Journal Of Cardiovascular Disease Research
ISSN: 0975-3583,0976-2833 VOL15, ISSUE6, 2024

POSTOPERATIVE DAY 1 PARATHYROID HORMONE AS A PREDICTOR OF HYPOCALCEMIA AFTER TOTAL THYROIDECTOMY -A PROSPECTIVE STUDY.

Divya G [1],Gowbath Marliya S[2]

(*1) (2) Junior Resident, Department of general surgery,Sree Mookambika institute of medical sciences, Kanyakumari, Tamilnadu*

Corresponding author : Gowbath Marliya S,Junior Resident, Department of general surgery,Sree Mookambika institute of medical sciences, Kanyakumari, Tamilnadu,Email: marliyagowbath@gmail.com.

ABSTRACT

Background: PTH as a predictor of hypocalcemia has a good sensitivity and specificity. But there is no consensus regarding the best time of its measurement and the absolute value to be used for discharging patients early a recent prospective study done at institution, half and hour postoperative PTH was found to be a reliable predictor of hypocalcemia with a cut off at 15pg/ml

Material methods:This study was conducted in Department of General Surgery, sree mookambika institute of medical sciences , Kanyakumari. Study conducted from November 2022 to September 2023.775cases admitted in General Surgery Ward Patients presenting with thyroid swellings undergoing total thyroidectomy during the study period

Result: Sensitivity, specificity, positive predictive value and negative predictive value of PTH 15 pg/ml in predicting hypocalcemia was 50.0%, 74%, 5.0% and 98.2%. Hence the PTH cut off with good sensitivity and specificity for predicting normocalcemia is > 15pg/ml.

Conclusion: In our study PTH >15 pg/ml was present in 73.33% and it was an accurate cut off level permitting safe, early discharge and none of these patients suffered signicant delayed hypocalcemia. Our study disclosed there is very significant relationship (p value – 0.007) between vitamin D levels and hypocalcemia. Majority of patients with vitamin D deficiency were hypocalcemic.

Keywords: Parathyroid hormonr, hypocalcemia,Thyroid swelling.

INTRODUCTION:

Thyroidectomy is a commonly performed surgical procedure. Traditional inpatient surgical care has followed a pattern of discharge that waits for the patient to be pain free, ambulant and consuming a normal diet with a low risk of complications. With modern anesthesia and surgical techniques, the patient usually recovers within 24 hours, so the limiting factor for discharge is the occurrence of complications. Early complications of thyroidectomy which are life threatening includes hemorrhage, severe hypocalcemia and bilateral recurrent laryngeal nerve palsy. Hemorrhage is rare between 1-3% and bilateral recurrent laryngeal nerve palsy with stridor is a very rare calamity at <1%; both classically manifest within a few hours though bleeding has been reported up to as late as one week after surgery. Transient hypocalcemia is the commonest

complication encountered, the median rate reported in a meta-analysis being 27%. It may not be noticeable until 24 to 36 hours after surgery. This traditionally required inpatient monitoring of patients for a prolonged period with serial monitoring of serum calcium levels. Prompt intervention is needed occasionally when the patient is symptomatic with tingling or cramps in the form of supplementation with oral calcium and vitamin D, rarely even intravenous calcium injections if the hypocalcemia is severe[(14)]. Serial calcium levels need to be measured in hypocalcemic patients until they are normocalcemic or an upward trend is observed. Hypocalcemia is therefore the main limiting factor for early discharge.

Normal blood calcium levels are a prerequisite for the safe discharge of post-thyroidectomy patients from the controlled hospital environment. Pre-emptive prolongation of patient hospitalization after the operation extends patient discomfort. It is not a cost-effective approach, since most patients do not develop clinical symptoms or laboratory-confirmed hypoparathyroidism. Therefore, strategies that may predict patients at risk for post-thyroidectomy symptomatic hypocalcemia could be useful. A decline in serum calcium from its preoperative values at 24 h has been reported to have a high sensitivity for predicting transient hypocalcemia. However, parathyroid hormone levels allow a more direct and precise determination of the long-term function of the parathyroid glands.

PTH as a predictor of hypocalcemia has a good sensitivity and specificity. But there is no consensus regarding the best time of its measurement and the absolute value to be used for discharging patients early[7]. In a recent prospective study done at institution, half and hour postoperative PTH was found to be a reliable predictor of hypocalcemia with a cut off at 15pg/ml. Based on this value we formulated a protocol for safe and effective early discharge, the day after surgery. However, we had concerns whether our patients would perceive early discharge as risky and prefer to stay for our default 2 days post operatively . Therefore we decided to test the protocol applicability and compliance to it in our department.

MATERIALS AND METHODS

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This study was conducted in Department of General Surgery, sree mookambika institute of medical sciences , Kanyakumari. Study conducted from November 2022 to September 2023.775cases admitted in General Surgery Ward Patients presenting with thyroid swellings undergoing total thyroidectomy during the study period

Inclusion criteria

- All the patients who undergo total thyroidectomy or completion thyroidectomy
- Age above 18 years
- Both genders

Exclusion criteria

- Age below 18 years
- Patients who had locally advanced thyroid malignancy.

- Patients with retrosternal extension of goiter.
- Patients with hyperthyroidism.

All the patients presented to surgical OPD with thyroid associated complaints who underwent total thyroidectomy or completion thyroidectomy were screened for eligibility and included in this study. Patients were explained about the procedure and its complications. Signs and symptoms of complications expected postoperatively were explained in detail. Patients were explained about the study being performed and an informed written consent was obtained.

Patients were taken up for surgery after informed written consent. Postoperative period on the day of surgery patients were monitored for complications – hemorrhage, recurrent laryngeal nerve palsy, hypocalcemia. Patients symptomatic for hypocalcemia were supplemented with calcium and vitamin D supplements. Next day following surgery early morning samples of calcium , albumin and PTH were sent. Patients with no symptoms and signs of hypocalcemia and with normal serum calcium and PTH according to the protocol were discharged. Rest of the patients were remain as inpatients, not discharged till stable or rising serum calcium on supplements.

Patients with serum calcium < 8 mg/dl or PTH < 15 pg/ml were supplemented with calcium and vitamin D. If PTH < 15 pg/ml irrespective of serum calcium – T.CaCO3 500 mg BD and T>Calcitriol 0.25 mcg BD given , supplements were increased according to symptoms. If PTH >15 pg/ml but calcium is low, the following protocol was followed.

RESULTS:

PTH in study patients

Table 5: DISTRIBUTION OF PTH

PTH Post-op Day1	No. of Subjects	Percentage
< 15	20	26.7%
15 & Above	55	73.3%
Total	75	100%

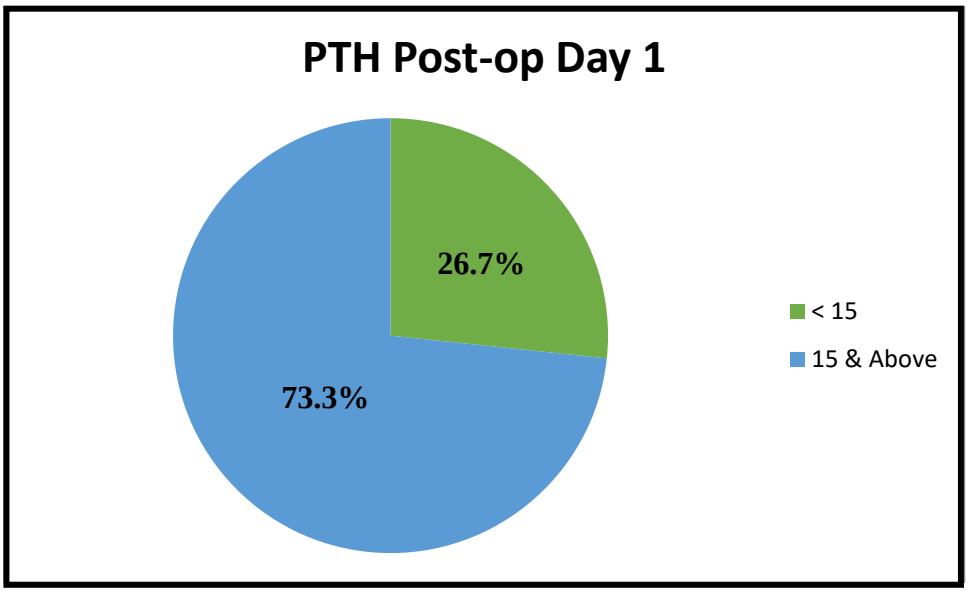

Figure 5: DISTRIBUTION OF PTH

- PTH can be used to predict the likelihood of hypocalcemia and therefore safety of early discharge of patients. Most of the patients had good PTH with a mean of 27.6 pg/ml. PTH ≥15pg/ml was present in 73.33% patients.

PTH and Hypocalcemia after 48 hours

Table 6: CORRELATION OF PTH WITH SERUM CALCIUM LEVELS AFTER 48 hrs.

PTH ON POD 1	NORMOCALCEMIA	HYPOCALCEMIA	TOTAL
<15	6 (30%)	14 (70%)	20 (100%)
15 and Above	30 (54.5%)	25 (45.5%)	55 (100%)
Total	36	39	75

*P value – 0.018 (P<0.05 significant)

(Chi square test)

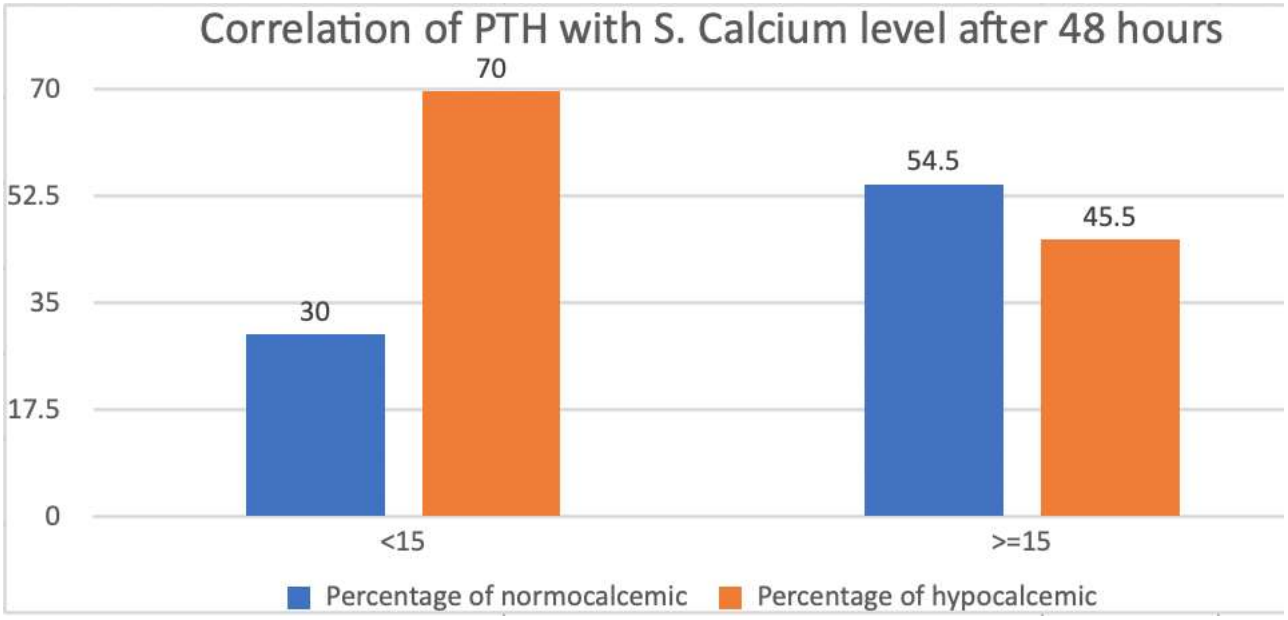

Figure 6: CORRELATION OF PTH WITH SERUM CALCIUM LEVELS AFTER 48 HOURS

- Majority of patients with normal PTH (> 15 pg/ml) had normocalcemia and also among patients with low PTH (<15 pg/ml), majority had hypocalcemia. PTH was found to be significant (p<0.01) in differentiating normocalcemia and hypocalcemia patients. In the group with PTH >15pg/ml hypocalcemia was seen in 70%, but the hypocalcemiawas mild .

PTH AND HYPOCALCEMIA AFTER 1 WEEK

Table 7: CORRELATION OF PTH WITH SERUM CALCIUM LEVELS AFTER 1 WEEK

PTH ON POD 1	NORMOCALCEMIA	HYPOCALCEMIA	TOTAL
<15	6 (30%)	14 (70%)	20 (100%)
15 and Above	30 (54.5%)	25 (45.5%)	55 (100%)
Total	36	39	75

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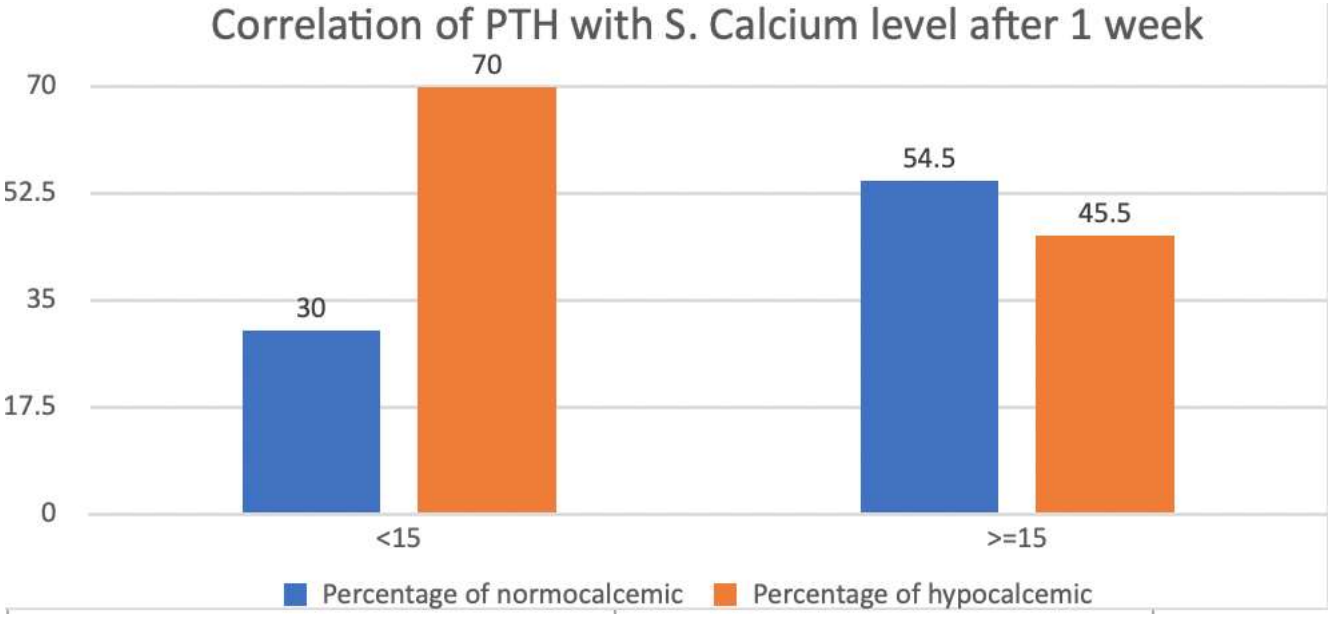

Figure 7: CORRELATION OF PTH WITH SERUM CALCIUM LEVELS AFTER 1 WEEK

- Majority of patients with normal PTH (> 15 pg/ml) had normocalcemia and also among patients with low PTH (<15 pg/ml), majority had hypocalcemia. PTH was found to be significant (p<0.01) in differentiating normocalcemia and hypocalcemia patients.

PTH AS A PREDICTOR OF HYPOCALCEMIA

Table 10: SENSITIVITY, SPECIFICITY, PPV AND NPV FOR VARIOUS PTH CUT OFF

PTH Post-op Day1	Sensitivity	Specificity	PPV	NPV	P Value
<6	0.0%	94.5%	0.0%	97.2%	0.734
<9.8	0.0%	87.7%	0.0%	97.0%	0.597
<15	50.0%	74.0%	5.0%	98.2%	0.449
<21	100.0%	67.1%	7.7%	100.0%	0.049

- Sensitivity, specificity, positive predictive value and negative predictive value of PTH 15 pg/ml in predicting hypocalcemia was 50.0%, 74%, 5.0% and 98.2%. Hence the PTH cut off with good sensitivity and specificity for predicting normocalcemia is > 15pg/ml.

RECEIVER OPERATOR CURVE FOR PTH

Table 11: ROC for PTH

Hypocalcemia Symptoms After 48 Hours Discharge	Valid N (listwise)
Positive	2
Negative	73
Total	75

Area under the Curve

Test Result Variable(s): PTH Post-op Day1

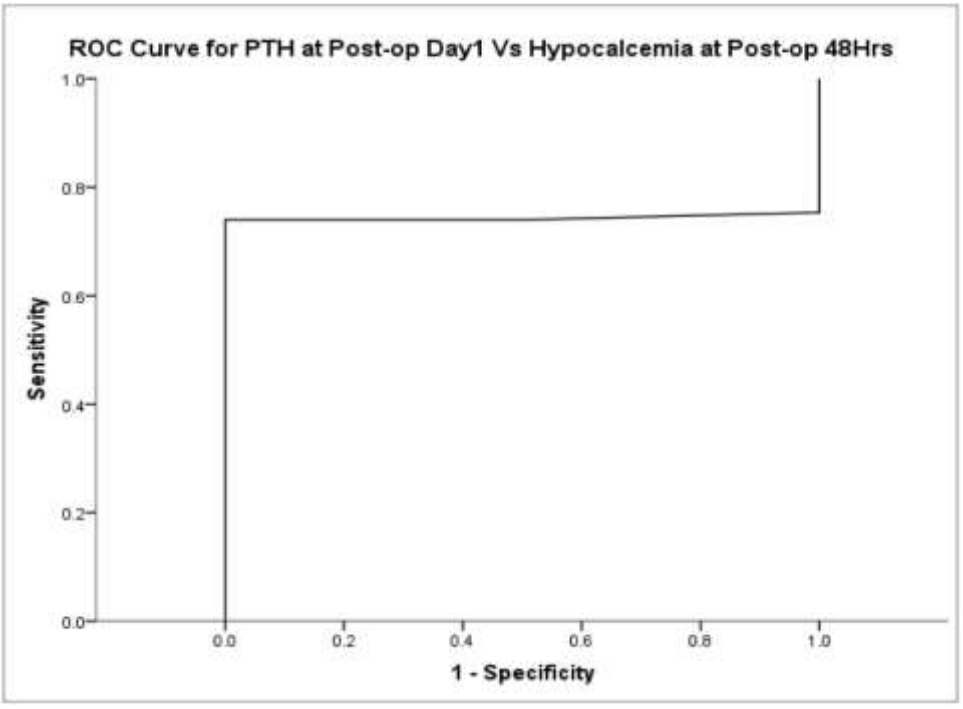

Figure 10: ROC CURVE FOR PTH

- Area under the receiver operator curve (ROC) was 0.743, indicating PTH as a reliable test for differentiating hypocalcemia and normocalcemia at post op 48 hrs .

AREA UNDER THE CURVE

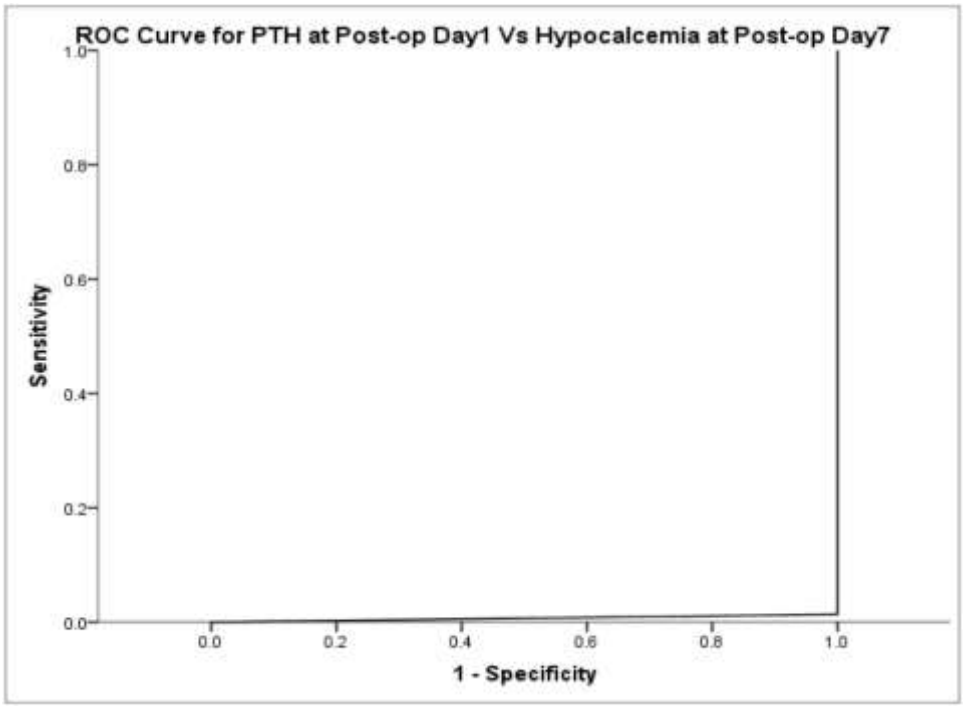

Figure 11: ROC CURVE FOR PTH

DISCUSSION:

Postoperative hypocalcemia remains the single greatest predictor of length of stay after total or completion thyroidectomy. Transient hypocalcemia has been reported to occur in up to 27% of patients. In our study, the estimated rate of transient hypocalcemia was 53.4%. The mechanism of transient hypocalcemia remains elusive. Numerous theories have been described in the literature. Hemodilution secondary to intraoperative fluid administration, calcitonin release after manipulation of the thyroid, “hungry bone syndrome” secondary to skeletal uptake of calcium in patients with thyrotoxic osteodystrophy, and, ultimately the earliest proposed

mechanism, after injury/removal or devascularization of the parathyroid glands. PTH achieves calcium homeostasis through a number of physiologic mechanisms including renal distal tubule calcium re-absorption, vitamin D mediated intestinal calcium absorption, and bone resorption. Early attempts at identifying patients at risk of hypocalcemia primarily attempted to use the change in sequential calcium over time and calculate slope to predict risk of hypocalcemia.

Routine supplementation with calcium and vitamin D has certain disadvantages including cost, inability to predict duration of supplementation and the risk of hypercalcemia. PTH as a tool was shown to reduce hypocalcemia rate by guiding early supplementation compared to calcium values only. Sabour S et al [(26)] compared group 1- using PTH to guide supplementation with group 2 - routinely supplemented irrespective of PTH and a control group which was supplemented based on calcium values; hypocalcemia in group 1(14%) and group 2 (4.5%), was lower than the control group (35%). Another study by Chow T-L et al [(4)] has also shown significantly low rate of symptomatic hypocalcemia in the group managed using PTH as a guide for supplementation compared to control group managed based on serum calcium alone. Our

study showed 4 (12%) cases with normal calcium and low PTH . PTH was shown in various studies as a good predictor of hypocalcemia at different cut off values (3-20 pg/ml) and timing of PTH measured (intraoperative to 24 hours post surgery) [(8,27,28,13,7,19)]. In our study PTH <15 pg/ml measured in the morning after surgery had sensitivity and specificity of 50% and 74% for predicting hypocalcemia. In an Australian multicenter study, data pooled from different centers with different timing and cut off values of PTH used, the overall sensitivity and specificity of PTH for predicting hypocalcemia is higher to our study (70.7% and 92.6%) [(16).].However single value of PTH <8 pg/ml with a sensitivity of 100% and PTH <10 pg/ml with 94% sensitivity and 100% specificity are also reported [(20,22).]

PTH as a reliable guide for safe and early discharge is published in many studies. Patients were discharged early in few studies based on PTH value but with routine calcium and vitamin D supplementation or discharged after day care surgery with routine supplementation without using PTH as a predictor of hypocalcemia [(12,11,31,32).] . Very few studies discharged patients early without calcium supplementation using PTH as a guide, similar to our study [(8,29).] The group with normal PTH and hypocalcemia (1.81o%) had higher mean calcium (7.7mg/dl) with mild symptomatic hypocalcemia only in few patients (3%), managed successfully with oral calcium supplementation. In the Australian society guidelines recommending early discharge based on PTH, 7% patients of

their multicenter data had normal PTH and hypocalcemia. They developed only minor symptoms of hypocalcemia, similar to our study group and were managed with supplements [16]. One of our patients discharged early based on the protocol with normal calcium and PTH had symptomatic delayed hypocalcemia on follow up. In the studies done by Chow TL et al and Cayo AK et al [8,29] patients were discharged early without supplementation based on PTH >6 pg/ml and >10 pg/ml, none of the discharged patients had hypocalcemia.

CONCLUSION:

In our study PTH >15 pg/ml was present in 73.33% and it was an accurate cut off level permitting safe, early discharge and none of these patients suffered signicant delayed hypocalcemia.The low PTH also predicted hypocalcemia to guide early supplementation of calcium and all the severe hypocalcemic patients had PTH lower than cut off 15 pg/ml.Majority of patients with normal PTH (> 15 pg/ml) had normocalcemia and also among patients with low PTH (<15 pg/ml), majority had hypocalcemia. PTH was found to be significant ($p<0.01$) in differentiating normocalcemia and hypocalcemia patients.Our study disclosed there is very significant relationship (p value – 0.007) between vitamin D levels and hypocalcemia. Majority of patients with vitamin D deficiency were hypocalcemic.

FINANCIAL SUPPORT AND SPONSORSHIP:

Nil.

CONFLICTS OF INTEREST:

There are no conflicts of interest

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