Original Article

Primary Hyperparathyroidism: Clinical, Biochemical, and Radio-Pathological Profiles of 804 Patients – A Retrospective Study from South India

Dhalapathy Sadacharan, Mano Z. Mathews, Anjali Sathya[1], Shanmugasundar Gopal[2], Sruti Chandrasekaran[3], Sivasubramaniam Murthy[4], Vijaya B. Reddy[5], Jayashree Gopal[6], Muthukumaran Jeyapaul[7], Sakthivel Sivasubramanian[8], Vignesh Gopalakrishnan[9], Bharath Ramji[7], Dinesh Goli, Gokulakrishnan Sundararaman[10], Shriraam Mahadevan[11]

Department of Endocrine Surgery, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai, Tamil Nadu, [1]Department of Endocrinology, Vijaya Group of Hospitals, Chennai, Tamil Nadu, [2]Department of Endocrinology, Magna Centres for Obesity, Diabetes and Endocrinology, Chennai, Tamil Nadu, [3]Department of Endocrinology, Dr. Rela Institute of Medical Centre, Chennai, Tamil Nadu, [4]Director and Consultant Endocrinologist, Endocrine Diagnostic and Research Centre, Chennai, Tamil Nadu, [5]Director and Consultant Endocrinolgist, Vijay Daibetes, Thyroid and Endocrine Clinic, Puducherry, [6]Department of Endocrinology, DiabEndoIndia and Apollo Hospitals, Chennai, Tamil Nadu, [7]Department of Endocrinology, Arka Center for Hormonal Health, Chennai, Tamil Nadu, [8]Department of Endocrinology, The Hormone Clinic, Trichy, Tamil Nadu, [9]Department of Endocrinology, Dr. Vignesh's Endocrine and Diabetes Centre, Trichy, Tamil Nadu, [10]Department of Endocrinology, Billroth Hospital, RA Puram, Chennai, Tamil Nadu, [11]Department of Endocrinology, Diabetes and Metabolism, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamil Nadu, India

Abstract

Introduction: Primary hyperparathyroidism (PHPT) is a common endocrine disorder with variable clinical presentation. We intend to describe the clinical, biochemical, and radio-pathological profiles of PHPT patients managed over 13 years from South India. **Methods:** We analysed all patients who underwent evaluation and surgery for PHPT from July 2011 to April 2024. **Results:** A total of 862 PHPT patients underwent parathyroidectomy, with female preponderance (61.2%). Analysis was done on 804 patients (>20 years of age) excluding adolescent and paediatric age groups. The mean age was 43.8 years. The presentation in decreasing order of frequency was weakness and fatigue (84.2%); bone pain (35%); renal disease (20.8%) in the form of nephrolithiasis, nephrocalcinosis, or renal dysfunction; and neuropsychiatric manifestations (23.8%). Pathological fractures were observed in 4.5%, hypercalcaemic crisis in 2.6% of patients, and 1% had MEN I (Multiple Endocrine Neoplasia) syndrome. The mean albumin adjusted serum calcium level was 12.3 ± 1.01 mg/dl, and the median serum PTH level was 338 (80–3864) pg/ml. The sensitivity of the ultrasound neck and ^{99m}Tc Sestamibi scan was 97.5% and 98.3%, respectively, with a concordance of 93.4%. 25% underwent bilateral neck exploration and parathyroidectomy. Lesions were ectopic in 20 (2.4%) patients. The mean parathyroid gland weight was 1.45 ± 0.75 g. Histopathology revealed parathyroid adenoma (93.5%), parathyroid hyperplasia (1.6%), and parathyroid carcinoma (2.2%). The cure rate was 99.3%, while three patients had persistent disease. Hungry bone syndrome was observed in 12.1%. **Conclusion:** There is a changing trend in the clinical and biochemical profiles of PHPT patients in India to a milder form of the disease. The incidence of parathyroid carcinoma was slightly higher compared to a few other centres in India.

Keywords: Asymptomatic hyperparathyroidism, hypercalcaemia, primary hyperparathyroidism, South India

Introduction

Primary hyperparathyroidism (PHPT) in the Indian population has a wide spectrum of clinical presentations ranging from bone disease and renal stone disease to asymptomatic disease. It is more common in the middle and elderly age group. Symptomatic disease is still prevalent in India (>90%) and can be attributed to the lack of awareness, delay in case

Supplementary material available online: https://journals.lww.com/indjem/

Access this article online

Quick Response Code:

Website: https://journals.lww.com/indjem/

DOI: 10.4103/ijem.ijem_468_24

Address for correspondence: Dr. Shriraam Mahadevan, Department of Endocrinology, Diabetes and Metabolism, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamil Nadu, India.
E-mail: mshriraam@gmail.com

Submitted: 12-Nov-2024 **Revised:** 20-Dec-2024
Accepted: 10-Jan-2025 **Published:** 28-Feb-2025

How to cite this article: Sadacharan D, Mathews MZ, Sathya A, Gopal S, Chandrasekaran S, Murthy S, *et al*. Primary hyperparathyroidism: Clinical, biochemical, and radio-pathological profiles of 804 patients – A retrospective study from South India. Indian J Endocr Metab 2025;29:69-76.

detection, and the higher prevalence of vitamin D deficiency. In the Western world, asymptomatic disease has been the dominant clinical phenotype. The advent of multi-channel serum auto-analysers and the inclusion of serum calcium as part of annual screening paved the way for this dramatic change in the West. The prevalence of the disease is estimated between 1 and 7 cases per 1000 adults.[1] According to a few recent studies from the developing world, there has been a distinct trend towards a milder form of disease presentation and biochemical profile.[2] In this study, we aim to present our 13-year clinical experience with PHPT and compare our findings with previously published Indian studies.

Materials and Methods

This study is a retrospective analysis of data from patients evaluated and treated surgically for PHPT between July 2011 and April 2024 at a high-volume centre in South India. All surgeries were performed by a single endocrine surgeon and their team. During this period, a total of 862 patients with PHPT underwent surgery, including 52 patients under the age of 20, among whom seven were neonates with neonatal severe hyperparathyroidism (NSHPT).[3,4] Data on young patients and those with neonatal severe PHPT have been previously published in studies from 2020 and 2024.[3-5] The current study focusses on PHPT patients over the age of 20, with an average follow-up period of 6 months. The study flowchart outlining the inclusion and exclusion criteria is presented in Figure 1. Biochemical assays were performed using FUJI DRI-CHEM, model NX500 (manufacturer: Fujifilm) by methods as specified against each parameter, calcium (Calcium-CLIII complex reflectance spectrophotometry) with a coefficient of variation (CV) <5%, phosphate (PNP-XOD-POD colorimetric, reflectance spectrophotometry) with CV < 6%, and alkaline phosphatase (P-nitro phenol phosphate, reflectance spectrophotometry) with CV < 5%. Parathyroid hormone (PTH) levels and serum 25-hydroxy vitamin D were determined by chemiluminescence immunometric assay (CLIA) using a Beckman Coulter DXI 800 platform

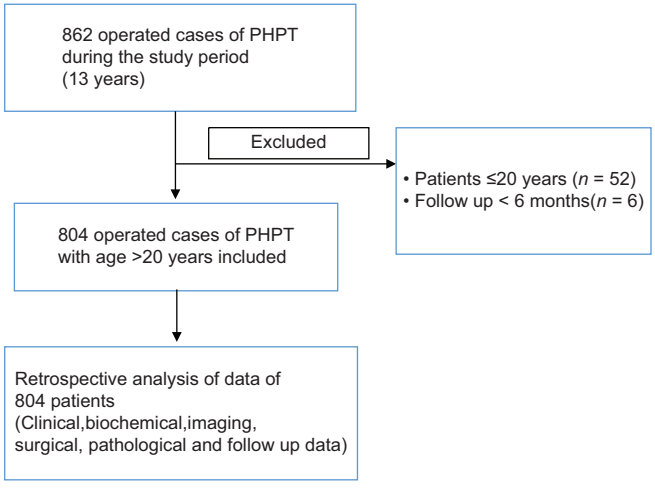


Figure 1: Study flowchart with inclusion and exclusion criteria

with a CV of 4.6% and 7%, respectively. Diagnosis of PHPT was established by inappropriately elevated serum parathyroid hormone (PTH >65 pg/ml) and elevated albumin-corrected serum calcium (>10.5 mg/dl). Vitamin D levels <20 ng/ml were considered as deficiency. Pre-operative localisation was done in all the cases using neck ultrasound (USG) and ^{99m}Tc Sestamibi scan. In cases where localisation failed, 4D CT (four-dimensional computed tomography) or MRI (magnetic resonance imaging) was performed. Additionally, an abdominal ultrasound was conducted to assess for any renal involvement. The bone mineral density (BMD) at the left femoral neck, lumbar spine (L1-L4), and distal 1/3rd of left radius were determined using a Hologic Dual energy X-ray absorptiometry (DXA) machine (Discovery- Wi series). BMD change was considered significant when it exceeds 0.022 g/cm2 for the spine, 0.027 g/cm2 for the total hip, and 0.029 g/cm2 for the femoral neck. T-scores were derived using the manufacturer's reference data. Osteoporosis was defined as T-score ≤ −2.5, and osteopenia as T-score between −1.0 and −2.5. A CV of 2.2% was noticed for BMD measurement at the forearm and lumbar spine and 3.1% at the femoral neck.

Presenting symptoms, previous medical history, and pre-operative findings regarding parathyroid gland location, size, weight, histopathology, and post-operative follow-up were reviewed. A diagnosis of hypercalcaemic crisis was established in patients having serum calcium >14 mg/dl along with acute symptoms and signs of hypercalcaemia. Normal calcium levels more than 1 year after surgery were considered as criteria for cure of PHPT. Genetic profiling was done in patients less than 30 years of age and those with multi-glandular disease and syndromic features. Genomic DNA was extracted using a Qiagen kit from whole blood EDTA. Mutation analysis was performed using next-generation sequencing (NGS) to analyse MEN1/2 genes. Cases where serum calcium either does not return to normal level or rises again within 6 months of the initial parathyroidectomy were considered as having persistent disease, and those cases that recurred after being normocalcaemic for more than 6 months were defined as recurrent hypercalcaemia.

Statistical analyses: SPSS 17 (SPSS Inc, Chicago, Illinois) was used for data analysis. The data are expressed as mean ± standard deviation (SD). Categorical data were expressed in percentages. Analysis of categorical variables was done by Chi-square test. $P \leq 0.05$ was considered statistically significant. The sensitivity of neck ultrasound and ^{99m}Tc Sestamibi scans in localising parathyroid lesions was calculated by comparing the imaging findings with intra-operative findings and was defined as the proportion of true positive cases correctly identified by the respective imaging modality.

Ethical aspect

The study was approved by IEC, Madras Medical College, Chennai 600003 [EC Reg No (DHR).EC/NEW/INST/2021/1618] (IEC No. 01032024) on 5.03.24. Written and informed consent was obtained for participation in the

study and use of the patient data for educational and research purposes. The procedures followed the guidelines laid down in Declaration of Helsinki 1964 and as revised later.

Results

A total of 862 patients underwent parathyroidectomy during the study period, of which 804 were included in the present study. Among these, 312 (38.8%) were men and 492 (61.2%) were women. Of the women, 62 were post-menopausal. The mean age at presentation was 43.8 ± 7.8 years. The age distribution of patients is shown in Supplementary Figure 1 as a bar graph. On analysing the clinical profile, it was observed that 126 (15.7%) patients were asymptomatic. Fatigue and weakness were the most common clinical presentation, observed in 84.2% of patients. Skeletal involvement was noted in 35% of patients, manifesting as bone pain (35%), pathological fractures (4.5%), and brown tumors (4.1%). Two-thirds of the patients reported pain in the lower limbs, particularly involving the femur and tibia, while one-third experienced back pain. Vertebral fractures were documented in 12 patients (non-traumatic). Additionally, femur fractures were observed in 20 patients, tibial fractures in three patients, and a humerus fracture in one patient, all resulting from trivial trauma. The fracture sites showed a positive correlation with the reported sites of bone pain. Renal stone disease was observed in 20.8% of patients. Nephrolithiasis was identified in 130 patients (16.1%), while a combination of nephrolithiasis and medullary nephrocalcinosis was seen in 37 patients (4.6%). Nephrolithiasis was more commonly observed on the left side (53.8%), with the renal calyx (78%) and ureter (22%) being the most frequently affected sites. Renal dysfunction was observed in 10 patients; however, none had chronic kidney disease (CKD) at stage 4 or 5. Hypercalcaemic crisis was observed in 21 (2.6%) patients, who were initially managed conservatively with hydration, saline diuresis, bisphosphonates, and calcimimetics. Surgery was performed during the same admission once the patients were clinically stabilised. Pancreatitis was seen in 5.4% of patients, whereas 20.5% of patients had complaints of constipation. 18.2% of patients were hypertensive in our study. Twenty-six patients (3.2%) presented with a palpable neck mass, five of whom had a hard neck swelling. Pre-operative imaging and intra-operative findings raised suspicion of parathyroid carcinoma in 15 patients among them, which was subsequently confirmed by post-operative histopathology. In contrast, 11 patients with a palpable mass but no suspicious intra-operative features were diagnosed with parathyroid adenomas. The clinical characteristics of the patients are summarised in Table 1.

Table 1: Demographic and clinical profiles (n=804)

Variable	Mean (SD)
Age (years)	43.8±7.8
Clinical features	**Frequency (%)**
Generalised weakness	677 (84.2%)
Bone pain	281 (35%)
Neuropsychiatric	191 (23.8%)
Renal stones	167 (20.8%)
Constipation	165 (20.5%)
Hypertension	147 (18.2%)
Asymptomatic	126 (15.7%)
Pancreatitis	44 (5.4%)
Pathological fracture	36 (4.5%)
Palpable mass	26 (3.2%)
Hypercalcaemic crisis	21 (2.6%)
Gall stones	15 (1.86%)

*SD-Standard deviation

Multiple Endocrine Neoplasia type 1 was genetically confirmed in 8 patients (1%). Five patients had associated prolactin secreting pituitary adenoma, and one patient had acromegaly due to growth hormone secreting adenoma. Four patients with prolactinomas had associated enteropancreatic neuroendocrine tumors. The majority of pathogenic mutations in the MEN1 gene were observed in exons 2, 3, and 5, and these mutations primarily involved missense and frameshift mutations. The biochemical profile showed hypercalcaemia in 99.12% of patients. Normocalcaemic PHPT was seen in 0.87% of cases. The mean (± SD) serum calcium level was 12.3 ± 1.02 mg/dL. The median serum PTH level was 338 (80–2842) pg/ml. The mean serum inorganic phosphorus level was 2.2 ± 0.35 mg/dL. The serum total ALP (alkaline phosphatase) was elevated (>140 IU/L) in 52.1% of patients. The mean (± SD) serum total ALP was 162.4 ± 109.5 IU/L. The mean (± SD) 25-hydroxy vitamin D level was 17.5 ± 7.07 ng/mL. Vitamin D deficiency (<20 ng/mL) was present in 70.1% of patients. Cholecalciferol was not given any patients pre-operatively. DXA scan report was available only in 434 (53.9%) patients. 38% had osteopenia (t-score –1 to -2.5), and 32% had osteoporosis (t-score ≤ -2.5) at any of the sites (hip, lumbar spine, and forearm). The mean (± SD) pre-operative BMD (T-scores) at the hip and lumbar spine measured were -2.98 ± 1.52 and -2.76 ± 1.43, respectively. All patients with pathological fracture had a T-score in the osteoporotic range. Pre-operative USG neck was performed on all patients. A 99mTc-Sestamibi scan was conducted in 98% of the patients, with imaging results being concordant in 751 (93.4%) cases. For patients in whom the lesion was not localised using ultrasound and Sestamibi scan, 4D CT or MRI was performed in 12 cases. PET-CT (positron emission tomography–CT), done for other indications, identified a parathyroid lesion in seven cases. The sensitivity of ultrasound and 99mTc-Sestamibi scan was 97.5% and 98.3%, respectively.

Surgical management: Focussed parathyroidectomy was done in all cases more than 40 years with a concordant pre-operative imaging (n = 578). For all other patients with discordant or non-localised imaging and patients less than 40 years of age (n = 201), a bilateral neck exploration and parathyroidectomy was done according to the department protocol. This protocol was made from our observations in the early years of the study where a few patients <40 years of age were found to have a double adenoma or multi-glandular

disease intra-operatively, in spite of concordant pre-operative localisation of a single gland disease. Three patients in our study underwent hemithyroidectomy due to the intra-capsular location of the parathyroid gland, and 15 patients underwent a hemithyroidectomy with CCLND (central compartment lymph node dissection) along with parathyroidectomy, given clinical suspicion of parathyroid carcinoma, later confirmed on histopathology. Sternotomy was required in seven patients for excision of the mediastinal parathyroid lesion [Figure 2]. Sub-total parathyroidectomy with thymectomy was done in the eight cases of MEN 1 syndrome. Five patients had concomitant papillary thyroid carcinoma and had undergone thyroidectomy along with parathyroidectomy. All cases were done under general anaesthesia. Parathyroid glands were approached laterally after mobilising the sternocleidomastoid muscle on the respective side. Recurrent laryngeal nerve was identified and preserved in all cases. Superior parathyroid glands are posterolateral and inferior parathyroid glands are anteromedial to the recurrent laryngeal nerve. The lesion was ectopic in 21 (2.6%) patients [Table 2]. 97.8% (786 cases) had a single lesion causing the disease. The weight of the resected glands varied from 0.45 g to 10 g (mean 1.45 g). Although the size of the gland was larger in patients with vitamin D deficiency, this difference did not reach statistical significance. The histopathological profile of the patients is summarised in Table 2. All 18 patients diagnosed with parathyroid carcinoma were symptomatic, with four presenting in hypercalcaemic crisis along with encephalopathy. All patients had serum calcium levels >14 mg/dl, with the highest recorded value reaching 20.1 mg/dl and a mean PTH level of 1240 ± 876.2 pg/ml. Pre-operative imaging was concordant in all cases.

Post-operative status: All virgin PHPT patients experienced normalisation of calcium and PTH levels following the excision of the parathyroid tumour. However, there were three cases of failed exploration, and these patients continued to have persistent disease. One patient had undergone surgery twice at another facility, but the lesion could not be localised during re-exploration. The other two patients had previous surgeries elsewhere, and despite re-exploration, we were unable to localize the parathyroid gland. All three cases remained non-localising despite extensive imaging efforts. Symptomatic hypocalcaemia was noted post-operatively in 12.3% of patients. Patients were supplemented with calcium until they became symptom-free. Eleven patients

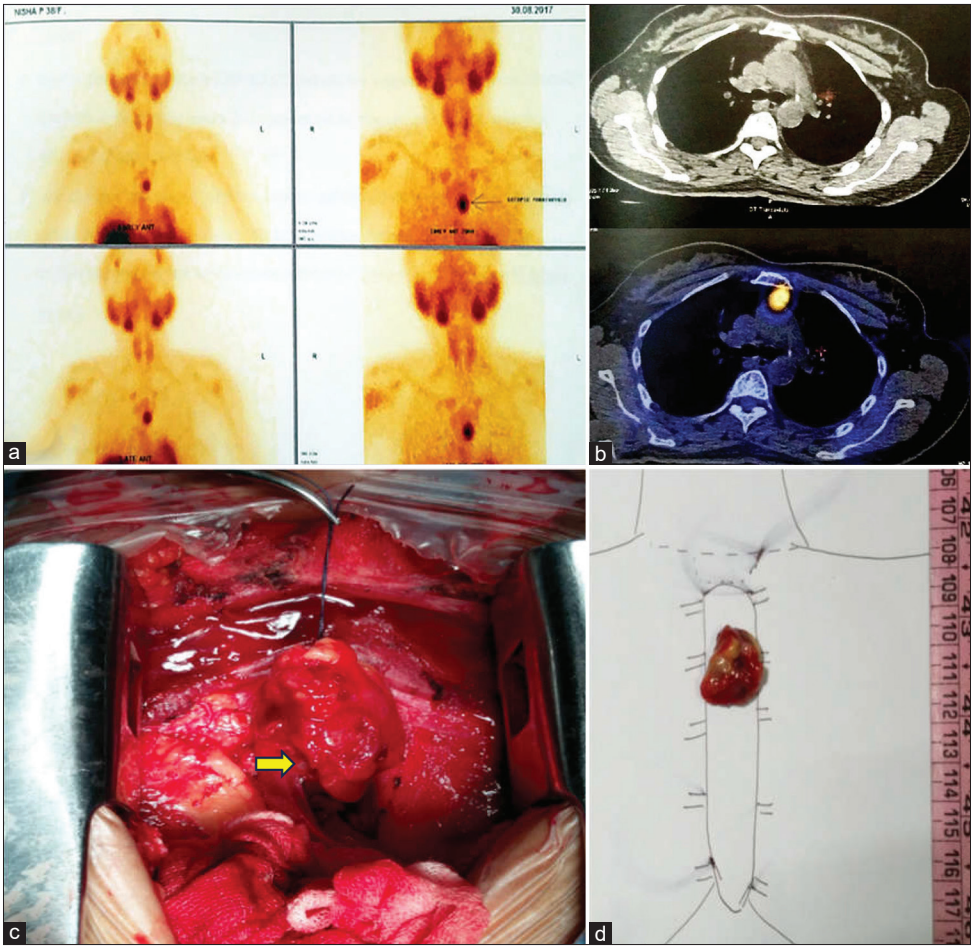


Figure 2: Mediastinal parathyroid a and b: ^{99m}Tc Sestamibi SPECT/CT showing a superior mediastinal parathyroid lesion c: Median sternotomy and exploration showed a parathyroid tumour (arrow) in the superior mediastinum behind manubrium sterni. d: Specimen picture showing a 2.5 × 2.8 cm parathyroid lesion

Table 2: Surgical technique and post-operative complications (*n*=804)

Procedure	Frequency (%)
Focussed Parathyroidectomy	578 (71.9%)
Bilateral neck exploration + Parathyroidectomy	201 (25%)
Hemithyroidectomy	3 (0.3%)
Hemithyroidectomy + CCLND	15 (1.8%)
Subtotal Parathyroidectomy + Thymectomy	8 (0.9%)
Sternotomy + Parathyroidectomy	7 (0.8%)
Parathyroidectomy + Thyroidectomy	5 (0.6%)
Complications	**Frequency (%)**
Temporary voice change	2 (0.2)
Seroma	16 (2)
Pedal oedema	139 (17.3)
Histopathological profile (*n*=804)	
HPE diagnosis	**Frequency (%)**
Adenoma	752 (93.5)
Atypical adenoma	9 (1.1)
Carcinoma	18 (2.2)
Double adenoma	12 (1.5)
Hyperplasia	13 (1.6)
Location of the abnormal gland	**Frequency (%)**
Superior	388 (48.2%)
Inferior	416 (51.7%)
Ectopic:	21 (2.6%)
• Thyrothymic ligament	12
• Intra-thyroidal	4
• Retro-oesopageal	3
• Carotid sheath	2

required both intravenous (IV) and oral calcium, while 88 patients needed only oral calcium treatment. Most patients who required IV calcium received it for 3 days, except for one patient who required it for 7 days. The majority of patients did not require calcium supplements beyond 1 month. Hungry bone syndrome was seen in 97 patients (12.1%). Four patients among them received zoledronic acid pre-operatively for the management of hypercalcaemic crisis. In the post-operative period, 139 (17.3%) patients complained of pedal oedema and two patients had temporary voice change [Table 2]. The cure rate was 99.3%, while three patients had persistent disease. The mean post-operative serum calcium was 8.75 ± 0.75 (7.2–15.2) mg/dL, and PTH was 9.93 ± 28.7 (2.4–422) pg/mL. On histology, the majority of our patients (93.5%) were found to have a parathyroid adenoma, 13 (1.6%) patients had hyperplasia of all glands, and 12 (1.5%) patients had a double adenoma [Figure 3]. Parathyroid carcinoma was seen in 18 (2.2%) patients [Supplementary Figure 2], whereas nine (1.1%) patients had an atypical adenoma. In three patients, parathyroid carcinoma diagnosis was a histological surprise; however, no additional procedures were performed due to the tumour's non-invasive nature. On follow-up, none of the patients had a recurrence of the disease. The median follow-up duration was 60 months (range 7–147 months).

Discussion

Our study looked into the clinical, biochemical, surgical, and histopathological characteristics of PHPT patients from South India over 13 years. We have observed a changing trend in the clinical profile of the patients with lower incidence of symptoms and a change in biochemical profile with low PTH levels compared to other centres from India. A study investigating the secular trends in the incidence of PHPT from the Mayo clinic has shown that the clinical spectrum of PHPT has shifted from a symptomatic disease with complications to uncomplicated, asymptomatic PHPT in older individuals (median 50–60 years) with the advent of serum auto-analysers.[6] In India, the majority of PHPT patients present as symptomatic disease with varied clinical manifestations, although there has been a gradual rise in the asymptomatic form of the disease over the past decade as reported by other centres.[7,8]

The mean age of presentation in our study was 43.8 ± 7.8 years, with a predominance of females. This is consistent with data from the Indian PHPT registry, which reported a mean age of 42 ± 14 years.[7] Another study from South India showed a mean age of 37 ± 10 years.[9] Compared to developed regions, PHPT in developing countries tends to present at a younger age. The exact reasons for this difference remain unclear, but possible explanations include the high prevalence of vitamin D deficiency and genetic dysregulation associated with the pathology in the Indian PHPT patients.[10] In our study, 70.1% of PHPT patients were found to have vitamin D deficiency.

The most common presenting symptom in our patients was generalised weakness (84.2%) in contrast to other studies where musculoskeletal symptoms were more predominant. Skeletal symptoms account for most of the morbidity in PHPT patients. Even though skeletal disease and renal disease were seen in 35% and 20.8% of patients, respectively, in our series, it was less compared to other series from India.[9-11] In a study of 332 patients, SK Bhadada *et al*.[12] reported skeletal manifestations including bone pain (56%), pathologic fractures (27%), and osteitis fibrosa cystica (40%). Mallikarjuna *et al*.[13] found a fracture rate of 3.6% in a study of 54 patients from South India. Another study from Kashmir, involving 78 PHPT patients, reported bony symptoms in 44% of patients, with a pathologic fracture rate of 10.1%.[14] In our study, pathologic fractures were observed in 4.5% of patients. This lower prevalence of fractures could be attributed to the early diagnosis of the disease in this region. A recent prospective study from South India by S Shetty *et al*.[15] showed a higher incidence of renal calculi (37.3%), while skeletal involvement (35.3%) and vitamin D deficiency (71%) were comparable to our series.

Renal involvement in the form of renal dysfunction, nephrolithiasis, and nephrocalcinosis was seen in 28.8% of our patients. This is comparatively low in contrast to other large series from India where the prevalence of renal stone disease is 30–50%.[11,12] The Indian PHPT registry data show

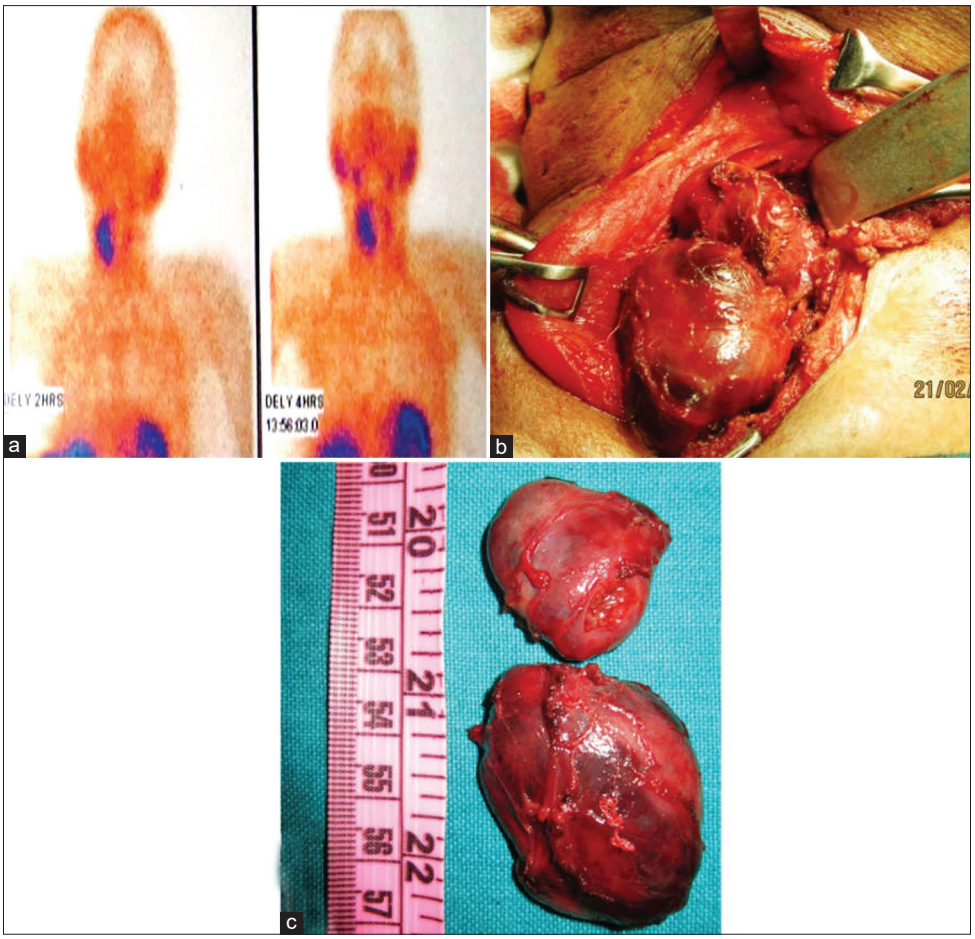


Figure 3: Double adenoma a: ^{99m}Tc Sestamibi scan showing right side parathyroid lesion b: Intra-op image showing double parathyroid adenoma on the right side c: Specimen picture showing 3.5 × 3cm and 2.5 × 2 cm parathyroid tumours

a higher prevalence of bone disease (72%) in the western part of India and renal stone disease (47.2%) in the eastern part.[12] In a study by Cristiana Cipriani *et al.*[16] from Italy which included 140 PHPT patients, the overall prevalence of nephrolithiasis was 55% in symptomatic and 35% in asymptomatic patients. Renal involvement can be seen in both symptomatic and asymptomatic forms of the disease. The incidence of hypercalcaemic crisis was 2.6% in our patients, whereas a study from North India by SK Yadav *et al*.[11] reported hypercalcaemic crisis in 21.3% of patients.

Asymptomatic PHPT is usually discovered by biochemical screening. Target organ involvement may or may not be present without overt symptoms and signs. 126 patients (15.6%) were diagnosed to have asymptomatic disease in our study. Data from the PHPT registry showed a progressive rise in asymptomatic PHPT cases with a prevalence of 10% among 554 patients.[8] Another study from South India also reported a higher prevalence (39%) of asymptomatic disease among 54 patients.[13] Similarly, Mithal *et al.*[17] reported a prevalence of 38% in a series from North India. All these studies highlight the changing clinical profile of PHPT in India from an overt symptomatic disease to an asymptomatic disease over the past decade. This can be attributed to increased health awareness among the general public, physician awareness, improved screening programmes, and a better referral pattern. In our series, all asymptomatic cases were detected by the evaluation of hypercalcaemia by endocrinologists.

Hypercalcaemia was present in 99.1% of patients in our study, and the mean serum calcium and serum phosphorous were similar to data from other Indian studies.[11-13] The mean serum PTH level in our study was 376.5 ± 278.7 pg/ml, which was lesser than the mean PTH reported in the Indian Parathyroid Registry (766 ± 773 pg/mL)[12] and in the study by Mallikarjuna VJ *et al.*[13] from South India (602.6 ± 721 pg/ml). The mean serum 25-OHD (17.5 ± 7.07 ng/ml) in our study was lower than that reported by previous Indian studies.[12,18] Higher PTH in PHPT is usually attributed to the severity of vitamin D deficiency. However, concomitant magnesium deficiency or other factors may also play a role in the rise of PTH secondary to vitamin D deficiency.[19]

PHPT due to syndromic association was observed in eight patients in our study. All were diagnosed to have MEN 1 syndrome and had a younger age of disease onset with multi-glandular disease. We used ultrasound and ^{99m}Tc Sestamibi scan for pre-operative localisation of the lesion

in our patients. Sensitivity was almost similar for both imaging modalities with a concordance of 93.4%. Sensitivity of ^{99m}Tc Sestamibi scan was less in multi-glandular disease compared to single gland disease. A study by Bhansali *et al.*[20] showed that the sensitivity and PPV of USG for detecting a single abnormal gland were 73% and 100%, respectively, whereas the sensitivity and positive predictive value were 98% for ^{99m}Tc Sestamibi scan. 4D-CT localised the lesion in 15 cases where the imaging findings were discordant. Patients (>40 years) with a concordant imaging finding were subjected to unilateral neck exploration or a focussed parathyroidectomy. In a study of 15,000 parathyroidectomies by James Norman *et al.,*[21] unilateral parathyroidectomies carried a 1-year failure rate of 3% to 5% and a 10-year recurrence rate of 4% to 6%. The mean tumour weight in our study (1.4 ± 0.75 g) was lower than the weight reported in other Indian studies.[9-11] Our study showed a predominance of adenoma (93.5%) similar to other studies. Parathyroid carcinoma accounts for 1% of cases of PHPT, and there has been an increase in the incidence of parathyroid carcinoma in the western part of the world.[22,23] The incidence of parathyroid carcinoma in our study was 2.2%, which was slightly higher compared to a few other centres in India. Most cases of PHPT are sporadic (95%) with the inherited form accounting for 2–5% of cases.[24]

The incidence of post-operative hungry bone syndrome (HBS) was higher in other Indian studies including the data from the Indian PHPT registry (40%).[12,25] Post-operative HBS was seen in 12.1% of patients in our study, and most of them occurred within the first 72 hours. This could be attributed to the relatively low serum PTH and ALP in our cohort. The mean PTH level (698 ± 533.3 pg/ml) and mean ALP level (256 ± 194.2 IU/L) in patients with HBS were found to be significantly elevated, suggesting a potential predictive role. Post-operative supplementation of calcium and vitamin D plays a crucial role in preventing HBS. An unusual finding of bilateral pedal oedema that worsened in the initial post-operative period which then regressed spontaneously was observed in 17.3% of our patients. The mechanism behind this is unclear and may need further exploration. The overall cure rate in our study was 99.3%, which is similar to other studies from India.[9,11] The recurrence rate of PHPT ranges from 0 to 4.16% according to a few studies.[25,26] None of the patients in our study developed recurrent disease during the follow-up period. A comparison of our study with previous Indian studies on PHPT is given in Table 3.

The limitations of this study include the unavailability of 24-hour urinary calcium and bone mineral density data for all patients, as well as its retrospective design.

Conclusion

Our study suggests a changing trend in the clinical and biochemical profiles of PHPT in the South Indian population, with a shift towards milder and asymptomatic forms of the disease. This change may be attributed to increased health awareness and improved socio-economic conditions. The incidence of parathyroid carcinoma was slightly higher, while the occurrence of HBS was lower compared to reports from other centres in India. Early detection of PHPT is crucial in preventing systemic complications and promoting overall bone health.

Acknowledgement

We acknowledge Dr Adlyne Reena Asirvatham, MBBS,DNB,DM (ENDO) from departemnt of Endocrinology, diabetes and metabolism, Sri Ramachandra Institute of Higher

Table 3: Comparison of our study with other Indian studies

	Present study (*n*=804)	Jha S *et al*.[9] (*n*=59)	SK Yadav *et al*.[11] (*n*=187)	Mallikarjuna VJ *et al*.[13] (*n*=54)	SK Bhadada *et al*.[12] (*n*=332)
Time period	2011-2024	2007-2015	2010-2016	2011-2015	2005-2015
Mean Age (years)	43.8±7.8	37±10	47	48.1±15.8	40.5±13.9
Male: Female	1:1.5	1:2.9	1:2.2	1:1.8	1:2.44
Most common symptom	**Weakness and fatigue (84.2%)**	**Musculoskeletal (72.8%)**	**Musculoskeletal (61%)**	**Bone pain (33.3%)**	**Weakness and fatigue (58.7%)**
Asymptomatic disease	15.7%	Nil	Nil	38.9%	4.2%
Skeletal disease (%)	35%	72%	61%	37%	58.6%
Renal disease (%)	28.8%	11.8%	53.5%	27.7%	36.7%
Hypercalcemic crisis (%)	2.6%	-	21.3%	7.4%	-
Serum Calcium (8.5-10.5 mg/dL)	12.3±1.01	-	12.8±1.6	12.7±2.0	11.7±1.6
Serum Phosphate (2.8-4.5 mg/dL)	2.2±0.35	-	2.3±0.6	2.43±0.7	3.0±1.2
Serum 25-OHD (30-50 ng/ml)	17.5±7.07	-	25.3±17.3	11.34±9	24.8±28.6
Serum PTH (15-65 pg/ml)	376.5±278.7	1153±338.7	635.7±444.9	602.6±721	766±773
Total ALP (44-147 IU/L)	162.4±109.5	-	414.8±318.8	375.5±314	420±563
Surgical profile					
Mean tumour weight (g)	1.4±0.72	2.5	3.3	4.9	5.6
Parathyroid carcinoma	2.2%	1.6%	3.2%	1.8%	1%
Ectopic parathyroid gland	2.4%	-	-	-	2.1%

Education and Research, Porur, Chennai, for referring and managing Hyperparathyroidism patients.

Author contribution

Study's conception and design-Dr Dhalapathy Sadacharan, Dr Shriraam Mahadevan. Material preparation, data collection, and analysis- Dr Dhalapathy Sadacharan, Dr Shriraam Mahadevan, Dr Dinesh Goli. Manuscript preparation- Dr Dhalapathy Sadacharan, Dr Shriraam Mahadevan, Dr Mano Z Mathews. Manuscript editing- Dr Dhalapathy Sadacharan, Dr Shriraam Mahadevan, Dr Mano Z Mathews, Dr Anjali Sathya, Dr Shanmugasundar Gopal, Dr Sruti Chnadrasekaran, Dr S Murthy, Dr VijayBhaskar Reddy, Dr Jayashree Gopal, Dr Muthukumaran Jeyapaul, Dr Bharath Ramji, Dr Sakthivel S, Dr Vignesh Gopalakrishnan, Dr Gokulakrishnan Sundararaman,

Financial support and sponsorship

Nil.

Conflicts of interest

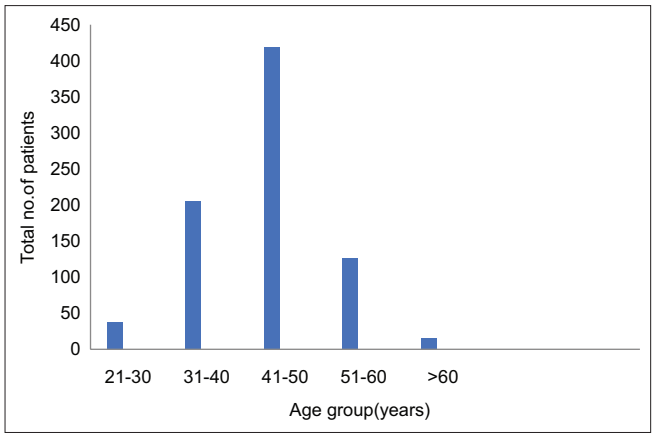
There are no conflicts of interest.

Data availability statement

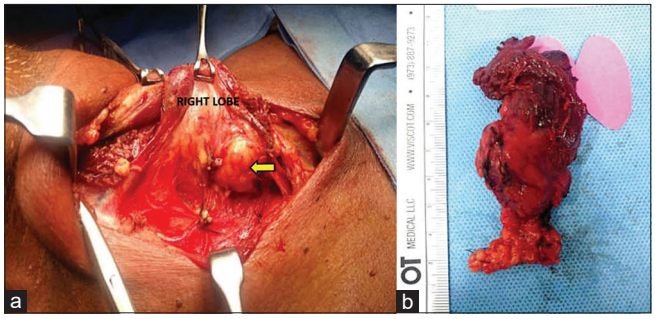
The details of the information provided in the study as ecxel sheet is available with primary author.

References

1. Yeh MW, Ituarte PH, Zhou HC, Nishimoto S, Liu IL, Harari A, *et al*. Incidence and prevalence of primary hyperparathyroidism in a racially mixed population. J Clin Endocrinol Metab 2013;98:1122-9.
2. Viswanathan G, Mathew V, Jeeragi M, George B, Bantwal G, Ayyar V, *et al*. Emerging pattern of asymptomatic hyperparathyroidism in South India-A six-year retrospective study. Folia Med (Plovdiv) 2024;66:221-6.
3. Sadacharan D, Mahadevan S, Rao SS, Kumar AP, Swathi S, Kumar S, *et al*. Neonatal severe primary hyperparathyroidism: A series of four cases and their long-term management in India. Indian J Endocr Metab 2020;24:196-201.
4. Sadacharan D, Rao SS, Mahadevan S, Shanmugasundar G, Murthy S, Chandrashekaran S, *et al*. Primary hyperparathyroidism in young and adolescents: Alike or unlike adult hyperparathyroidism?-A series from South India. Indian J Endocrinol Metab 2024;28:22-8.
5. Sadacharan D, Mahadevan S, Rao SS, Jeevarathnam D, Rajakumar U. Neonatal severe primary hyperparathyroidism—Presentation, management, and follow-up of seven cases. Indian J Surg 2024;86:1132-41.
6. Griebeler ML, Kearns AE, Ryu E, Hathcock MA. Secular trends in the incidence of primary hyperparathyroidism over five decades (1965-2010). Bone 2015;73:1–7.
7. Arya AK, Kumari P, Bhadada SK, Agrawal K, Singh P, Mukherjee S, *et al*. Progressive rise in the prevalence of asymptomatic primary hyperparathyroidism in India: Data from PHPT registry. J Bone Miner Metab 2021;39:253–9.
8. Shah VN, Bhadada S, Bhansali A, Behera A, Mittal B. Changes in clinical and biochemical presentations of primary hyperparathyroidism in India over a period of 20 years. Indian J Med Res 2014;139:694–9.
9. Jha S, Jayaraman M, Jha A, Jha R, Modi KD. Primary hyperparathyroidism: A changing scenario in India. Indian J Endocrinol Metab 2016;20:80–3.
10. Varshney S, Bhadada SK, Saikia UN, Sachdeva N, Behera A, Arya AK, *et al*. Simultaneous expression analysis of vitamin D receptor, calcium-sensing receptor, cyclin D1, and PTH in symptomatic primary hyperparathyroidism in Asian Indians. Eur J Endocrinol 2013;169:109–16.
11. Yadav SK, Mishra SK, Mishra A, Mayilvagnan S, Chand G, Agarwal G, *et al*. Changing profile of primary hyperparathyroidism over two and half decades: A study in tertiary referral center of North India. World J Surg 2018;42:2732-7.
12. Bhadada SK, Arya AK, Mukhopadhyay S, Khadgawat R, Sukumar S, Lodha S, *et al*. Primary hyperparathyroidism: Insights from the Indian PHPT registry. J Bone Miner Metab 2017;36:238–45.
13. Mallikarjuna VJ, Mathew V, Ayyar V, Bantwal G, Ganesh V, George B, *et al*. Five-year retrospective study on primary hyperparathyroidism in South India: Emerging roles of minimally invasive parathyroidectomy and preoperative localization with methionine positron emission tomography-computed tomography scan. Indian J Endocr Metab 2018;22:355-61.
14. Misgar RA, Dar PM, Masoodi SR, Ahmad M, Wani KA, Wani AI, *et al*. Clinical and laboratory profile of primary hyperparathyroidism in Kashmir Valley: A single-center experience. Indian J Endocr Metab 2016;20:696-701.
15. Shetty S, Cherian KE, Shetty S, Kapoor N, Jebasingh FK, Cherian A, *et al*. Does Baseline PTH influence recovery of bone mineral density, trabecular bone score and bone turnover markers? A prospective study following curative PArathyroidectomy in primary hyperparathyroidism. Endocr Pract 2020;26:1442-50.
16. Cipriani C, Biamonte F, Costa AG, Zhang C, Biondi P, Bilezikian JP, *et al*. Prevalence of kidney stones and vertebral fractures in primary hyperparathyroidism using imaging technology. J Clin Endocrinol Metab 2015;100:1309–15.
17. Mithal A, Kaur P, Singh VP, Sarin D, Rao DS. Asymptomatic primary hyperparathyroidism exists in North India: Retrospective data from 2 tertiary care centers. Endocr Pract 2015;21:581–5.
18. Gopal RA, Acharya SV, Bandgar T, Menon PS, Dalvi AN, Shah NS. Clinical profile of primary hyperparathyroidism from Western India: A single center experience. J Postgrad Med 2010;56:79-84.
19. Kannan S, Mahadevan S, Velayutham P, Bharath R, Kumaravel V, Muthukumaran J, *et al*. Estimation of magnesium in patients with functional hypoparathyroidism. Indian J Endocrinol Metab 2014;18:821-5.
20. Bhansali A, Masoodi SR, Bhadada S, Mittal BR, Behra A, Singh P, *et al*. Ultrasonography in detection of single and multiple abnormal parathyroid glands in primary hyperparathyroidism: Comparison with radionuclide scintigraphy and surgery. Clin Endocrinol (Oxf) 2006;65:340-5.
21. Norman J, Lopez J, Politz D. Abandoning unilateral parathyroidectomy: Why we reversed our position after 15,000 parathyroid operations. J Am Coll Surg 2012;214:260-9.
22. Machado NN, Wilhelm SM. Parathyroid cancer: A review. Cancers 2019;11:1676.
23. Brown S, O'Neill C, Suliburk J, Sidhu S, Sywak M, Gill A, *et al*. Parathyroid carcinoma: Increasing incidence and changing presentation. ANZ J Surg 2011;81:528–32.
24. English KA, Lines KE, Thakker RV. Genetics of hereditary forms of primary hyperparathyroidism. Hormones 2024;23:3–14.
25. Pradeep PV, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Long-term outcome after parathyroidectomy in patients with advanced primary hyperparathyroidism and associated Vitamin D deficiency. World J Surg 2008;32:829-35.
26. Bhansali A, Masoodi SR, Reddy S. Primary hyperparathyroidism in North India: A description of 52 cases. Ann Saudi Med 2005;25:29–35.



Supplementary Figure 1: Age distribution of the patients



Supplementary Figure 2: Parathyroid carcinoma a: Intra-op picture showing a right inferior parathyroid lesion (arrow) infiltrating the right lobe of thyroid suspicious of parathyroid carcinoma b: Specimen – en-bloc resection of tumour with right hemithyroidectomy + CCLND