INTRODUCTION

Thyroid surgeries are common surgical procedures worldwide and transient hypocalcaemia is common and potentially life-threatening complication after total or completion thyroidectomy.[1,2] Post-operative PTH assay can be used to stratify the risk of patients developing hypocalcaemia after thyroidectomy.[3] Routine administration of oral calcium with vitamin D4 for all the patients following total thyroidectomy irrespective of their parathyroid hormone level has been widely practiced in India.[4] However, an intact PTH level during the early post-operative period has been found to be accurate in predicting the risk of developing hypocalcaemia and thereby facilitate decreased hospital stay and prevents un necessary routine calcium prescription.[5]

Aim
We aimed to assess the clinical efficacy and cost effectiveness of routine PTH assay during the early post-operative period in predicting acute hypocalcaemia and its management.
MATERIALS AND METHODS

A review of the prospectively collected data of patients who underwent either total or completion thyroidectomy in a tertiary endocrine surgery center was done over a period of 5 years from April 2013 to April 2018.

Based on the inclusion and exclusion criteria, 190 patients were selected for the study out of 370 patients of thyroid surgeries. All patient and surgery related details were recorded in a database. All patients had a single post-operative PTH assay within the first 4th hour following surgery further serum calcium assays and treatments were based on the early PTH levels accordingly.

The patients were divided into 4 groups according to their PTH level.

<table>
<thead>
<tr>
<th>Group</th>
<th>Serum pth level</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>&lt;5pg/ml</td>
<td>10</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>5-10pg/ml</td>
<td>10</td>
</tr>
<tr>
<td>Low risk</td>
<td>10-15pg/ml</td>
<td>8</td>
</tr>
<tr>
<td>No risk</td>
<td>&gt;15pg/ml</td>
<td>162</td>
</tr>
</tbody>
</table>

Among the 190 patients, 162 were categorized as no risk group, 8,10 patients at low risk, intermediate risk group respectively and there were 10 patients at high risk group. All the patients were monitored for the development of clinical symptoms of hypocalcemia and serum calcium levels were measured in 28 patients.

Cost comparison of PTH assay performed at a standard lab versus the overall cost of routine calcium prescription and the associated increase in duration of hospital stay was done.

RESULTS

190 patients were included in the study from a total of 370 thyroid surgeries. Among these, there were 165(86.8%) total thyroidectomies and 25(13.2%) completion thyroidectomies. Majority 90.5% (172/190) were female patients and the age range was from 25 to 64 (mean 38 years).

Gender-wise distribution of the study population. Patients were stratified in to 4 groups based upon the PTH results, Values more than 15 pg/ml considered normal (15 – 60pgms/dl). There were 14.75 % (28/190) cases of temporary and 1.6%(3/190) cases permanent biochemical hypoparathyroidism.

Table 1:

<table>
<thead>
<tr>
<th>PTH levels pg/dl</th>
<th>Normal range 15 – 60</th>
<th>Total patients n=190</th>
<th>Serum Calcium measured n=28</th>
<th>No. of symptomatic hypocalcaemia Calcium&lt;8mg/dl</th>
<th>asymptomatic hypocalcaemia Calcium&lt;8</th>
<th>No. of calcium replacements patients</th>
<th>No. of Permanent hypocalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 No risk group</td>
<td></td>
<td>n=162</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10 – 15 low risk</td>
<td></td>
<td>n=8</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5 – 10 Intermediate risk</td>
<td></td>
<td>n=10</td>
<td>10</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>&lt;5 High risk</td>
<td></td>
<td>n=10</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Total N=190</td>
<td></td>
<td></td>
<td>13</td>
<td>3</td>
<td>15</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

No risk group – 85.25% (162/190): no cases of symptomatic hypocalcemia, serum calcium levels are not measured.

Further statistical analysis of PTH, in prediction of hypocalcaemia showed following outcomes.

The above data shows that there was no incidence of hypocalcemia in the no risk group and therefore a serum PTH level >15pg/ml, essentially rules out the risk of development of postoperative hypocalcemia.
The results revealed that, only 7.8% (15/190) patients requiring daily calcium carbonate and Vit D4 supplementation for variable period of time and the most of the patients (92.2%) did not require any form calcium or Vit D4 support. Majority of the patients were discharged from the hospital within 24 to 48 hours. All the patients with low PTH levels were reviewed at 1st and 4th week post-operatively and in selected patient’s serum PTH also assayed and calcium, Vit D4 treatments were tailored off as per requirement.

The results shows that the sensitivity and NPV of PTH assay in predicting the risk of hypocalcemia is 100% and therefore can be used to avoid unnecessary calcium supplementation. Also, the test is particularly useful in the no risk and high risk group indicating that a serum PTH value of more than 15pg/ml eliminates need for calcium supplementation, while in patients with serum PTH level < 5 pg/ml, calcium supplementation should be started early to avoid the hypocalcemic symptoms. The high sensitivity and NPV of PTH in prediction of hypocalcaemia avoided unnecessary, routine prescription of costly calcium in 162 patients and also allowed safe early hospital discharge culminating significant reduction of overall hospital cost without compromising the care. It also helps in early identification of patients who will benefit from early calcium supplementation.

Cost Analysis
The cost of PTH assay in a standard lab is around 750 -1000 INR, and the cost of Calcium carbonate/Vit D4 (3 gms and 1mcg a day) 30- 45 INR/day along with prolonged hospital day with hospital surcharges range from Rs. 500 to upto INR. 5000 per day. Therefore, the total cost of calcium supplementation and hospital stay can be around INR 1200 to INR 13,350. A single PTH assay can lead to financial savings of INR 450 to INR 13,350 for every patient.

DISCUSSION
Parathyroid hormone (PTH) plays a major role in calcium metabolism by directly acting on the kidneys, bone and gastrointestinal tract and it has a short half life of around 3-5 minutes. Postoperative hypocalcemia may occur due to trauma to the parathyroid gland or its blood supply, or the unintentional removal of the gland during surgery. Permanent hypoparathyroidism is defined as the continuing need for calcium and / or vitamin D replacement at 1 year after thyroidectomy and associated with increased morbidity. Majority of the patients, however, have transient hypocalcemia which usually resolves by within few weeks to months. Therefore, a definitive strategy for identifying patients at risk of developing hypocalcemia is essential. In 1989, a study by N Hamada et al showed the correlation between the postoperative parathormone levels and the calcium levels indicating a strong association between them. The common symptoms of hypocalcemia includes, circumoral and digital numbness or parasthesias, carpopedal or laryngeal spasm, cardiac arrhythmias. Chvostek sign and Trousseau sign are typical signs of latent hypocalcemia. Chung Yau Lo et al in 2002 evaluated the applicability of intraoperative parathyroid hormone assay in predicting post-operative hypocalcemia. PTH levels were measured preoperatively, a quick PTH assay was done 10 minutes after induction of anesthesia and 10 minutes after completion of thyroidectomy and the PTH levels were also measured in the post-operative period. The study showed that hypocalcemic patients had significantly lower PTH levels compared to normocalcemic patients.

Monitoring the postoperative calcium levels is the current practice being carried out after thyroidectomy in India. However fall in calcium levels have been found not to be specific for thyroid surgery. Also the prophylactic supplementation of calcium in unwarranted cases may hinder the early identification of symptoms of hypocalcemia. In contrast, PTH levels are more specific for thyroid surgeries compared to serum calcium levels and can help to detect parathyroid injury earlier. A prospective study of 76 patients by Simon Grodski and Stephen Farell in 2007 demonstrated that PTH measurement at 4-12 hours postoperatively predicted hypocalcemia accurately.

In our study, patients with normal PTH level did not develop hypocalcemia and required no calcium supplementation postoperatively. This showed the effectiveness of the routine use of PTH assay in early prediction of hypocalcemia and its cost effectiveness. We feel our study is unique in that, apart from the clinical efficacy the cost effectiveness analysis was also performed to elucidate the financial benefits to the patient.

CONCLUSION
Routine measurements of PTH levels in the early postoperative period following thyroid surgery accurately predict the risk of hypocalcemia. It has the advantages of reducing unwanted calcium supplementation and decreases the period of postoperative stay in the hospital. Therefore routine use of PTH assay in the post-operative period following thyroidectomy can offer significant benefits to the patient and aid in the early diagnosis of hypocalcemia.

REFERENCES
2. Ignjatović M, Cuk V, Ozegović A, Cerović S, Kostić Z, Romić P.


