Original Research Article

IMAGING FEATURES AND POST SURGICAL DATA OF INDIAN PATIENTS WITH PHPT

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ABSTRACT

Background: To study the Imaging Features and post-Surgical data of Indian patients with primary hyperparathyroidism.

Materials and Methods: This was a prospective study conducted at tertiary care center, Mahatma Gandhi Medical College and Hospital, Jaipur consecutive patients with primary hyperparathyroidism from year 2022 to 2024. The analysis included profiling of patients on different demographic, clinical and biochemical and radiological parameters. Quantitative parameters were expressed as means and standard deviation.

Results: In This study total of 100 patients were diagnosed as primary hyperparathyroidism. Ultrasound KUB showed nephrolithiasis in 22 (22%) and nephrocalcinosis in 7 (7%) patients. Both were present in 5 (5%). Nephrocalcinosis alone was present in 2 (2%) patients. The greatest reduction in bone mineral density was found at the site of predominantly cortical bone, the radius (0.73±0.13 g/cm2), whereas the site of predominantly cancellous bone, the lumbar spine (0.94±0.13 g/cm2). The site of mixed composition, the femoral neck (0.87±0.13 g/cm2), gave an intermediate value. Parathyroid adenoma was the most common histological change noted in the parathyroid glands. 85 (96.59%) patients had adenoma and 3 (3.4%) patients had hyperplasia of parathyroid gland. The mean total parathyroid gland weight was 2.75±3.53 g (0.1-18.5). In asymptomatic group mean adenoma weight was 1.87±1.89 (0.1-6.2) g and in symptomatic group mean adenoma weight was 3.59±4.45 g (0.2-18.5) . In asymptomatic group had a significantly lower mean adenoma weight (1.87 vs. 3.59 g, $P<.05$) compared to the symptomatic group.

Conclusion: Our study showed 49% patients were asymptomatic. Asymptomatic PHPT has not been described in India, this is the first prospective study to show increasing incidence of asymptomatic PHPT in India.

This study provides valuable insights into the clinical, imaging, and surgical outcomes of Indian patients with Primary Hyperparathyroidism (PHPT). Imaging techniques, particularly ultrasound and bone mineral density measurements, play a critical role in identifying renal and skeletal complications associated with PHPT, such as nephrolithiasis, nephrocalcinosis, and reduced bone mineral density. The study also highlights the significant correlation between adenoma size and the presence of symptoms, with symptomatic patients having larger adenomas compared to asymptomatic ones.

Post-surgical outcomes following parathyroidectomy demonstrate significant improvements in calcium levels, symptoms, and overall quality of life for most patients. The majority of patients achieve normalization of serum calcium, and those with nephrolithiasis or nephrocalcinosis often experience reduced stone formation post-surgery. These findings emphasize the importance of early diagnosis, appropriate imaging, and timely surgical intervention to achieve optimal outcomes in PHPT patients.

Overall, this study underscores the need for a tailored approach in the management of PHPT, where imaging and surgical strategies are personalized based on the clinical presentation and adenoma characteristics. Continued follow-up and monitoring are essential to ensure the long-term success of treatment and the prevention of recurrence.

Keywords: Imaging, Post Surgical Data, PHPT.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the disease characterized by hypercalcemia due to autonomous production of parathyroid hormone (PTH) by one or more glands. PHPT is caused by adenoma (85%), hyperplasia (14%) or carcinoma (1%). PHPT is present in 1% of the adult population, and its incidence increases to 2% after the age of 55 years in Western series.[1]

By far the most common lesion found in patients with primary hyperparathyroidism is the solitary parathyroid adenoma . Several risk factors have been identified in the development of primary hyperparathyroidism.[2,3]

In approximately 15 % of cases, all four parathyroid glands are involved in the hyperparathyroid process. There are no clinical features that differentiate primary hyperparathyroidism due to adenoma versus hyperplasia.4 it is associated with a familial hereditary syndrome, such as multiple endocrine neoplasia (MEN) types I and IIa. 5 While the pathophysiology of the sporadic cases is unknown, the calcium set point does not seem to be altered.6

Parathyroid carcinoma causes a severe form of primary hyperparathyroidism and is responsible for less than 1 % of cases of primary hyperparathyroidism

Apart from operator inexperience, the usual cause of initial surgical failure (“persistent disease”) is the presence of either unrecognized (often very asymmetric) parathy¬roid hyperplasia or ectopic parathyroid tissue (i.e., intra¬thyroidal, undescended, retroesophageal, or mediastinal glands).[7] Recurrent disease, defined as that occurring after an interval of at least 6 to 12 months of normo calcemia, varies in incidence from 2% to 16%. Recurrent hyperparathyroidism usually arises in unresected hyperplastic glands, but rarely it may be caused by para¬thyroid carcinoma, a second adenoma, or a multicentric or miliary “parathyromatosis” engendered by inadvertent local seeding of parathyroid tissue (usually hyperplastic) into the neck during previous parathyroid surgery.[8,9]

At present, preoperative imaging enables consideration of a minimally invasive unilateral parathyroidectomy in approximately 70% of those patients thought preopera¬tively to have sporadic primary hyperparathyroidism due to a solitary adenoma. Surgical cure rates in appropriately selected patients are comparable to those achieved after bilateral neck exploration (i.e., 95% to 97%), Although a recent study in which all patients selected for minimally invasive surgery were also subjected to immediate bilateral neck dissection demonstrated a failure to recognize mul¬tiglandular disease in 16% of the subjects. Patients with known or suspected multiglandular disease, such as those with MEN1 and those younger than 30 years of age, should undergo bilateral neck exploration.[10,11,12]

Options for patients with hyperplasia include resection limited to visibly abnormal glands, subtotal parathyroidectomy with cryopreservation of tissue, and total parathyroidectomy with immediate autotransplantation (i.e., in the forearm) of some excised tissue. In patients with MEN1, consider¬ations of the rate (30% to 50% or higher with long-term follow-up) and the timing of recurrences versus the poten¬tial morbidity of surgical hypoparathyroidism tend to favor subtotal parathyroidectomy as the preferred approach at present.[13,14]

The immediate postoperative management of parathy¬roidectomy focuses on establishing the success of the surgery and monitoring the patient closely for symptomatic hypocalcemia and for uncommon but potentially serious acute complications such as bleeding, vocal cord paralysis, and laryngospasm.[15,16] After successful resection of a parathyroid adenoma, serum levels of intact PTH decline rapidly, often to undetectable concentrations, with a disap-pearance half-time of about 2 minutes. Serum calcium typi¬cally reaches a nadir between 24 and 36 hours after surgery.[17] Serum PTH returns to the normal range within 30 hours, although measurements of the parathyroid secretory response to hypocalcemia suggest that it does not fully normalize for at least several weeks.[18,19]

oral calcium supplements routinely are provided as soon as oral intake is reestablished. Moderate doses of calcitriol (0.5 to 1.0 µg daily) are added for those with large adenomas and severe hyperparathyroidism and for those in whom alkaline phosphatase had been elevated preoperatively—that is, patients in whom an impressive calcium requirement can be anticipated, often for many weeks postoperatively, as they remineralize their skeletons. This so-called hungry bone syndrome is associated with hypocalcemia, hypophosphatemia, and low urinary calcium excretion.[20,21]

Preoperative localization studies are recommended for patients with persistent or recurrent disease after a first operation. Scanning with 99mTc-sestamibi offers the highest sensitivity and accuracy, although other studies (ultraso¬nography, computed tomography [CT], magnetic reso¬nance imaging) may provide additional or confirmatory information.

(Sestamibi does localize to thyroid nodules,[22,23] which may accompany parathyroid disease in 20% to 40% of patients, although it tends to wash out from thyroid tissue much more rapidly than from parathyroids. 99mTc-sestamibi can be combined with iodine 123 (123I) scanning to improve distinction of parathyroids from thyroid nodules or with single-photon emission computed tomo¬graphic (SPECT) imaging to achieve accuracy in localiza¬tion not possible with planar imaging.[24,25] On the other hand, sestamibi scanning may fail to reveal small glands (uptake is related to gland size and PTH levels(133) or to demonstrate multiple abnormal glands in cases of para¬thyroid hyperplasia, the most common cause of persistent postoperative hyperparathyroidism. Recently, the use of so-called four-dimensional CT with synchronous contrast-enhanced multiplanar anatomic reconstruction was shown in one study to provide sensitivity superior to sestamibi scanning alone for localizing functioning para¬thyroid tissue in candidates for reoperation.[26,27,28]

More invasive techniques have been used, including angiography and selective venous sampling for measure¬ment of PTH. Ultrasound- or CT-guided fine-needle aspiration of suspected parathyroid tissue may be used to obtain cytologic or immunochemical confirmation before surgery, and intraoperative ultrasonography has been useful in some cases to locate cervical or intrathyroi¬dal glands.[29,30]

After successful surgery for primary hyperparathyroid¬ism, bone mass typically improves by as much as 5% to 10% during the first year at sites rich in trabecular bone (spine, femoral neck),31whereas improvement at cortical sites (distal radius) is less predictable. Increases at tra-becular sites may continue for several years, to as much as 12% to 15% after 10 years, although normal bone mineral density may not be achieved. This improvement, which is most apparent in those with the greatest preoperative reductions in bone mass, may be related in part to rapid remineralization of the previously enlarged bone remodel¬ing volume, but the continued improvement over years suggests a more sustained increase in net bone formation and total bone volume as well.[32,33]

MATERIALS AND METHODS

This was a prospective study conducted at Mahatma Gandhi Medical College and Hospital, Jaipur. consecutive patients with primary hyperparathyroidism from year 2022 to 2024. The Study was Prospective, cross sectional and observational An abbreviated skeletal survey (including X-ray of bilateral hands, skull, spine) was carried out for all patients. Bone mineral density (BMD) at hip, forearm and lumbar spine was determined using a dual-energy X-ray absorptiometer (GE Lunar). Localization of parathyroid adenoma was done by technetium-99m (2-methoxyisobutylisonitrile) (99 mTc MIBI) scan and USG neck in all patients. CT/MRI neck was done whenever indicated. For those patients who meet the criteria for parathyroidectomy,[20] surgery was performed. Weight and number of parathyroid glands resected was recorded. Histopathological diagnosis of surgically dissected tumor specimens was established using conventional histological criteria. Postoperative samples for serum total calcium and intact PTH concentration was taken for three consecutive postoperative days, and the minimal value recorded. Postoperative hypocalcemia was managed by intravenous calcium gluconate infusion and oral calcium and calcitriol wherever indicated.

Statistical Methods

The analysis included profiling of patients on different demographic, clinical and biochemical parameters. Quantitative parameters were expressed as means and standard deviation. Categorical data was expressed as absolute number, percentage & median. Independent student t test was used to compare the mean value of continuous parameter between asymptomatic and symptomatic groups. Cross table were generated and chi square test was used for testing of association between asymptomatic and symptomatic groups .Pearson’s correlation coefficient (r) was calculated to determine the correlation between parameters. P-value < 0.05 is considered statistically significant. All analysis was done using SPSS version 24.0.

RESULTS

This table shows imaging methods used for gland localization. Sonography localized a single adenoma or suggested multiglandular disease in 94 patients (94%). Falsely localized in 3 patients. Technetium 99m sestamibi was done in 99 patients. One patient was pregnant so this scan was not done. Technetium 99m sestamibi localized a single adenoma or suggested multiglandular disease in 90 patients (90.90 %). False localized in one case. C methionine PET was done in 3 patients and the diseased gland was localized in two patients. Diseased gland was not localized in one patient with any modality.

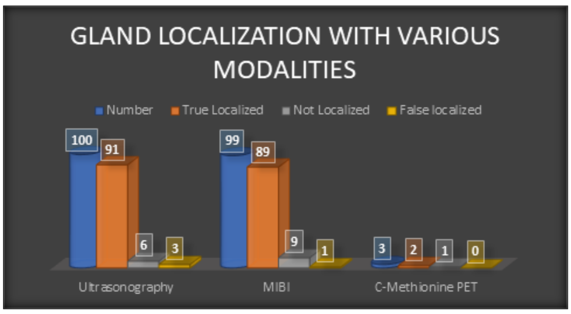

Figure 1:

This figure shows imaging methods used for gland localization. Sonography localized a single adenoma or suggested multiglandular disease in 94 patients (94%), falsely localized in 3 patients. Technetium 99m sestamibi was done in 99 patients. One patient was pregnant so this scan was not done. Technetium 99m sestamibi localized a single adenoma or suggested multiglandular disease in 90 patients (90.90 %), false localized in one case. C methionine PET was done in 3 patients and the diseased gland was localized in two patients. Diseased gland was not localized in one patient with any modality.

This table shows the localization of diseased glands. The most common diseased glands were right inferior gland 43 (43%) and left inferior gland 43 (43%) . Left superior gland was localized in 1 (1%) and right superior gland 3(3%) patients . Multiple glands were localized in 5 (5%) patients . Ectopic gland localized in 4 (4%) patients. [Table 2]

This table shows findings of ultrasound of the kidney, ureters and bladder (KUB)- USG – KUB was done in 100 cases . Ultrasound KUB showed nephrolithiasis in 22 (22%) and nephrocalcinosis in 7 (7%) patients . Both were present in 5 (5%) . Nephrocalcinosis alone was present in 2 (2%) patients. [Table 3]

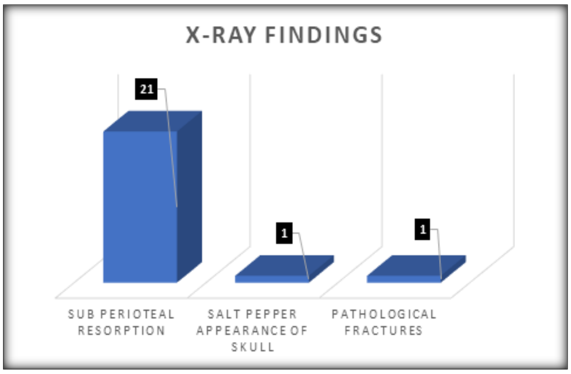

Figure 2:?

This figure shows X-ray findings of patients with PHPT- Ninety nine patients had X-ray results documented as part of their preoperative surgical assessment. X-ray hand showed sub periosteal resorption in 21 (21.21%), X ray skull showed salt pepper appearance in one case. Only one patient presented with pathological fractures.

Table 1: Gland localization with various imaging techniques

Imaging	Number	True localized	False localized	Not localized
Ultrasonography	100	91	3	6
MIBI	99	89	1	9
C-Methionine PET	3	2	0	1

Table 2: Sites of gland localization

Site of localization	Number
Right Superior	3
Right Inferior	43
Left Superior	1
Left Inferior	43
Multiple	5
Ectopic	4
Not Localized	1

Table 3: USG – KUB of patients with PHPT

USG-KUB	Number
Nephrolithiasis	22
Nephrocalcinosis	7
Both	5

This was a prospective study conducted at Mahatma Gandhi Medical College and Hospital, Jaipur. We enrolled consecutive patients with primary hyperparathyroidism from 2022 to 2024. A total of 100 patients were diagnosed as primary hyperparathyroidism.

Localization of parathyroid gland

Patients with PHPT underwent Tc^{99m}-sestamibi scanning and high-resolution ultrasound (US) scanning. One hundred patients underwent high-resolution ultrasound (US) scanning. Sonography localized a single adenoma or suggested multi-glandular disease in 94 patients (94%). Falsely localized in 3 patients. (table 1). Technetium 99m sestamibi was done in 99 patients. One patient was pregnant so this scan was not done. Technetium 99m sestamibi localized a single adenoma or suggested multiglandular disease in 90 patients (90.90 %). False localized in one case. 3 out of 4 ectopic glands were localized by technetium 99m sestamibi scan. No ectopic gland was localized by ultrasonography. MRI neck was done in one patient and the diseased gland was localized. C- methionine PET was done in 3 patients and the diseased gland was localized in two patients. Diseased gland was not localized in one patient with any modality.

The most common diseased gland were right inferior gland 43 (43%) and left inferior gland 43 (43%) patients. Left superior gland and right superior gland were localized in 1 (1%) and 3(3%) patients respectively. Multiple glands were localized in 5 (5%) patients. Ectopic gland localized in 4 (4%)

patients . The sites of ectopic glands were left parasternal groove, left intrathyroidal, right intratyroidal, and tracheo esophageal groove (table 8).

Ultrasound of the Kidney, Ureters and Bladder (KUB)

Ultrasound of the Kidney, Ureters and Bladder (KUB) was done in 100 cases (table 3). Ultrasound KUB showed nephrolithiasis in 22 (22%) and nephrocalcinosis in 7 (7%) patients. Both were present in 5 (5%). Nephrocalcinosis alone was present in 2 (2%) patients (table 3).

Dual-energy *X-ray* absorptiometry scan (DXA scan)

Ninety nine patients had DXA scan results documented as part of their preoperative surgical assessment. One patient was pregnant so DXA scan was not done. Out of 99 patients, 85 had bone involvement (85.85%). Based on the World Health Organisation classification, 40 (40.4 %) had osteopenia and 45 patients (45.45 %) had osteoporosis. The greatest reduction in bone mineral density was found at the site of predominantly cortical bone, the radius (0.73±0.13 g/cm^2), whereas the site of predominantly cancellous bone, the lumbar spine (0.94±0.13 g/cm^2) inety nine patients had X-ray results documented as part of their preoperative surgical assessment. One patient was pregnant so X-ray was not done.

DISCUSSION

PHPT is present in 1% of the adult population, and its incidence increases to 2% after the age of 55 years in Western series.[1] With the advent of multichannel biochemical screening in the 1970s, the incidence of PHPT increased around the world. Subsequently, the clinical entity of asymptomatic hyperparathyroidism was recognized.[3,4]

Dual-energy X-ray absorptiometry scan (DXA scan)

The greatest reduction in bone mineral density was found at the site of predominantly cortical bone, the distal third radius (0.75±0.12 g/cm2), whereas the site of predominantly cancellous bone, the lumbar spine (0.94±0.13 g/cm2). 34,35The site of mixed composition, the femoral neck (0.87±0.13 g/cm2), gave an intermediate value. This finding is similar to Castellano et al (151) study but the mean BMD is higher at all sites in present study. Out of 99 patients, 40 (40.4 percent) had osteopenia and 45 patients (45.45 percent) had osteoporosis. This finding in contrast to Castellano et al study where osteoporosis was 74%(151). These differences may be due to different age profile of patients.[36]

Surgery and Histopathology of the parathyroid glands

The mean adenoma weight in our study was 2.745 ±3.53 g, which is lower than the mean adenoma weight reported in previous Indian studies (4.5-8.6 g). Parathyroid gland weight not correlated with other parameters in our study. This is in contrast with earlier reports that parathyroid tumor weight was positive correlated with serum calcium , i PTH, and alkaline phosphatase.[37]

Parathyroid carcinoma accounts for <1% of sporadic PHPT.[2] In our cohort, no patient had parathyroid carcinoma with surgically treated PHPT. Our finding is similar with retrospective study that have been conducted in Australia.[8] In the Australian series, although parathyroid carcinoma overall only accounted for 0.5% of all parathyroid tumors

from 1958 to 2010. This finding is in contrast to high prevalence rate of parathyroid carcinoma has been reported previously from India. Also, in a recent study of PHPT in a Chinese population, 14/235 (5.96%) patients had parathyroid carcinoma. The reasons behind such a change in these countries are not clear. Increased calcium screening and operations on asymptomatic patients may be contributing factors.[38,39]

The difference in skeletal manifestations of PHPT between western and eastern populations has been proposed to due to a high prevalence of vitamin D deficiency in east and differences in prevailing surveillance patterns.[8] Our finding supports this because in our series the mean concentration of vitamin D is similar to west.

However, despite the prevalence of vitamin D deficiency reported from Asian countries, there seems to be a change in the clinical presentation of disease, with an increasing number of patients with non skeletal or minimal manifestations being reported. A recent study on Chinese PHPT patients from 2000 to 2010 showed that asymptomatic PHPT increased to 50% of all cases after 2007.[16]

Thus, our study cohort had features midway between those reported from the western countries and those reported from India. There is a trend toward early detection of PHPT in the asymptomatic form especially in the affluent population from India.

It is important to identify asymptomatic PHPT because it is not just earlier recognition of patients who would progress to develop classical PHPT as previously hypothesized. Instead, observational data over 1 to 2 decades of follow-up suggest that most patients do not evolve over time to become overtly symptomatic.[20,21] Such data support the decision to withhold surgical intervention in such patients. However treatment of asymptomatic PHPT remains controversial, and some experts feel that all patients with PHPT should be treated surgically, regardless of severity

CONCLUSION

Our study showed 49% patients were asymptomatic. Asymptomatic PHPT has not been described in India, this is the first prospective study to show increasing incidence of asymptomatic PHPT in India.

This study provides valuable insights into the clinical, imaging, and surgical outcomes of Indian patients with Primary Hyperparathyroidism (PHPT). Imaging techniques, particularly ultrasound and bone mineral density measurements, play a critical role in identifying renal and skeletal complications associated with PHPT, such as nephrolithiasis, nephrocalcinosis, and reduced bone mineral density. The study also highlights the significant correlation between adenoma size and the presence of symptoms, with symptomatic patients having larger adenomas compared to asymptomatic ones.

Post-surgical outcomes following parathyroidectomy demonstrate significant improvements in calcium levels, symptoms, and overall quality of life for most patients. The majority of patients achieve normalization of serum calcium, and those with nephrolithiasis or nephrocalcinosis often experience reduced stone formation post-surgery. These findings emphasize the importance of early diagnosis, appropriate imaging, and timely surgical intervention to achieve optimal outcomes in PHPT patients.

Overall, this study underscores the need for a tailored approach in the management of PHPT, where imaging and surgical strategies are personalized based on the clinical presentation and adenoma characteristics. Continued follow-up and monitoring are essential to ensure the long-term success of treatment and the prevention of recurrence.

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