

PRIMARY HYPERPARATHYROIDISM: EPIDEMIOLOGICAL, CLINICAL, AND THERAPEUTIC FEATURES IN A TERTIARY HOSPITAL COHORT

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ABSTRACT

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by inappropriate secretion of parathyroid hormone (PTH), leading to hypercalcemia. Although biochemical screening has increased the diagnosis of asymptomatic forms in developed countries, PHPT continues to be diagnosed at symptomatic stages in other regions. Data from North Africa are limited. The aim of this study was to describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of patients with PHPT treated in two referral hospitals in Rabat, Morocco. Materials and methods: A descriptive study was conducted including adult patients with a confirmed diagnosis of PHPT managed between January 2015 and December 2022 at Ibn Sina University Hospital and Mohamed V Military Hospital. Clinical, biochemical, imaging, therapeutic, and outcome data were analyzed. Results: Eighty-three patients were included, with a mean age of 53.27 ± 16.86 years and a marked female predominance (90.4%). PHPT was asymptomatic in 39.7% of cases. Osteoarticular manifestations were the most frequent (56.6%). Mean serum calcium level was 122.8 ± 21.4 mg/L, and PTH levels were elevated in all patients. Cervical ultrasound and sestamibi scintigraphy showed sensitivities of 89.1% and 92%, respectively. Surgical treatment was performed in 95.18% of patients. Postoperative hypoparathyroidism occurred in 34.9%. Conclusion: In this cohort, PHPT was frequently diagnosed at symptomatic stages, with a high burden of skeletal involvement. Early detection through systematic serum calcium measurement and timely surgical management are essential to prevent complications and improve long-term outcomes.

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HIPERPARATIROIDISMO PRIMARIO: CARACTERÍSTICAS EPIDEMIOLÓGICAS, CLÍNICAS Y TERAPÉUTICAS EN UNA COHORTE HOSPITALARIA DE TERCER NIVEL

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RESUMEN

El hiperparatiroidismo primario (HPTP) es una endocrinopatía caracterizada por la secreción inapropiada de hormona paratiroidea (PTH), que conduce a hipercalcemia. Si bien el cribado bioquímico ha incrementado el diagnóstico de formas asintomáticas en países desarrollados, en otras regiones continúa diagnosticándose en etapas sintomáticas. Los datos provenientes del norte de África son limitados. El objetivo del estudio fue describir las características epidemiológicas, clínicas, paraclínicas y terapéuticas de pacientes con HPTP atendidos en dos hospitales de referencia en Rabat, Marruecos. Materiales y métodos: Se realizó un estudio descriptivo que incluyó pacientes adultos con diagnóstico confirmado de HPTP (enero de 2015 y diciembre de 2022) en el Hospital Universitario Ibn Sina y el Hospital Militar Mohamed V. Se analizaron datos clínicos, bioquímicos, de imágenes, terapéuticos y evolutivos. Resultados: Se incluyeron 83 pacientes, con una edad media de 53,27±16,86 años y predominio femenino (90,4%). El HPTP fue asintomático en el 39,7% de los casos. Las manifestaciones osteoarticulares fueron las más frecuentes (56,6%). El calcio sérico medio fue 122,8±21,4 mg/L y la PTH estuvo elevada en todos los pacientes. La ecografía cervical y la gammagrafía con sestamibi mostraron sensibilidades del 89,1% y 92%, respectivamente. El tratamiento quirúrgico se realizó en el 95,18%. El hipoparatiroidismo posoperatorio ocurrió en el 34,9%. Conclusión: En esta cohorte, el HPTP se diagnosticó con frecuencia en etapas sintomáticas, con elevada carga de compromiso óseo. La detección precoz mediante medición sistemática del calcio sérico y el manejo quirúrgico oportuno son fundamentales para prevenir complicaciones y mejorar los resultados a largo plazo.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders and is characterized by inappropriate overproduction of parathyroid hormone (PTH) from one or more pathological parathyroid glands, leading to hypercalcemia and disturbances in calcium–phosphate homeostasis [1].
Hypercalcemia associated with PHPT may be detected incidentally during routine biochemical testing or identified in the context

of related complications, particularly skeletal and renal involvement. Over recent decades, the widespread use of automated biochemical screening has led to a shift in the clinical presentation of PHPT, with an increasing proportion of patients being diagnosed at asymptomatic or mildly symptomatic stages [2,3].
In approximately 95% of cases, PHPT occurs sporadically. The underlying pathology is most commonly a single parathyroid

adenoma, accounting for nearly 85% of cases, followed by multiglandular disease, including multiple adenomas or parathyroid hyperplasia, in 10-15% of patients. Parathyroid carcinoma remains a rare cause, representing less than 1% of cases [4]. In contrast, hereditary forms of PHPT—such as multiple endocrine neoplasia (MEN) types 1 and 2A and isolated familial hyperparathyroidism—account for approximately 5% of cases and are typically associated with earlier onset and multiglandular involvement [4,5].

Parathyroidectomy is the definitive treatment for PHPT and is recommended for all symptomatic patients, as well as for asymptomatic individuals who meet established surgical criteria, including younger age and evidence of renal or skeletal involvement. In patients who do not fulfill surgical indications or are not suitable surgical candidates, careful biochemical and clinical surveillance remains an accepted management strategy [6,7].

Despite the availability of international guidelines, the epidemiological and clinical characteristics of PHPT vary across regions, influenced by differences in diagnostic practices, access to biochemical screening, and healthcare systems. Data from North African and developing countries remain limited. Therefore, the present study aimed to describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of patients hospitalized and followed for PHPT at the University Hospital Center of Rabat and the Mohamed V Military Hospital over a 7-year period (2015-2022).

MATERIALS AND METHODS

Study design and setting

A retrospective descriptive study was conducted in the Departments of Endocrinology and Metabolic Diseases of Ibn Sina University Hospital and Mohamed V Military Hospital in Rabat. The study included patients diagnosed and managed for PHPT over a 7-year period, from January 2015 to December 2022.

Study population

All adult patients (≥ 18 years) with a confirmed diagnosis of PHPT who were hospitalized or followed in the participating centers during the study period were eligible for inclusion. Patients with secondary or tertiary hyperparathyroidism were excluded.

Diagnostic criteria

The diagnosis of PHPT was established based on the presence of hypercalcemia associated with elevated serum PTH levels, in accordance with current international recommendations. Hypercalcemia was defined as a total serum calcium level above the upper limit of normal for the local laboratory reference range. PTH concentrations were measured using standardized immunoassays.

Localization studies

All patients underwent cervical ultrasound as the first-line imaging modality for lesion localization. Additional imaging techniques were employed when ultrasound findings were inconclusive or discordant, including cervical and mediastinal computed tomography (CT), sestamibi scintigraphy, magnetic resonance imaging (MRI), and positron emission tomography (PET) using ^{18}F -fluorocholine, according to availability and clinical judgment.

Data collection

Data were collected retrospectively from medical records using a standardized extraction form and included:

- Epidemiological data: age, sex, history of cervical irradiation, sporadic or familial forms of PHPT, and associated comorbidities.
- Diagnostic data: time to diagnosis, circumstances of disease discovery, clinical manifestations, biochemical parameters (serum calcium and PTH levels), imaging findings, and histopathological results.
- Therapeutic data: medical management, surgical treatment, or conservative observation.
- Outcome data: postoperative complications, biochemical evolution, recurrence, and disease persistence.

Therapeutic management and follow-up

Surgical treatment was proposed according to established indications and consisted of parathyroidectomy with intraoperative assessment at the discretion of the surgical team. Histopathological examination of excised specimens was systematically performed. Postoperative follow-up included clinical evaluation and serial biochemical monitoring of serum calcium and PTH levels to assess remission, persistence, or recurrence of disease. Complications such as hypoparathyroidism, hungry bone syndrome, recurrent laryngeal nerve injury, and mortality were recorded.

Statistical analysis

Quantitative variables were expressed as mean $\pm$ standard deviation, while qualitative variables were reported as frequencies and percentages. Data analysis was performed using standard descriptive statistical methods.

RESULTS

A total of 83 patients diagnosed with PHPT were included during the study period. The mean age at diagnosis was 53.27 ± 16.86 years, with a marked female predominance (90.4%).

Clinical presentation

Clinical manifestations were heterogeneous. Osteoarticular involvement was the most frequent presentation, observed in 56.6% of patients, followed by general symptoms in 36.1% and urinary manifestations in 10.8%. Digestive, cardiovascular, neuropsychiatric, and neuromuscular symptoms were less frequently reported. Notably, PHPT was asymptomatic at diagnosis in 39.7% of cases, reflecting the increasing detection of the disease at earlier stages (Figure 1).

Biochemical findings

Mean serum calcium level was 122.8 ± 21.4 mg/L and was within the normal range in 9.6% of patients. PTH levels were elevated in all cases, with a mean concentration

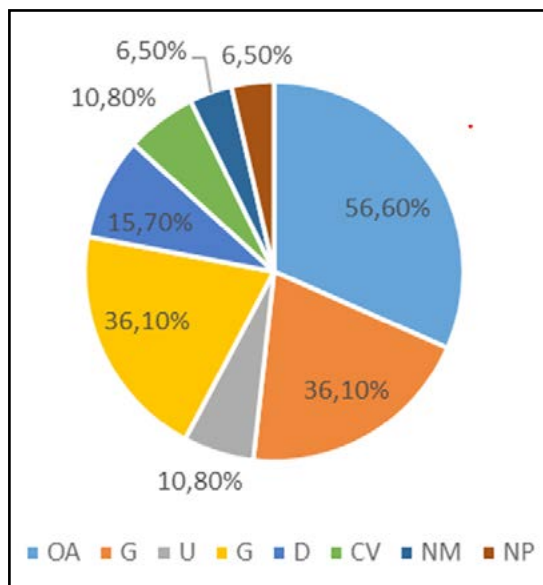


Figure 1. Clinical manifestations at diagnosis in patients with primary hyperparathyroidism. Abbreviations: OA: osteoarticular manifestations; G: general symptoms; U: urinary manifestations; D: digestive manifestations; CV: cardiovascular manifestations; NP: neuropsychiatric manifestations; NM: neuromuscular manifestations.

of 261.7 ± 186.8 pg/mL, confirming the diagnosis of PHPT in the entire cohort.

Imaging and localization studies

Cervical ultrasound was performed in all patients and demonstrated a sensitivity of 89.1% for parathyroid lesion localization. Sestamibi scintigraphy was performed in 64 patients, yielding a sensitivity of 92%. Additional imaging modalities, including CT scan, MRI, and ^{18}F -fluorocholine PET, were used selectively in cases with inconclusive or discordant findings.

Therapeutic management

Surgical treatment was performed in 79 patients, representing 95.18% of the cohort. Parathyroidectomy was the primary therapeutic approach. Histopathological examination of surgical specimens revealed parathyroid adenoma in most cases.

Postoperative outcomes and complications

Postoperative hypoparathyroidism was observed in 29 patients (34.9%), while hungry bone syndrome occurred in 3 patients (3.6%). One case of transient recurrent laryngeal nerve palsy was recorded. Persistent PHPT was observed in one patient, who required three surgical interventions before achieving remission. There was one case of postoperative mortality of unknown cause. Disease recurrence was documented in three patients and was attributed to ectopic parathyroid adenoma.

DISCUSSION

PHPT is a frequent endocrine disorder whose incidence increases with age, particularly among women in the fifth and sixth decades of life. In line with previous reports, our cohort showed a mean age at diagnosis of 53.2 years and a marked female predominance (90.4%), with a high proportion of postmenopausal women. This epidemiological profile is consistent with data reported in large population-based and review studies and reinforces the role of hormonal and metabolic factors in disease expression [3,8].

As described in the literature, the sporadic form represents the majority of PHPT cases, while hereditary forms—mainly associated with multiple endocrine neoplasia types 1 and 2A or isolated familial hyperparathyroidism—account for approximately 5-10% of cases [4,5]. Our findings confirm this distribution, supporting the representativeness of our population.

The clinical presentation of PHPT has evolved over recent decades, largely due to the widespread use of routine biochemical screening. While older series reported symptomatic disease as the rule, contemporary studies from developed countries describe asymptomatic PHPT in up to 70-80% of cases [3,8]. In contrast, 39.7% of patients in our study were asymptomatic at diagnosis, a lower proportion than that reported in Western cohorts. This finding

likely reflects delayed diagnosis and limited systematic calcium screening, underscoring the importance of routine serum calcium measurement, particularly in postmenopausal women and high-risk populations [3,9].

Osteoarticular manifestations were the most frequent clinical presentation in our series (56.6%), consistent with reports from referral and surgical cohorts, where skeletal involvement remains a common mode of presentation [8,10]. Urinary manifestations were less frequent, in line with previously published clinical series [10]. These data suggest that, despite increasing detection of asymptomatic forms worldwide, PHPT in our setting still frequently presents clinically significant skeletal disease.

Biochemical diagnosis was based on the association of hypercalcemia with inappropriately elevated or high-normal PTH levels, in accordance with established diagnostic criteria [1,8]. Notably, normocalcemic PHPT accounted for a small proportion of cases, consistent with previously reported data [11].

Preoperative localization relied primarily on cervical ultrasound and sestamibi scintigraphy, both of which demonstrated high sensitivity in our cohort. These findings are consistent with international data highlighting the complementary role of ultrasound and functional imaging in parathyroid localization [12,13]. Advanced imaging modalities were reserved for selected cases with inconclusive or discordant findings.

Parathyroidectomy remains the definitive treatment for PHPT and was performed in most of our patients. Surgical indications for asymptomatic PHPT were based on international consensus criteria, as defined by the Fifth International Workshop on the Evaluation and Management of PHPT [7] and reinforced by the American Association of Endocrine Surgeons guidelines [6]. More recently, the 2024 recommendations of the Société Française d'Endocrinologie (SFE) have emphasized the importance of ionized calcium measurement in cases of diagnostic

uncertainty, systematic skeletal and renal evaluation, and early surgical management when clinical impact or risk of progression is present [14].

Postoperative complications in our cohort were dominated by hypoparathyroidism, while hungry bone syndrome and recurrent laryngeal nerve injury were rare. Although the rate of postoperative hypoparathyroidism was notable, most cases were transient and managed conservatively. These findings are comparable to those reported in surgical series, particularly in patients with more advanced disease at presentation [6,10].

In non-operated patients, medical management—including vitamin D supplementation—was implemented in accordance with international recommendations, given the high prevalence of vitamin D deficiency in PHPT and its role in aggravating bone involvement [15]. Regular follow-up was essential to monitor biochemical evolution and detect potential renal, skeletal, and cardiovascular complications [9].

This study has several limitations. First, its retrospective design may have introduced information bias due to incomplete or heterogeneous documentation in medical records, particularly regarding non-specific symptoms and the timing of clinical manifestations. Second, the study was conducted in two tertiary referral hospitals, which may have resulted in referral bias and an overrepresentation of symptomatic or complicated cases, potentially limiting the generalizability of our findings to the broader population. Third, localization imaging modalities beyond ultrasound and sestamibi scintigraphy (CT, MRI, and ^{18}F -fluorocholine PET) were performed selectively rather than systematically, which may have influenced the assessment of diagnostic performance. Finally, postoperative outcomes were reported based on available follow-up data; longer follow-up

would be necessary to better quantify long-term recurrence and persistent disease. Despite these limitations, the study provides valuable regional data on the epidemiological profile, clinical presentation, diagnostic approach, and therapeutic management of PHPT in a North African setting.

This study shows that PHPT in our setting is still frequently diagnosed at a symptomatic stage, with a marked female predominance and a substantial burden of skeletal involvement. Despite the availability of reliable diagnostic tools and established international guidelines, delayed diagnosis remains common, likely reflecting insufficient systematic biochemical screening. Early detection through routine serum calcium measurement, together with timely referral and appropriate surgical management, is crucial to prevent irreversible skeletal and renal complications and to improve long-term outcomes.

Conflicts of interest

The authors declare no conflicts of interest.

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Author contributions

All authors participated in the study design. They contributed to data collection, analysis, and interpretation of results. All authors participated in drafting the manuscript, critically reviewed its content, and approved the final version for publication.

Ethics committee approval

This observational study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Due to its retrospective nature and anonymization of data, formal ethics committee approval was not required.

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