Open Access Journal

Indian Journal of Medical Research and Pharmaceutical Sciences

October 2020;7(10) ISSN: ISSN: 2349-5340

Impact Factor: 4.054

PROFILE OF PATIENTS OPERATED ON FOR PRIMARY HYPERPARATHYROIDISM AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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Keywords: *thyroidectomy, Routine intensive, Patients, endocrine operation.*

Abstract

Introduction: The presentation of primary hyperparathyroidism is protean, making the early diagnosis difficult. The routine use of automated calcium analyser has solved the problem where it is available. This is not the case for Chris Hani Baragwanath Academic hospital (CHBAH), where, according to our observations, the diagnosis is still a challenge and often made in the complication-related stage. Worldwide, women are more affected than men, especially after menopause. The morbidity associated with hyperparathyroidism can be disastrous for a condition that can be readily treated. The aim of this study is to assess the profile of patients operated on for primary hyperparathyroidism.

Objective: To determine the clinical presentation, the calcium level, and the cause of primary hyperparathyroidism

Method: Review of all patients operated on for primary hyperparathyroidism at CHBAH from 2013 to 2019.

Results: Most patients presented with various conditions not directly related to hyperparathyroidism and had mild to moderate hypercalcemia. Over 90% of hypercalcemia resolved post-parathyroidectomy, and parathyroid adenoma was the most common histopathological report.

Conclusion: Primary hyperparathyroidism was mainly established in the workup of patients who presented with various conditions and was associated with significant comorbidities. Most cases were due to parathyroid adenoma that was successfully treated with parathyroidectomy.

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Introduction

Primary hyperparathyroidism is the third most common endocrine disorder of calcium metabolism characterised by hypercalcemia and elevated or inappropriately normal concentrations of parathyroid hormone[1]. It affects 0.3% of the general population and 1–3% of postmenopausal women[2]. Worldwide, women are affected three times more often than men[3]. It commonly affects women over 50 years old, and therefore the highest prevalence is seen in postmenopausal women[4]. Hypercalcemia has systemic manifestation throughout the body, making the clinical presentation nonspecific. It encompasses musculoskeletal, neuropsychiatric, gastrointestinal, cardiovascular, urogenital, and renal symptoms. The most common presentation is fatigue, but it is difficult in the setting of chronic disease to equate fatigue with hyperparathyroidism. The delay in diagnosis has led to the classical presentation of "pain, moan, groan stones" in advanced cases[5,6]. The clinical profile of primary hyperparathyroidism in most western countries has changed. With the introduction of routine biochemical screening in 1970 (automated calcium analyser), the diagnosis is made early[7,8]. This has led to the introduction of the term "asymptomatic hyperparathyroidism", which describes the patients who lack the clinical signs and symptoms associated with hypercalcemia[9]. The routine biochemical screening has also translated into fivefold increased detection because the signs and symptoms of hyperparathyroidism are protean[10]. This has not been the narrative for the patients in our setting, in which such biochemical screening is not routinely practised. Therefore, it is our observation that the patients at Chris Hani Baragwanath Academic Hospital (CHBAH) are still being diagnosed and recognized in the symptomatic and

complication-related stages. Delayed presentation can lead to significant morbidity and disability for a condition that is readily diagnosed by routine blood test. Unfortunately, in low- to middle-income countries, to our knowledge the automated calcium analyser is not common practice even in tertiary health facilities. Limited medical services in rural communities and delayed referrals are hypothesized to affect the profile of our patients at presentation. There is also a scarcity of publications on hyperparathyroidism in South Africa[11]. But the report from India mirrors our observations[11,12]. We therefore endeavour in this study to review the parathyroidectomies performed for primary hyperparathyroidism at CHBAH over the past 7 years to determine the clinical presentation and the associated comorbidities/complications.

Objective

To determine the clinical presentation of patients operated on for primary hyperparathyroidism.
To determine the level of hypercalcemia at diagnosis and post-operative outcome.
To determine the cause of primary hyperparathyroidism.

Method

This descriptive study was conducted retrospectively at CHBAH on all patients operated on for primary hyperparathyroidism from January 2013 to December 2019. Parameters analysed included the patients' demographics, comorbidities, surgery, histopathological report, clinical presentation, calcium result, parathyroid hormone (PTH) result, and imagings. The exclusion criterion was all parathyroidectomy performed for other indications (secondary and tertiary hyperparathyroidism). Data was obtained from the department of record and theatre registry at CHBAH. Ethical approval was obtained from the human ethics committee of the University of the Witwatersrand and the research review board of CHBAH (clearance certificate number: M191125).

Statistical analysis

The results in this observational descriptive study are expressed as proportion by ratio or percentage for continuous variable and as mean/median (for non–normally distributed parameters) and standard deviation for categorical variables. Data was analysed using STATA software.

Results

Table 1. Demographics

Parameters	Results
Female (number, %)	62 (80.52)
Male (number, %)	15 (19.48)
Female to male ratio	4:1
Mean age, years (range)	61 (24–85)
Median age, years	62
Race, blacks vs. others (number, %)	67 vs. 10 (87.01 vs. 12.99)

Table 2. Clinical presentation

Clinical Presentation	Number	Percentage (%)
Gastrointestinal (constipation, , PUD, pancreatitis)	13	17.11
Rheumatology (bone pain, osteoarthritis)	26	35.14
Cardiovascular (MI, palpitations, arrhythmia)	2	2.63
Neuropsychiatric (mood disorder, confusion, forgetfulness, insomnia, anxiety, CVA	18	23.68
Urogenital (stones)	7	9.21

Orthopaedic (fracture)	4	5.26
Non-specific (fatigue, tinnitus, weight loss)	16	21.05
Incidental finding of elevated calcium	7	9.21

Note: CVA = Cerebrovascular accident MI = myocardial infarction. PUD = Peptic ulcer disease. Some patients presented with multisystemic symptoms and therefore each symptom was included under the system affected. That is why the total is more than the number of patients (77).

Table 3. Underlying comorbidities

Underlying Conditions	Number (%)
Human immunodeficiency virus	8 (10.53)
Musculoskeletal	21 (27.63)
Gastrointestinal tract	12 (15.73)
Respiratory system	3 (3.95)
Central nervous system	7 (9.21)
Diabetes	13 (17.11)
Malignancy	7 (9.21)
Cardiovascular system	46 (60.3)

Note: Some patients presented with multisystemic symptoms and therefore each symptom was included under the system affected. That is why the total is more than the number of patients (77)

Biochemical findings

All patients had elevated calcium with a mean value of 2.95 mmol/l (2.53–3.56). Mild hypercalcemia (2.55–3.0 mmol/l) represented the majority of cases (50/77; 64.94%); 33.77% (26/77) of patients presented with moderate hypercalcemia (3.0–3.5 mmol/l), and one patient (1.30%) had severe hypercalcemia (3.5–4.0 mmol/l). The PTH was equally elevated with a mean of 20.34 pmol/L (7.30–53.80). Of the 49 patients (63.63%) who had Vitamin D results available, 26 (53.06%) had a normal value and the remaining 23 (46.93%) had a low value. Their respective mean was 106 nmol/L (73.92–185) and 50.74 (21.73–72.31), the normal value of vitamin D being >72.50 nmol/L

Post-operatively (on day one), hypercalcemia resolved in the majority of patients (90.91%), of which 62.33% were rendered normocalcemic with a mean of 2.33 mmol/L (2.21–2.53), and 28.57% developed transient hypocalcemia with a mean of 1.89 mmol/L (1.06–2.14). The remaining patients (9.09%) had unresolved hypercalcemia after the index operation (mean of 2.75 mmol/L ranging from 2.63 to 2.9). The patient with parathyroid carcinoma had the most profound hypocalcemia (1.06 mmol/L) post-operatively whereas the pre-operative value was not the highest (3.06 mmol/L).

Imagings

Because pre-operative localization was mandatory before surgery, 97.4% (75/77) had Tc-99m-Sestamibi scan, and 93.5% (72/77) had ultrasound. In 12% of Tc-99m-Sestamibi and 6.9% of ultrasound scans, the tumour could not be localized. All ultrasounds were performed by or under the supervision of a single experienced sonographer.

Surgery

Besides the parathyroid exploration, thyroidectomy was performed as an added procedure in 7 cases (4 total and 3 lobectomy). The 4 total thyroidectomy cases were equally divided between malignancies and Graves' disease. The 3 lobectomies were for intrathyroidal parathyroid adenoma (2 cases) and one benign goitre. Three parathyroid explorations failed (histopathology revealed lymph node).Two additional failed exploration (fat tissue) were successful on re-exploration, and the parathyroid was discovered in the carotid sheath. In two other cases with confirmed adenoma, the calcium remained high after a transient decrease. These two cases were treated medically although the repeat Tc-99m-Sestamibi scan revealed a second intrathoracic adenoma in one of them.

Histopathological report

Sixty-four cases were reported as adenoma (83.1%), and in 9 cases (11.6%) the report was either hyperplasia or adenoma (to correlate with the clinical presentation). There was one parathyroid carcinoma (1.2%), and three failed procedures (3.8%) reported as lymph nodes.

Discussion

The presentation of our patients was varied in keeping with the non-specificity of the clinical picture. It is not surprising that the majority of the patients presented with organ-specific complications related to various sub-specialities because it is not possible to diagnose hyperparathyroidism apart from routine calcium analysis. Likewise, it is difficult to establish to what extent the hypercalcemia worsened the underlying condition. Most patients had mild to moderate hypercalcemia (98.18%) despite the delayed presentation. The high number of patients with post-operative hypocalcemia is what is expected because the dominant gland (adenoma) is removed[13]. The natural history is toward normalization of calcium as the suppressed normal glands recover.

The paucity of oxyphilic cells, the size of the adenoma below the resolution of the gamma camera (<1 cm), and the presence of the MDR 1 gene, which encodes for P-glycoprotein are known reasons for a failed Tc-99m-Sestamibi scan.[14,15] On ultrasound the non-localizations are due to ectopic site (retro-esophageal, tracheoesophageal groove, carotid sheath, mediastinum, intrathyroidal, intrathymic), the size being smaller than 5 mm, the quality of the machine, and the expertise of the sonographer[15].

The high incidence of adenoma in our study is in line with the literature where adenoma represents 87%, hyperplasia 9%, multiple adenoma 3%, and malignancy less than 1%[10]. It is not easy to differentiate hyperplasia from adenoma at histopathology without the additional information provided by clinical picture, imaging, and intra-operative findings, so some of the histopathology was reported by the pathologist as either adenoma or hyperplasia even though their clinical behaviour and imaging favoured adenoma. Most of our patients were female and advanced in age.

Limitations

Retrospective nature with possibility of missing data.

Conclusion

Primary hyperparathyroidism was discovered mainly in the work-up or follow-up of the underlying conditions and was associated with significant complications related to the various target organs involved. Almost all patients had mild to moderate hypercalcemia, most of which resolved after surgery, and the adenoma was by far the most common histopathological report.

Recommendation

Because the only reliable way to diagnose hyperparathyroidism is routine calcium measurement, it will be of benefit to routinely test calcium at least in critically ill patients and in patients with chronic conditions.

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