

Original Article

Clinical Profile and Management Outcome of Parathyroid Adenoma - A 7 Years Retrospective Study

Md. Arif Hossain Bhuyan¹, Abu Yusuf Fakir², Md. Nurullah³, Md Abdullah Hil Kafi⁴, Sk. Nurul Fattah Rumi⁵, Md. Sumon Hossain⁶

Abstract

The study aims to present the clinical profile and management outcomes of parathyroid adenoma patients in our institutions. This retrospective study included ten patients with parathyroid adenoma presented to Department of Otolaryngology and Head-Neck Surgery at Dhaka Medical College Hospital and Ibn Sina Medical College Hospital, Dhaka from January 2004 to January 2011. Out of 10 patients, 8 were female. Average age of presentation was 50 years. 6 patients were symptomatic and 4 were asymptomatic. In 8 patients, serum creatinine level was within normal limits and 2 patients had elevated serum creatinine level. All 10 patients had hypercalcaemia and increase parathormone level, from mild to severe. CT guided fine needle aspiration cytology diagnosed 2 cases preoperatively. 6 patients diagnosed with ^{99m}Tc Sestamibi scan and 3 patients diagnosed by single photon emission computed tomography (SPECT-CT) dual isotope (I-123/^{99m}Tc-MIBI) subtraction for imaging parathyroid adenoma. All the patients underwent parathyroidectomy except for 1 patient in whom hemithyroidectomy was done. Postoperative period was not without complications but has been managed with strong monitoring. Long term follow up was done up to 1 year with 100% cure rate.

Key Words: *Hypercalcaemia, hyperparathyroidism, parathyroid adenoma, parathyroidectomy.*

1. Associate Professor, Department of Otolaryngology and Head-Neck Surgery, Ibn Sina Medical College, Dhaka.
2. Professor, Department of Otolaryngology and Head-Neck Surgery, Dhaka Medical College, Dhaka.
3. Assistant Professor, Department of Anaesthesia, Ibn Sina Medical College, Dhaka
4. Professor, Department of Otolaryngology and Head-Neck Surgery, Ibn Sina Medical College, Dhaka.
5. Associate Professor, Department of Otolaryngology and Head-Neck Surgery, Dhaka Medical College, Dhaka.
6. Registrar, Department of Otolaryngology and Head-Neck Surgery, Ibn Sina Medical College, Dhaka.

Address of correspondence: Dr. Md. Arif Hossain Bhuyan, Associate Professor, Department of Otolaryngology and Head-Neck Surgery, Ibn Sina Medical College, Dhaka.

Introduction

Rationale of the study: Parathyroid adenoma is not a common disease. Its diagnosis is often missed. In many cases, patients are unaware of the tumours. Proper diagnosis and preoperative localization is necessary. Primary hyperparathyroidism due to parathyroid adenoma has an adverse effect on long term mortality. Patient with parathyroid adenoma gets benefit symptomatically, metabolically and from a survival point of view after a successful parathyroidectomy. Surgery should be done by an experienced surgeon as it results in excellent cure rate. Postoperative period is not without complications. Strong monitoring is required. Long time follow up of the same is necessary.

Parathyroid adenoma is a benign tumour of the parathyroid glands and most common disorder of the gland¹. The gland increases in size and produces parathormone in excess. This is called primary hyperparathyroidism. The parathyroid glands in the neck help control calcium use and removal by the body. They do this by producing parathormone. Parathormone helps control calcium, phosphorus and vitamin D levels within the blood and bone². The elevated parathormone levels result in hypercalcaemia and hypophosphataemia. The majority of cases of primary hyperparathyroidism (80%) are due to a single adenoma³. In approximately 15% of cases, the disease is due to multiple gland hyperplasia and double adenomas account for about 2-5% of cases³. Parathyroid carcinoma is rare and accounts for less than 1% of patients with primary hyperparathyroidism³. Radiotherapy to head and neck during childhood can predispose to either adenoma or hyperplasia⁴. The majority of patients with primary hyperparathyroidism have no symptoms or only mild symptoms and are picked up on biochemical screening for another reason. Although the classic presentation of 'stones, bones, moans and abdominal groans' is often quoted, many patients have mild symptoms or are asymptomatic. Its frequency increases with age and it is more common in females⁵. Symptoms widely varies. The longer one has hyperparathyroidism, the more symptoms he will develop. The diagnosis of primary hyperparathyroidism can be accurately made in the presence of an elevated serum calcium and parathormone level. Occasionally, it may be difficult to identify milder form of primary hyperparathyroidism, as parathormone is not released at an even rate, so repeated measurements of serum parathormone and calcium may be required to make a biochemical diagnosis⁶.

A positive family history of hypercalcaemia should raise the suspicion of hereditary hyperparathyroidism and multiple endocrine neoplasia (MEN) syndrome. When presented with familial hyperparathyroidism, other endocrine neoplasms (especially a phaeochromocytoma) associated with multiple endocrine neoplasia syndrome need to be excluded. The common biochemical tests performed are plasma calcium, albumin, vitamin D and parathormone. Complementary tests that may be helpful to support the diagnosis are plasma phosphate, creatinine and magnesium. Preoperative localization of parathyroid tumours can locate abnormal glands in 80- 85% of cases⁷. High resolution ultrasound and ^{99m}Tc-sestamibi scan are very helpful. CT and MRI are required for preoperative localization of the tumour. Ultrasound is cheap, non-invasive and can only be used to locate adenomas in the neck, with a sensitivity of around 85% in the unexplored neck, dropping to 40% in patients who have had a previous exploration⁸. SPECT (single photon emission computerized tomography) scan can detect 87% of solitary adenomas, 55% of abnormal glands in patients with multiglandular disease and 75% of persistent or recurrent lesions in the previously explored neck⁹. Diffuse hyperplasia will often lead to negative scan as the parathyroid glands are less mitochondria-rich¹⁰. PET (positron emission tomography) scan is clinically useful in highly preselected patients with recurrent primary hyperparathyroidism with a sensitivity of 83% and specificity of 100%. All patients with parathyroid adenoma should have parathyroidectomy.

Opinions differ as to the correct management of patients without symptoms. The National Institute of Health (NIH) Consensus Development Conference held in 1990 provided some guidelines. Patients with

calcium level above 3.00 mmol/L should have parathyroidectomy with or without symptoms. Patients with mild hyperparathyroidism (calcium 2.85- 3.00 mmol/L) should have surgery if any of the following criteria are fulfilled¹¹:

- Creatinine clearance reduced by at least 30%.
- Urine calcium excretion above 400 mg/ 24 hours.
- Age below 50 years.
- Recent history of kidney stone.
- Apparent neuromuscular or psychiatric symptoms.

The treatment of parathyroid adenoma is surgery. Prior to the surgery, the medical treatment of hypercalcaemia will depend on its severity. Mild (<3.0 mmol/L) to moderate (3-3.5 mmol/L) hypercalcaemia can generally be managed on an outpatient basis, whereas severe (>3.5 mol/L) hypercalcaemia requires more vigorous inpatient treatment. Acute treatment of hypercalcaemia includes rehydration with intravenous normal saline, diuretics and the use of biphosphanates intravenously. Longer treatment requires maintenance of adequate hydration, a low calcium diet, oral biphosphanates and parathyroidectomy. Many patients will require post-operative calcium and vitamin D supplementation until the suppressed glands recover their function.

Objectives

1. To determine clinical profile of patients diagnosed with parathyroid adenoma.
2. To determine the clinical outcome of patients within one year of parathyroidectomy including early and late postoperative complications.
3. Whether calcium supplement should be given after parathyroidectomy.

4. To present the indications for parathyroidectomy in our hospitals.

Materials and Methods

This is a retrospective and descriptive study which included ten patients with parathyroid adenoma presented to Dhaka Medical college Hospital and Ibn Sina Medical college Hospital from January 2004 to January 2011. Data has been collected from the patient's case history files. So it is a study based on document review. Out of 10 patients, 8 were female and average age was 50 years. We have divided the patients into symptomatic and asymptomatic group. The data of each patient included age, sex, presenting symptoms and signs, preoperative investigations, operation notes, histopathological examination, complications, postoperative biochemical studies and state at follow up. Collected data were tabulated. Diagnosis was confirmed by post-surgical histopathology. Follow up was done up to 1 year postoperatively. Other investigations done as routine pre-requisite for operation. The study did not include patients who underwent repeat parathyroidectomy or histopathological examination reported other than parathyroid adenoma.

Results

From January 2004 to January 2011, total ten patients diagnosed as parathyroid adenoma on final histopathology after operation. Table I shows that out of 10 patients, 8(80%) were female. Average age was 50 years. In the symptomatic group, patients were comparatively younger (Average 42 years) than asymptomatic group (Average 55 years). Table II shows that 6(60%) out of 10 patients were symptomatic and 4(40%) were asymptomatic. In the symptomatic group, presentations were muscle cramps, recurrent headache, hypertension, polydypsia, nausea, vomiting, kidney stone, bone fracture and psychiatric symptoms(Table III).

Table I
Male, Female ratio N= 10

Sex	Number (%)
Male	2/10(20%)
Female	8/10(80%)

Table II
Clinical presentation N= 10

	Number (%)
Asymptomatic	4/10(40%)
Symptomatic	6/10(60%)

Table III
Presenting symptoms and sign N = 6

	Number of patients
Muscle cramps	5(83.3%)
Recurrent headache	3(50%)
Hypertension	3(50%)
Polydypsia	2(33.3%)
Nausea and vomiting	2(33.3%)
Kidney stone	2(33.3%)
Bone fracture	1(16.6%)
Psychiatric symptoms	1(16.6%)

More than one symptoms and/or signs were present in a patient.

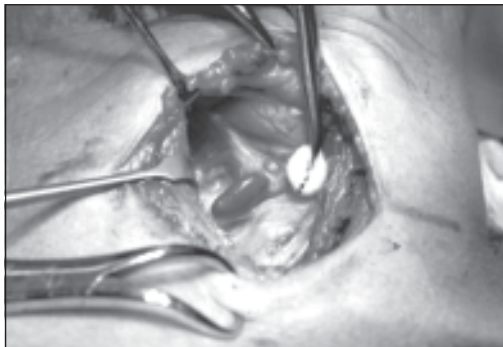


Fig.-1: *Per-operative view of parathyroidectomy*

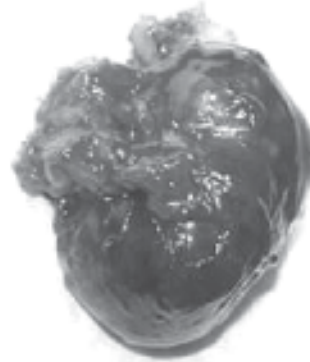


Fig.-2: *Post-operative specimen of parathyroidectomy*

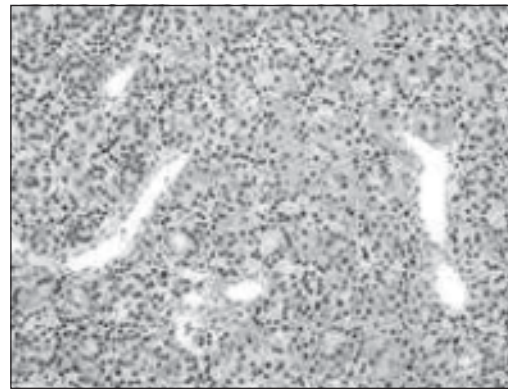


Fig.-3: *Histopathological picture of parathyroid adenoma*

In 8 patients, serum creatinine level was within normal limit, 1-1.2 mmol/L. On the other hand, 2 patients had elevated serum creatinine level of 2.4 – 4.8mmol/L. These 2 patients had severe hypercalcaemia simultaneously. All 10 patients had hypercalcaemia varying from mild to severe. In the symptomatic group average of serum calcium was 2 ± 0.5 mmol/L, but in the asymptomatic group, it was 1.8 ± 0.3 mmol/L (Table IV). In all patients serum parathormone level was above the normal limits. High parathormone levels were noted in the symptomatic group as compared to asymptomatic group. CT guided fine needle

aspiration cytology was done in 6 patients. 2 were diagnosed as parathyroid adenoma.

Table IV

Preoperative serum calcium level

	Serum calcium level
Symptomatic group	2 ± 0.5 mmol/L
Asymptomatic group	1.8 ± 0.3 mmol/L

Preoperative parathyroid scan was done in all patients. Table V shows that, 6 patients diagnosed with ^{99m}Tc Sestamibi scan. 3 patients diagnosed by single photon emission computed tomography (SPECT CT) dual isotope (I-123/^{99m}Tc-MIBI) subtraction for imaging parathyroid adenoma. One patient was diagnosed as parathyroid adenoma after routine histopathological examination. In this case there was high calcium and parathormone level but scan failed to identify the same. It was diagnosed as parathyroid adenoma on frozen section biopsy. Except for 2 cases, others were diagnosed on the operation table on frozen section biopsy. Ultrasound of the neck and either CT scan or MRI of the neck were done in 6 patients as routine pre-operative localization. Table VI shows that, out of 4 asymptomatic patients, one fit the criteria for the age of less than 50 years. All the patients satisfied the criteria for elevated serum calcium level more than 1 gm/dl from normal level. 2 out of 4 patients satisfied two out of four criteria for parathyroidectomy in asymptomatic patients.

Table V

Neck imaging studies

	Number of patients
^{99m} Tc Sestamibi scan	6
SPECT CT scan	3
Ultrasound of the neck	6
CT/ MRI of the neck	6

More than one imaging studies were done in a patient.

Table VI

Indications for parathyroidectomy in asymptomatic patients National Institute of Health (NIH) criteria N= 4

	Number of patients
Age less than 50 years	¼
Creatinine clearance	2/4
Bone mineral density	0/4
Serum calcium(more than 1 gm/dl than normal level)	4/4

Table VII shows that 9 patients underwent unilateral parathyroidectomy and 1 underwent hemithyroidectomy that was diagnosed as parathyroid adenoma after routine histopathological examination. Figure 1 shows preoperative parathyroidectomy in a patient and figure 2 shows postoperative specimen of the same. All 10 cases were diagnosed as parathyroid adenoma after routine histopathological examination. Figure 3 shows microscopic picture of a patient with parathyroid adenoma. In postoperative period, 8 patients (80%) developed hypocalcaemia (Table VIII). There was marked decrease of parathormone level from as high as 2490 pg/ml (preoperative value) to as low as 30 pg/ml (postoperative value). In all patients there was decrease of parathormone level at least 60% postoperatively (Table VIII). Complications of hypocalcaemia were strongly monitored by us in all postoperative patients. In the first postoperative day, 3 patients developed circumoral numbness. On the 2nd to 3rd postoperative day, 5 patients developed carpopedal spasm (Table IX). All the patients were managed with injectable calcium gluconate. Average stay of patients postoperatively in the hospital was 5 days.

Ultimately all the patients were discharged with oral calcium and calcitriol. Follow up was done 1 week, 1 month, 3 months, 6 months and 1 year after discharge. All patients came for follow up 1 year after surgery and had normal calcium and parathormone level.

Table VII
Surgical procedure N= 10

	Number of patients
Unilateral parathyroidectomy	9/10(90%)
Hemithyroidectomy	1/10(10%)

Table VIII
Postoperative Follow-up N= 10

	Number of patients
Hypocalcaemia	8/10(100%)
Decrease of parathormone	10/10(100%)

Table IX
Symptoms of Hypocalcaemia in postoperative patient N= 8

	Number of patients
Circumoral numbness	3/8(37.5%)
Carpopedal spasm	5/8(62.5%)

Discussion

Majority of patients in our study were female. Bailey BJ showed, parathyroid adenoma is three times more common in female than male¹². Same study shows peak incidence occurs in 5th and 6th decade and it rarely occurs below 15 years of age¹². Our study shows the same result. In our study, we have divided patients into symptomatic and asymptomatic group. In the symptomatic group, patients were comparatively younger (Average 42 years) than asymptomatic group (Average 55 years), but Mittendorf EA observed opposite result in his study¹³. In a study by Wilkinson, Leight et al of

management of primary Hyperparathyroid disease, they showed parathyroid adenoma occurs more frequently in patients exposed to neck radiation⁷. In our series, none had history of irradiation.

Presentation of parathyroid adenoma widely varies. It ranges from asymptomatic to wide range of symptoms. Hyperparathyroidism may be asymptomatic and is detected only on further work-up of patients with hypercalcaemia⁴. In our study clinical presentation also widely varies. Preoperative investigations, both biochemical and imaging studies are very important for diagnosis and to treat the case. Biochemical tests include serum calcium, serum parathormone, serum electrolytes and serum creatinine. In a study by Reber PM in 1995, it was shown that all parathyroid adenoma patients had hypercalcaemia and increase parathormone level¹⁰. High parathormone levels were noted in the symptomatic group as compared to asymptomatic group¹⁰. Our study shows the same result. All of our 10 patients had hypercalcaemia preoperatively varying from mild to severe.

CT guided fine needle aspiration cytology is worth doing as it may on rare occasion diagnose the case⁸. In our study CT guided fine needle aspiration cytology was done in 6 cases and 2 were diagnosed as parathyroid adenoma. Parathyroid scan is necessary for focused approach. With recent advances in the field of imaging technique particularly parathyroid scans, none of them had to undergo repeat parathyroidectomy⁷. In our series, preoperative parathyroid scan was done in all patients. Except for 1 case others were diagnosed by ^{99m}Tc Sestamibi scan and single photon emission computed tomography (SPECT CT) dual isotope (I-123/^{99m}Tc-MIBI) subtraction for imaging parathyroid adenoma. Computerized tomography (CT scan) and Magnetic

resonance imaging (MRI) may be useful for parathyroid localization in selected cases⁶. In our study CT scan or MRI were done in 6 patients for preoperative localization. Frozen section selectively used to confirm parathyroid tissue³. In our series, we have done frozen section biopsy in 8 cases on operation table and all were diagnosed as parathyroid adenoma. Intraoperative sestamibi probe is useful for localizing parathyroid adenomas by using a probe which detects a radioactive molecule administered preoperatively that accumulates in the parathyroid adenoma¹⁴. Probe-guided surgery may be more useful in reoperative cases of missed adenomas, recurrent disease or ectopic glands¹⁴. In our study we have not done any probe-guided surgery. Cryopreservation of parathyroid tissue in some cases is beneficial to save some parathyroid tissue that was removed in order that it may be utilized in the future if a patient's parathyroid function is found to be too low following surgery. Tissue may be frozen and stored for an individual patient and can be used at a later date if necessary¹⁴. We have not preserved any tissue in our study.

According to the National Institution of Health (NIH) guidelines¹¹ for parathyroidectomy for asymptomatic patients, most of our patients met one to two criteria, which were serum creatinine levels above 1 mg/dl and reduction in creatinine clearance. One patient aged 32 years, satisfied the age criteria, which is less than 50 years. In all asymptomatic patients, bone mineral densitometry (BMD) was normal.

Immediate postoperative (following parathyroidectomy) hypocalcaemia is desirable¹⁵. Development of hypocalcaemia could be secondary to surgical manipulation of the opposite parathyroid gland or suppressed parathormone from normal gland due to hyper secretion of the diseased

gland¹⁵. Development of hypocalcaemia after parathyroidectomy though expected should be closely monitored for early intervention. In our study, eighty percent of our patient had already experienced symptoms of hypocalcaemia before adequate management was given. It was observed in our study that the drop in ionized calcium levels were noted most often on the 2nd and 3rd postoperative day. Similar result has been observed in other studies^{12,13}.

Postoperative fall of parathormone is an operative success¹⁵. In the present series, there was marked decrease of parathormone level from as high as 2490 pg/ml (preoperative value) to as low as 30 pg/ml (postoperative value). In all patients there was decrease of parathormone level at least 60% postoperatively. Hypercalcaemia in postoperative period is an operative failure¹⁵. None of our patient developed hypercalcaemia at one year of follow up. In the present study, we can infer that our patients had 100% cure rate.

Acknowledgement

Department of ENT and Head-Neck surgery, Ibn Sina Medical College and Dhaka Medical College have sponsored the study. We acknowledge the help extended by all the staff of the said departments as well as our patients for their active participation.

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