

High prevalence of cholelithiasis in primary hyperparathyroidism: a retrospective analysis of 120 cases

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Primary hyperparathyroidism (PHPT) due to parathyroid adenoma is the most common cause of hypercalcemia, which is characterized by high parathyroid hormone (PTH) level despite elevated serum calcium levels [1]. With the advent of autoanalyzer and serum calcium is a part of routine screening in West. The presentation of PHPT is asymptomatic and hence, attention has been diverted to the features like hypertension, mental changes, peptic ulcer disease and gallstone disease [2, 3]. Few studies have shown the association of cholelithiasis with PHPT [4, 5]. Hypercalcemia and elevated PTH have been implicated as a cause for cholelithiasis in patients with PHPT.

This retrospective study was conducted by the Endocrinology department at our institution. PHPT was diagnosed based on elevated calcium and PTH levels. Patients with hyperparathyroidism due to secondary and tertiary causes were excluded. Cholelithiasis was diagnosed by either ultrasonographic evidence of gallstone(s) and/or history of cholecystectomy. Prevalence of cholelithiasis in PHPT patients was compared with that in the normal north Indian population using a study [6] conducted by the Gastroenterology and Hepatology department of our institution.

Serum calcium (reference range [RR]: 8.5–10.2 mg/dL), phosphate (RR: 3.5–5 mg/dL), alkaline phosphatase (RR 28–129 IU/L), and creatinine (RR: 0.5–1.4) were measured

by standard methods. Serum iPTH (RR: 15–65 pg/mL) was measured by chemiluminescence assay and vitamin D (RR: 9–37 ng/mL) by radioimmunoassay (RIA) using commercially available kits. SPSS 10® software was used to analyze the data. Continuous variables were described as mean (SD) and categorical data were expressed in *n* (%). Correlation analysis was used to correlate two variables. $P < 0.05$ was considered as statistically significant.

One hundred and twenty patients (mean [SD] age 39 [14] years, 80 women) with PHPT were studied. Eighty-three patients were below 50 years of age. Their mean weight was 55.1 (14.6) kg and mean BMI 20.8 (4.7) kg/m². All PHPT patients were symptomatic with the most common presenting symptom being bone pain ($n=68$, 56.7%). Fifty-four (45.4%) patients had renal stones. The mean serum calcium level was 11.5 (1.8) mg/dL, phosphorus 2.9 (0.8) mg/dL, alkaline phosphatase 217.0 (489.4) IU/L (median 316), vitamin D 25.8 (27.8) (median 15.2) ng/mL and iPTH 819 (700) pg/mL (median 818). Thirty-one patients had cholelithiasis (25.8%). Cholelithiasis was more frequent in women (26 vs. 5) as compared to men; the prevalence in women increased with advancing age (Table 1). Overall the prevalence of gallstones in the reference published study [6] was 3.1% in healthy northern Indian population, and was higher among women (4.2%). After standardization of rates of gallstones for gender, the proportion of gallstones was 2.89% in the reference study, and was 21.24%. ($p < 0.04$) in the present study. No correlation between preoperative serum calcium ($r=0.042$, $p=0.66$), phosphate ($r=-0.07$, $p=0.42$) and PTH ($r=0.03$, $p=0.7$) was seen with cholelithiasis. Using unconditional logistic regression analysis, the only factor that predicted development of gallstone was age (odds ratio -1.05, 95% CI -0.99–1.11, $p=0.02$).

This study showed high prevalence of cholelithiasis in PHPT (25.8%) compared to the general population (3.1%)

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Table 1 Age-wise distribution of frequency of gall stones in patients with primary hyperparathyroidism (PHPT)

Age (years)	Men		Women		Total gallstones
	All PHPT	Gallstones	All PHPT	Gallstones	
<30	15 (12.5)	0	19 (15.8)	3 (2.5)	3 (2.5)
30–39	12 (10)	1 (0.8)	16 (13.3)	8 (6.7)	9 (7.5)
40–49	2 (1.6)	0	19 (15.8)	4 (3.3)	4 (3.3)
≥50	11 (9.2)	4 (3.3)	26 (21.6)	11 (9.2)	15 (12.5)
Total	40 (33.3)	5 (4.16)	80 (66.7)	26 (21.66)	31 (25.8)

Data are as *n* (%)

of north India. Higher prevalence of cholelithiasis was noted in women; this increased with advancing age, which is in consonance with the other studies [6–8]. Animal studies have shown a decreased biliary flow and increased biliary ionized calcium concentration with hypercalcemia thus favoring a lithiatic milieu [9]. One study found that PTH is a smooth muscle relaxant [10], resulting in lazy gallbladder; both factors can lead to cholelithiasis in PHPT. However, we did not find any correlation between serum calcium and cholelithiasis. Despite the study being a retrospective one, and done only on northern Indians, the finding of high prevalence of gallstone in PHPT compared to general population should not be ignored and PHPT may be considered a risk factor for cholelithiasis.

References

1. Weber CJ, Sewell CW, McGarity WC. Persistent and recurrent sporadic primary hyperparathyroidism: histopathology, complications, and results of reoperation. *Surgery*. 1994;116:991–8.
2. Mundy GR, Cove DH, Fiske R. Primary hyperparathyroidism: changes in the pattern of clinical presentation. *Lancet*. 1980;1:1317–20.
3. Silverberg SJ, Shane E, Jacobs TP, Siris E, Bilezikian JP. A 10-year prospective study of primary hyperparathyroidism with or without parathyroid surgery. *N Engl J Med*. 1999;341:1249–55.
4. Werner S, Hjerm B, Sjöberg HE. Primary hyperparathyroidism. Analysis of findings in a series of 129 patients. *Acta Chir Scand*. 1974;140:618–25.
5. Amann R. Cholelithiasis in primary hyperparathyroidism. *Therapiewoche*. 1978;28:657–9.
6. Singh V, Trikha B, Nain C, Singh K, Bose S. Epidemiology of gallstone disease in Chandigarh: a community-based study. *J Gastroenterol Hepatol*. 2001;16:560–3.
7. Malhotra SL. Epidemiological study of cholelithiasis among railroad workers in India with special reference to causation. *Gut*. 1968;9:290–5.
8. Broulik PD, Haas T, Adámek S. Analysis of 645 patients with primary hyperparathyroidism with special reference to cholelithiasis. *Intern Med*. 2005;44:917–21.
9. Ahrendt SA, Ahrendt GM, Pitt HA, Moore EW, Lillemoe KD. Hypercalcemia decrease bile flow and increase biliary calcium in the prairie dog. *Surgery*. 1995;117:435–42.
10. Mok LL, Nickols GA, Thompson JC, Cooper CW. Parathyroid hormone as a smooth muscle relaxant. *Endocrinol Rev*. 1989;10:420–36.