

Clinical Profile, Diagnostics, and Short-term Outcomes of Parathyroid Surgery for Hyperparathyroidism in a Tertiary Hospital in the Philippines: A Retrospective Study

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ABSTRACT

Objective. This study aimed to describe the demographics, clinical presentations, diagnostic workup, and short-term biochemical outcomes of parathyroidectomy among patients with hyperparathyroidism in a tertiary hospital in the Philippines.

Methods. A retrospective review of patients who underwent parathyroidectomy in the University of the Philippines-Philippine General Hospital from 2014 to 2021 was done. Demographics, symptoms, laboratory and imaging findings, surgical approach, and post-operative outcomes were recorded. Descriptive statistics and paired t-tests were used for analysis.

Results. Thirty-two patients underwent surgery: 23 had primary, six had secondary, and 3 had tertiary hyperparathyroidism. The mean age was 47 years, and 72% were female. The average symptom duration before surgery was 24 months. Bone pain was the most frequent symptom, and five patients presented with brown tumors. Pre-operative laboratory evaluation showed severe hypercalcemia and markedly elevated iPTH, especially in primary HPT. Sestamibi scans were the most commonly used imaging modality (84%). Surgery resolved hypercalcemia in 95.2% and normalized iPTH in 93.8% of patients. No complications were recorded within 30 days post-operatively.

Conclusion. Parathyroidectomy is an effective and safe treatment strategy in achieving normal PTH levels among patients with hyperparathyroidism. Patients with hyperparathyroidism in this study underwent surgery late in the course of the disease process. Strategies must be employed to promote earlier diagnosis and subsequent treatment. Further studies with larger population sizes are recommended to investigate the long-term outcomes of operated HPT patients.

Keywords: parathyroidectomy, hyperparathyroidism, hypercalcemia

INTRODUCTION

Hyperparathyroidism (HPT) is an endocrine disorder characterized by excessive secretion of parathyroid hormone (PTH), leading to disturbances in calcium, phosphate, and bone metabolism. It is classified as primary, secondary, or tertiary depending on etiology. Primary hyperparathyroidism (PHPT), the most common form, is typically due to parathyroid adenoma, hyperplasia, or carcinoma and results in autonomous PTH secretion and hypercalcemia.^{1,2} Secondary hyperparathyroidism (SHPT) arises as a compensatory response to chronic hypocalcemia, frequently due to chronic kidney disease (CKD), whereas tertiary hyperparathyroidism

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(THPT) represents autonomous PTH secretion after prolonged SHPT, particularly in patients undergoing renal replacement therapy.³

Surgery is the definitive treatment for symptomatic PHPT and is considered in asymptomatic patients who meet criteria including significantly elevated serum calcium, reduced bone density, kidney stones, or decreased glomerular filtration rate.^{4,5} For SHPT and THPT, parathyroidectomy is indicated when medical management fails to correct persistent hyperparathyroidism and end-organ complications emerge.

Pre-operative evaluation involves laboratory investigations such as serum calcium, phosphorus, creatinine, and PTH. Imaging modalities to localize the gland pathology including ultrasonography, 4D CT Scan and technetium-99m sestamibi scans are also critical in pre-operative planning. Intraoperative PTH monitoring is done to confirm localization and success of removing the pathology.

While international guidelines inform current diagnostic and treatment protocols⁵, data from the Philippine setting are scarce. This study reviews the profiles, diagnostic approaches, and short-term post-operative outcomes of patients who underwent parathyroidectomy for HPT at a tertiary government hospital in the Philippines.

METHODS

This is a retrospective cross-sectional study approved by the ethics review board (UPMREB code 2022-0323-01) and included all patients who underwent parathyroidectomy from January 1, 2014 to June 30, 2021 at the Department of Otolaryngology-Head and Neck Surgery of University of the Philippines-Philippine General Hospital. Adult patients (18 years old and above) who underwent surgery for planned parathyroidectomy from the years specified were included in this study. The exclusion criteria were as follows: patients who had unplanned removal of their parathyroid glands such as in thyroidectomy or in other neck/chest surgeries and patients who did not undergo parathyroid surgery in the specified years but are seeking follow-up in the Department for parathyroid-related conditions.

Data was collected through review of medical records. The investigators retrieved the following from the patient's charts: demographic data (age, sex), clinical data (duration of illness, symptoms), laboratory tests results (intact PTH, calcium, phosphorus, creatinine), imaging study results, operative findings, and histopathologic findings. Data was also collected from their follow-up up to six months post-operatively, including intact PTH, calcium, phosphorus, and creatinine. Included patients were anonymized by assigning them a unique control number. Participants were referred through their control numbers throughout the study and none was directly identified to ensure confidentiality and avoid bias.

Baseline demographics and perioperative clinical data was analyzed using descriptive statistics (means, proportions

and standard deviations). Pre-operative and post-operative clinical parameters were compared using paired t-test. All statistical analyses were performed using SPSS.

RESULTS

A total of 32 patients met the inclusion criteria, comprising 23 cases of PHPT (72%), six of SHPT (19%), and three of THPT (9%). The cohort included 23 females (72%) and nine males (28%), with a mean age of 47 years (range: 26–75). The mean duration from onset of symptoms to surgery was 24 months while time from diagnosis to surgery averaged at eight months. The clinical profile of patients are detailed in Table 1.

Clinical presentation varied across subtypes. Musculoskeletal complaints, particularly bone pain, were reported in 14 patients (44%). Brown tumors were documented in five individuals (16%), affecting sites such as the mandible, shoulder, and long bones. Nephrolithiasis or nephrocalcinosis was noted in six patients (19%). Additional symptoms included generalized weakness, neuropsychiatric disturbances, and gastrointestinal complaints.

Table 2 summarizes the pre-operative laboratory parameters of patients who underwent surgery for hyperparathyroidism. Mean corrected serum calcium and intact PTH levels were highest for primary hyperparathyroidism. As expected, phosphorus levels were markedly elevated for both secondary and tertiary hyperparathyroidism. Since all cases of secondary and tertiary hyperparathyroidism were secondary to chronic kidney disease, serum creatinine pre-operatively was noted to be markedly elevated.

The surgical procedures performed are summarized in Table 3. In cases of primary HPT, excision of the hyperfunctioning parathyroid gland or suspected adenoma was guided by pre-operative imaging findings. The imaging modalities used for localization are detailed in Table 4, with a noted institutional preference for technetium-99m sestamibi scans. For secondary and tertiary HPT, patients underwent either subtotal parathyroidectomy (3½ glands) or total parathyroidectomy with autotransplantation. Concurrent partial or total thyroidectomy was performed in 63% of patients.

Table 5 summarizes the operative times. In the absence of intraoperative rapid intact PTH testing at our institution, frozen section analysis of suspected lesions was performed in 78% of cases to confirm the pathologic parathyroid gland. Operative durations were highly variable, reflecting the heterogeneity of procedures performed since many cases included additional surgeries beyond parathyroidectomy.

Post-operative laboratory parameters were also documented and contrasted to baseline measures as shown in Table 6. Table 7 summarizes the proportion of patients with documented resolution of hyperparathyroidism and hypercalcemia. Data collected was delimited by patients who were lost to follow-up and who were not able to facilitate laboratory tests within the designated follow-up period.

Table 1. Clinical Profile of Patients who Underwent Parathyroidectomy

| | All cases | Primary N=23 (72%) | Secondary N=6 (19%) | Tertiary N=3 (9%) |
|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Mean age at the time of OR | 47 (26-75) ^a | 49 (30-75) ^a | 45 (27-70) ^a | 37 (35-40) ^a |
| Sex | | | | |
| Male | 9 (28%) | 7 (30%) | 1 (17%) | 1 (33%) |
| Female | 23 (72%) | 16 (70%) | 5 (83%) | 2 (67%) |
| Mean duration of symptoms prior to surgery in months | 24 (1-120) ^a | 25 (1-120) ^a | 18 (4-36) ^a | 28 (8-48) ^a |
| Mean time between diagnosis and surgery in months | 8 (1-48) ^a | 7 (1-19) ^a | 4 (2-6) ^a | 25 (1-48) ^a |
| Presentation | | | | |
| Specific: | | | | |
| Nephrolithiasis/Nephrocalcinosis | 6 (19%) | 6 | 0 | 0 |
| Pathologic fracture | 4 (13%) | 2 | 1 | 1 |
| Osteopenia/Osteoporosis | 3 (9%) | 1 | 0 | 2 |
| Suspected brown tumor | 5 (16%) | 3 | 1 | 1 |
| Nonspecific symptoms: | | | | |
| Bone pains | 14 (44%) | 9 | 2 | 3 |
| Generalized weakness | 5 (16%) | 1 | 3 | 1 |
| Abdominal pain | 4 (13%) | 4 | 0 | 0 |
| Nausea vomiting | 3 (9%) | 2 | 1 | 0 |
| Mood changes | 1 (3%) | 1 | 0 | 0 |
| Seizures | 1 (3%) | 0 | 1 | 0 |

^a presented as range**Table 2.** Mean Pre-operative Laboratory Parameters of Patients who Underwent Parathyroidectomy

| | Reference Range | Primary HPT (N= 23) | Secondary HPT (N= 6) | Tertiary HPT (N=3) |
|---|-----------------|-----------------------------------|-----------------------------------|---------------------------------|
| Corrected Serum calcium (mmol/L) | 2.10-2.55 | 3.08 ± 0.42 | 2.67 ± 0.12 | 2.67 ± 0.07 |
| Serum Phosphorus (mmol/L) | 0.81-1.49 | 0.99 ± 0.51 | 2.68 ± 1.24 | 2.77 ± 0.67 |
| Serum Creatinine (mmol/L) | 58-110 | 82.1 ± 38.6 | 640.0 ± 261.1 | 758.0 ± 137.7 |
| iPTH (pg/mL) | 10-65 | 1044.0 (56.4-3604.0) ^a | 528.74 (13.8-1782.3) ^a | 510.9 (27.8-994.0) ^a |

^a presented as range

DISCUSSION

Clinical data from this case series have highlighted that patients with hyperparathyroidism undergo surgery late in the course of the disease process. On average, patients have endured 24 months of symptoms, most commonly bone pains, prior to surgery. The average time between diagnosis and surgery is eight months. None of the patients were asymptomatic.

In developed nations, asymptomatic primary hyperparathyroidism is described as the most common clinical phenotype among patients⁶, with only 15% presenting with overt symptoms⁷. This is attributed to programs for routine serum calcium screening. Our series has bias over symptomatic patients since our population only included patients who underwent surgery. However, in contrast to described rates of surgical treatment in asymptomatic patients at 20-30%, our patients await clinically overt symptoms prior to surgery.⁸

Looking at the presenting symptoms, almost half of the patients suffer from bone pains - which likely represents an undocumented end-organ effect such as osteoporosis, osteopenia or pathologic fractures. A large cohort of early-

diagnosed patients with primary hyperparathyroidism has shown that end-organ effects occur in a median of 3.7 years from diagnosis.⁶ This infers that our patients may have been suffering from a hyperparathyroid state long before the onset of their symptoms and that they seek consultation late in the course of the disease once they already have end-organ effects.

Table 3. Type of Surgeries Done for Hyperparathyroidism

| | For all cases (N=32) |
|--|-------------------------|
| Type of surgery performed | |
| Excision of suspected adenoma | 23 (72%) |
| Subtotal (3 ½ parathyroidectomy) | 6 (19%) |
| Total parathyroidectomy with autotransplantation | 3 (9%) |
| Frozen section (parathyroid lesion) | |
| Performed | 25 (78%) |
| Not performed | 7 (22%) |
| Procedure included | |
| Total thyroidectomy | 13 (41%) |
| Thyroid lobectomy | 7 (22%) |
| No thyroidectomy | 12 (38%) |
| Thymectomy | 3 (9%) |
| Submandibular gland excision | 1 (3%) |

Table 4. Imaging for Preoperative Localization Performed for Hyperparathyroidism

| Imaging Modality | Number of patients (%) |
|------------------|------------------------|
| Neck ultrasound | 17 (53.1%) |
| Sestamibi scan | 27 (84.4%) |
| Neck CT scan | 4 (12.5%) |

Table 5. Frozen Section and Mean OR Time of Parathyroid Surgeries

| | | Cases | mean OR time (min) |
|--|---------|-------|--------------------|
| Surgeries for primary HPT (N=23) | with FS | 17 | 187 |
| | no FS | 6 | 118 |
| Surgeries for secondary/tertiary HPT (N=9) | with FS | 8 | 236 |
| | no FS | 1 | 97 |
| All parathyroid surgeries (N=32) | with FS | 25 | 199 |
| | no FS | 7 | 108 |

Table 6. Mean Pre-operative and Post-operative Laboratory Parameters of Patients who Underwent Parathyroid Surgery

| Mean laboratory values | Reference Range | Primary HPT (pre-op) | Primary HPT (post-op) | Secondary HPT (pre-op) | Secondary HPT (post-op) | Tertiary HPT (pre-op) | Tertiary HPT (post-op) |
|----------------------------------|-----------------|----------------------|-----------------------|------------------------|-------------------------|-----------------------|------------------------|
| Corrected Serum calcium (mmol/L) | 2.10-2.55 | 3.08 | 2.32 | 2.67 | 1.89 | 2.66 | 1.90 |
| Serum Phosphorus (mmol/L) | 0.81-1.49 | 0.99 | 1.04 | 2.68 | 1.29 | 2.77 | 1.23 |
| Serum Creatinine (mmol/L) | 58-110 | 82.1 | 88.78 | 640.0 | 525.67 | 758.0 | 658.50 |
| iPTH (pg/mL) | 10-65 | 1036.0 | 48.43 | 215.4 | 66.76 | 510.9 | 9.40 |

Table 7. Resolution of Hyperparathyroidism and Hypercalcemia among Patients who Underwent Parathyroidectomy

| | Achieved normal intact PTH within D7PO | Achieved normal intact PTH within D30PO | Total |
|---------------------|--|---|------------|
| Primary HPT (N=16) | 14 (87.5%) | 1 (6.3%) | 15 (93.8%) |
| Secondary HPT (N=3) | 2 (66.7%) | 0 | 2 (66.7%) |
| Tertiary HPT (N=2) | 2 (100%) | 0 | 2 (100%) |
| | Hypercalcemia resolved within D7PO | Hypercalcemia resolved within D30PO | |
| Primary HPT (N=21) | 19 (90.4%) | 1 | 20 (95.2%) |
| Secondary HPT (N=6) | 6 (100%) | 0 | 6 (100%) |
| Tertiary HPT (N=3) | 3 (100%) | 0 | 3 (100%) |

The series also included five patients (16% of cases) which presented with a new bony mass (mandible - 3, shoulder - 1, leg - 1). Four of the cases had histopathologic confirmation of giant cell rich lesions typical of brown Tumors. Brown tumors are slow-growing, painful skeletal lesions occurring as a terminal process in the bone remodeling of primary and secondary hyperparathyroid patients. Long standing excessive levels of PTH results in an imbalance in osteoclastic and osteoblastic processes causing these fibrous growths in the skeleton. Modern authors describe osteoclastomas as having almost disappeared for primary hyperparathyroid cases since the 1970s due to early detection and treatment.⁹ Multiple occurrences of suspected brown tumors in our case series is suggestive of late diagnosis and management of our hyperparathyroid patients. Future studies are recommended to investigate and describe osteoclastoma cases secondary to parathyroid pathologies.

In 2016, the American Association of Endocrine Surgeons (AAES) published indications for surgical intervention in primary hyperparathyroidism. Indications for surgery include serum calcium levels 1 mg/dL above normal (11.5 mg/dL or 2.88 in mmol/L) even in asymptomatic patients.⁵ In our series, mean calcium levels were 3.09 mmol/L or 12.3 mg/dL, which is almost 2 mg/dL higher than normal. This implies that we operate on our patients when their serum calcium is markedly elevated and more at risk of hypercalcemia complications.

Unfortunately, even as of writing, our institution is still incapable of doing rapid serum PTH determination which is the recommended modality to confirm localization.¹⁰ Frozen section was alternatively utilized in 78% of cases including primary, secondary, and tertiary cases.

In terms of biochemical outcomes, most of the patients had resolution of their hyperparathyroidism and hypercalcemia within seven days from the OR. One patient documented resolution at one month post-operatively. No morbidities and mortalities were noted within the 30-day follow-up. These results suggest that parathyroid surgery is a safe and effective management strategy to resolve hyperparathyroidism.

In this study, we described our experience in doing surgeries for all forms of hyperparathyroidism. We noted that we operate on our cases late in the course of the disease when patients already have severe hypercalcemia and end-organ effects including cases of brown tumors. The preferred diagnostic modality for localization in our institution was sestamibi scan and neck ultrasonography, both of which demonstrated good agreement with final histopathologic results. Most of our cases included frozen section to confirm the pathologic parathyroid lesion intraoperatively due to unavailable rapid intact PTH.

This study is limited by its single-center design, small sample size, and potential referral bias toward advanced cases, which may restrict external validity and generalizability. A larger local series including several institutions would give a

better picture of our practices in parathyroid surgery. A larger series is also recommended for comparison of diagnostic modalities for localization including ultrasound, parathyroid scintigraphy, and 4D CT scan. Separate studies are also recommended to further investigate our series of Brown tumor cases identified in this paper. Studies looking into outcomes after longer follow-up are also recommended to further evaluate the safety and efficacy of parathyroid surgeries in hyperparathyroidism. Routine screening for serum calcium levels, which is practiced in developed nations, should also be investigated. It can also be recommended in a focused subset of patients with higher risks of developing hyperparathyroidism for early detection and definitive management.

CONCLUSION

Parathyroidectomy is an effective and safe treatment strategy in achieving normal PTH levels among patients with hyperparathyroidism. Patients with hyperparathyroidism in this study underwent surgery late in the course of the disease process. Strategies must be employed to promote earlier diagnosis and subsequent treatment. Further studies with larger population sizes are recommended to investigate the long-term outcomes of operated HPT patients.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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