

## Clinical Presentation and Management of Primary Hyperparathyroidism: A Single Centre Experience

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**Background:** Primary Hyperparathyroidism (PHPT) is the 3<sup>rd</sup> most common endocrine disorder. The clinical presentation of primary hyperparathyroidism has undergone a paradigm shift with asymptomatic PHPT being the predominant form in the western world. In developing countries like India PHPT still presents as a severe symptomatic disorder typically described by Fuller Albright as “Stones, Bones, Groans, & Moans”.

**Aim:** The study aims to present the clinical profile and management outcome of PHPT at our centre in western India.

**Method:** In this retrospective study, we analyzed the clinical presentation, biochemical profile, radiological features, management and its outcome in 30 histopathologically proven patients of PHPT over a period of 3 years (2018-2021) at a tertiary care Centre in western India.

**Results:** The disease was seen predominantly in the age group of 50-60 years. The median age of presentation was 50.5 years. There was female preponderance with the female to male ratio being 3:1. The majority of patients in this study were overtly symptomatic (94%) and only 6% of cases presented as asymptomatic PHPT. In symptomatic group 50% of patients had skeletal manifestations, around 43% of patients had renal calculi and 40% had GI symptoms like gastric or duodenal ulcer & acute pancreatitis. The mean preoperative calcium and iPTH levels were 11.2mg/dl & 304.4pg/ml respectively. The diseased parathyroid was localized radiologically in all cases. For preoperative localization The sestamibi scan had the highest sensitivity (88.8 %) whereas USG had the greatest positive predictive value (94.7%). Most of the patients (70%) in this study had single gland adenoma & were subjected to focused parathyroidectomy. At the end of 6 months, only 2 patients (6.6%) had a persistent disease and were subsequently managed by bilateral neck exploration.

**Conclusion:** The majority of patients of PHPT at our institute had a classical symptomatic presentation with skeletal and renal manifestations. The surgical cure rate was 90% with Focused parathyroidectomy being the main surgical approach.

**Keywords:** Primary Hyperparathyroidism (PHPT), Solitary Parathyroid Adenoma, Hypercalcemia, Endocrine Disorder.

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## Introduction

In the early twentieth century, PHPT was considered a rare disorder. Since the introduction of routine biochemical screening in 1970, PHPT has become the third most common endocrine disease, preceded by diabetes and thyroid disorders.

Primary hyperparathyroidism (PHPT), is clinically characterized by hypercalcemia and elevated or inappropriately normal levels of parathyroid hormone due to autonomous secretion of parathyroid hormone (PTH) from one or more glands. PHPT is caused by a solitary parathyroid adenoma in 80–85% of cases, parathyroid hyperplasia in 10–15% of cases and rarely by parathyroid carcinoma which is responsible for less than 1% of cases. The incidence of Primary hyperparathyroidism increases with age, but the incidence peaks in the 5<sup>th</sup> to 6<sup>th</sup> decade of life. Women are more affected than men in a ratio of 3:1'. The prevalence of primary hyperparathyroidism shows regional variation. In the western world, the prevalence of primary hyperthyroidism varies from 1 in 200 to 1 in 100000. Comparatively, it is difficult to determine the prevalence rate in developing countries like India as there is very limited data on primary hyperparathyroidism published in the literature from these countries.

The Classical clinical symptoms of PHPT popularly termed “bones, stones, abdominal groans and psychic moans”, were the original form of the disease. Over the years the clinical presentation of primary hyperparathyroidism (PHPT) has undergone a paradigm shift in the western world from symptomatic to asymptomatic PHPT. The majority of cases (75% to

80%) in these countries present as asymptomatic PHPT. These patients do not have a classical clinical presentation but have mild and nonspecific symptoms. Conversely in developing countries like India, most of the cases of PHPT still present as a classical Symptomatic disease. The symptomatic PHPT has myriads of symptoms which include Renal manifestations, skeletal manifestation, GI manifestations and neuropsychiatric manifestations

The diagnosis of PHPT primarily is biochemical, consisting of elevated sr. Calcium and PTH levels. The biochemical work-up in patients suspected of PHPT should include Sr. Creatinine, and Vitamin D levels to Rule out secondary HPT. The standard biochemical panel for PHPT must include 24-hour urinary calcium clearance to Rule out Familial hypocalciuric hypercalcemia (urinary calcium < 100mg/24hr).

Preoperative localization of the hyperfunctioning parathyroid gland is usually obtained with ultrasonography, Sestamibi scan or 4D CT scan. Preoperative Imaging studies have no role in the diagnosis but are a useful adjunct to deciding the surgical approach. The surgical removal of the affected parathyroid gland remains the only definitive cure for PHPT. As per revised National Institute of Health (NIH) guidelines, Parathyroidectomy is recommended in all symptomatic patients. Surgery in patients with asymptomatic PHPT though controversial is recommended in individuals with any of the criteria depicted in table 1.

**Table 1 (as per NIH criteria)**

Age	Less than 50
Serum levels of calcium	>1mg/dl above the upper limit
EGFR	Less than 60ml/min
24hr urinary calcium level	>400mg per day
Biochemical stone profile	Increased risk
Renal imaging	Nephrolithiasis or nephrocalcinosis
DXA(dual-energy x-ray absorptiometry)	T-score < 2.5
Vertebral imaging	Presence of vertebral fracture

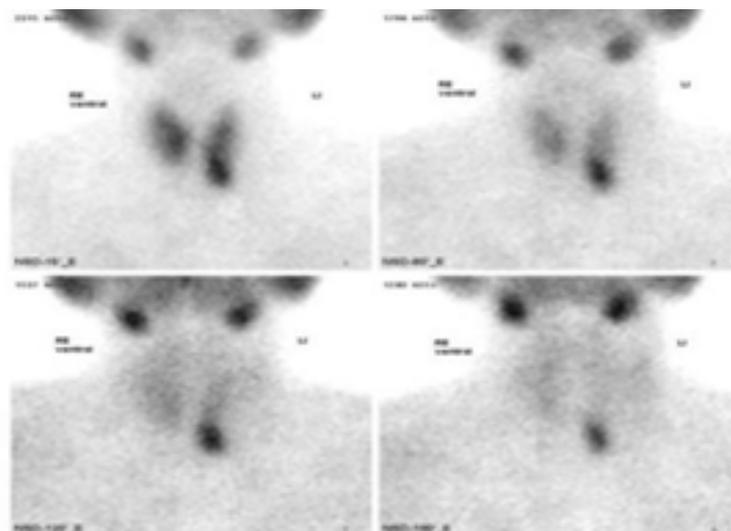
Bilateral neck exploration is the traditional surgical approach and has cure rates of more than 95% with a low risk of complications. However, with improved preoperative localization studies and intraoperative adjuncts like intraoperative iPTH monitoring, focused parathyroidectomy is performed with equal success and is appropriate for solitary adenoma.

#### Method:

**Study Design:** In this retrospective study, a review of medical records of all patients who underwent

parathyroidectomy for PHPT at our institute during a period of 3 years, from 2018 to 2021 was done. This resulted in 30 histologically proven cases of PHPT, which were analyzed.

The clinical data of each patient including age, sex, presenting symptoms, preoperative biochemical investigations, preoperative localization techniques, operative approach and findings, histopathology report, complications, postoperative biochemical studies and postoperative disease status were recorded in case record form. The Collected data were tabulated. The Data was analyzed using SPSS 17. For descriptive statistics like gender, presenting clinical features, frequency and percentages were calculated, while means were calculated for age, pre-operative and post-operative biochemical parameters, like serum PTH and calcium (Ca). The sensitivity and positive predictive values of the imaging studies (USG, Sestamibi scan, 4D CT Scan) were calculated ROC curve in SSPS 17 to assess the effectiveness of the localization studies.

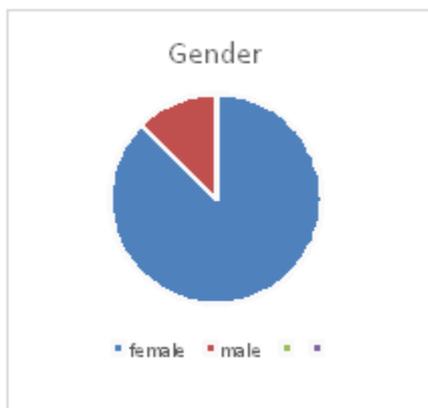


Sestamibi Scan showing left inferior parathyroid adenoma



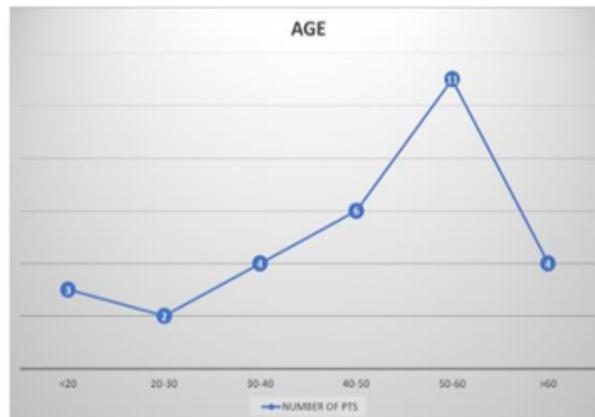
USG neck showing left inferior parathyroid adenoma

**Result:**



Gender distribution of PHPT

Gender distribution of PHPT



Age distribution of PHPT

In this study out of 30 patient majority were females (76.66%) with the male-to-female ratio being 1:3. The mean age of presentation was  $50.5 \pm 9.87$  yrs. The commonest affected age group was between 50 -60 yrs. (36.66 %) followed by 40-50 yrs. (20%). The majority of patients (94%) with PHPT had a classical symptomatic disease and only 2 patients (6.66%) had nonspecific symptoms and were classified as asymptomatic PHPT.

The mean preoperative Sr. calcium and iPTH level were 11.6 mg/dl & 305.4 pg/dl respectively.

The symptomatic group of the patients had varied clinical presentations. Around 50% of patients had skeletal manifestations (bone pain, osteoporosis, and pathological fractures). Renal calculi were present in 43.33% of patients and 40% of patients had GI symptoms like gastric or duodenal ulcer or acute pancreatitis.

**Table 2: Distribution of patients according to presenting symptomatology**

Skeletal complaints	50%
Renal calculi	43.33%
Gastrointestinal symptoms	40 %
Muscular symptoms	20%
Neuropsychiatric symptoms	33.33%
Asymptomatic	6.66%

The fall in mean pre-operative calcium from 11.2 to 9.6mg/dl post-operatively.

The sensitivity of the preoperative imaging modalities for localization of the

affected parathyroid gland was highest for the Sestamibi scan (88.8%) followed by the 4D CT scan (84.6%), and the sensitivity of USG was lowest at 62.2%. The positive predictive value for USG was highest (94.7%) followed by the Sestamibi scan (89%) and 4D CT scan (88%).

The main surgical approach used in 70% of cases was focused parathyroidectomy. Bilateral neck exploration was used in the rest of the patients. The intra-operative IPTH monitoring was done for all patients by MIAMI protocol.

The 10 min drop in mean IPTH levels was from 305.4 pg/dl to 56.8 pg/dl (more than 80%).

On Postoperative histopathology, 21 patients had parathyroid adenoma (70%) and 9 patients showed parathyroid hyperplasia and no patients had carcinoma.

At the end of 6 months, 27 patients (90%) were declared cured as they had achieved normal calcium homeostasis. Only 2 patients (6.6%) had persistence of disease and were sub-sequentially managed by bilateral neck exploration.

The main postoperative complication in our study was hypocalcemia, which was treated with oral and intravenously calcium supplementation and no patient had recurrent laryngeal nerve injury. There was a mortality of 1 patient on postoperative day 35 due to severe cardiac complications.

### Discussion

In our study, PHPT was predominantly seen in the age group of 50 -60 yrs. (36.66 %) followed by 40-50 yrs. (20%). The mean age of presentation was  $50.5 \pm 9.87$  yrs. These results were comparable to a retrospective study from south India conducted by Mallikarjuna et al [1]. They had reported the mean age of PHPT as  $48.1 \pm 15.8$  years. There were more females (76.66%) affected than males

(23.3%) in our study with the M:F ratio being 1:3. This is similar to classic female predominance seen in PHPT. According to a study by Dipti Sarma et al [2] from northeast India, there was equal gender distribution with M:F ratio of 1:1.25.

In this study, the majority of patients (94%) had a severe symptomatic disease. Clinically the patients with PHPT had varied symptomatology. The most common presenting symptoms were skeletal manifestation (50%), Renal calculi (43%), and GI symptoms (40%). Only 2 (6.66%) patients were diagnosed as asymptomatic PHPT. In a study by Sanjay Yadav et al [3], 79.6% of all included patients had symptomatic PHPT with Musculoskeletal (52.9%) and renal disease (34.9%) being the most common presenting symptom, suggesting that the symptomatic disease is the most common form of presentation in developing countries.

The mean pre-operative calcium in our study dropped from 11.2 to 9.6mg/dl post-operatively and the drop in mean IOPHTH (intra-operative IPTH) level was seen from 305.4 pg/dl to 56.8 pg/dl. A study by A. Raman [4] conducted in 2019, had shown a similar drop in the mean calcium and mean IOPHTH in cases of primary hyperparathyroidism from 13.1 mg/dl to 9.1 mg/dl and 256.5 pg/dl to 128.4 pg/dl respectively.

The accuracy of pre-operative imaging studies has promoted the use of minimally invasive surgery, resulting in reduced duration and complication of surgery. In our study, the sensitivity was highest for the Sestamibi scan (88.8%) followed by 4D CT (84.6%) and USG (62.6 %). The positive predictive value was greatest for USG (94.7%) followed by Sestamibi scan (88.8%) and 4-D CT (88%). In comparison a meta-analysis by Cheung et al6. Reported that the positive predictive value of USG is comparable to both the Sestamibi scan (90.7%) and 4-dimensional

CT (93.5%). In this meta-analysis, the sensitivity of the <sup>99m</sup>Tc-Sestamibi scan for detecting parathyroid adenoma was 88% whereas the preoperative ultrasonography had an average sensitivity of 76%.

The adenoma was localized to the neck in 90% of cases and the rest was localized to the mediastinum. The concordance between Sestamibi scan and USG was seen in 63.33%. A similar concurrence of 70 % was seen in the study conducted by R.S.Munk et al [5,6].

On the postoperative histopathological evaluation, in our study, 70% of patients had single gland adenoma and 30% of patients had parathyroid hyperplasia. There was no case of parathyroid carcinoma reported. In the study conducted by S.S. Avad [7], 92% of cases had adenomas (11 single, 3 double), and 8% of patients had PTH hyperplasia with no cases of parathyroid carcinoma.

In the study conducted by CF Russell et al, the majority of patients had no complications. permanent unilateral vocal cord paralysis was seen in 2 % of patients. In our study there was no incidence of recurrent laryngeal nerve injury however a high incidence of postoperative hypocalcemia (33.34%) was observed which may be due to the late presentation and severity of the disease. [8]

90% of the patients were cured after primary cervical exploration and 2 patients had persistence of disease at the end of 6 months there was the mortality of 1 patient due to cardiac illness which is comparable to another study by CF Russell [9] et al where 92.2 % of patients were cured after primary cervical exploration and 0.2% died during the postoperative period. [10,11]

### Limitation

The retrospective nature of this study was a major limitation. The study was conducted on a small cohort which was

another limiting factor. In future, further prospective studies of large groups of patients are needed to establish the true clinical scenario in less industrialized countries like India.

### Conclusion

Though there is a dramatic shift in the clinical spectrum of PHPT in the industrialized world, patients with PHPT at our centre still present as an overtly symptomatic disease. The severity of PHPT may be due to delayed diagnosis and widely prevalent vitamin D deficiency. As most of the cases of Primary hyperparathyroidism were due to solitary adenoma and the availability of adjuncts like preoperative localization techniques and intraoperative PTH monitoring had facilitated focused parathyroidectomy as the main surgical approach at our centre.

The surgical cure rate was 90%. As the patients of PHPT had a variety of clinical manifestations in our study, screening of serum calcium should be of prime importance in patients with renal stones, bone pains and neuropsychiatric symptoms.

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