Original Article

Parathyroid Adenoma: an experience in BIRDEM General Hospital

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Abstract:

Background: Parathyroid adenoma is most commonly associated with primary hyperparathyroidism which leads to hypercalcaemia. Hypercalcaemia results in multiple stone formation in Kidney and biliary tract which indicates surgical removal of tumor. Perioperative management of patient is essential to prevent mortality and morbidity. The purpose of this study is to analyze a case series of patient having parathyroid adenoma with difficulties, to localize the adenoma and to take the measures to maintain the normal level of calcium in pre, per and postoperative period.

Methods: This retrospective study was carried out in BIRDEM General Hospital and Ibrahim Medical College from May 2017 to December 2019. 14 patients who were diagnosed as primary hyperparathyroidism due to parathyroid adenoma who had been managed at the BIRDEM General Hospital, Dhaka, Bangladesh from May 2017 to December 2019 were reviewed and included.

Result: Among 14 patients 8 were female and 6 male (M: F=3:4). Age ranges from 26 to 71 years with mean age was 52 years. Serum PTH were above normal (>65 pg/ml) in all cases. Serum calcium level were above normal in 12 cases (85.71 %) and 2 (14.29%) had normal levels. Serum phosphate levels were within normal range. Excision of adenoma done in all cases which were confirmed by frozen section per-operatively. None of our patients develop any complication during and after surgery.

Conclusion: Successful management of parathyroid adenoma requires combined skills of surgeons, endocrinologists, anesthesiologists and pathologists. Improvement after operation is quite remarkable and rewarding.

Key words: Parathyroid adenoma, Hypercalcaemia, Scintigraphy.

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Introduction:

Parathyroid adenoma is a benign tumour of the parathyroid glands¹. The parathyroid glands are located in the neck, near or attached to the back side of the thyroid gland². The normal parathyroid gland weighs approximately 50-70 mg³. Parathyroid hormone produced by chief cells of parathyroid gland which regulates calcium, phosphate and vitamin D homeostasis⁴.

Primary hyperparathyroidism (PHPT) is a disorder of one or more of the parathyroid glands⁵. It is the third most common endocrine disorder after diabetes mellitus and thyroid disease⁶. The parathyroid gland(s) become overactive and secret excess amounts of parathyroid hormone^{7,8}. As a result blood calcium rises to a level that is higher than normal (called hypercalcaemia)⁹.

The incidence of PHPT is increasing with a rate of 42 in 100,000 per year. While in women over 60 years of age the average annual incidence approaches 190:100,000 per year¹⁰.

Approximately 80 percent of people with primary hyperparathyroidism (PHPT) have few or no symptoms. In this people PHPT is typically diagnosed after an elevated calcium is detected when a blood test is done for some other reason¹¹.

However, there are sometimes nonspecific symptoms that might be related to the elevated calcium level. This includes- Joint aches, fatigue, weakness, loss of appetite, mild depression, difficulty concentrating, excessive thirst, frequent urination, constipation¹².

In majority of the patients parathyroid adenoma are associated with hyper-calcaemia.

Hypercalcaemia is usually managed by 13:

 Intravenous fluids and diuretics-Extremely high calcium can be a medical emergency. Patient needs hospitalization for treatment with intravenous fluid and diuretics to prompt lower the calcium level to prevent arrhythmia or damage to the nervous system. Fluids are usually given 2.5-3 ml/kg/hr (range 4-6 litre/day). And diuretics, usually frusemide, which decreased tubular reabsorption of calcium.

- Bisphosphonates: Intravenous antionsteoporotic drugs, which can quickly lower calcium level, are often used to treat hypercalcaemia due to cancer (risk associated with this treatment include osteonecrosis of the jaw and certain types of thigh fractures).
- Corticosteroid (Prednisolone): If hypercalcaemia is caused by high level of vitamin D, short term use of prednisolone is useful. It decreases the absorption of calcium from gut.
- Calcitonin: Subcutaneous or intravenous, may also be used.

Methods:

Medical records of 14 patients with a diagnosis of parathyroid adenoma who had been managed at the BIRDEM General Hospital, Dhaka, Bangladesh from May 2017 to December 2019 were reviewed and included.

Patient's age, sex, presenting symptoms and duration of these symptoms prior to diagnosis, clinical findings, side and site of the adenoma were noted. Preoperative serum parathyroid hormone, serum calcium and serum phosphate were recorded.

For localizing the tumour^{99m}Tc Sestamibi parathyroid scintigraphy was done preoperatively. Scintigraphy shows the site of the parathyroid adenoma, number and size of the parathyroid adenoma, relation with the thyroid gland which helps the surgeon during surgery.

The operative findings were recorded. Any operative complications (if any) both immediate and delayed were noted.

Preoperative preparations taken:

Commonly associated conditions that were checked and/ or managed preoperatively are: hypercalcaemia, hyperphosphataemia, hypomagnesaemia, electrolytes imbalance, low albumin, low creatinine clearance. The day before surgery the department of Histopathology was informed for frozen section biopsy.

Surgical technique:

Normal level of calcium, acid base balance and electrolytes were ensured.

Scintigraphy of parathyroid adenoma was again reviewed by surgeon before starting the surgery.

Experienced and skilled anesthesiologists were present during surgery to tackle any unwanted situations during surgery like cardiac arrhythmia, heart failure and neurovascular irritability like complications.

Our all the 14 patients were operated under general anesthesia. Cervical collar incision was made. Flap was raised and strap muscles were retracted on the site of parathyroid adenoma. Then the lobe of the thyroid gland was mobilized, recurrent laryngeal nerve was identified on that side. After that parathyroid adenoma was searched and possible tissues were dissected and sent for frozen section.

At the same time blood sample was also collected for intraoperative rapid parathormone measurement for biochemical documentation for successful removal of parathyroid adenoma.

After getting confirmation result of frozen section and intraoperative rapid parathormone level, surgery proceeded and the wound was closed in layers.

Postoperative period:

Post operatively patients might develop hypocalcaemia. So all the patients were monitored closely to observe any features of hypocalcaemia. Monitoring of serum calcium level were also done in the laboratory, initially 4 to 6 hours after surgery then every 12 hourly to avoid severe hypocalcaemia or hungry bone syndrome.

Results:

14 patients with a mean age of 52 were included in the study (Table I). Female sex was dominant (57.1%) (Table II). Among the patients 9 (64.2%) were diabetic and 5 (35.7%) were hypertensive (Table III).

On clinical presentation, most of the patients were asymptomatic hypercalcaemic, and it was 8 (57.1%) in number. Skeletal manifestations constituted in 35.7% (n=5). Osteoporotic changes were present in 21.4% (n=3) and compression fractures were in 14.2% (n=2).

In 35.7% (n=5) patients were associated with renal stone. 7.2% (n=1) patient presented with abdominal pain (chronic pancreatitis). Clinical presentations of the patients are shown in Table IV.

On laboratory investigations, the preoperative calcium level were raised in 12 cases (85.71 %) and 2 (14.29%) had normal levels. The preoperative parathyroid level were above normal (>65 pg/ml) in all cases (100%). Among the patients there were vitamin D deficiency 4 (28.5%), electrolytes imbalances 3 (21.4%) and dyslipidaemia 3 (21.4%) shown in Table V. Vitamin D deficiency and electrolytes imbalances were corrected before surgery.

In all the patients scintigraphic examinations were performed for preoperative localization of adenoma(s) (100%). Variation of location of parathyroid adenoma are shown in Table VI.

Among them 11 (78.6%) patients only underwent parathyroidectomy. And 1 (7.2%) patient underwent parathyroidectomy along with hemithyroidectomy as the parathyroid adenoma was intrathyroidal, 1 (7.2%) patient underwent parathyroidectomy along with partial lobectomy, 1 (7.2%) patient underwent parathyroidectomy along with nodulectomy (Table VII).

Peroperatively parathyroid adenoma was confirmed in every case by frozen section.

Post operatively among the 14 patients 12 (85.7%) needed intravenous calcium supplementation and 2 patients (14.2%) had normal calcium level and didn't need any form of calcium supplementation. Up to 1 year of follow up none of our patients develop any complication.

Table I:
Age distribution of study population (n=14)

Age group in years	Frequency	Percent %
21-30	1	7.14
31-40	1	7.14
41-50	3	21.42
51-60	7	50
61-70	1	7.14
71-80	1	7.14
Total	14	100

Table II:
Sex distribution (n=14)

Sex	Frequency	Percent %
Male	6	42.9%
Female	8	57.1%
Total	14	100%

Table III:
Comorbidities among study subjects (n=14)

Comorbidities	Frequency	Percent %
Type II diabetes	9	64.2%
mellitus		
Hypertension	5	35.7%
Chronic kidney disea	ses 2	14.2%
Renal stone	5	35.7%
Osteoporosis	3	21.4%
Compression fracture	2	14.2%
Chronic pancreatitis	1	7.2%
Dyslipidemia	3	21.4%
Parkinson's diseases	1	7.2%

Table IV:
Clinical presentation of study population (n=14)

Presentation	Number (%)
Asymptomatic hypercalcaemia	8(57.1%)
Diffuse body pain	3(21.4%)
Back pain	3(21.4%)
Abdominal pain	1(7.2%)
Renal stone	5(35.7%)
Fatigue	4(28.5%)
Nausea and vomiting	1(7.2%)

Table V: Important laboratory findings (n=14)

Variable	Values
Hypercalcaemia (>11 mg/dl)	12(85.7%)
Elevated PTH (>65pg/ml)	14(100%)
Vitamin D deficiency (<40ng/ml)	4(28.5%)

Table VI:Location of parathyroid adenoma by scintigraphy in study subjects(n=14)

Laterality	Superior	Inferior
Right	2(14.2%)	5(35.7%)
Left	3(21.4%)	4(28.5%)

Table VII :Operative procedures (n=14)

Surgical approach	Number (%)
Parathyroidectomy	11(78.6%)
Parathyroidectomy+	01(7.2%)
hemithyroidectomy	
Parathyroidectomy+lobectomy	01(7.2%)
Parathyroidectomy+nodulectom	ny 01(7.2%)

Discussion:

This study was done in a single nationally representative tertiary care institution to evaluate trends, presentation, management and outcome in patients with parathyroid adenoma underwent parathyroidectomy.

In case of primary hyperparathyroidism, patients usually are of sixth or seventh decade in contrast to the younger age group¹⁴. In this cohort study, mean age of the patient was 52 (ranges from 26 to 71).

Moreover the prevalence of primary hyperparathyroidism was often observed in female of post-menopausal age (2.1-3.4%)¹⁵. In our study number of female was also predominant.

In our study, clinical presentations, perioperative management and outcome was similar in both male and female. Here majority of the patient was asymptomatic and detected during routine biochemical screening.

Parathyroid tumours are generally not visible or palpable clinically¹⁶. But one of our patients who was very lean and thin, the parathyroid mass was visible on the neck. The other patients had symptomatic presentation including renal compromise and stone, musculoskeletal disorder, gastrointestinal complaints and psychiatric symptoms.

Nephrolithiasis is the most frequent presentation in patient with renal disorder, where as severe bone disorder has been identified in less than 3% of cases¹⁷. In our study presentation of renal and bone disorder was equal 37.5% in each.

Hyperparathyroidism increases bone turn over and reduces mineral density causing osteopenia, osteoporosis and fracture which is the frequent complication in late diagnosed hypercalcaemia¹⁸. Radiologic findings of osteopenia, osteoporosis and fracture were documented in the present study.

In our study, preoperative parathormone levels were above normal in all cases (100%). Preoperative serum calcium level in 12 (85.7%) cases were elevated and in 2 (14.2%) cases were in normal ranges.

The lower levels of vitamin D (in 28.5% cases) in our study also support the hypothesis that vitamin D deficiency might play a role in the pathogenesis of primary hyperparathyroidism¹⁹.

In our study all the patient had done preoperative scintigraphy for localization of adenoma.

There are usually 4 parathyroid glands in human. Two of the glands are usually located on the bottom and the other two are on top of thyroid gland. Generally superior glands are smaller than the inferior glands. Parathyroid adenoma usually developed from one of the lower glands. Very rarely, parathyroid glands may be intrathyroidally localized (less than 2%)²⁰.

In this current study, 64.2% cases parathyroid adenoma originated from lower glands and one cases was intrathyroidal. All patients were suffering from a single parathyroid adenoma.

In our 14 cases, 12 cases were hypercalcaemic preoperatively, they were managed with intravenous fluid and frusemide diuretics.

Intraoperative rapid parathormone measurement has been used in all the cases.

In this method surgeon can be sure that hyperfunctional parathyroid glands are removed. Parathyroid hormone is produced only in the parathyroid glands and the intact parathyroid hormone has half-life of less than 5 minutes. Therefore, blood concentration of parathyroid hormone will rapidly decrease shortly after removal of all over expressing parathyroid tissue²¹.

Alhefdhi et al. showed that parathyroid hormone level decreased by 50% in 96.5% of patients²².

For further confirmation in all the cases intraoperative frozen section were done.

Previously as a surgical technique, bilateral neck exploration was accepted as gold standard. But now-a-days precise preoperative localization of parathyroid adenoma causes minimally invasive surgical procedure.

Only parathyroidectomy has the advantages of shorter operative time, decreased surgical dissection, lower costs, shorter hospital stay and a decreased risk of transient post-operative hypocalcaemia compared with bilateral neck exploration²³.

Transient hypocalcaemia is the most common complication after parathyroid surgery ranges from 5-52% and the most commonly accused condition is hungry bone syndrome^{24,25}. The syndrome has been reported to develop in 13% cases²⁶. In this series, 12 (85.7%) cases developed transient hypocalcaemia and required calcium supplementation. But none of the patient developed hungry bone syndrome.

Recurrence rate of primary hyperparathyroidism is 3-5%²⁷. We have followed up the patients for 1 year after operation, there was no recurrence.

Conclusion:

Parathyroidectomy is the only treatment of parathyroid adenoma. Due to lack of facilities,

skill and limitation of knowledge regarding perioperative management of parathyroidectomized patients, parathyroidectomy is difficult to done in many institutions. A successful parathyroidectomy needs appropriate preoperative evaluation, localization, experienced and skilled surgeon and meticulous surgery. The important limitation of our study was its retrospective nature and the study population was small. However, the incidence of primary hyperparathyroidism is reported to be rare. We believe that our study provides comprehensive data on clinical features of parathyroid adenoma, perioperative management and contributes to valuable reference data.

References:

- Al-Thani H, El-Metbouly M, Al-Sulaiti M. Management and outcomes of hyperparathyroidism: a case series from a single institution over two decades. Therapeutics and Clinical Risk Management 2018;14: 1337-1345.
- Mohamed Mahmoud HG. Clinical presentation and outcome of surgical management of primary hyperparathyroidism: A single centerbased case series in Egypt. J Head Neck Physicians Surg 2017;5: 17-22.
- Topal U, Dalci K, Unal AG. Clinical and surgical approach to parathyroid adenomas: A single-center experience. Annals of Medical Research, 2019; 26(10):2259-65.
- Prihantono P, Palinggi E. Surgical Treatment for Parathyroid Adenoma: A Case Report. Open Access Maced J Med Sci. 2019 Aug 15; 7(15):2497-2501.
- Pierce KA, Willis MS. Hypercalcemiain a 56-Year-Old Female. LABMEDICINE: January 2008 Volume 39 Number 1.

- 6. Udelsman R, Åkerström G. The Surgical Management of Asymptomatic Primary Hyperparathyroidism: Proceedings of the Fourth International Workshop. J Clin Endocrinol Metab, October 2014, 99(10):3595–3606.
- 7. Al-Hassan MS, Mekhaimar M. Giant parathyroid adenoma: a case report and review of the literature. Journal of Medical Case Reports (2019) 13:332
- Wilhelm SM, S.Wang T.The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism. *JAMA* Surg. 2016; 151(10):959-968.
- 9. Parnell KE, Oltmann SC. The surgical management of primary hyperparathyroidism: an updated review. *Int. J. Endo. Oncol.* (2018) 5(1).
- 10. Hindie E, Ugur O. 2009 EANM parathyroid guidelines. Eur j Nucl Med Mollnmaging (2009) 36:1201-1216.
- 11. Khan AA, Hanley DA. Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. A Canadian and international consensus. OsteoporosInt (2017) 28:1–19
- Reiher AE, Mazeh H, Schaefer S, Gould J, Chen H, Sippel RS. Symp-toms of gastroesophageal reflux disease improve after parathyroidec-tomy. *Surgery*. 2012; 152:1232–1237.
- 13. Kunstman JW, Kirsch JD, Mahajan A, Udelsman R (2013) Clinical review: Parathyroid localization and implications for clinical management. J Clin Endocrino IMetab 98:902–12.
- Karateke F. Surgical Approach for Parathyroid Adenoma (Uzmanlýktezi). Adana, Çukurova Üniversitesi 2010.

- 15. McClenaghan F, Qureshi YA. Parathyroid cancer. Gland Surgery. 2015; 4(4):329.
- Bhansali A, Gogate Y. Hyperparathyroidism. Clinical Rounds in Endocrinology. Springer, New Delhi, 2015:309-339.
- 17. Lundgren E, Hagström EG, Lundin J, et al. Primary hyperparathyroid-ism revisited in menopausal women with serum calcium in the upper normal range at population-based screening 8 years ago. *World J Surg.* 2002; 26:931–936.
- 18. R, Mahajan G, Gliwa A. Primary hyperparathyroidism: Skeletal and non skeletal effects, diagnosis and management. Maturitas 2011; 70:246 55.
- Callender GG, Udelsman R. Surgery for primary hyperparathyroidism. *Cancer*. 2014; 120:3602–3616.
- 20. Rossi RL, Cady B: Surgery of Parathyroid Glands, In: Surgery of the Thyroid and Parathyroid Glands. Cady B, Rossi RL (eds), WB Saunders, Philadelphia, 1991. pp: 283-94.
- 21. Gawrychowski J, Bula G. Imaging diagnostics for primary hyperparathyroidism. *Endokrynol Pol.* 2013; 64:404–408.
- 22. Bilezikian JP, Khan AA, Potts JT Jr; Third International Workshop on the Management of Asymptomatic Primary Hyperthyroidism. Guide-lines for the management of asymptomatic primary hyperparathyroid-ism: summary statement from the third international workshop. *J ClinEndocrinolMetab*. 2009; 94(2):335–339.
- 23. Khan A, Bilezikian J, Bone H, et al. Cinacalcet normalizes serum calcium in a double-blind randomized, placebo-

- controlled study in patients with primary hyperparathyroidism with contraindications to surgery. *Eur J Endocrinol*. 2015; 172(5):527–535.
- 24. Alhefdhi A, Pinchot SN, Davis R, et al. The necessity and reliability of intraoperative parathyroid hormone (PTH) testing in patients with mild hyperparathyroidism and PTH levels in the normal range. World J Surg 2011; 35:2006–9.
- 25. Schneider DF, Mazeh H, Sippel RS, Chen H. Is minimally invasive parathyroidectomy associated with

- greater recurrence compared with bilateral exploration? Analysis of more than 1,000 cases. *Surgery* 152(6), 1008–1015 (2012).
- 26. Temiz A, Turgut MS. Clinical, diagnosis, localization studies and treatment in primary hyperparathyroidism. J Harran University Med Facult 2018; 15:40-44.
- 27. 23-Usta A, Alhan E, Cinel A, Turkyilmaz S, Erem C A 20-year study on 190 patients with primary hyperparathyroidism in a developing country: Turkey experience. IntSurg 2015; 100:648–55.