from 1 to 50 percent [1-7] but most surgeons reported an incidence of 20 to 30 percent for postoperative hypocalcaemia. Its symptoms vary widely from peripheral numbness to Tetany [8-15]. Also, the postoperative hypocalcaemia incidence varies widely depending on the type of thyroid surgery and the underlying disease which is present 28 percent following total thyroidectomy, 23 percent following subtotal thyroidectomy due to thyrotoxicosis [16], and less than 1.5% following subtotal thyroidectomy due to other diseases [17].

Depending on the extent of parathyroid gland damage during thyroidectomy surgery, hypocalcaemia may be transient or permanent which develops in 2 percent of patients. Hypocalcaemia following total thyroidectomy must be considered permanent in patients requiring calcium replacement more than 6 months [17].

## AIM

We aimed to identify the onset of clinical symptoms of hypocalcaemia following subtotal and total thyroidectomy in Rasool-e-Akram hospital from 2013 to 2014, to reduce the health care costs by preventing routine measurement of serum calcium after thyroidectomy.

## MATERIALS AND METHODS

This was a hospital-based cross-sectional observational study conducted on 108 patients who underwent thyroidectomy, of whom 47.2 percent (51 patients) underwent total thyroidectomy and 52.8 percent (57 patients) underwent subtotal thyroidectomy, to determine the clinical onset of postoperative hypocalcaemia.

After obtaining the written informed consent, we prepare a check list which includes patients' demographic information, type of operation, underlying thyroid problems and different hypocalcaemic symptoms and their onset such as; tingling, peri-oral numbness, lips numbness, Petechia, fingertips tingling and limbs muscle spasms, convulsions, Trousseau and Chvostek sign. The check lists were filled by the general surgery residents. Finally Statistical analysis was conducted using SPSS, version 22, with statistical significance defined as p <0.05.

## RESULTS

There were 65 females and 43 males. The median age of patients was 42.6±12.2 years (range: 20-72). There was no statistically significant difference in age and gender between patients who underwent total thyroidectomy and those underwent subtotal thyroidectomy. The patients' thyroid underlying problems is listed in [Table/Fig-1].

As can be seen from the [Table/Fig-2], among all hypocalcaemia clinical signs and symptoms only Trousseau sign had statistically significant difference distribution between patients underwent total thyroidectomy and those underwent subtotal thyroidectomy.

	Subtotal thyroidectomy (57 patients)	Total thyroidectomy (51 patients)	Overall Mean
Age	43.3±12.7	41.7±11.6	42.6±12.2
Male/Female	22/35	21/30	65/43
<b>Thyroid underlying pathology</b>			
-Cancer	34 (59.6%)	40 (78.4%)	74 (68.5%)
-Benign Goiter	15 (26.3%)	6 (11.8%)	21 (19.4%)
-Hyperthyroidism	8 (14%)	5 (9.8%)	13 (12%)

[Table/Fig-1]: Thyroidectomy patient demographics and clinical characteristics.

	Subtotal thyroidectomy	Total thyroidectomy	p-value
peri-oral numbness	18 (31.6%)	12 (23.5%)	0.35
Lips numbness	16 (28.1%)	13 (25.5%)	0.76
fingertips tingling	9 (15.8%)	10 (19.6%)	0.6
Hand and foot muscles spasms	5 (8.8%)	8 (15.7%)	0.27
Limbs proximal muscles spasms	8 (14%)	7 (13.7%)	0.9
Trousseau sign	5 (8.8%)	12 (23.5%)	0.03
Chvostek sign	3 (5.3%)	6 (11.8%)	0.2
all of the above symptoms	18 (31.6%)	13 (25.5%)	0.4

**[Table/Fig-2]:** Hypocalcaemia clinical manifestations distribution.

	The average onset of postoperative hypocalcaemia (hours)	p-value
<b>Age (years) :</b>		0.15
39-20	43.5±11.5	
59-40	36.5±10.5	
> 60	47.5±11	
<b>Gender :</b>		0.001
Male	51.5±8.5	
Female	36.5±9.5	
<b>Underlying thyroid pathology:</b>		0.4
-Cancer	42.5±11.5	
-Benign Goiter	33.5±3.5	
-Hyperthyroidism	31±2.5	
Overall average	41.25±11.5	

**[Table/Fig-3]:** The average onset of postoperative hypocalcaemia by patient demographics characteristics.

	The average onset of postoperative hypocalcaemia (hours)	p-value
peri-oral numbness	41±11.5	0.2
Lips numbness	41.5±11.5	
fingertips tingling	43±13.5	
Hand and foot muscles spasms	41±12.5	
Limbs proximal muscles spasms	44.5±13	
Trousseau sign	39.5±11.5	0.7
Chvostek sign	40±14	

**[Table/Fig-4]:** The average onset of postoperative hypocalcaemia by patient Clinical signs and symptoms.

	The average onset of postoperative hypocalcaemia (hours)	p-value
Type of thyroid surgery:		0.002
Subtotal thyroidectomy	46.5±10	
Total thyroidectomy	34±9.5	

**[Table/Fig-5]:** The average onset of postoperative hypocalcaemia by type of thyroid surgery.

As can be seen from the [Table/Fig-3] there was no statistically significant difference between patient's age and the average onset of postoperative hypocalcaemia. There was statistically significant gender difference and the average onset of postoperative hypocalcaemia ( $p=0.001$ ). There was no statistically significant difference between underlying thyroid pathology and the average onset of postoperative hypocalcaemia.

Hypocalcaemic seizure was the earliest symptom and muscle spasms were the latest symptoms of hypocalcaemia. There was no statistically significant difference time interval between onset of Trousseau sign and onset of Chvostek sign [Table/Fig-4].

As can be seen from the [Table/Fig-5] there was a statistically significant difference between the two type of surgery and the average onset of postoperative hypocalcaemia ( $p=0.002$ ).

## DISCUSSION

The first cause of post-thyroidectomy hypocalcaemia is the accidental removal of parathyroid glands or damage to the glands or their blood supply during thyroid surgery [18].

Whereas other probable complications of thyroidectomy, such as recurrent laryngeal nerve paralysis, laryngeal oedema or cervical haematoma, generally occur within the first 24 hours after surgery, the lowest point of hypocalcaemia classically occurs at 24-48 hour after surgery. Infrequently, it can be postponed until the fourth postoperative day. This postponement in the appearance of hypocalcaemia is the cause why hospital stay after total thyroidectomy lasts longer than 24 hour, to avoid probable complications of late-onset hypocalcaemia [19,20].

Different strategies for the diagnosis and treatment of hypocalcaemia have been proposed. Older methods include serial measurements of calcium during the first 48 hours of hospitalization is still used in many areas. Some surgeons suggest that providing calcium and vitamin D to all patients in hospital can reduce duration of admission [21]. For instance Blanton et al., investigated the effect of calcium + vitamin D and calcium supplementation in these patients and showed that both these protocols were to effectively reduce symptoms of hypocalcaemia in these patients [22]. Tartaglia and colleagues studied the effect of calcitriol and oral calcium supplement in more than 200 patients who were undergoing total thyroidectomy therapy, and demonstrated that profilactic 1mg calcitriol twice daily and oral calcium 500mg three times a day can effectively reduce postoperative severe hypocalcaemia [23]. The similar results derived from Uruno et al., study in Japan [24]. They ministered infusion of 78-156 mg intravenous calcium, 3-8 hours after surgery. Roh and Park from South Korea showed decrease in incidence and severity of post thyroidectomy hypocalcaemia by administration of oral vitamin D and calcium [25].

However, some other surgeons not agree with the effect of vitamin D and calcium on decreasing the risk of post thyroidectomy hypocalcaemia [26].

More recent studies have shown that PTH levels may be helpful for early diagnosis of hypocalcaemia [27]. Although some surgeons agree with PTH measurements, some claim that it is not useful [28]. In a recent systematic review by doctor Grodski and colleagues, the accuracy of PTH in determining cases of early hypocalcaemia was precocious [29]. It was shown that PTH levels after thyroidectomy can predict hypocalcaemia, but its accuracy is not 100%.

The authors concluded that although the PTH level can be used to predict hypocalcaemia and the time of hospital discharge with caution after the first 24 hour after surgery, it is rarely possible for a patient with normal PTH to encounter hypocalcaemia. Moreover PTH levels can be used as a criterion for calcium and vitamin D treatment.

In all mentioned studies the laboratory signs of hypocalcaemia, the prevalence and the treatment were investigated, and there are few studies about the onset of clinical symptoms of hypocalcaemia which has a wide range from peripheral paresthesia like tingling around the mouth, muscular spasm like carpedal spasm to a prolonged Q-T interval in ECG. Besides, Shuvstok and Trousseau signs are mostly positive.

In this study the prevalence of clinical hypocalcaemia was reported about 28.7% which is approximately equal to the previous studies. The prevalence of clinical hypocalcaemia in patients with subtotal thyroidectomy was 31.6% and in patients with total thyroidectomy was 25.5% which were in previous studies, respectively, 23% due to thyrotoxicosis and 28% after total thyroidectomy [15,16].

The most common clinical symptom of hypocalcaemia was tingling and numbness around the mouth then lips numbness and finger tips paresthesia [Table/Fig-2]. Regarding to gradual drop of serum calcium levels, symptoms such as paresthesia and numbness manifest prior to the catastrophic symptoms like seizure. However, considering the new guidelines suggestion of the early prescription of calcium and vitamin D at the onset of mild hypocalcaemia symptoms, the likelihood of the catastrophic symptoms has been decreased due to early treatment.

Among the symptoms of hypocalcaemia in patients undergoing subtotal thyroidectomy and total thyroidectomy Troussau sign prevalence had statistically significant differences. High prevalence of Troussau sign after total thyroidectomy may be due to the possibility of further damage to the parathyroid glands or its vessels. Removal of parathyroid glands during total thyroidectomy has been followed by permanent hypocalcaemia; one of the first could be a positive Trousseau sign [17].

### Onset of clinical symptoms of hypocalcaemia

The average time for clinical symptoms of hypocalcaemia to be manifested in this study was  $41.25 \pm 11.5$  hours, after the thyroidectomy. It was previously mentioned that hypocalcaemia usually occurs between 24-48 hours after surgery. The maximum time of hypocalcaemia occurrence in this study was 64 hours (the third day after surgery). Consequently, based on these results, it seems reasonable to discharge patients after 3 days.

On the other hand the mean time of onset of clinical symptoms of hypocalcaemia was longer in men than women though it seems to be an accidental finding. Patient characteristics such as age, type of primary pathology, and the type of clinical symptom of hypocalcaemia were ineffective in the onset of clinical symptoms manifestation.

In patients who underwent total thyroidectomy time, of hypocalcaemia symptoms was significantly shorter than patients who had undergone subtotal thyroidectomy. This is most probably due to the more thyroid tissue removal and more damage to the parathyroid glands. Thus a faster decline in serum calcium occurred.

To consider clinical symptoms in the diagnosis of hypocalcaemia after thyroidectomy can be very helpful. Doctor Kim et al., also found that 72.5% of patients have both clinical symptoms and laboratory hypocalcaemia [30]. So, they concluded that both clinical symptoms and laboratory hypocalcaemia should be considered to evaluate and to discharge of patients. Moreover, PTH level for the symptomatic patients and serum calcium levels of the day after surgery for laboratory hypocalcaemic patients could be used to detect hypocalcaemia. Additionally the PTH levels were studied in other studies too. For example Dr Toniato et al., claimed that PTH levels in the first day after surgery can predict hypocalcaemia as well [31].

In Lecerf et al., study in which the authors evaluated the sensitivity, specificity, and positive and negative predictive values for iPTH which were respectively; 84.6%, 92.9%, 82.5%, and 93.8% (general accuracy, 90.5%) [32]. But PTH evaluation is not accessible everywhere like in Dr Rehman et al., studies that the diagnosis of hypocalcaemia was upon clinical symptoms and serum calcium levels only [33]. All in all it does not appear to be helpful to measure PTH levels in emergency situations.

### LIMITATIONS

Short term follow up of patients is one the limitations of study as sometimes the hypocalcaemia manifests with late onset. Furthermore serum calcium levels in this study were not consistent with clinical disease. On the other hand, in this study did not evaluate other diagnostic procedures such as EKG.

### CONCLUSION

This study showed that although clinical examination in the diagnosis of hypocalcaemia can be useful, laboratory tests are needed. None of patients showed hypocalcaemia under 26 hours, thus it can be concluded that the laboratory testings could be postponed until this time and avoid extra charges for patients. However, we suggest a physical exam for early detection of hypocalcaemia after thyroidectomy. Paying special attention to symptoms in patients underwent total thyroidectomy is needed because of their symptoms develop faster.

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