

The prevalence of primary hyperparathyroidism in Korea: a population-based analysis from patient medical records

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Purpose: Because primary hyperparathyroidism (PHPT) is difficult to recognize, it has a high likelihood of being underdiagnosed. In this study, we estimated the incidence of PHPT and evaluated PHPT diagnosis in Korea.

Methods: To calculate the prevalence of PHPT, we examined the medical records of patients that were hospitalized for urolithiasis between 2013 and 2016 at a single institute, and then identified those who were diagnosed with PHPT from the same group. A Korea-wide insurance claim database was used to ascertain the number of urolithiasis patients and the number of parathyroidectomies performed in Korea. The incidence of PHPT in the Korean population was estimated using the ratio of patients who presented with urolithiasis as the initial symptom of PHPT.

Results: During the 4-year study period, 4 patients from the 925 urolithiasis patients enrolled in this study (0.4%) were diagnosed with PHPT. During this same period, there were 85,267 patients with urolithiasis in Korea, and the estimated number of PHPT patients was 341, which was 0.4% of 85,267. Considering that 12% to 23% of patients with PHPT are initially diagnosed with urolithiasis, the total number of PHPT patients was estimated to range from 1,483 to 2,842. The number of patients who underwent parathyroidectomy due to PHPT was 1,935 during the study period.

Conclusion: The number of patients we estimated to have PHPT corresponded closely with the number of patients undergoing parathyroidectomy during the study period. Considering the number of nonsymptomatic PHPT patients, PHPT may be properly diagnosed in Korea.

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Key Words: Primary hyperparathyroidism, Incidence, Urolithiasis, Parathyroidectomy, Population

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a complex endocrine disorder characterized by elevated parathyroid hormone (PTH)

levels resulting in hypercalcemia [1]. Surgical removal of the parathyroid is the only curative treatment for PHPT and is recommended in all cases of symptomatic PHPT, and in some cases of asymptomatic PHPT depending on the patient's age,

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bone density, serum calcium levels, creatinine clearance, 24-hour urine calcium levels, and/or nephrolithiasis on imaging [2].

Untreated, symptomatic PHPT can dramatically impact quality of life and has been linked to various short and long-term complications of the musculoskeletal, renal, gastrointestinal, cardiovascular, neuromuscular, and neuropsychiatric systems [3]. Clinical manifestations include urolithiasis, diabetes insipidus, osteoporosis, depression, memory loss, and psychosis – with urolithiasis the most common [4]. Therefore, correct diagnosis of PHPT is important. Korean population exceeds 50 million, it is possible that PHPT may be underdiagnosed in South Korea.

Because diagnosis is largely based on laboratory tests, PHPT can be difficult to diagnose. The incidence of PHPT is approximately 1 per 1,000 people (0.1%) [5]. In the United States 23–30 new cases are reported per 100,000 people per year [6]. Meanwhile, the number of parathyroidectomies performed in South Korea is significantly low and it is less 20 cases even in the tertiary teaching hospitals [7,8]. Based on these figures and the South Korean population (50 million), it is possible that PHPT may be underdiagnosed in South Korea.

In this study, we estimated the incidence of PHPT and compared it with the number of parathyroidectomies performed to evaluate whether PHPT has been properly diagnosed in South Korea.

METHODS

Nationwide insurance claim database analysis

To obtain the number of parathyroidectomies and urolithiasis treatment procedures performed in South Korea, we used longitudinal data from a nationwide insurance claims database, called the Health Insurance Review and Assessment Service (HIRA) database. HIRA database contains the diagnosis, treatment, procedures, surgical history, and prescription drug information for 46 million patients per year, accounting for 90% of the total Korean population, and covering 99.9% of all medical claims in South Korea [9].

All cases of one gland parathyroidectomy (claim code P4511), and urolithiasis treatments, including percutaneous ureterolithotomy (claim code R3211, R3213), uerteroscopic ureterolithotomy (claim codes R3216, R3217, R3218, R3219), percutaneous nephropithotomy (claim code R3375), pyelolithotomy (claim code R3390), operative ureterolithotomy (claim codes R3421, R3422, R3423), flexible ureterorenoscopic calculi removal (claim codes R3424, R3425, R3426, R3427, R3428, R3429), and removal of urethral calculi (claim code R3671, R3672, R3673) were identified from the HIRA database. The South Korean population was obtained from the Korean Statistical Information Service (http://kosis.kr/nsportalStats/nsportalStats_0102Body.jsp?menuId=10).

The incidence of PHPT diagnosis among urolithiasis patients at a single medical institute

We retrospectively reviewed the medical records of patients who were hospitalized for treatment of urolithiasis at single center from January 2013 to December 2016. We collected laboratory data including serum intact PTH, calcium, ionized calcium, phosphorus, 24-hr urine calcium, and 25-OH Vitamin D levels. We then collected the data of patients from the same group who were diagnosed with PHPT. PHPT was diagnosed when serum intact PTH was higher than the normal range without evidence of Vitamin D deficiency or chronic kidney disease. Serum intact PTH was routinely measured in all patients. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital (approval number: 16-2016-156).

RESULTS

Incidence of parathyroidectomy due to PHPT in South Korea

Fig. 1 shows that 1,935 patients in South Korea underwent parathyroidectomy due to PHPT from 2013 to 2016 (468, 441, 450, and 576, annually). During this period, the annual population of South Korea was 50,428,893, 50,746,659, 51,014,947, and 51,245,707, respectively. The incidence of PHPT treated by parathyroidectomy in South Korea was 0.001%.

Incidence of PHPT in urolithiasis patients at a single institution

From 2013 to 2016, 925 patients underwent treatment for urolithiasis at a single institution (Fig. 2). Of these patients, 45 showed elevated serum intact PTH, 4 of whom (0.4%) were diagnosed with PHPT and underwent subsequent parathyroidectomy.

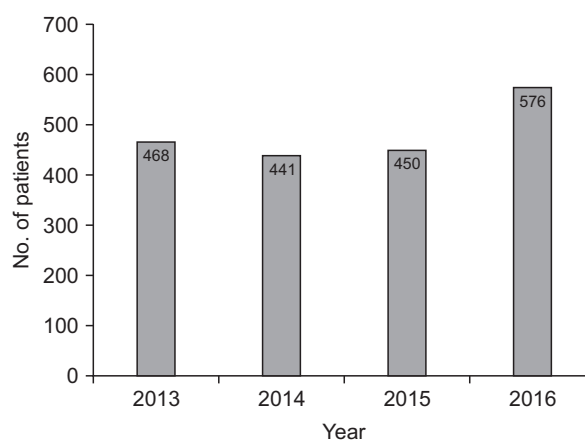


Fig. 1. The number of the patients who underwent parathyroidectomy due to primary hyperparathyroidism from 2013 to 2016.

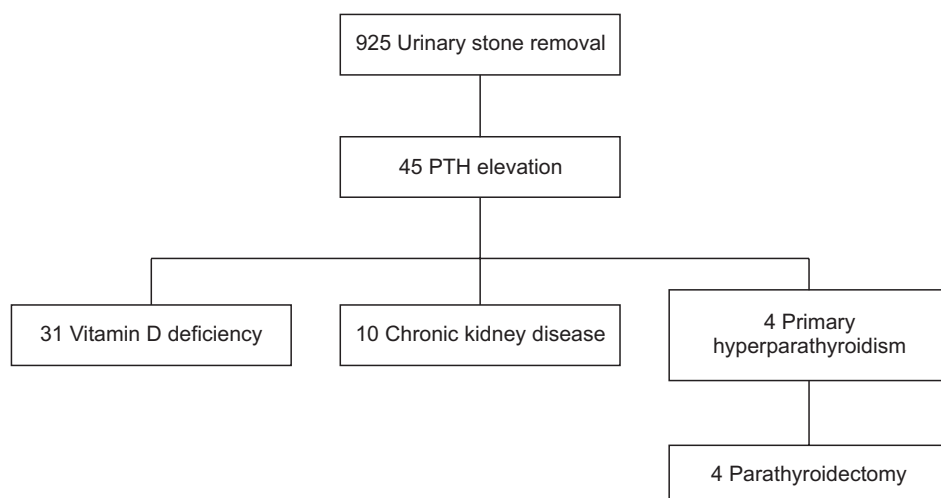


Fig. 2. The prevalence of primary hyperparathyroidism from the urolithiasis patients between 2013 and 2016.

Table 1. Clinical characteristics of the four patients who were diagnosed with primary hyperparathyroidism during treatment for urolithiasis

No.	Sex	Age (yr)	Ca (mg/dL)	P (mg/dL)	PTH (pg/dL)	24-Hr urinary Ca (mg/day)	Interval between diagnosis of urinary stone and PHPT (mo)	Parathyroid pathology	Size (cm)
1	F	77	11.9	2.5	361	169.6	2	Adenoma	1.2
2	F	29	14.1	2.7	317.2	847.6	0	Adenoma	1.6
3	F	75	11.3	2.2	169	156.2	27	Adenoma	1.6
4	M	57	11.2	2.6	107	262.8	11	Adenoma	2.7

dectomy. The remaining 41 patients had elevated PTH due to Vitamin D deficiency (n = 31) or chronic kidney disease (n = 10). The clinical characteristics of the 4 patients who underwent parathyroidectomy are shown in Table 1.

Estimated incidence of PHPT in the general South Korean population

From 2013 to 2016, a total 85,267 patients underwent treatment for urolithiasis (16,774, 18,716, 20,557, and 29,220, annually) in South Korea. When we postulated that 0.4% (incidence of PHPT in our institute) of urolithiasis patients in South Korea during the study period might have been diagnosed with PHPT, the estimated number of PHPT patients from urolithiasis patients was 341. Considering 12% to 23% of PHPT patients are first diagnosed with urolithiasis in South Korea [7,8], the number of PHPT in the general population was estimated to have ranged from 1,483 to 2,842 during the 4-year study period. During this time, the accumulated population of South Korea was 203,436,206 (50,428,893, 50,746,659, 51,014,947, and 51,245,707, annually from 2013 to 2016, respectively). Therefore, the annual incidence of PHPT appears to range from 0.007% to 0.0014% (1,483 to 2,842 of 203,436,206).

DISCUSSION

The biochemical characteristic of PHPT is hypercalcemia caused by excessive excretion of PTH from one or more parathyroid gland [10]. The classic diagnosis of PHPT is when corrected calcium is high in the presence of elevated PTH [11]. PHPT is often missed because PTH is not measured during routine health screening, and is not routinely measured without probable cause. PHPT is often picked up when there are abnormal serum calcium levels although slightly elevated calcium levels may be overlooked without measuring PTH. As such, the incidence of PHPT is likely to be underestimated making it quite impossible to evaluate the true incidence of PHPT in the general population, which makes it difficult to evaluate if the disorder is properly diagnosed and treated. Interestingly, at our institute, PTH is routinely measured in patients who were hospitalized for treatment of urolithiasis, and so we were able to estimate the incidence of PHPT in the general Korean population using this information.

This is the first study to estimate the prevalence of PHPT in South Korea. Our results show that the estimated incidence of PHPT in Korea is 0.007% to 0.0013%, which was similar to that of parathyroidectomy due to PHPT (0.001%). We therefore suggest that PHPT is adequately diagnosed in South Korea.

Previous studies from Western countries have shown annual incidences of PHPT ranging from 0.004% to 0.3% (0.004% in Switzerland [12], 0.016% in Denmark [13], 0.02% in the United States [6], 0.04%–0.11% in United Kingdom [14], and 0.3% in Italy [15]).

The incidence of PHPT in South Korea appears to be lower than that of Western countries. The differences in the incidence of PHPT may be attributed to differences in the diagnostic environment of the countries where the studies were conducted [16,17] such as lack of availability of automated blood biochemistry analyzers [16]. However, we believe the most convincing reason for the low prevalence of PHPT in South Korea may be owing to body habitus considering medical environment. In fact, the PHPT patients had higher body weight and body mass index compared to the normal subject [18]. It is obvious that South Koreans had lower body weight and body mass index than Western people [19], and we believe that body habitus is the major factor contributing low incidence of PHPT in Korean population. Although PHPT does not always lead to urolithiasis [20], it is known to be linked with hypercalcemia and hypercalciuria which are well known complications of the disorder. Detecting PHPT among patients who have already developed urolithiasis is important as parathyroidectomy has shown clear advantage in reducing the recurrence of urolithiasis [21]. Previous studies have shown that more than 90% of urolithiasis patients with PHPT did not experience reoccurrence of their symptoms post parathyroidectomy [21,22]. In this study, we showed that the incidence of PHPT in urolithiasis patients (0.4%) was as high as 400 times the incidence of PHPT in the general population (0.001%). Therefore, we suggest that PTH screening be considered for all urolithiasis patients to improve diagnosis and treatment.

This study has several limitations. First, it is the presumption that the percentage of PHPT in the urolithiasis patients in a single medical institute is the same as in the general Korean population. Results could be biased if patient characteristics at the study institution were not representative of the general

population. However, the site is a secondary hospital, and patients are mostly from the local community. Therefore, we consider the characteristics of the study population to be similar to those of the general population. Second, we could only obtain data about the number of parathyroidectomies performed, not the number of patients actually diagnosed with PHPT. In fact, however, the number of patients actually diagnosed with PHPT is much higher than that of parathyroidectomies as shown in one study which reported that only around half of symptomatic PHPT patients underwent parathyroidectomy [23]. Therefore, the number of patients diagnosed with PHPT might be higher than the estimated number of PHPT patients in this study. Third, we classified 31 patients as vitamin deficiency. However, it is possible that those patients had PHPT accompanied with vitamin D deficiency, since they did not undergo work-ups for PHPT such as parathyroid scan, parathyroid ultrasonography, or PTH measurement after normalization of vitamin D level. This was an inevitable limitation of this study due to its retrospective nature. Future prospective studies are essential to determine the more exact incidence of PHPT.

In conclusion, the estimated incidence of PHPT in South Korea is 0.007% to 0.0014% which correlates with the number of the patients who underwent parathyroidectomy during the study period, suggesting that PHPT is properly diagnosed in South Korea.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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