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BIOLIFE RESEARCH ARTICLE

Evaluation of the Role of Serum Phosphorus and Serum Magnesium in the Early Detection of Post Thyroidectomy Hypocalcaemia

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ABSTRACT

Background: Hypocalcemia remains a common complication after thyroid surgery, particularly total thyroidectomy. By further evaluation of the relationship between phosphorus, magnesium and calcium, faster discharge of the patient may be achieved, and prophylactic medical treatment will be spared to the more serious complications.
Objective: The aim of this study was to evaluate the accuracy of hyperphosphatemia and hypomagnesemia for early prediction of post thyroidectomy hypoparathyroidism, in an attempt at earlier discharge from hospital.
Methods: Sixty patients were evaluated and admitted to HNESU for total or completion thyroidectomy. Serum calcium, phosphorus, and magnesium levels were measured pre-operatively and at 12, 24 hours, 1 and 6 months post-operatively.
Results: The mean age was 44+/-2 years old. Twelve patients (20%) developed hypocalcaemia post-operatively, and 6 of them (10%) experienced permanent hypocalcaemia. Among the permanent hypocalcaemic patients 5 had low calcium and magnesium 24 hours post-operatively and only 1 of them had low calcium and normal magnesium. None of them had elevated phosphorus 24 hours post-operatively.
Conclusion: Transit hypocalemia is quite significant in patients post-total Thyroidectomy. Serum phosphorus and magnesium have no role in predicting early (24 hours) post-thyroidectomy hypocalcaemia; however serum magnesium has a very effective role in the early prediction of transient versus permanent hypocalcaemia following total thyroidectomy operation. This can substitute the measurement of PTH which in turn can be cost effective since the P and Mg tests are cheap and widely available compared to PTH test.

KEYWORDS: Thyroid-Posphorus-Magnesium-Hypocalcemia-Parathormone.

INTRODUCTION

The parathyroid hormone (PTH) helps regulate the body's level of calcium (Ca) and phosphorus (P). It stimulates bone to slowly release Ca and P into blood. The PTH stimulates the kidneys to increase re-absorption of Ca, while simultaneously signaling the kidneys to excrete P, this process balances Ca and P levels in the blood by creation of an inverse relationship [1-4]. Temporary hypoparathyroidism leads also to a

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reduction in renal reabsorption of magnesium (Mg), and expansion of the extracellular volume increases Mg excretion [5]. According to Wilson et al, [5] 10% of patients who undergo total thyroidectomy (TT), develop hypomagnesemia and hypocalcemia [4,5]. Temporary hypocalcaemia occurs in 10–40 % of patients who undergo a TT while permanent hypocalcaemia occurs in 0.5-10 %. Surgical technique has evolved to preserve parathyroid function wherever possible [6-10]. However, transient hypoparathyroidism still occurs owing to parathyroid manipulation, devascularization, venous engorgement or inadvertent removal with the thyroid specimen [11.12].

Following TT, patients are closely observed for bleeding in the first 24 hours. The main discharge-limiting factor thereafter is the development of hypocalcaemia as patients not at risk of hypocalcaemia may be discharged on day 1 following surgery [11.12]. Implementation of protocols using postoperative PTH measurement has been shown to facilitate day 1 discharge after thyroidectomy. However, rapid PTH measurement is not readily available in many hospitals [13-21]. The measurement of serum phosphate is a widely available test, with a low cost and quick turnaround time than PTH [22-24].

The present prospective study was conducted to evaluate the accuracy of hyperphosphatemia and hypomagnesemia as an early predictor of post thyroidectomy hypoparathyroidism, in an attempt at performing TT as a safe day case surgery, and predicting permanent hypoparathyroidism (at 6 months post-operatively).

SUBJECTS AND METHODS

Study population

This prospective study included 60 consecutive patients admitted for TT or completion thyroidectomy at the Head and Neck and Endocrine Surgery Unit, Alexandria Main University Hospital, from January 2013 to January 2014. The studied population included 43 females and 17 males. Their ages ranged between 9 and 73 years with a mean of 43±15 years.

The protocol of the study was approved by the ethical committee of the hospital. It was explained in details to the patients and their care-givers (relatives) and an informed written consent was obtained before enrollment in the study.

Preoperative evaluation

All patients were subjected to thorough history-taking, complete physical examination and assessment of vocal cord mobility by indirect laryngoscopy. Laboratory investigations included complete blood count, renal function tests (urea and creatinine), thyroid function tests (T3, T4 and TSH), serum P, serum Mg, and serum Ca. Neck ultrasonography (US) was done for all patients preoperatively as well as fine needle aspiration cytology (FNAC) from suspicious thyroid lesions and suspicious cervical lymph nodes (LNs).

Postoperative assessment

Serum Ca, P, and Mg levels were measured at 12 and 24 hours post-operatively. Serum PTH level was measured for patients with low levels of serum Ca, 24 hours, one and 6 months post-operatively. The normal serum levels of Ca, P, and Mg are ranging between (9-10.5 mg/dL), (2.5 to 4.5 mg/dL) and (1.8 to 2.5 mEq/L) respectively. All patients were discharged on daily oral Ca supplement dose for one week.

Statistical analysis

Data were analyzed using the SPSS software package version 22.0. (SPSS Inc., Chicago, IL, USA). Quantitative data were described using mean and standard deviation and the median, and compared between the two groups using the student t test Comparison between the two groups regarding categorical variables was done using the Chi-square (X^2) test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's exact test or Monte Carlo correction. P value of <0.05 was considered to be statistically significant.

RESULTS

The preoperative findings related to history, laboratory investigations, and thyroid morphology are shown in Table 1.

The chief complaint was a cervical neck mass (81.7%) with a mean duration of 33 months, ranging 1 month to 25 years. Forty two patients (70%) complained of dyspnea and 21 (35%) complained of dysphagia. Eight patients (13.3%) had a positive family history of benign thyroid diseases, and no one had a family history of malignant thyroid disease. Nineteen patients (31.67%) had co-morbidities. Eleven patients had diabetes mellitus (DM), with a concomitant hypertension (HTN) in ten of them. Seven patients (11.67%) had history of thyroid surgery as subtotal in 4 and hemithyroidectomy in 3 of them. Two patients had low T3 and T4, and high TSH, while two other patients had a high TSH only. Fourteen patients (23.3%) had controlled toxic goiter with low TSH.

By US examination of the neck, the mean size of the left lobe was 3.64 cm, and of the right lobe was 3.80 cm. The size of the dominant nodule ranged from 0.3 to 8.8 cm with a mean of 2.94 ±1.93 cm.

Fifty three patients (88.3%) underwent TT, while 7 underwent completion thyroidectomy either on both sides or on one side only. Central neck dissection was performed in two patients (3.3%). Thirteen patients (21.6%) had postoperative numbness and/or hoarseness. Histo-pathological examination of the submitted specimens showed that multinodular goiter (MNG) was the commonest diagnosis (46.7%), followed

by papillary thyroid carcinoma (PTC) (18.3%) then controlled toxic goiter (CTG) (16.7%) (Table 2).

Table 1: Distribution of the studied patients (n=60) according to history, laboratory investigations, and thyroid texture

			N	%
Complaints	Midline neck mass		49	81.7
	Dyspnea		42	70.0
	Dysphagia		21	35.0
	Toxic manif.		13	21.7
	Voice Changes		9	15.0
Family History	-Ve		52	86.7
	+Ve (Benign)		8	13.3
Medical History	DM + HTN		10	52.6
	HTN		5	26.3
	IHD		3	15.8
	DM		1	5.3
History of thyroidec-tomy	Subtotal		4	6.7
	Hemithyroide-ctomy		3	5.0
Thyroid function tests	T3	L	2	3.3
		N	58	96.7
	T4	L	2	3.3
		N	58	96.7
	TSH	L	14	23.3
		N	42	70.0
Thyroid texture	Multinodular		39	65.0
	STN		13	21.7
	Diffuse		8	13.3

DM; Diabetes Mellitus – HTN; Hypertension – IHD; Ischemic heart disease

Table 2: Distribution of the studied patients (n=60) according to operations performed, postoperative complications and histo-pathological diagnosis.

		N	%
Thyroidectomy operations	Total	53	88.3
	Completion (Both lobes)	4	6.7
	Completion (One lobe)	3	5.0
CND	No	58	96.7
	Yes	2	3.3
Postoperative complications	Hoarseness	5	38.5
	Numbness	5	38.5
	Hoarseness & Numbness	3	23.0
Histopathological diagnosis			
MNG		28	46.7
PTC		11	18.3
CTG		10	16.7
Thyroiditis		5	8.3
Follicular adenoma		3	5.0
Amyloid goiter		1	1.7
FTC		1	1.7
Poorly differentiated carcinoma		1	1.7

CND; Central neck dissection – MNG; Multinodular goiter – PTC; papillary thyroid carcinoma – CTG; Controlled toxic goiter`- FTC; Follicular thyroid carcinoma

All patients were normo-calcemic pre-operatively. Also it could be noticed that only one patient had high pre-operative phosphorus level. Six patients had permanent hypocalcaemia with low PTH level at six months post-operatively (Table 3). The same results were illustrated at (Figure 1)

Table-4 shows the classification of post-operative calcium, phosphorus and magnesium levels according to time intervals.

Table-4. Classification of patients according to post-operative Ca, P and Mg serum levels.

		N	%
Ca	Normal	34	56.7
	Low 12 hr only	14	23.3
	Low Transient(24 hr-6m)	6	10.0
	Low Permenant	6	10.0
P	Normal	55	91.7
	High 12 hr only	4	6.7
	High 12 hr and 24 hr	1	1.7
Mg	Normal	35	58.3
	Low 12 hr only	17	28.3
	Low 24 hr only	3	5.0
	Low 12 and 24 hr	5	8.3
Total		**60**	**100.0**

Calcium level at 12 and 24 hours post-operatively was related significantly to magnesium level (p=0.029 and 0.006 respectively). There was no significant correlation, however, between calcium and phosphorus levels post-operatively (Figure-2).

Table-5 illustrates the relation between post-operative changes in calcium level by time and post-operative phosphorus and magnesium level at 12 and 24 hours, showing that post-operative permanent hypocalcaemia was statistically related to post-operative magnesium, as five of the six patients with low permanent hypocalcaemia had low magnesium level at 24 hours ($p<0.001$). It was noticed also that permanent hypocalcaemia was not related to phosphorus level post-operatively.

Table-6 shows that permanent hypocalcaemia was significantly related to patients with low levels of calcium and magnesium at 24 hours post-operatively, ($p<0.001$). It was noted also that 85.7% of patients with low calcium level combined with normal magnesium level at 24 hours (6/7), had transient hypocalcaemia.

This reveals the importance of the combination of 24 hours post-operative calcium and magnesium levels in predicting the occurrence of permanent hypocalcaemia.

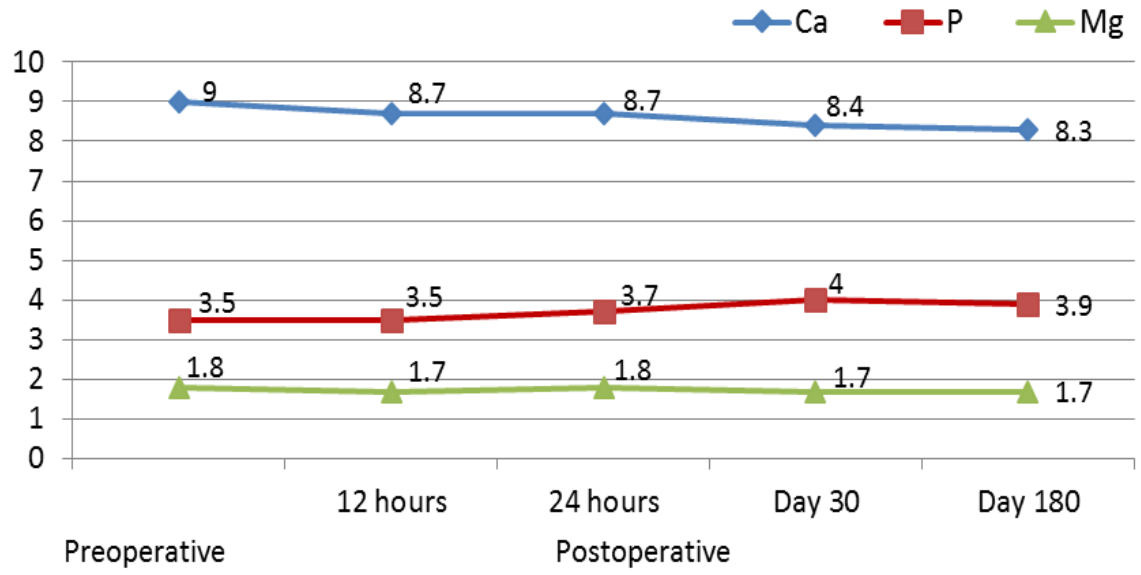
DISCUSSION

Thyroidectomy is a clean surgical procedure with a small exposed area, minimal blood and fluid loss and

Table 3: Pre and post-operative levels of serum Ca, P, Mg and PTH.

		Preoperative		Postoperative							
				12 hours		24 hours		Day 30		Day 180	
		N	%	N	%	N	%	N	%	N	%
Ca	Min. – Max.	8.20 – 10.0		6.20 - 10.10		6.80 - 9.80		7.0 – 9.80		7.0 – 9.30	
	Mean ± SD	9.03 ± 0.35		8.69 ± 0.68		8.69 ± 0.57		8.38 ± 0.94		8.34 ± 0.85	
	Median	9.0		8.65		8.80		8.55		8.75	
	Low	0	0.0	22	36.7	12	20.0	6	9.8	6	9.8
	Normal	60	100.0	38	63.3	48	80.0	10	16.4	10	16.4
	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
P	Min. – Max.	2.20 – 5.0		1.80 - 7.50		1.60 - 5.20		2.90 – 4.90		3.0 – 4.60	
	Mean ± SD	3.51 ± 0.62		3.52 ± 1.03		3.65 ± 0.69		4.01 ± 0.62		3.93 ± 0.33	
	Median	3.50		3.40		3.65		4.05		4.0	
	Low	1	1.7	6	10.0	1	1.7	0	0.0	0	0.0
	Normal	58	96.7	49	81.7	57	95.0	16	26.2	1	26.2
	High	1	1.7	5	8.3	2	3.3	0	0.0	0	0.0
Mg	Min. – Max.	1.40 – 2.30		0.90 – 2.70		1.10 - 3.50		1.20 – 2.0		1.20 – 2.0	
	Mean ± SD	1.80 ± 0.18		1.72 ± 0.36		1.78 ± 0.31		1.68 ± 0.22		1.68 ± 0.24	
	Median	1.80		1.75		1.80		1.75		1.70	
	Low	7	11.7	22	36.7	8	13.3	6	9.8	6	9.8
	Normal	53	88.3	38	63.3	52	86.7	10	16.4	10	16.4
	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Figure-1. Description of the studied cases according to pre and post-operative level of serum Ca, P, and Mg



no involvement of the digestive tract. Dietary intake can be resumed a few hours after the operation, in most cases. The endocrine and metabolic response is slight and short-lived. Consequently, both fluid volumes and ion concentrations promptly return to their baseline preoperative states [25-27].

Although the incidence of postoperative complications is acceptable, they may be extremely uncomfortable and incapacitating. The most common metabolic complications are disorders of calcium ion concentrations [28].

Homeostasis of magnesium ions is directly related to calcium levels. An abrupt fall in calcium concentration leads to increase of the production and release of parathormone (PTH) and exacerbates the secondary clinical manifestations, because of hypocalcemia. Posphorus concentration is inversely related to calcium and is regulated by Ca, PTH and vitamin D [26].

In this study, 53 patients were subjected to TT and 7 had completion thyroidectomy. Temporary and permanent hypocalcaemia were encountered post-operatively, 6 patients each (10%).

In accordance with the results presented herein, the mean rate of post-operative temporary hypocalcaemia, permanent hypocalcaemia and hoarseness of voice measured in literature ranged between 10-40%, 0.5-10% and 10%-12%, respectively [6-10, 28, 29].

Postoperative serum calcium, phosphorus and magnesium were measured in the present study at 12 hours, 24 hours, one month and 6 months intervals. Most of the reviewed studies measured them at 24 hours and\or 48 hours [4-6, 24].

Hammerstad et al [6] measured serum calcium and magnesium post-operatively after 6 hours, 48 hours, one month, 6 months and 12 months. They defined hypocalcaemia as “permanent” at one year after operation, and transient if it normalizes within a year after surgery.

Sousa et al [5] had a different strategy in their work, as they measured postoperative serum calcium, phosphorus and magnesium at 24 and 48 hours interval only with no scheduled follow up measurements. They correlated post-operative magnesium and phosphorus levels with transient hypocalcaemia, and they found that neither Mg nor P levels had any role in post-thyroidectomy Ca level.

Sam et al [24] studied only the relation between post-operative serum calcium and phosphorus at 24 hours and 2 weeks intervals. They did not study the influence of post-operative magnesium level on hypocalcaemia. They said that serum P may predict post-thyroidectomy hypocalcaemia.

In the present study, it was noticed that serum calcium and magnesium levels were related to each other at 12 and 24 hours post-operatively. These results were in agreement with the results of Hammerstad et al [6] as they also noticed significant relation between calcium and magnesium. Wilson et al [4] also found that hypomagnesaemia correlated with hypocalcaemia, and that patients were more likely to be symptomatic when both cations are low. Conversely, Sousa et al [5] stated that magnesium level has no significant relation with hypocalcaemia. After revising the literature, the relation between post-operative calcium and magnesium was noticed to be not well studied, demonstrating the necessity of more studies in this topic.

Serum magnesium level in hypocalcaemic patients at 24 hours post-operative seems to have a significant role in predicting the development of permanent hypocalcaemia (p=<0.001). In other words, patients with combined low calcium and magnesium levels 24 hours post-operatively are likely to have permanent hypocalcaemia, and serum calcium level tends to return to normal levels before 6 months post-operatively in

Table-5: Relation between post-operative Ca and post-operative P and Mg.

		Classification of patients according to post-operative Ca								^{MC}p
		Normal (n = 34)		Low 12 hrs (n = 14)		Low transient (n = 6)		Low permenant (n = 6)		
		N	%	N	%	N	%	N	%	
P	Normal	31	91.2	12	85.7	6	100.0	6	100.0	0.904
	High 12 hr	2	5.9	2	14.3	0	0.0	0	0.0	
	High 12 and 24 hr	1	2.9	0	0.0	0	0.0	0	0.0	
Mg	Normal	25	73.5	6	42.9	3	50.0	1	16.7	<0.001*
	Low 12 hr	6	17.6	8	57.1	3	50.0	0	0	
	Low 24 hr	1	2.9	0	0.0	0	0.0	2	33.3	
	Low 12 and 24 hr	2	5.9	0	0.0	0	0.0	3	50.0	

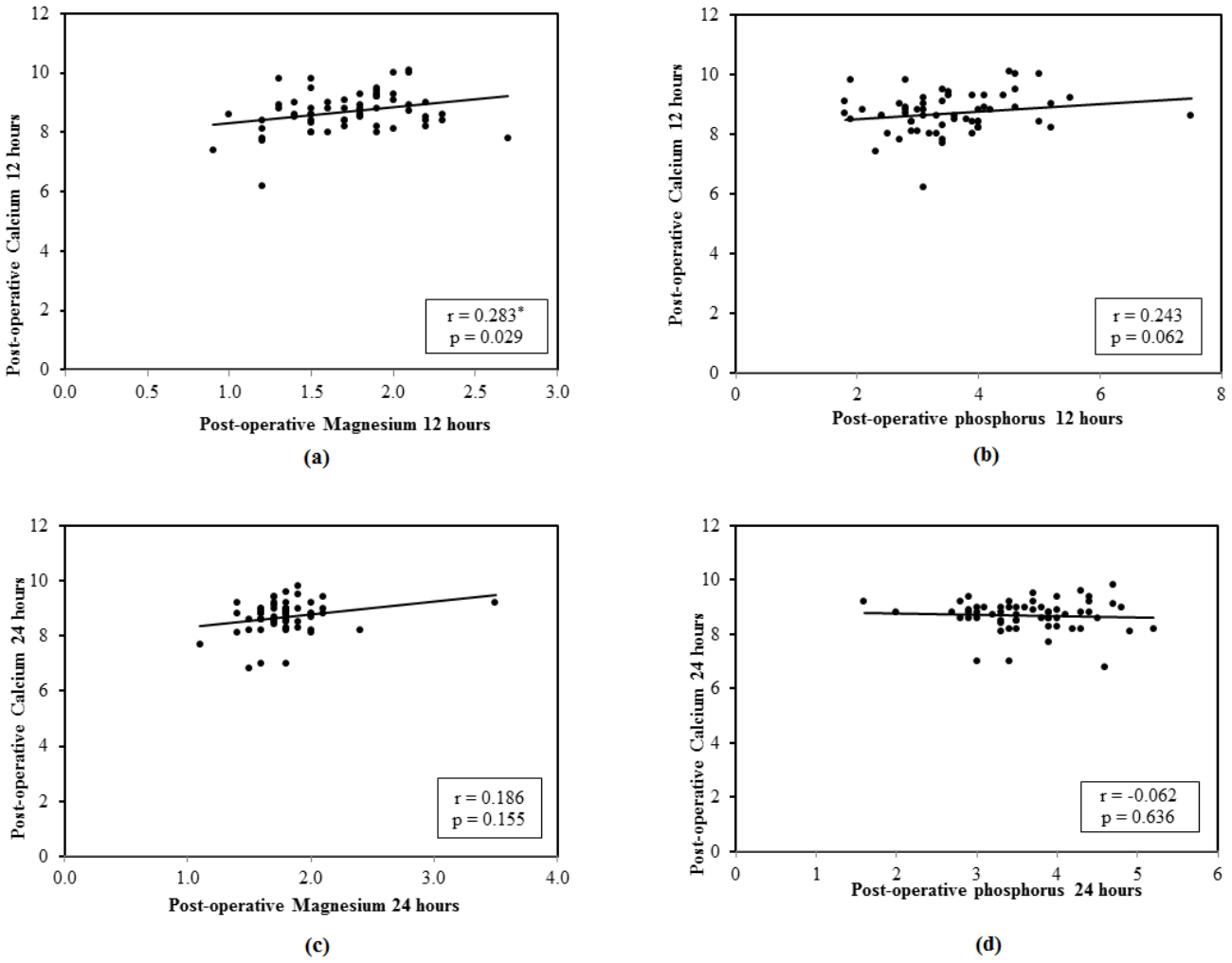
*: Statistically significant at p ≤ 0.05

Table-6: Relation between classification of patients according to post-operative Ca and Ca, Mg 24 hr

24 hrs postoperative level of Ca and Mg	Classification of patients according to post-operative Ca								^{MC}p
	Normal (n = 34)		Low 12 hrs (n = 14)		Low transient (n = 6)		Low permenant (n = 6)		
	N	%	N	%	N	%	N	%	
Normal Ca - Normal Mg	31	91.2	14	100.0	0	0.0	0	0.0	<0.001*
Normal Ca - Low Mg	3	8.8	0	0.0	0	0.0	0	0.0	
Low Ca - Normal Mg	0	0.0	0	0.0	6	100.0	1	16.7	
Low Ca - Low Mg	0	0.0	0	0.0	0	0.0	5	83.3	

MC: Monte Carlo test
X2: Chi-square test

Figure-2. Correlation between calcium and both phosphorus and magnesium at 12 and 24 hours intervals (a. Ca with Mg in post-operative 12 hours. b. Ca with P in post-operative 12 hours. c. Ca with Mg in post-operative 24 hours, d. Ca with P in post-operative 24 hours).



hypocalcaemic patients with normal 24 hours magnesium level (Table 6).

In accordance with our results, Hammerstad and colleagues[Error! Reference source not found.] stated that the degree of decrease in magnesium levels in serum 48 h after operation may predict development of permanent hypocalcemia. On reviewing literature, no other study discussed the relation between permanent hypocalcaemia and early post-operative serum magnesium level measurement. Further studies are recommended to consider 24 hours combined serum calcium and magnesium levels measurement as a predictor of permanent hypocalcaemia

In this study it was noticed that post-operative serum phosphorus level had no significant relation with calcium level confirming what was stated by Sousa et al[Error! Reference source not found.] they found that phosphorus levels had no role in post-thyroidectomy hypocalcaemia.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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