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Evaluation of quality of life in primary hyperparathyroidism patients: Pre- and post-parathyroidectomy outcomes in an Indian cohort

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ABSTRACT

Objective: Primary hyperparathyroidism (PHPT) is a common endocrine condition that causes hypercalcemia and other symptoms due to improper parathyroid hormone (PTH) secretion. With fatigue, bone pain, and neuropsychiatric difficulties, the disorder drastically lowers quality of life (QoL). This study uses Pasieka's parathyroid symptoms score to evaluate parathyroidectomy's impact on Indian PHPT patients' QoL.

Material and Methods: This 18-month prospective observational study was conducted at an Indian academic tertiary care facility. Parathyroidectomy was performed on 42 PHPT patients. Pasieka's parathyroid symptoms questionnaire and baseline clinical and biochemical parameters were completed preoperatively and three months postoperatively. The questionnaire uses a linear analog scale to assess 13 symptoms, including weariness, bone pain, mood issues, and cognitive issues.

Results: Preoperatively, patients demonstrated markedly increased calcium and PTH levels. Post-parathyroidectomy, notable enhancements were noted across various QoL dimensions. Significant reductions in bone pain, joint pain, weariness, and muscle weakness were seen ($p<0.001$). Neuropsychiatric symptoms, such as irritability and mood fluctuations, shown considerable improvement ($p<0.001$). Cognitive symptoms, including amnesia, exhibited some improvement, although dermatological symptoms such as itching and polydipsia were mitigated.

Conclusion: PHPT patients benefit greatly after parathyroidectomy in both physical and mental ways. In order to reduce the systemic effects of PHPT, surgery must be performed quickly. Parathyroidectomy improves patient well-being.

Keywords: Primary hyperparathyroidism, parathyroidectomy, quality of life, postoperative outcomes

INTRODUCTION

Primary hyperparathyroidism (PHPT) is caused by an intrinsic abnormality in one or more of the parathyroid glands, leading to inappropriate secretion of parathyroid hormone (PTH) independent of serum ionized calcium levels (1). As a result, patients with PHPT develop an altered calcium regulatory set point, maintaining elevated circulating calcium levels through increased renal calcium absorption, enhanced gastrointestinal absorption, and heightened osteoclastic activity in bone (2).

The diagnosis of PHPT is predominantly biochemical, marked by increased intact PTH levels and hypercalcemia in individuals with normal renal function (3). PHPT exerts considerable systemic effects, encompassing renal symptoms such as nephrolithiasis, nephrocalcinosis, renal tubular acidosis, nephrogenic diabetic insipidus, and both acute and chronic renal insufficiency (4). Bone-related problems, such as osteopenia and osteoporosis, are also common (5). Furthermore, PHPT is linked to a wide array of non-specific symptoms, such as cognitive deficits, fatigue, irritability, sleeplessness, digestive disorders, and musculoskeletal pain, all of which diminish quality of life (QoL) (6).

QoL evaluation in patients with PHPT is essential for understanding the disease's wider implications beyond biochemical irregularities. A variety of instruments exist for this objective, such as Pasieka's parathyroid symptoms score, the short-form

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health survey-36 (SF-36), the primary hyperparathyroidism quality of life questionnaire (PHPQoLQ), and the disease-specific quality-of-life questionnaire for patients with PHPT (7). Pasieka's parathyroid symptoms score is essential for assessing patient-reported outcomes post-parathyroidectomy (PTX), as it encompasses both physical and neuropsychiatric symptoms (8).

However, there is a paucity of data from India evaluating QoL in PHPT patients, despite differences in disease presentation, healthcare access, and treatment timelines compared to Western populations (9). Understanding patient-reported outcomes in this context is essential for guiding clinical decision-making and health policy.

Therefore, the aim of this study is to objectively assess the QoL in Indian patients with PHPT before and after curative parathyroidectomy using Pasieka's parathyroid symptoms score. This study provides valuable insight into the symptomatic burden of PHPT in an underrepresented population and highlights the tangible benefits of surgery beyond biochemical correction, contributing novel data to a globally relevant yet locally underexplored issue.

MATERIAL and METHODS

This prospective observational study was performed at an academic tertiary care institution in India over an 18-month period, from July 2019 to December 2020. Written informed consent was acquired from all participants. The study was approved by Institution Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh on March, 2021 under letter no. NK/6980/MS/175.

Patient Selection

Patients diagnosed with PHPT were included in the study. The inclusion criteria were persons with biochemically verified PHPT (elevated PTH levels alongside hypercalcemia). Exclusion criteria encompassed those with secondary or tertiary hyperparathyroidism, chronic kidney disease (stage 3 or above), or a history of neck surgery.

Data Collection and Preoperative Assessment

Prospective data collection included demographic information, medical history (including comorbidities), clinical manifestations of PHPT, and relevant biochemical, radiological, operative, and histological findings. All patients underwent parathyroid imaging, comprising of neck ultrasound and Tc-99m-sestamibi scans, to identify the afflicted gland(s).

Surgical Approach

Parathyroidectomy was conducted utilizing either a minimally invasive approach through a restricted cervical incision or via bilateral neck exploration, contingent upon preoperative imaging results and intraoperative evaluation.

QoL Assessment

All patients completed Pasieka's parathyroid symptoms questionnaire both preoperatively and at a three-month follow-up, which was originally developed in English. For patients who were not proficient in English, bilingual healthcare professionals assisted in translating the questionnaire into Hindi or other vernacular languages during the interview process. While this approach ensured patient comprehension, a formal forward-backward translation and validation process of the questionnaire in these languages was not performed. The questionnaire comprises 13 items assessing symptoms such as abdominal discomfort, bone pain, mood disorders, weakness, headaches, irritability, joint pain, exhaustion, amnesia, trouble standing from a seated posture, pruritus, and polydipsia. Symptoms were evaluated using a linear analog scale from 0 (absence of symptoms) to 100 (maximum severity), resulting in a cumulative score between 0 and 1300, based on multiple evaluations or a specified formula, not described here.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was employed to assess the distribution of continuous variables for normality. Continuous variables demonstrating normal distribution were expressed as mean ± standard deviation, while non-normally distributed variables, if any, were reported as median and interquartile range (IQR). Preoperative and postoperative comparisons of continuous variables were performed using the paired Student's t-test for normally distributed data and the Wilcoxon signed-rank test for non-parametric data.

Categorical variables were summarized as frequencies and percentages. Comparisons between categorical variables were conducted using the chi-square test or Fisher's exact test, as appropriate, based on the expected cell counts.

Effect sizes were calculated where relevant to assess the magnitude of differences observed. All statistical tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant. Graphs and plots were generated to visualize the distribution of scores and, where applicable, changes in symptom severity over time.

RESULTS

The study included 42 patients with a mean age of 41.62±13.32 years (range: 18-72 years). The predominant age group among patients was 41-50 years, comprising 38.1%, while females represented 66.7% of the study cohort (Table 1). The average systolic and diastolic blood pressures were 130.60±11.27 mmHg and 77.74±6.64 mmHg, respectively. The average weight and height of the group were 69.95±11.81 kg and

161.07±5.85 cm, yielding a mean body mass index (BMI) of 26.60±3.15 kg/m^2. Over half of the patients (54.8%) exhibited a BMI within the overweight range (25.0-29.9 kg/m^2), while 14.3% were categorized as obese (BMI ≥30.0 kg/m^2) (Table 1).

Biochemical analyses indicated considerable abnormalities in calcium and phosphate metabolism preoperatively. The average serum calcium level was 2.80±0.30 mmol/L (range: 1.99-3.57 mmol/L), whereas the adjusted calcium level was 2.81±0.31 mmol/L (range: 2.20-3.65 mmol/L). The average serum phosphate level was 0.90±0.42 mmol/L, while the median (IQR) value of serum PTH levels was elevated to 237.50 (179.00-417.00) ng/L, with its extreme values reaching 2293.00 ng/L (Table 1).

PTX, patients demonstrated significant improvements in various aspects of health-related quality of life (HRQoL), particularly concerning musculoskeletal symptoms, neuromuscular function, fatigue, and mood (Table 2).

1. Musculoskeletal Manifestations: Patients experienced significant pain relief. Bone pain scores decreased from 40.71±19.68 to 15.71±5.9 (p<0.001), while joint pain scores dropped from 36.4320.82± to 15.24±5.52 (p<0.001). Joint pain reduction averaged -21.19±17.28, with reductions of up to -60.0. Abdominal pain also showed significant improvement, with scores declining from 30±20.12 to 13.33±6.5 (p<0.001), highlighting the clinical benefits of surgical intervention (Table 2).

Table 1. Summary of clinical details

Clinical parameters	Mean ± SD	Range	Frequency (%)
Age (years)	41.62±13.32	18.00-72.00	
Age distribution			
18-30 years			10 (23.8%)
31-40 years			7 (16.7%)
41-50 years			16 (38.1%)
51-60 years			6 (14.3%)
61-70 years			2 (4.8%)
71-80 years			1 (2.4%)
Gender			
Male			14 (33.3%)
Female			28 (66.7%)
Systolic BP (mmHg)	130.60±11.27	110.00-160.00	
Diastolic BP (mmHg)	77.74±6.64	70.00-90.00	
Weight (kg)	69.95±11.81	45.00-98.00	
Height (cm)	161.07±5.85	150.00-175.00	
BMI (kg/m^2)	26.60±3.15	20.00-34.50	
BMI distribution			
18.5-22.9 kg/m^2			4 (9.5%)
23.0-24.9 kg/m^2			9 (21.4%)
25.0-29.9 kg/m^2			23 (54.8%)
30.0-34.9 kg/m^2			6 (14.3%)
Investigations			
S. magnesium (mg/dL)	2.16±0.60	1.24-4.10	
S. calcium (mg/dL)	11.19±1.20	7.98-14.29	
S. albumin (g/dL)	3.95±0.44	2.89-4.77	
Corrected calcium (mg/dL)	11.21±1.22	8.80-14.60	
S. phosphate (mg/dL)	2.79±1.29	0.60-6.25	
S. PTH (pg/mL)	362.70±368.84	67.30-2293.00	
S. vitamin D (ng/mL)	32.17±18.79	9.75-93.40	
ALP (U/L)	213.03±182.20	63.00-737.00	

SD: Standard deviation, BMI: Body mass index, PTH: Parathyroid hormone, BP: Blood pressure, ALP: Alkaline phosphatase

2. Neuromuscular Function and Fatigue: Fatigue and muscle weakness, common symptoms of hyperparathyroidism, have improved markedly. Fatigue scores reduced from 47.62±15.9 to 16.9±5.63 (p<0.001). Similarly, weakness scores improved from 45.71±20.62 to 17.38±5.87 (p<0.001) (Table 2). Patients reported better physical endurance and reduced difficulty in daily tasks. The ability to rise from a chair, a key mobility indicator, improved from 17.14±15.19 to 10.95±3.7 (p=0.003) (Table 2).

3. Neuropsychiatric and Cognitive Manifestations: Patients experienced significant reductions in irritability (27.38±17.54 to 14.05±7.34, p<0.001), mood fluctuations (18.57±13.36 to 11.43±3.54, p<0.001), and feelings of sadness (14.52±9.42 to 10.95±2.97, p=0.002) (Table 2). Headaches, another frequently reported symptom, decreased significantly from 25.71±20.02 to 13.1±6.04 (p<0.001), with an average reduction of 12.62±18.62 (Table 2).

Cognitive symptoms showed mild improvements. Forgetfulness scores decreased from 15±11.32 to 12.14±7.5, though the change was not statistically significant (p=0.110) (Table 2).

Dermatological and additional symptoms - Symptoms such as polydipsia and pruritus improved significantly. The feeling of thirst decreased, with an average change of -6.43±11.44. Pruritus symptoms were reduced significantly (Table 2).

4. Comprehensive Symptomatic Alleviation and Clinical Consequences: The postoperative changes in HRQoL underscore the substantial benefits of parathyroidectomy. The most significant improvements were observed in fatigue (-30.71±14.38), bone pain (-25.00±18.25), joint pain (-21.19±17.28), and weakness (-28.33±16.81), with some patients achieving total symptom relief (Tables 2, 3). While symptom relief varied among individuals, the overall trend highlighted the effectiveness of surgery in improving QoL.

DISCUSSION

Our study provides significant evidence that parathyroidectomy substantially improves the QoL in patients with PHPT. Using Pasieka's parathyroid symptoms score, we observed significant decreases in the severity of a wide range of symptoms within three months post-surgery. These findings corroborate past research highlighting the diverse advantages associated with surgical intervention in PHPT and emphasize the particular symptomatic improvements that reflect the experiences of patients in India.

Symptomatic Burden and Surgical Outcomes

PHPT is recognized for its diverse clinical presentations, including traditional symptoms like nephrolithiasis and osteoporosis, as well as more subtle signs such as fatigue, cognitive impairment, and irritability. Our investigation revealed that preoperative symptom scores identified fatigue, weakness, and bone pain as the most significant complaints. These findings correspond with previous research by Pasieka et al. (7) and others, which similarly highlighted fatigue and bone pain as defining characteristics of PHPT and key contributors to diminished QoL. A study by Pasieka et al. (7) indicated that 89% of patients with PHPT experienced fatigue, whereas 76% reported bone pain preoperatively,

Table 2. Summary of changes in individual parameter at 3 months after parathyroidectomy in 42 patients

HRQoL	Pre-operative Mean ± SD	Post-operative (after 3 months) Mean ± SD	p-value
Abdominal pain	30±20.12	13.33±6.5	0.000
Inability to move off a chair	17.14±15.19	10.95±3.7	0.003
Bone pain	40.71±19.68	15.71±5.9	0.000
Feeling thirsty	19.05±13.22	12.62±4.97	0.001
Feeling tired	47.62±15.9	16.9±5.63	0.000
Feeling weak	45.71±20.62	17.38±5.87	0.000
Feeling blue	14.52±9.42	10.95±2.97	0.002
Forgetfulness	15±11.32	12.14±7.5	0.110
Headache	25.71±20.02	13.1±6.04	0.000
Irritability	27.38±17.54	14.05±7.34	0.000
Itchy	15.95±13.26	11.19±3.28	0.011
Joint pain	36.43±20.82	15.24±5.52	0.000
Mood change	18.57±13.36	11.43±3.54	0.000

SD: Standard deviation, HRQoL: Health-related quality of life

Table 3. Summary of change in HRQoL

Change in HRQoL (post-operative)	Mean ± SD	Min-max
Abdominal pain	-16.67±16.03	-60.0-0.0
Ability to move off a chair	-6.19±12.48	-60.0-0.0
Bone pain	-25.00±18.25	-70.0-20.0
Feeling thirsty	-6.43±11.44	-40.0-10.0
Feeling tired	-30.71±14.38	-50.0-10.0
Feeling weak	-28.33±16.81	-60.0-0.0
Feeling blue	-3.57±6.92	-30.0-0.0
Forgetfulness	-2.86±11.32	-40.0-40.0
Headache	-12.62±18.62	-60.0-30.0
Irritability	-13.33±16.48	-60.0-0.0
Itchy	-4.76±11.53	-50.0-10.0
Joint pain	-21.19±17.28	-60.0-0.0
Mood change	-7.14±12.15	-50.0-0.0

SD: Standard deviation, HRQoL: Health-related quality of life

aligning with our findings on symptom prevalence. The post-surgical improvements observed in our study validate the results of prior research. A 2011 study by Wilhelm et al. showed that parathyroidectomy normalizes biochemical markers and significantly alleviates musculoskeletal and neuropsychiatric symptoms, often within a few months of surgery (10). Similarly, our study found that fatigue, weakness, and bone pain exhibited the most substantial reductions in symptom scores, with improvements of over 60% in these domains. This highlights the significance of parathyroidectomy as a conclusive procedure for both biochemical normalization and alleviation of symptoms.

Neuropsychiatric Enhancements and Ongoing Symptoms

Neuropsychiatric symptoms in PHPT, including depression, irritability, and memory loss, are often overlooked despite their significant impact on QoL. Our study noted significant post-surgical improvements in symptoms like irritability and mood swings, consistent with the findings of Roman (11), who documented substantial gains in emotional well-being after surgery. The improvement in symptoms like "feeling blue" and irritability aligns with the hypothesis that hypercalcemia-related neurochemical imbalances are reversible after surgery. However, certain symptoms in our cohort, such as forgetfulness and itchy skin, showed minimal improvement. This observation corresponds with other research, including a study by Westerdahl and Bergenfelz (12), which indicated that although parathyroidectomy efficiently alleviates symptoms directly related to hypercalcemia, symptoms with a multifactorial origin or less direct connection to parathyroid function may endure. Forgetfulness may be affected by age-related cognitive alterations or other concomitant conditions, highlighting the necessity for supplementary care techniques in addition to surgery.

Global Comparisons and Cultural Context

Our research provides significant insights into the global comprehension of PHPT, especially from an Indian viewpoint, where QoL data are limited. Studies conducted in Western populations, such as those by Szalat et al. (13) and VanderWalde (14), have consistently demonstrated QoL improvements after parathyroidectomy, with reductions in symptoms like fatigue, joint pain, and depression. These parallels emphasize the widespread advantages of parathyroidectomy among many populations, while also underscoring the necessity of regional studies, to include cultural and healthcare system disparities. In our investigation, the preoperative symptom load was significantly elevated, with mean scores for fatigue and bone pain surpassing those documented in comparable studies from Western nations. This gap may indicate postponed diagnosis and extended disease duration in Indian patients, potentially attributable to restricted awareness and access to specialized care. The increased symptom load highlights the critical necessity for prompt diagnosis and care in resource-limited environments.

Strengths and Novel Contributions

A principal strength of our study is its prospective design, facilitating a rigorous comparison of symptom profiles pre- and post-surgery. Furthermore, by employing disease-specific instrument such as Pasieka's parathyroid symptoms score, we obtained a detailed and thorough understanding of the clinical enhancements observed in PHPT patients. This methodology differentiates our research from others that have utilized generic QoL instruments, such as the SF-36, which may inadequately encompass the symptomatology specific to PHPT.

Our study's original contribution lies in its emphasis on an Indian cohort, offering context-specific data that were previously absent. With the growing recognition of PHPT in India due to enhanced diagnostic capabilities, our findings underscore the essential significance of parathyroidectomy in the management of this ailment and provide a standard for future studies in the area.

Study Limitations

Despite its strengths, our study has several limitations. The brief three-month follow-up duration may inadequately reflect the long-term advantages or possible symptom return following parathyroidectomy. Extended follow-up studies are essential to ascertain the sustainability of these enhancements and their effect on patients' overall QoL.

One of the key limitations of our study is that while the questionnaire was translated into the vernacular language with the assistance of bilingual healthcare professionals, a formal forward-backward translation and validation process was not performed. The single-center design and limited sample size restrict the generalizability of our results. Multicenter studies with larger cohorts could yield more extensive insights and facilitate subgroup analysis, including the effects of surgical procedures or variations in outcomes related to preoperative calcium levels. Ultimately, although Pasieka's parathyroid symptoms score serves as an effective instrument for evaluating disease-specific symptoms, the inclusion of other tools such as the PHPQoLQ or the SF-36 may yield a more comprehensive evaluation of patient outcomes.

CONCLUSION

The results of our research hold considerable significance for clinical practice. They underscore the significance of acknowledging the symptomatic burden of PHPT and the role of parathyroidectomy in attaining not just biochemical resolution, but also substantial enhancements in QoL. These findings should motivate doctors to emphasize early diagnosis and prompt surgical referral for symptomatic patients. The continuation of specific symptoms after surgery underscores the necessity for a multidisciplinary approach to patient care, incorporating supportive interventions like cognitive therapy or dermatological treatment where suitable.

Ethics

Ethics Committee Approval: The study was approved by Institution Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh on March, 2021 under letter no. NK/6980/MS/175.

Informed Consent: Written informed consent was acquired from all participants.

Footnotes

Author Contributions

Concept – M.R., C.T., D.D., S.K.B.; Design – M.R., C.T., D.D.; Supervision – C.T., D.D., A.B., S.K.B.; Data Collection or Processing – M.R., D.D., M.T., S.K.B., A.B.; Analysis or Interpretation – M.R., M.T., S.V.P.; Literature Search – C.T., M.T., S.V.P.; Critical Review – A.B., S.K.B., D.D.; Writing – M.R., C.T.

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