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# The Surgical Management of Primary Hyperparathyroidism: The Experience in Tikur Anbessa Specialized Tertiary Referral and Teaching Hospital, Addis Ababa, Ethiopia

**Sahilu Wondimu[1], Berhanu Nega[2]**
[1]General and HPB surgeon, Assistant professor of Surgery, Addis Ababa University School of Medicine, Addis Ababa Ethiopia, E-mail: sahlu.wondimu@gmail.com
[2]Associate Prof of surgery, Consultant General and cardiothoracic surgeon, E-mail: b_nega@yahoo.com

***Primary hyperparathyroidism is an endocrine disorder characterized by excessive and inappropriate release of Parathormone (PTH) from parathyroid glands resulting in diverse clinical manifestations involving the skeletal system in the form of bone and joint pains and pathological fractures, the gastrointestinal system in the form of dyspepsia from Peptic ulcer disease and pancreatitis, nephrolithiasis and other neuropsychiatric and nonspecific symptoms. There is nothing known about the epidemiology of this condition in our country and experience in Para-thyroidectomy is very limited. In the biggest tertiary referral and teaching hospital in the country, only seven cases have been seen and treated over a period of seven years from 2007-2014 and only three had complete medical documents. We therefore present these three cases in detail and review the available literature in the management of primary hyperparathyroidism.***

**Key words:** Primary hyperparathyroidism, hungry bone disease, parathyroid adenoma
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## Introduction

Primary Hyperparathyroidism is an endocrine disorder of the parathyroid glands resulting in excessive and sustained release of Parathormone (PTH) with an overall effect of elevated serum calcium level in the majority of patients. The clinical manifestation is protean and involves a number of organs and systems and includes bone and joint pains, pathological fractures, renal stones, Peptic ulcer disease, pancreatitis, neuropsychiatric symptoms like depression, polyuria, polydipsia and other nonspecific manifestations. The most common cause is solitary adenoma of the parathyroid gland but may also be occasionally caused by double adenomas, hyperplasia or carcinoma. It is commonly seen in females and diagnosis is confirmed by determination of serum PTH and calcium levels. The lesion is localized by Ultrasound and/or Sestamibi scan and Para thyroidectomy is curative.

No literature is available describing the state of primary hyperparathyroidism in our country and the surgical experience in Para thyroidectomy is very limited. In the country's biggest tertiary referral and teaching hospital only seven cases had been diagnosed and treated over a period of seven years from 2007-2014. According to the Operation theatre registration book, four were males and the rest three were females and the age ranges from 16-59. Unfortunately the complete medical file could be retrieved only for three of these cases and we therefore present each of them in detail and review the available literature on the current surgical management of primary hyperparathyroidism.

## Case 1:

A 30 year old female patient presented with generalized bone and joint pain of 4 years duration which initially began around the knee and ankles of the lower extremities but later involved the upper extremities as well. She also complained of back pain, generalized weakness, epigastric burning pain with occasional vomiting and excessive thirst. She could walk only with the help of crutches until 4 months prior to admission where she couldn't move at all and confined to bed. She denied history of fever and swelling of any of her joints. Physical examination revealed a chronically sick, cachectic patient with normal vital signs and an enlarged right lobe of the thyroid gland. She had limitation of movement of the right hip joint with fixed flexed deformity of the left knee joint. Laboratory investigations revealed, normal Haemogram, elevated calcium, low phosphorus, significantly elevated alkaline phosphatase level and normal albumin (Table.1). Serum PTH level has not been determined. Plane x-rays of the skull (Figure 1), both hands and pelvis showed generalized osteoporosis and pathological fracture of the inferior ramus of the pubic bone on the right side (Figure 2). Ultrasound of the neck revealed a well-defined 1.8 cm by 2.4cm hypo-echoic mass on the right side of the neck medial to carotid artery and

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poster inferior to the right lobe of the thyroid possible parathyroid mass (Figure 3). FNAC of the enlarged right lobe of the thyroid gland was suggestive of follicular neoplasm.

**Table 1.** Summary of Pre- and post-operative Relevant Laboratory Results

| Date | calcium | phosphorus | Alkaline phosphatase |
|---|---|---|---|
| **Preoperative- 25/5/2007** | 13.1(8.4-10.2 mg/dl) | 2.4 (2.5-5mg/dl) | 2174(32-92IU/dl) |
| **25/7/2007** | 12.1 | | 1494 |
| **14/12/2007** | 15.2 | | |
| **Post-operative- 10/1/2008** | 6.6 | | |
| **7/2/2008** | 6.3 | | |
| **1/8/2008** | 7.1 | | |
| **21/9/2008** | 8.6 | | |

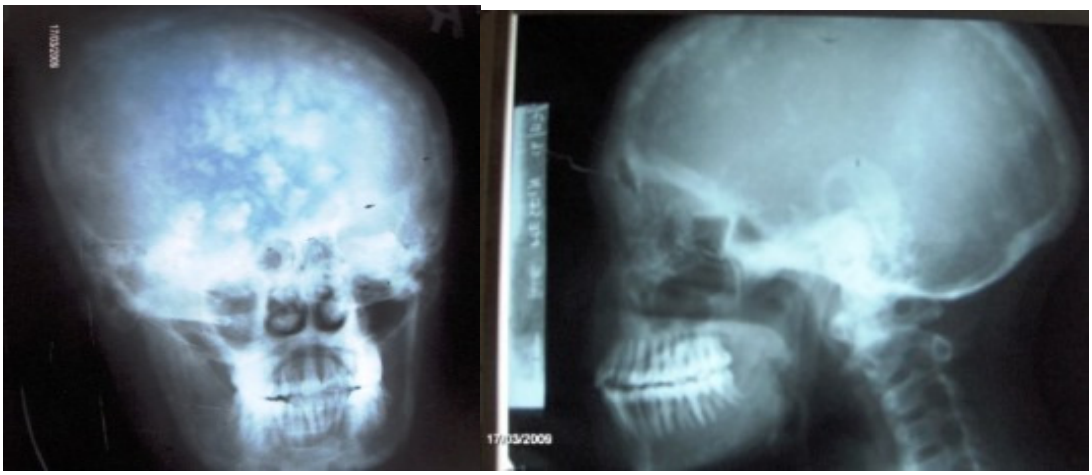

**Figure 1**. Plane x-rays of the skull (AP and Lateral views)

With an impression of metabolic bone disease secondary to primary hyperparathyroidism, she was prepared and operated. Intraoperative findings were enlarged right and left inferior parathyroid glands with normal superior glands. The right lobe of the thyroid was also found to be enlarged and nodular. The enlarged inferior parathyroid glands and the right lobe of the thyroid gland were resected out. Operation time was 100 minutes.

The post-operative course was smooth and the patient was put on IV calcium gluconate which were later changed to oral form and given for several weeks. Post-operative serum calcium level was low but gradually increased to approach normal level. Bone pain significantly improved and patient was instructed to exercise her joints and gradually did better. She was discharged after 96 days of stay in the hospital.

**Biopsy**: ***Gross*** *–two nodular specimen of size 3x1.5x1 cm and 1.5x0.8x0.7 cm respectively which are yellowish brown, indistinctly nodular seemingly capsulated with smooth surface. There was a distinct 0.5 cm sized whitish node in the larger gland.*

***Microsxopy:*** *lobulated and nodular glandular and epithelial elements with clear cells having granular eosinophilic cytoplasm, small round nuclei arranged in clusters and wide thin walled blood vessels*

***Index:*** *chief cell hyperplasia of the inferior parathyroid glands with oxyphilic adenoma on the bigger hyperplastic right inferior parathyroid gland. No evidence of malignancy on the right lobe of thyroid gland.*

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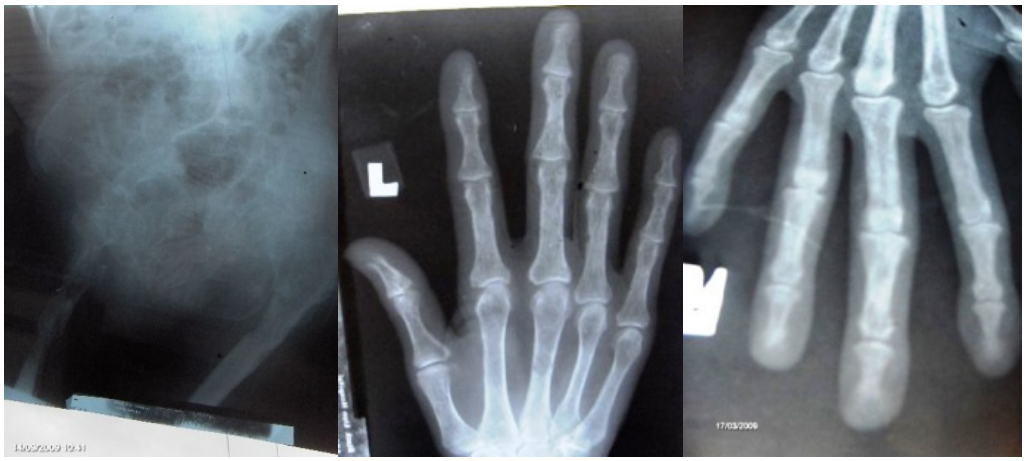

**Figure 2.** X-rays both hands and pelvis with Generalized Osteoporosis and Pathological Fracture of Inferior Ramus of the Right Pubic Bone

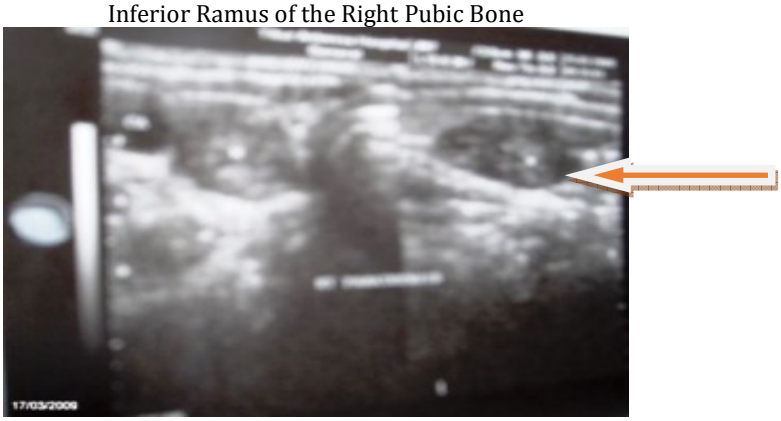

**Figure 3.** Ultrasound of the Neck

## Case 2

A 28 yr old female patient presented with progressively worsening pain in the region of the right hip joint of 3 months duration associated with generalized body weakness. A year prior to her present complaint, she sustained fall down accident to her left hip for which partial hip replacement had been done abroad. She denied any other symptoms and any known medical illness. Physical examination revealed tenderness and limitation of movement of the right hip joint with no swelling and sign of acute inflammation. Laboratory investigations indicated a normal Haemogram, renal, thyroid, and liver function tests except a significantly elevated alkaline phosphatase, highly elevated serum PTH level with normal serum calcium (Table 2).

**Table 2.** Summary of Pre- and post-operative Relevant Laboratory Results

| Date | calcium | ALP | PTH |
|---|---|---|---|
| **Preop 19/3/2009** | 10.4mg/dl( 8.4-10.2) | 2000IU/L (64-306) | |
| **16/2/2009** | 9.6mg/dl (8.9-11.0) | 1107IU/L (0-483) | |
| **25/3/09** | | | 1060pg/ml (14-72) |
| **Post op 2/4/09** | 3.55mg/dl(4.5-5.6mg/dl ionized | | |
| **23/4/09** | 11mg/dl(8.9-1mg/dl) | | |

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Plane x-ray of both hands showed generalized osteoporosis with sub periosteal erosion and CT scan of the lower extremities indicated multiple lytic lesions on the femurs tibia (Figure 4) and pelvic bones with no pathological fracture and a replaced prosthetic left hip (Figure 5). Ultrasound of neck was consistent with normal thyroid gland and a 1.9x1.6cm sized hypo echoic lesion in the region of projection of the right parathyroid gland.With an impression of metabolic bone disease secondary to primary hyperparathyroidism she was prepared and operated on. Neck exploration revealed enlarged right inferior and superior parathyroid glands with normal left parathyroid and thyroid gland. Resection of both right parathyroids was done.

***Biopsy Report:*** *Gross: two yellow brown nodular masses of size 2.5x1.5x0.5 cm and2x1.5x1cm*
*Mic: proliferation of chief cells arranged in cords and solid sheets with no features of malignancy*
*Index: parathyroid Adenoma*

Her post-operative course was smooth except few episodes of hypocalcemic tetany during the first 5 post-operative days that was successfully treated with IV calcium gluconate which was later changed to oral calcium that the patient took for some weeks. Her symptom significantly improved and she was discharged well.

**Case: 3**

A 30 yr old male patient presented with bilateral hip and lower extremity pain of nine months duration.The pain was constant and dull aching in type and severe enough to limit his movement and confine him to bed. He also complained of bilateral flank pain and reddish discoloration of the urine, generalized weakness, anorexia and significant weight loss. He didn't have history of swelling in the joints and denied history of polydipsia and polyuria. Physical examination revealed a chronically sick and cachectic patient with normal vital signs and mild limitation of movement of both hip joints.

Laboratory investigation is consistent with mild anemia (Hct-27.2%), Elevated creatinin (2.5mg %), Elevated Ionized calcium 2.07mmol/l (0.62-1.54 mmol/l), significantly elevated alkaline phosphatase (2930IU/l),highly elevated PTH level of 2620pg/ml(14-20 Pg/ml)(Table 3), ultrasound of the abdomen showed bilateral renal stones, ultrasound of the neck showed 2.3x2.0cm hypo echoic solid mass in the projection of the right parathyroid gland with normal thyroid gland, plane x-ray of the hands showed generalized osteoporosis, saucerisation of the cortices of phalangeal bones with areas of lytic changes and tuft resorption ,CXR revealed multiple pathological fracture of the ribs with resorption of the distal end of the clavicle and generalized osteoporosis (Figure 6), lumbosacral x-ray showed bilateral renal stones (Figure 6) with generalized osteoporosis and multiple lytic expansile lesions in the iliac bones and proximal femur (Figure 6) .

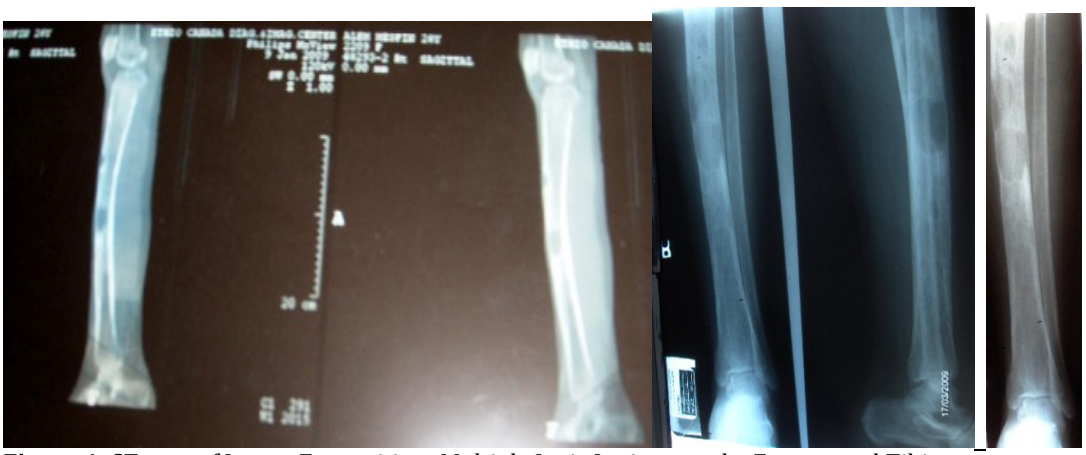

**Figure 4.** CT scan of Lower Extremities: Multiple Lytic Lesions on the Femurs and Tibia

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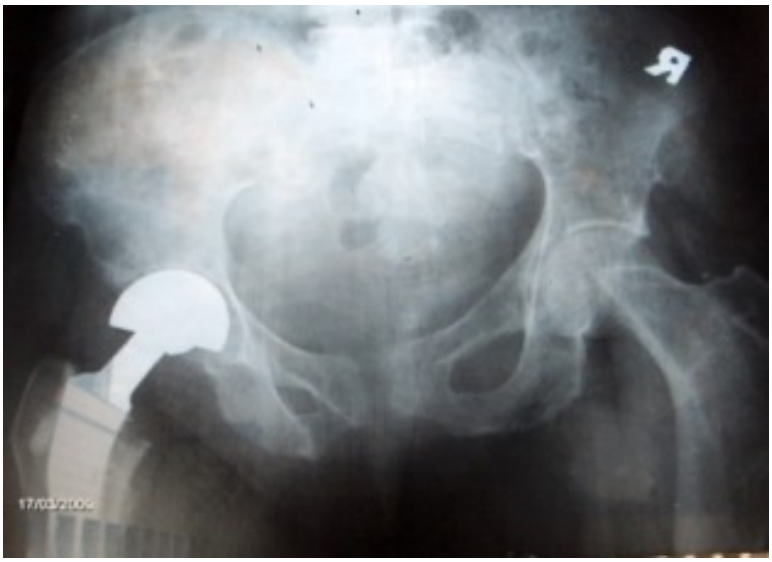

**Figure 5.** Pelvic Bones with no pathological Fracture and a Replaced Prosthetic Left Hip

With an impression of metabolic bone disease secondary to primary hyperparathyroidism, he was prepared and operated. Neck exploration revealed enlarged right superior parathyroid gland with the rest three being normal, no lymphadenopathy and normal thyroid. Excision of the enlarged right superior parathyroid gland was done (Figure 7).

***Biopsy Report: Gross -*** *Grey brown nodular, encapsulated 4x3x2cm single tissue fragment weighing12gm*

***Microscopy –****Round to polygonal cells with eosinophilia cytoplasm that is water clear peripherally, hyper chromatic granular nuclei and prominent nucleoli arranged in cords and tubules and surrounded by thick fibrous capsule, with areas of calcification hemorrhage and cystic spaces. The overall finding is consistent with parathyroid adenoma.*

The patient had uneventful post-operative course with calcium supplementation and discharged improved with a hospital stay of 56days.

**Table 3.** Summary of pre- and post-operative relevant lab results

| Date | Calcium | ALP | Creatinin | PTH |
|---|---|---|---|---|
| **Preop - 9/3/08** | | | 2.5mg/dl(0.7-1.4) | |
| **30/4/08** | | | | 2620pg/ml (14-72) |
| **10/5/08** | | | 1.7mg/dl(0.7-1.4) | |
| **16/5/08** | 8.5mg/dl(8.8-10.2) | | | |
| **20/5/08** | 10.4mg/dl(8.9-11) | | | |
| **14/6/08** | | 2930IU/l(0-483) | | |
| **Postop-27/6/08** | 2.07mmol/l(0.621.54) | | | |
| **30/6/08** | 8.6mg/dl (8.9-11) | 554IU/l(0-483) | | |
| **14/7/08** | | | 1.5mg/dl(0.7-1.4) | |

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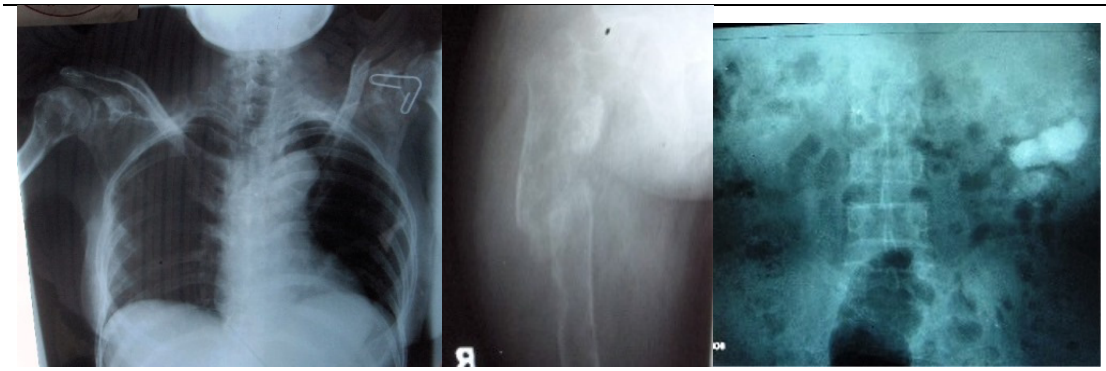

**Figure 6.** CXR with multiple pathological fracture of the ribs with resorption of the distal end of the clavicle and generalized osteoporosis Lumbosacral x-ray showed bilateral renal stones with generalized osteoporosis and multiple lytic expansile lesions in the iliac bones and proximal femur

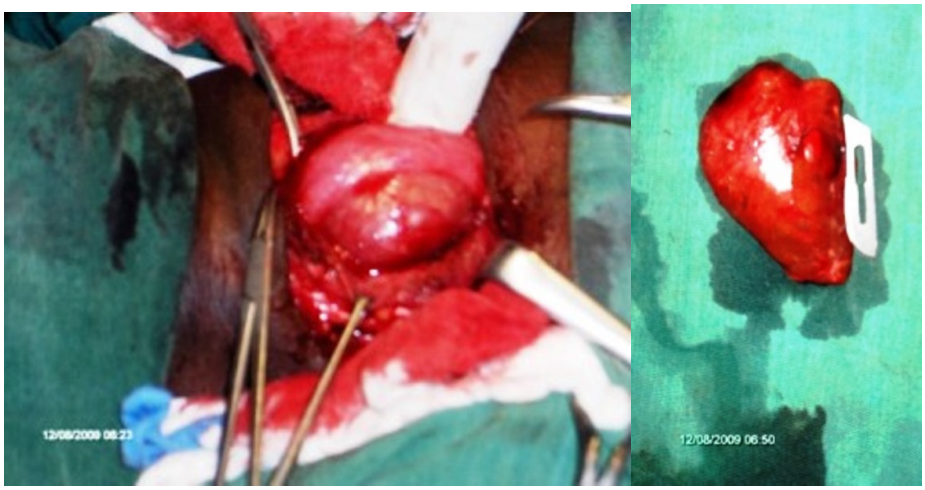


**Figure 7.**

## Discussion

Primary hyperparathyroidism is an endocrine disorder characterized by excessive and inappropriate release of Parathormone (PTH) from parathyroid glands resulting in diverse clinical manifestations involving the skeletal system in the form of bone and joint pains and pathological fractures, the gastrointestinal system in the form of dyspepsia from PUD and pancreatitis, nephrolithiasis and other neuropsychiatric and nonspecific symptoms. Truly asymptomatic cases of primary hyperparathyroidism have been described mainly in developed countries like Canada and it is usually detected during screening by serum calcium measurement[5]. It is commonly seen in females with a F:M of 2-3:1 [1, 8].

All our patients presented with advanced skeletal involvement as was also reported from Pakistan [2] and India [8] and unlike what is described in the literature [1, 2, 8]. Four (57%) out of 7 of our patients were males.

The most common cause is a solitary adenoma involving one of the four glands usually the right inferior but may also be caused by double adenomas, hyperplasia and rarely carcinoma. Of the seven cases we operated on, two had double adenomas and one had three adenomatous parathyroid gland. Diagnosis requires a high index of suspicion based on clinical evaluation and demonstration of elevated serum levels of PTH along with raised or occasionally normal serum calcium level. The most commonly used localization studies are ultrasound of the neck with a sensitivity of 65%, Technetium- 99 Sestamibi scan with a sensitivity of 80% alone or in combination increasing the sensitivity to 96% [4]. None of our cases had Sestamibi scan done but all had ultrasound examination of the neck which showed the parathyroid lesion preoperatively in all cases.

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Traditionally the treatment of primary hyperparathyroidism has been bilateral neck exploration with examination of all the four glands and excision of the affected one [1]. Recently this approach has been questioned given the fact that about 85% of the disease is caused by adenoma involving only one of the four glands and preoperative localization of this affected gland is possible nearly accurately using ultrasound and Sestamibi scan. Furthermore in centers with best set ups, intraoperative determination of serum PTH level following excision of the affected gland has decreased the number of unnecessary bilateral neck explorations in effect reducing the rate of complications like hypocalcaemia and recurrent laryngeal nerve injury [3] .This has led to a practice of unilateral targeted neck exploration as the most favored approach in the current management of primary hyperparathyroidism [6]. The list of new developments in the surgical management of primary hyperparathyroidism goes on to include endoscopic neck and mediastinal exploration making parathyroidectomy much less invasive and a quite safe procedure [7].

The commonest complications following parathyroidectomy are recurrent laryngeal nerve injury and hypocalcaemia [7]. The latter is usually due to the so called hungry bone disease where most of the free serum calcium returns to the skeleton following rapid drop in PTH after the surgery and will get better as the remaining parathyroid glands start to produce and secrete PTH which maintains calcium homeostasis. From the seven cases operated in our hospital, only one developed this complication and was successfully treated with IV calcium gluconate and later with oral calcium and Vitamin D. All the others had a smooth post-operative course.

Post-operative follow up of patients is done by serial determination of serum calcium and PTH level and cure is declared if the level of calcium normalizes and stays so at least for six months after surgery[7]. Persistent and recurrent primary hyperparathyroidism is also described according to this definition of cure. Only one of the three cases presented had a long term post-operative follow up and she became normocalcemic and stayed so for over six months and so can be declared cure. Complete information couldn't be found in all the rest and so it is difficult to comment on their long term outcome.

## Recommendation

The few cases we operated on had significant skeletal manifestations with bone pains and multiple fractures causing severe disability. This usually results from advanced disease due to late diagnosis. Therefore high index of suspicion and proper screening using serum calcium and PTH measurement is required to detect this disorder at the earliest stage.

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