

Determining Factors in Post Thyroidectomy Hypocalcemia

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Abstract

Introduction: Hypocalcemia is an alarming common complication after thyroidectomy. However, post-operative hypocalcemia incidence reported by various authors was very variable. Several factors are accused in the appearance of post-thyroidectomy hypocalcemia. The aim of this study was to determine predisposing factors and hypocalcemia etiology after thyroid surgery on the basis of our experiences.

Method: We conducted a descriptive and analytical retrospective study carried out between June 2017 and June 2019, concerning patients having undergone thyroidectomy. This study was conducted within the Otolaryngology department of the University hospital of Andohatapenaka Antananarivo Madagascar. We included patients with clear operative report, postoperative calcaemic blood level and thyroid gland histological findings. We excluded patients with past medical history of parathyroid ablation, calcic homeostasis disorder and patients dealing with calcic treatment.

Results: On 176 patients, we noted female prevalence (sex-ratio: 0, 09) and an average Age of 43, 73 years (extreme from 16 to 69 years). Hypocalcemia was found in 39 patients (22, 16%). Male gender is a protective factor against hypocalcemia. Thyroid totalization surgery is a significant risk factor of hypocalcemia. Parathyroid discovery higher than one during the operation is a significant protective factor against hypocalcemia. Parathyroid gland reimplantation is a significant protective factor against hypocalcemia.

Conclusion: Procedure control by discovering and respecting parathyroid glands are the warrant of avoiding hypocalcemia, as well as their reimplantation when parathyroids were torn. Thyroid surgical revision may often cause hypocalcemia.

Keywords: *Determining Factors; Hypocalcemia; Thyroidectomy*

Introduction

Post thyroidectomy hypocalcaemia is defined by a decrease of the calcium level in the blood less than 2mmol/l found after thyroid surgery, with or without clinical manifestations [1-3].

Thyroid nodules are commonly managed by thyroidectomy [4]. Hypocalcaemia is a clinical and biological abnormality frequently seen after thyroid surgery due to parathyroid glands impairment [5]. This setting stretches considerably the hospitalisation time and worsen the post-operative management. In some cases, a substitutional calcic treatment is taken lifetime [6,7].

The incidence of hypocalcaemia measured 24 hours after surgery varies from 1% to 50% according to the literature [6,8]. Post thyroidectomy hypocalcaemia mechanism involve multiples factors, which are not well individualised [9].

Aim of the Study

In that study, we aim to determine the aetiological factors of post thyroid surgery hypocalcaemia.

Materials and Methods

We enrolled every patients, seen in the otolaryngology consult, showing a thyroid gland disease and underwent thyroid surgery. Two days of hospital stay after surgery were required. No calcaemic blood level was taken before thyroidectomy, although it was measured at the first postoperative day. We included patients with clear operative report, postoperative calcaemic blood level and thyroid gland histological findings. We excluded patients with past medical history of parathyroid ablation, calcic homeostasis disorder and patients dealing with calcic treatment.

We conducted a descriptive retrospective and analytical study between June 2017 and June 2019 involving patients undergoing thyroidectomy. This study was implemented in the otorhinolaryngology and head and neck surgery department at the Andohatapenaka University Hospital Center in Antananarivo, Madagascar. The data were collected from medical records of hospitalized patients for thyroid surgeries meeting our criteria. We used Excel and Epi-info for data processing. The relationship between postoperative hypocalcemia and sex, age, surgical types, histological nature, hormonal status, race, intraoperative parathyroid finding, perioperative incidents, parathyroid reimplantation and surgeon experience were examined.

Results

Out of 176 patients, a female predominance was marked (91.48%) with a sex ratio at 0.09, the average age was 43.73 years with extremes of 16 to 69 years. Hypocalcemia was observed in 39 patients, or 22.16%. The male sex is a protective factor against hypocalcemia (OR = 0.86) after thyroidectomy, but the association is not significant (Table 1). The present study did not show a significant association between hypocalcemia and age (Table 2). Thyroid totalization surgery appears as a risk factor (OR: 2.77, 95% CI: [1.10 - 6.97]) of significant hypocalcemia for thyroid surgery (Table 3).

Hypocalcemia						
Sex	Yes	No	Case number	OR	CI 95%	p
Male	3	12	15	0,86	[0,23 - 3,24]	1
Female	36	125	161	Undefined		
Total	39	137	176			

Table 1: Post-thyroidectomy hypocalcemia and sex.

The male gender is a protective factor against hypocalcemia (OR = 0.86) compared to the female gender but the strength of the association is not significant (because the confidence interval of the odds ratio includes the value a).

Hypocalcemia						
Age	Yes	No	Case number	OR	CI 95%	p
< 20	1	3	4		Reference	
20 - 39	6	33	39	0,56	[0,05 - 6,16]	0,523
40 - 60	28	78	106	1,08	[0,11 - 10,78]	1
> 60	4	23	27	0,52	[0,04 - 6,36]	0,525
Total	39	137	176			

Table 2: Post-thyroidectomy hypocalcemia and age.

No significant association between hypocalcemia and age.

Hypocalcemia						
Surgery	Yes	No	Case number	OR	CI 95%	p
Total thyroidectomy	25	97	122		Reference	
Totalisation thyroidectomy	10	14	24	2,77	[1,10 - 6,97]	0,026
hemi thyroidectomy	00	4	4	undefined	undefined	0,583
Hemi thyroidectomy with isthmectomy	1	17	18	0,23	[0,03 - 1,80]	0,195
Thyroidectomy with lymph node dissection	3	3	6	3,88	[0,74 - 20,40]	0,118
Thyroidectomy + sternotomy	00	2	2	0	Undefined	1
Total	39	137	176			

Table 3: Post-thyroidectomy hypocalcemia and surgical procedure.

Thyroid totalization appears to be a risk factor (OR: 2.77, 95% CI: [1.10 - 6.97]) significant hypocalcemia for thyroid surgery.

In our case series, there is no significant association between the histologic type and hypocalcemia (Table 4). Hypocalcemia is not significantly associated with thyroid hormone biology (Table 5). There is no significant association between race and hypocalcemia (Table 6). This study shows that discovered parathyroid number more than 1 is a significant protective factor (OR = 0.07, 95% CI: [0.03 - 0.21]) of hypocalcemia (Table 7). Our research did not show a significant association between perioperative incidents and hypocalcemia (Table 8). Parathyroid glands reimplantation, removed intraoperatively, is a protective factor (OR = 0.00, 95% CI: Unknown) for hypocalcemia (Table 9). No significant association between surgeon’s experience and hypocalcemia is found during our research (Table 10).

Hypocalcemia						
Histology	Yes	No	Number	OR	95% CI	p
Malignant	12	28	40	1,73	[0,78 - 3,84]	0,174
Benign	27	109	136			
Total	39	137	176			

Table 4: Post-thyroidectomy hypocalcemia and histology.

No significant association between histology and hypocalcemia.

Hypocalcémie						
Hormone status	Yes	No	number	OR	95% CI	p
Euthyroidism	39	134	173		Reference	
Hypothyroidism	00	2	2	Undefined	Undefined	1
Hyperthyroidism	00	1	1	Undefined	Undefined	1
Total	39	137	176			

Table 5: Post-thyroidectomy hypocalcemia and thyroid hormone.

No significant association between thyroid hormone status and hypocalcemia.

Hypocalcemia						
Race	Yes	No	Case number	OR	95% CI	p
Black	39	132	171	Undefined	Undefined	0,588
White	00	5	5			
Total	39	137	176			

Table 6: Post-thyroidectomy hypocalcemia and race.

No significant association between hypocalcemia and race.

Hypocalcemia						
Parathyroid number	Yes	No	Case number	OR	95% CI	p
> 1	23	130	153	0,07	[0,03 - 0,21]	0,000
None	16	7	23			
Total	39	137	176			

Table 7: Post-thyroidectomy hypocalcemia and parathyroid discovery.

Parathyroid discovery greater than 1 is a protective factor against hypocalcemia (OR=0,07, IC à 95%: [0,03 - 0,21]).

Hypocalcemia						
Incidents	Yes	No	Case number	OR	95% CI	p
Removed Parathyroid	00	2	2		Reference	
Injured Parathyroid	4	8	12	Undefined	Undefined	1
Laryngeal nerve injury	00	1	1	Undefined	undefined	1
Vessels injury	00	4	4	Undefined	Undefined	1
No incidents	35	122	157	Undefined	Undefined	1
Total	39	137	176			

Table 8: Post-thyroidectomy hypocalcemia and intraoperative incidents.

No significant association between intraoperative incident and hypocalcemia.

Hypocalcemia						
Reimplantation	Yes	No	Case number	OR	95% CI	p
Yes	00	2	2	0	undefined	0,001
No	39	00	174			
Total	39	137	176			

Table 9: Hypocalcaemia post-thyroidectomy hypocalcemia and parathyroid reimplantation.

Parathyroid Reimplantation appears as a protective factor against hypocalcemia.

Hypocalcemia						
ENT surgeon	Yes	No	Case number	OR	95% CI	p
Specialist	33	102	135		Reference	
4 th year trainees	6	35	41	0,53	[0,20 - 1,37]	0,185
Less than 4 th year trainees	00	00	00	Undefined	Undefined	0,591
Total	39	137	176			

Table 10: Post-thyroidectomy hypocalcemia and surgeon's experience.

No significant association between hypocalcemia and surgeon's experience.

Discussion

Thyroidectomy is the most commonly used surgical procedure for suspicious thyroid nodules [4]. Operative techniques are based on paraclinical and clinical lesions. This is a very delicate surgical procedure that can cause life-threatening complications. Postoperative complications of thyroidectomy usually occur within the first 24 hours after surgery. Apart from the involvement of the laryngeal nerves, cervical hematoma, the most common is the occurrence of hypocalcemia due to iatrogenic parathyroid gland dysfunction [5]. Post-thyroidectomy hypocalcemia is a multifactorial issue and it would be inappropriate to define some etiological factors. The incidence of postoperative hypocalcemia varies considerably in the literature and the causes of this clinical-biological abnormality are not well established [10,11].

In our case series, post-thyroidectomy hypocalcemia accounts for 22.16% of the total study population. According to various authors in the literature, post-thyroidectomy hypocalcemia varies between 6.9% and 50% [12,13]. According to Salem's team and Bunyami, post-thyroidectomy hypocalcemia accounts for 22.42% and 23.97%, respectively [14,15]. The proportion of postoperative hypocalcemia was different from one author to another however our result is close to most of the literature findings. The results diversity may be related to the many clinical definitions used by different research institutions. Some authors consider the presence of hypocalcemia only during clinical manifestations, while others report on postoperative calcium levels [16,17]. Moreover, the reference value used by each analysis laboratory is sometimes different. In our study population, measurement of postoperative calcemia is performed only at 24 hours after thyroid surgery. Some authors include patients who have undergone not only total thyroidectomy, but also thyroid surgery with relatively low risk of hypocalcemia such as thyroid lobectomy [18].

The male gender is a protective factor against hypocalcemia (OR = 0.86) compared to the female gender but the association is not significant for this study. The same version was reported by the Senthil team in 2017 [19]. Most authors state that the female gender was very sensitive to developing post-thyroidectomy hypocalcemia but with a non-significant proportion [14,20-22]. Our study joins the data of the literature. This difference in distribution is related to the majority study population of the female gender and the thyroid pathology is also of interest to the female gender, which is the best studied. The high incidence of post-thyroidectomy hypocalcemia in women may be due to the deficiency of calcium and vitamin D in this gender compared to the male gender [23]. Erbil, *et al.* Reported preoperative levels of vitamin D significantly lower in women compared to men, whereas this vitamin determines the outcome of calcemia postoperatively [24,25].

The average age of our study population was 43.73 years with extremes of 16 to 69 years. The present study did not show a significant association between postoperative hypocalcemia and age. A study conducted by the Shrikanth team reveals an average age of 40.12 years with extremes of 14 to 63 years, but there is also no significant correlation between age and hypocalcemia [26]. In addition, Mostafa has returned to an average age of 43 but there is still no significant association between age and hypocalcemia [27]. According to some authors, patients over 50 years of age are most at risk of developing postoperative hypocalcemia and old age is not a protective factor for hypocalcemia [19,28]. In contrast, the Randall study reports the incidence of higher hypocalcemia in younger subjects and that old age is a protective factor for post-thyroidectomy hypocalcemia. Some authors have specified the same result; each one year increase from age 50 corresponds to a 1% decrease in the risk of postoperative hypocalcemia [29,30]. The proportion of postoperative hypocalcemia in the elderly is explained by a deficiency of vitamin D synthesis, inadequate nutrition and low sun exposure [18,31]. There is a contradictory version mentioned by some authors. The age of patients is one of the predictors of postoperative hypocalcemia, but the literature does not reveal any significant association [21].

The operative technique and the type of thyroid surgery are among the factors determining the occurrence of postoperative hypocalcemia. In our study, thyroid totalization surgery appears as a risk factor (OR: 2.77, 95% CI: [1.10 - 6.97]) of significant hypocalcemia after thyroidectomy. According to Senthil, thyroid surgery presents a risk of hypocalcemia in 100% of cases [19]. Our study coincides with the data of the literature. The fibrosis or tissue adhesion of the previous surgical procedure sets the difficulty of the remaining lesion excision that can cause parathyroid glands lesions. In addition, the exact operative protocol of previous thyroid surgery in other hospitals has not

always been reported in our research center; it is possible that there was already lesions of the parathyroids during this first intervention [19]. This explains the very high rate of hypocalcemia after thyroid totalization surgery.

This study did not show a significant association between the histological type of goitre and hypocalcemia (OR: 1.73, 95% CI: [0.78 - 3.84]). According to Sakouti and some authors, thyroidectomy indicated for thyroid cancer had a high incidence of postoperative hypocalcemia, but was not significant [19,32]. In addition, Randall reported a significant proportion of hypocalcemia after surgery for crawling goitre [29]. Our findings is close to the literature. If the thyroid tumor is removed, a larger dissection must be performed to obtain clearance of the tumor. A more aggressive surgical approach is often adopted, but this act constitutes a major risk for the parathyroid glands. In addition, parathyroid lesions may occur due to changes in thyroid anatomical structure [28,29,33].

This study does not show a significant correlation between hypocalcemia and the status of thyroid hormones before surgery. According to Noguchi, thyroidectomy in hyperthyroid patients is at greater risk for post-thyroidectomy hypocalcemia [34]. According to Salem, there is no difference in the proportion of postoperative hypocalcemia in patients with hyperthyroidism or in euthyroid patients [14]. In our case series, thyroidectomy was performed only in euthyroid patients. Patients with dysthyroidism were first referred to endocrinologists. This situation explains the difference between our research and those of some authors.

This study did not show a significant association between race and hypocalcemia. Randall states that the black race is a significant protective factor against post-thyroidectomy hypocalcemia [29]. Burge, *et al.* found that race is not a factor significantly associated with hypocalcemia, but Afro Americans are less at risk of postoperative hypocalcemia [35]. This parameter was difficult to assess in our research since almost all of our study population is black. Black race synthesizes vitamin D better, while this vitamin participates in production of parathyroid hormone (PTH) by a system of negative feedback. This explains the low risk of postoperative hypocalcemia in black race [25,36].

In this study, discovery of more than 1 parathyroid peroperatively is a significant protective factor (OR = 0.07, 95% CI: [0.03 - 0.21]) of post-thyroidectomy hypocalcemia. According to Kim and the Senthil team, discovery of parathyroids equal to or greater than 2 preoperatively is a good prognosis factor for post-thyroidectomy calcemia level [19,37]. Our study was comparable to the literature. In thyroid surgery, if two intact parathyroid glands are found and even the others are torn, those remaining glands are able to compensate for calcium homeostasis.

Intraoperatively, parathyroid glands can be traumatized, torn or devascularized. This study did not show a significant association between intraoperative incidents and hypocalcemia. Awad and the Erbil team reported the calcium blood level effects after parathyroid lesions, but not significantly [4,38]. Our study is comparable to the literature. In parathyroid trauma, parathyroid hormone (PTH) levels drop as a result of ischemia or even glandular infarction [4].

The present study shows that reimplantation is a significant protective factor (OR = 0.00, 95% CI: Not Defined) against hypocalcemia. Lo and Zedenius' teams report the same significant results through retrospective studies [39,40]. Our study is comparable to the literature. Despite the caution of surgeons during thyroid surgery, parathyroid glands can be damaged. In case of tearing of parathyroid gland, its reimplantation into sternocleidomastoid muscle will be adopted to prevent postoperative hypocalcemia and revascularization will be obtained from the 8th week [14,15].

Surgeon's experience is a predictor of postoperative hypocalcemia but is not significant in our study. According to Mishra, thyroidectomy performed by the trainees is more at risk of hypocalcemia but is not significant [41]. Our study was comparable to the literature. Most of the thyroidectomy performed in our series was performed by the otolaryngology specialist surgeon but some are performed by well-trained and supervised surgeon trainees.

Conclusion

Thyroidectomy is a surgical procedure that is at risk for hypocalcemia due to injured parathyroid glands. Several factors are incriminated in the appearance of this biological anomaly. Thyroid totalization is an operative technique with a significant risk of postoperative

hypocalcemia. Intraoperative discovery of parathyroid gland superior to 1 is one of the significant protective factors of postoperative hypocalcemia and intraoperative parathyroid gland reimplantation was also reported as a significant protector of hypocalcemia post-thyroidectomy.

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All authors have read and approved the final version manuscript.

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Conflicts of Interest

Authors do not declare any conflict of interest.

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