

Clinical Findings and Causes of Primary Hyperparathyroidism during 18 Years in Loghman Medical Center

Mahmoudi S. MD^{*}, Shadidi Asil R. MD^{*}, Zamani A. MD^{*}
Mirhashemi S. H. MD^{**}, Souri M. MD^{*}, Rashnow F. MD^{**}, Oshidori B. MD^{*}
Alishahi F. MD^{***}, Hajinasrillah E. MD^{****}

Abstract:

Background and Objective: Primary hyperparathyroidism is a relatively common endocrine disease that can be accompanied by non-specific symptoms such as weakness, fatigue, bone pain, and kidney stones. From the laboratory point of view, this disease is seen with an increase in the level of calcium and parathyroid hormone. Definitive treatment in these patients is parathyroidectomy surgery.

Materials & Methods: This study, which was conducted in a descriptive-retrospective manner, the files in the archives of Loghman Medical Center, which underwent parathyroidectomy from 1385 to 1402, were reviewed.

Results: Between 1385 and 1402, 43 patients underwent parathyroidectomy in Loghman Hospital, their mean age was 47.3 ± 15 years, the youngest patient was 15 years old, and the oldest patient was 79 years old. 6 cases were men (14%) and 37 cases were women (86%). The ratio of women to men in this study was 6.14 to 1. Adenoma is the most common cause of primary hyperparathyroidism.

Conclusion: Primary hyperparathyroidism is a relatively common disorder in Iran, which usually manifests with bone pain and a history of kidney stones. Unlike western countries, this disease in Iran is usually diagnosed after symptoms develop, but like others, parathyroid adenoma is the most common cause.

Keywords: Primary Hyperparathyroidism, Parathyroidectomy, Parathyroid Adenoma

* Assistant Professor of General Surgery, Shahid Beheshti University of Medical Sciences and Health Services, Loghman Hakim Hospital

** Associate Professor of General Surgery, Shahid Beheshti University of Medical Sciences and Health Services, Loghman Hakim Hospital

*** Resident of General Surgery, Shahid Beheshti University of Medical Sciences and Health Services, Loghman Hakim Hospital

**** Professor of General Surgery, Shahid Beheshti University of Medical Sciences and Health Services, Loghman Hakim Hospital

Received: 12/10/2024

Accepted: 15/04/2025

Corresponding Author: Dr. Esmail Hajinasrillah

Tel: 66469025

E-mail: e.hajinasrollah@gmail.com

Background and Objectives

Primary hyperparathyroidism is an endocrine disorder characterized by the excessive secretion of parathyroid hormone (PTH) from the parathyroid glands, which can lead to a variety of complications. It is essential to differentiate this condition from secondary hyperparathyroidism, typically caused by chronic kidney disease or phosphate-calcium imbalances,^{1,2} as the latter is not the focus of this study. Symptoms of primary hyperparathyroidism are chiefly associated with elevated serum calcium levels, which can precipitate gastrointestinal disturbances, kidney stones, bone disorders, and psychiatric issues.³

This condition is of relatively common prevalence, with an incidence rate of approximately 25 per 100,000 individuals, translating to about 1%.⁴ Research indicates that it occurs more frequently in women,⁴ and in countries with advanced screening programs, primary hyperparathyroidism is often diagnosed and treated prior to the onset of symptoms. Elevated PTH levels result in abnormal serum calcium concentrations,⁵ as the hormone facilitates the mobilization of calcium from bones while diminishing renal calcium excretion. Diagnosis of primary hyperparathyroidism frequently commences with the detection of elevated serum calcium levels, accompanied by increased PTH, a critical distinction that differentiates this condition from hypercalcemia resulting from other etiologies, such as malignancy-related metastases. While primary hyperparathyroidism can manifest in any age group, it is predominantly diagnosed in individuals over the age of 45,⁴ with women exhibiting a prevalence approximately double that of men. In less developed countries, patients often present with secondary symptoms, including fatigue, weakness, muscle pain, as well as renal and skeletal complications, and occasionally thrombophlebitis.⁶

Adenomas typically form in one of the four parathyroid glands, though multiple adenomas may be present concurrently, resulting in hyperactivity of the affected

glands. Other less common etiologies encompass hyperplasia and parathyroid cancers,⁷⁻⁹ which generally present greater challenges in treatment. In certain cases, sternotomy or thymus gland resection may be necessitated.

To date, only one study has explored medical treatment utilizing natural phosphate and estrogen;¹⁰ however, surgical parathyroidectomy remains the definitive treatment for this disorder.⁸ The type of surgical intervention is directly correlated with the underlying cause of hyperparathyroidism. This study seeks to investigate the clinical findings and underlying causes of primary hyperparathyroidism over an 18-year period at Laghman Hakim Hospital.

Materials and Methods

This descriptive retrospective cohort study analyzed the medical records of patients who underwent parathyroidectomy at Laghman Hakim Hospital from 2006 to 2023. Data collection encompassed 43 patients, including demographic information such as age and sex, clinical symptoms, serum calcium and parathyroid hormone levels both preoperatively and postoperatively, and tumor type and size as indicated by pathology reports. The collated data were imported into SPSS software for statistical analysis. The Shapiro-Wilk test was employed to assess the normality of the quantitative data distribution. Quantitative data characterized by a normal distribution were reported as means with standard deviations, whereas qualitative data were presented as percentages and frequencies. Results were further illustrated using graphs and tables to enhance clarity.

Findings

Between 2006 and 2023, a total of 43 patients underwent parathyroidectomy at Laghman Hakim Hospital, with a mean age of 47.3 years. The age of the patients ranged from 15 to 79 years. Gender distribution indicated that 6 patients (14%) were male

and 37 (86%) were female, establishing a female-to-male ratio of 6.14:1.

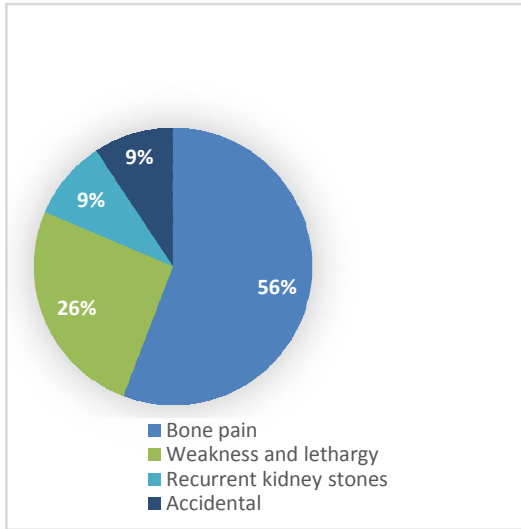


Figure 1 - Reasons for referral of patients with hyperparathyroidism in clinical findings and causes of primary hyperparathyroidism over a period of 18 years at Loghman Hakim Hospital

Notably, the study identified that 4 patients (9.3%) were asymptomatic and were

diagnosed with primary hyperparathyroidism solely through laboratory tests indicating hypercalcemia. Among the symptomatic patients, 24 (55.8%) experienced bone pain, 11 (25.6%) reported weakness and fatigue, while 4 patients (9.3%) presented with kidney stones and recurrent episodes of nephrolithiasis, as illustrated in Figure 1.

The average serum calcium level prior to surgery was 11.59 ± 2.6 mg/dL, which significantly decreased to 9.2 ± 1.2 mg/dL following the procedure. Parathyroid hormone levels were also evaluated both before and after surgery, with the comparative findings alongside serum calcium levels depicted in Figure 2.

In terms of etiology, the predominant indication for parathyroidectomy was the presence of parathyroid adenoma, affecting 37 patients (86%), while 5 patients (11.6%) were diagnosed with parathyroid hyperplasia. Only 1 patient (2.3%) was identified as having parathyroid cancer, as shown in Figure 3.

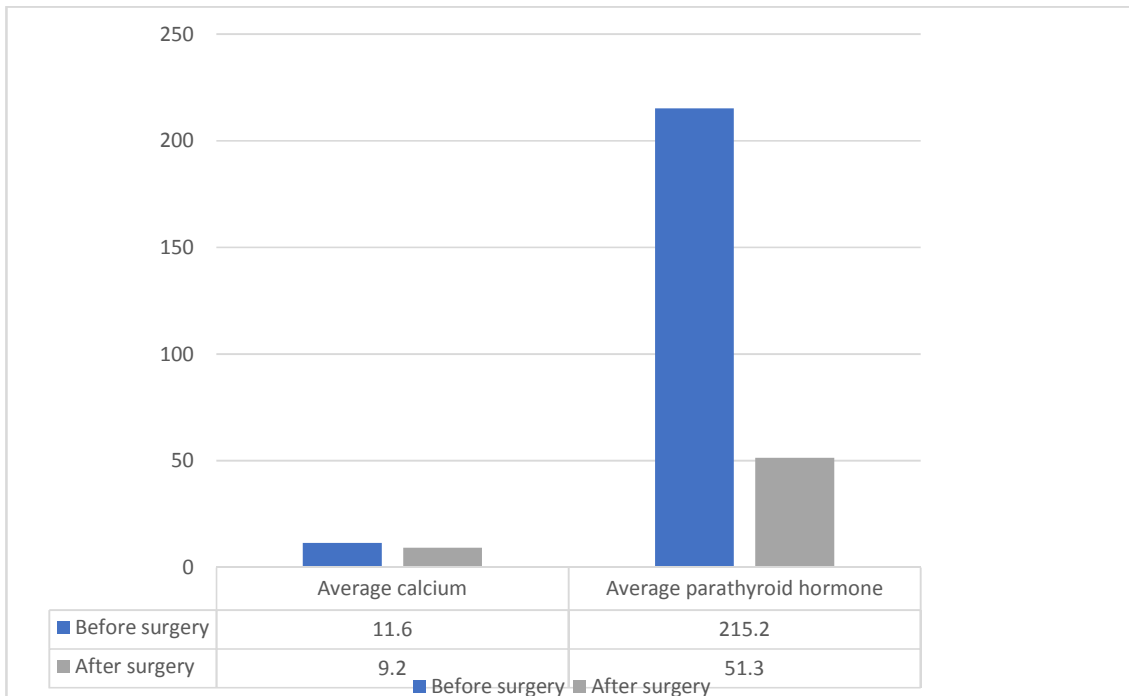


Figure 2 - Pre- and postoperative calcium and parathyroid hormone levels in clinical findings and causes of primary hyperparathyroidism over a period of 18 years in Loghman Hakim Hospital

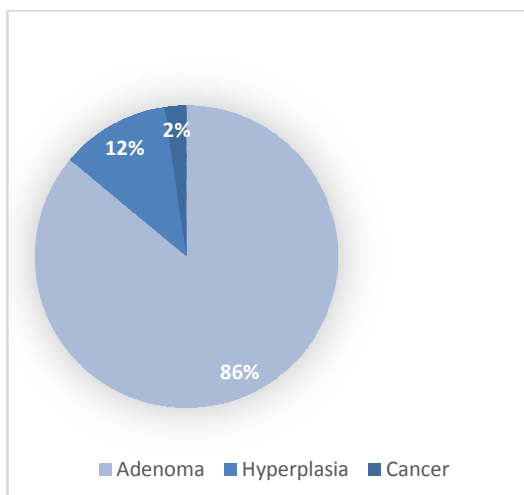


Figure 3 - Pathological causes of patients with hyperparathyroidism in clinical findings and causes of primary hyperparathyroidism over a period of 18 years in Loghman Hakim Hospital

The average tumor size among the 43 patients was less than 3 cm, with a mean size of 2.68 ± 0.3 cm; however, 15 patients had tumors exceeding 3 cm, averaging 3.4 ± 0.4 cm, as presented in Table 1.

Table 1 - Parathyroid gland size in patients with hyperparathyroidism in clinical findings and causes of primary hyperparathyroidism over a period of 18 years in Loghman Hakim Hospital

Mass size	Number	Percentage
Patients with a mass smaller than 3.5 cm	28	65.1
Patients with a mass larger than 3.5 cm	15	34.9
Total	43	100

Discussion and Conclusion

Primary hyperparathyroidism is an endocrine disorder characterized by the excessive secretion of parathyroid hormone by the parathyroid glands. This condition frequently leads to elevated serum calcium levels, resulting in a variety of clinical manifestations. Symptoms associated with hyperparathyroidism include bone pain, fractures, kidney stones, weakness, fatigue, polyuria, anorexia, nausea, vomiting, osteopenia, and constipation, all of which are commonly observed in affected patients. While numerous studies have documented an increase in serum calcium levels through routine laboratory tests,¹¹ our findings reveal a discrepancy, with many patients in this study diagnosed at more advanced stages of the disease due to a lack of regular monitoring.^{12,13} The majority of patients presented with clinical symptoms such as bone pain, weakness, fatigue, and kidney stones, ultimately leading to a diagnosis of hyperparathyroidism. These results underscore the critical importance of awareness and early detection in the effective management of this endocrine disorder.¹²

In the majority of reports, parathyroid adenoma is recognized as the primary etiology of primary hyperparathyroidism, a finding that is corroborated by our study, as the majority of our patients presented with adenomas. This disorder results from dysfunction in one or more of the four parathyroid glands. While adenomas are typically localized to a single gland, they may also be present in multiple glands, leading to hyperactivity.^{14,15}

Within our patient cohort, elevated levels of parathyroid hormone (PTH) and calcium were observed. Diagnosis was confirmed through scintigraphy, which subsequently prompted surgical resection of the adenoma from one of the parathyroid glands.

In cases involving hyperplasia, surgeries were often conducted in one or two stages. During these procedures, a portion of a parathyroid gland was sometimes transplanted subcutaneously into the

patient's arm as a precautionary measure.¹⁶ The necessity of two-stage surgeries frequently arose from the challenges associated with differentiating between hyperplasia and adenoma. Even when the enlargement and subtle brown discoloration of a gland suggested the presence of an adenoma, surgical manipulation could pose a risk of diminishing PTH levels in the remaining parathyroid glands. Following the initial surgical intervention, an increase in PTH and calcium levels was noted, indicating the potential presence of hyperplasia,¹⁷ which necessitates the removal of all glands in such circumstances.

Malignant tumors represent an exceedingly rare etiology of primary hyperparathyroidism. In one particular case, preoperative evaluation suggested a diagnosis of cancer due to the size and invasive characteristics of the mass. However, following the successful resection of the affected thyroid lobe and a partial

neck dissection of the lymph nodes, there was no evidence of metastasis observed for up to a year postoperatively.

Monitoring the treatment requires regular clinical evaluations alongside periodic assessments of calcium and PTH levels, which are essential for effective management.¹⁸ Our study indicated a significant reduction in symptoms, with patients reporting considerable alleviation during follow-up visits. Primary hyperparathyroidism is relatively common in Iran, typically presenting with musculoskeletal pain and a history of kidney stones. In contrast to Western countries, where routine screening often facilitates early identification of this condition, diagnosis in Iran typically occurs only after the manifestation of symptoms. Nevertheless, parathyroid adenoma continues to be the predominant cause in both regions.

References:

1. Ali Nawaz Khan, MBBS, FRCS, FRCP, FRCR; Chief Editor: Felix S Chew, MD, MBA, Secondary Hyperparathyroidism (SHPT) Imaging and Diagnosis. Medscape. Updated: Aug 27, 2020.
2. Vijayadershan Muppidi; Sreenath R. Meegada; Anis Rehman. Secondary Hyperparathyroidism. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
3. Binod Pokhrel; Stephen W. Leslie; Steven N. Levine. Primary Hyperparathyroidism. National library of medicine, StatPearls [Internet].
4. Bilezikian JP, Brandi ML, Eastell R, et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. The Journal of Clinical Endocrinology and Metabolism. 2014; 99(10): 3561-3569.
5. Marcella D. Walker and Shonni J. Silverberg. Primary hyperparathyroidism. Nat Rev Endocrinol. 2018 Feb; 14(2): 115-125. Published online 2017 Sep 8. doi: 10.1038/nrendo.2017.104.PMCID: PMC6037987.NIHMSID: NIHMS979180.PMID: 28885621.
6. Lawrence E. Mallette MD, PhD. Review: Primary Hyperparathyroidism, an Update: Incidence, Etiology, Diagnosis, and Treatment. The American Journal of the Medical Sciences, Volume 293, Issue 4, April 1987, Pages 239-249.
7. Robert A Wermers. Incidence of Primary Hyperparathyroidism in the Current Era: Have We Finally Reached a Steady State? The Journal of Clinical Endocrinology & Metabolism, Volume 108, Issue 12, December 2023, Pages e1749-e1750, <https://doi.org/10.1210/clinem/dgad267>.
8. STEPHEN J. MARX. Etiologies of Parathyroid Gland Dysfunction in Primary Hyperparathyroidism. JOURNAL OF BONE AND MINERAL RESEARCH Volume 6. Supplement 2, 1991 Mary Ann Liebert, Inc., Publishers.
9. Jessica MacKenzie-Feder, Sandra Sirrs, Donald Anderson, Jibrán Sharif, Aneal Khan. Primary Hyperparathyroidism: An Overview. International Journal of Endocrinology, 02 June 2011. <https://doi.org/10.1155/2011/251410>.
10. Parham M, Eshagh Hosseini SJ, Bagherzadeh M. The first manifestation of hyperthyroidism with deep vein thrombosis: A case report. Qom Univ Med Sci J 2015; 8(6): 81-84. [Full Text in Persian].
11. EDNA D. TANIEGRA, M.D. Hyperparathyroidism. American Family Physician. Jan 15 2004.
12. Mir Saeed Ghazi A A, Bostani I, Nasri H, Amiri Z, Rahimi F, Nafrabadi M T et al . Primary Hyperparathyroidism: A Report on 30 Cases of the Disease. Research in Medicine 1999; 23 (4): 301-308. URL: <http://pejouhesh.sbmu.ac.ir/article-1-2381-fa.html>.
13. Sohrab Atefie. Investigation of cases of primary hyperparathyroidism that underwent surgery during 20 years in Shiraz. Iranian Journal of Endocrine and Metabolism, Shahid Beheshti University of Medical Sciences and Healthcare Services, third year - number 4 - pages 281-277 (Winter 2008).
14. Ghada El-Hajj Fuleihan, MD, MPH, FRCP Shonni J Silverberg, MD. Primary hyperparathyroidism. Uptodate. Nov 08 2024.
15. Zubair W. Baloch, Virginia A. LiVolsi, in Encyclopedia of Endocrine Diseases, 2004. Primary Hyperparathyroidism.
16. Sandelin K. Parathyroid carcinoma. In: Holzheimer RG, Mannick JA, editors. Surgical Treatment: Evidence-Based and Problem-Oriented. Munich: Zuckschwerdt; 2001. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK7004/>.
17. Alexander L. Shifrin, L. Daniel Neistadt, Pritinder K. Thind. Atlas of Head and NECK PATHOLOGY PARATHYROID ADENOMA and HYPERPLASIA. ebook 2020. ISBN: 978-3-030-40958-6.
18. Zubair W. Baloch MD, PhD, Virginia A. LiVolsi MD. Pathology of the parathyroid glands in hyperparathyroidism. Seminars in Diagnostic Pathology, Volume 30, Issue 3, August 2013, Pages 165-177.