

Improved Mortality Outcomes in Primary Hyperparathyroidism: Significant Benefit of the Dedicated Indian PHPT Registry

BACKGROUND

Primary hyperparathyroidism (PHPT) is one of the most common chronic diseases in endocrinology. It is a multisystem condition with a possible wide array of involvement, including debilitating renal and skeletal disease. Since the identification of the disease in Captain Charles Martell who presented with multiple fractures, deformity, and renal stones, PHPT has undergone a transition to a more asymptomatic phenotype following automated serum calcium measurements.^[1] However, the predominant disease phenotype in India is symptomatic. While the debate on more symptomatic disease in India despite younger age at diagnosis remains unresolved, there is a paucity of evidence on the prevalence and predictors of mortality from the Southeast Asia region, and more specifically, from India. We recently analyzed mortality outcomes in patients from a single tertiary-care center in the country as part of the Indian PHPT Registry and noted an 8.8% prevalence of mortality.^[2]

Insights from the Indian PHPT Registry

There were 464 patients in the cohort (following exclusion of those lost to follow-up) of which 41 patients succumbed due to disease-related or unrelated causes. The study interval was divided into two halves, the first period extending from 1997-2007 and the second interval from 2008-2018. On analyzing the trends of mortality in the cohort, there was reduced mortality in the second study interval (2008-2018). It reduced from 14.4% in the first half to 7.2% in the second interval. CKD was the most common cause of mortality overall, and on analyzing the cause-distribution of mortality, CKD emerged as the most common cause of death in both study intervals. Age at diagnosis, age at death, and male gender were not significantly different between both time intervals. Renal dysfunction, anemia, and pancreatitis were not significantly different between both groups. Serum calcium and PTH were not significantly different between both intervals. Renal parameters (creatinine and estimated glomerular filtration rate) were also similar between both time intervals. Though there was a lower eGFR and higher percentage of patients with renal dysfunction in the later interval, mortality outcomes were better in the later period.

Clinical implications

Secular trends in the behavior of the disease have been noted in the form of both increased incidence as well as the evolution from symptomatic to asymptomatic phenotype.^[3] This is not only recognized in western countries but has also been reported in Indian settings.^[4,5] However, the trends in prevalence and patterns of mortality have not been well elucidated previously. The finding of an almost halved mortality rate in the latter half

of the cohort is not only encouraging but bears testimony to improved management, specifically in terms of surveillance following parathyroidectomy. The severity of disease and causes of mortality have remained unchanged with time. Despite this, there is a decrease in mortality. This is probably attributable to improvement in surveillance for complications and ensuring their timely management. Renal complications in PHPT can manifest as nephrolithiasis, nephrocalcinosis, hypercalciuria, and/or reduced eGFR. Prior experience suggests only partial resolution of these complications with curative parathyroidectomy.^[6,7] Therefore, ensuring regular follow-up is of utmost importance for managing the collateral damage that in fact, is the major contributor to morbidity and mortality in patients with PHPT.

How do we fare as compared to the west?

Survival after parathyroidectomy has been recently reported from the US, UK, and Europe.^[8-10] In these contemporary reports, the common finding is comparable mortality with respect to the general population. However, higher mortality rates in patients with symptomatic (associated with complications) or severe disease (serum calcium exceeding 10.8 mg/dl) have been reported even in these countries. The mortality rate in Indian patients with PHPT is higher than in some countries but lower than others. However, the finding of reduced mortality even with similar parameters of disease complications and severity as before is both reassuring and encouraging.

Proposed line of surveillance care for PHPT in India

The Indian PHPT registry has shown the way forward in long-term active surveillance of patients following curative parathyroidectomy, so as to improve outcomes. This suggests the significant benefit of a dedicated parathyroid registry and regular surveillance in improving outcomes, despite similar severity of disease and greater preponderance of patients with symptomatic PHPT in both intervals. Though follow-up protocols may not be as stringent as for those on medical management, biannual to annual frequency of follow-up, especially for patients with renal complications at baseline is imperative. Devising a simple strategy to calculate the estimated glomerular filtration rate in all patients with PHPT can aid in risk stratification at baseline. This subset of patients should be followed up more frequently both by the endocrinologist and urologist to provide definite management of the reversible causes such as nephrolithiasis. The non-reversibility of certain renal manifestations should be impressed upon, at each opportunity of interaction with the patient.

The way forward

Interestingly, Captain Martell succumbed to complications arising as a result of untreated nephrolithiasis.^[1] As we near the centenary of the recognition of PHPT in 1926, it is only apt that we remember the statement with regard to the death of Captain Martell i.e., “he died so that others may live”. Patterns of mortality are different in India as compared to the west, and renal complications need special mention in this context. Active surveillance of these complications in patients following curative parathyroidectomy can serve as a useful first step in averting premature mortality in these patients, especially in those with reversible causes.

Liza Das, Sanjay Kumar Bhadada, Poonam Kumari

Department of Endocrinology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence: Prof. Sanjay Kumar Bhadada, Department of Endocrinology, Post Graduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: bhadadask@rediffmail.com

REFERENCES

1. Casper S. Inexplicable patients: The case of Charles Martell and ward 4 at the Massachusetts general hospital. *CMAJ* 2016;188:1263-4.
2. Das L, Bhadada SK, Arvindbhai SM, Dahiya D, Behera A, Dutta P, *et al.* Baseline renal dysfunction determines mortality following parathyroidectomy in primary hyperparathyroidism: Analysis of Indian PHPT Registry. *J Bone Miner Metab* 2021. doi: 10.1007/s00774-021-01256-9.
3. Griebeler ML, Kearns AE, Ryu E, Hathcock MA, Melton III LJ, Wermers RA. Secular trends in the incidence of primary hyperparathyroidism over five decades (1965–2010). *Bone* 2015;73:1-7.
4. Arya AK, Kumari P, Bhadada SK, Agrawal K, Singh P, Mukherjee S, Sood A, Rao SD. Progressive rise in the prevalence of asymptomatic primary hyperparathyroidism in India: Data from PHPT registry. *J Bone Miner Metab* 2021;39:253-9.
5. Mithal A, Kaur P, Singh VP, Sarin D, Rao DS. Asymptomatic primary hyperparathyroidism exists in North India: Retrospective data from 2 tertiary care centers. *Endocr Pract* 2015;21:581-5.
6. Agrawal K, Arya AK, Sood A, Kumari P, Singh P, Sapara M, *et al.* A detailed appraisal of renal manifestations in primary hyperparathyroidism from Indian PHPT registry: Before and after curative parathyroidectomy. *Clin Endocrinol* 2021;94:371-6.
7. Nair CG, Babu M, Jacob P, Menon R, Mathew J. Renal dysfunction in primary hyperparathyroidism; effect of parathyroidectomy: A retrospective cohort study. *Int J Surg* 2016;36:383-7.
8. Wermers RA, Griebeler ML, Thapa P, Hathcock MA, Kearns AE. Survival in primary hyperparathyroidism over five decades (1965-2010) a population-based retrospective study. *Bone* 2021;152:116099.
9. Reid LJ, Muthukrishnan B, Patel D, Seckl JR, Gibb FW. Predictors of nephrolithiasis, osteoporosis, and mortality in primary hyperparathyroidism. *J Clin Endocrinol Metab* 2019;104:3692-700.
10. Nilsson M, Ivarsson K, Thier M, Nordenström E, Bergenfelz A, Almquist M. Mortality after surgery for primary hyperparathyroidism: Results from a nationwide cohort. *Br J Surg* 2021;108:858-63.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Quick Response Code:



Website:
www.ijem.in

DOI:
10.4103/ijem.ijem_346_21

How to cite this article: Das L, Bhadada SK, Kumari P. Improved mortality outcomes in primary hyperparathyroidism: Significant benefit of the dedicated Indian PHPT registry. *Indian J Endocr Metab* 2021;25:507-8.