



Characteristics of Primary Hyperparathyroidism Patients Based on One Saudi Center Experience

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Abstract

Introduction: The prevalence and presentation of the Primary Hyperparathyroidism (PHPT) geographically varies. There is a paucity of published literature on PHPT in Saudi Arabia, so this study aimed to investigate the characteristic features and the surgical outcome of PHPT patients.

Methods: A retrospective review of PHPT patients underwent parathyroidectomy at King Faisal Specialist Hospital and Research Center, from 2010 to 2016.

Results: There were 88 patients; 72 (81.8%) were female and 16 (18.2%) were male. The mean age was 46 ± 15 year. The mean preoperative serum level was 2.85 ± 0.33 for calcium and 407 ± 475 for parathyroid hormone. The majority of the cases presented with bone symptoms 50 patients (56.8%), followed by no symptoms in 25 patients (28.4%), fatigability 7 (7.9%), renal symptoms 4 (4.6%) and gastric symptoms 2 (2.3%). Sestamibi scanning localized diseased gland in 71 cases (81.6%). The causes of PHPT were single adenoma in 75 (85.2%), double adenoma in 6(6.8%) and hyperplasia in 7(8%). The persistent rate was 1.1% and the recurrent rate was 2.2%. Females found to have a lower preoperative vitamin D level comparing with males $39.7 \text{ nmol/L} \pm 28.6 \text{ nmol/L}$ vs. $73.87 \text{ nmol/L} \pm 19.73 \text{ nmol/L}$ ($p= 0.0001$). Moreover, patients with multiple gland disease had a higher rate of recurrence comparing with patients with single adenoma 0% vs. 15.4% ($p=0.020$).

Conclusion: While half of PHPT patients in Saudi Arabia still present with bone symptoms, one fourth of the cases are asymptomatic. Moreover, one third of the cases are younger than 40 years old.

Keywords: Primary hyperparathyroidism; Causes; Parathyroidectomy

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Introduction

Primary Hyperparathyroidism (PHPT) is the uncontrollable overproduction of Parathyroid Hormone (PTH) causing an abnormal calcium homeostasis [1-5]. PHPT is a common endocrine disorder worldwide [1-5]. The prevalence of PHPT varies from country to country [1-5]. While the reported literatures estimate the range of PHPT prevalence in the US, Europe and Australia to be 1 to 21 per 1,000 individuals [6], PHPT was as low as 61 cases over a decade in India [7].

In addition, patients' presentation can vary from asymptomatic to severe systemic manifestations [1-7]. Although routine calcium test was introduced in Saudi hospital since 2000 [8], the clinical features, and the overall pattern of PHPT patients in the Kingdom of Saudi Arabia (KSA) is still not clear. Few studies published in the literature discuss about the clinical features of PHPT patients in the KSA [8-10].

The aim of this study is to investigate the characteristic feature and the surgical treatment outcome of patients with primary hyperparathyroidism who were operated in King Faisal Specialist Hospital and Research Center (KFSH & RC), Riyadh, KSA. Such a study will enrich our literature and help health providers, endocrinologist and endocrine surgeons to develop an overall view about patients with PHPT in the KSA.

Methods

This is a descriptive study in which we systematically reviewed all the clinic-pathological features and the surgical treatment modalities for all adult patients with PHPT who underwent initial parathyroidectomy at KFSH&RC, Riyadh, KSA, for 6 years (January 2010-June 2016). However, we exclude patients who were on thiazide diuretics or lithium, pediatric patients, patients who were operated outside KFSH & RC, and patients with secondary or tertiary hyperparathyroidism. KFSH & RC is a single tertiary institution. In this study, we defined the persistence of disease as high

Table 1: PHPT characteristics based on gender.

Variables	Male	Female	p Value
(N)	-16	-72	
Age	44 ± 19	46 ± 14	0.678
Pre-op Ca mg/dl	2.95 ± 0.37	2.83 ± 0.32	0.191
Pre-op PTH pg/ml	411 ± 435	405 ± 486	0.966
Pre-op Vitamin D nmol/L	73.9 ± 19.7	39.7 ± 28.6	0.0001
Presentations:			
Bone	11 (68.7%)	39 (54.1%)	
Renal	0 (0%)	4 (5.6%)	
Asymptomatic	3 (18.8%)	22 (30.6%)	0.485
Fatigability	1 (6.3%)	6 (8.3%)	
Gastric	1(6.3%)	1 (1.4%)	
Causes:			
SA	12 (75%)	63(81.8%)	0.132
DA	3 (18.8%)	3 (3.9%)	
HP	1 (6.3%)	6 (7.8%)	
Post-op Ca, mg/dl	2.52 ± 0.61	2.35 ± 0.22	0.005
Post-op PTH pg/ml	88 ± 67	98 ± 108	0.006
Surgical Outcome			
Persistence	0 (0%)	1 (1.4%)	1
Recurrence	0 (0%)	2 (2.8%)	1

postoperative calcium level within 6 months, whereas the recurrent disease as manifested by high postoperative calcium after the 6 months.

Data was collected from the electronic medical records and missing information extracted from the patient's charts. The parameters include: Patient's demographics, age, gender, presenting symptoms, the preoperative radiological image findings, pre- and post-operative serum levels of calcium and Parathyroid Hormone (PTH), causes of PHPT which could be adenoma, double adenomas or hyperplasia, presence of coincidence thyroid gland pathology, type of surgery, follow up persistence and recurrent rate.

This study was approved by KFSH & RC's Research Advisory Council (RAC). Data was analyzed using SPSS version 20. Continuous data was summarized as means and Standard Deviation (SD), whereas categorical data was summarized as absolute values and percentages. Differences between continuous data were analyzed using unpaired Student's test: Whereas categorical data was analyzed using the chi-square test or fisher's exact test, as appropriate. p value of 0.05 or less was considered statistically significant.

Results

In total 88 patients met the inclusion criteria. The mean age was 46 ± 15 years and 72 (81.8%) were females and 16 (18.2%) were males. The mean preoperative serum levels were 2.85 mg/dl ± 0.33 mg/dl for calcium and 407 pg/ml ± 475 pg/ml for PTH. Moreover, 50 patients (56.8%) were presented with bone symptoms, 25 patients (28.4%) were asymptomatic, 7 patients (7.9%) were presented with fatigability, 4 patients (4.6%) were presented with renal symptoms (polyuria, nephritis and kidney stone) and 2 patients (2.3%) were presented with gastric symptoms (nausea, vomiting and abdominal pain).

Table 2: PHPT characteristics based on age.

Variables	≤ 40 Years	> 40 Years	p Value
(N)	-32	-56	
Gender			
Male	8 (25%)	8 (14.3%)	0.255
Female	24 (75%)	48 (85.7%)	
Pre-op Ca mg/dl	2.84 ± 0.31	2.86 ± 0.35	0.789
Pre-op PTH pg/ml	490.9 ± 580.8	358.3 ± 400.5	0.21
Presentations:			
Bone	22 (68.8%)	28 (50%)	
Renal	0 (0%)	4 (7.1%)	
Asymptomatic	7 (21.9%)	18 (32.1%)	0.234
Fatigability	3 (9.3%)	4 (7.1%)	
Gastric	0 (0%)	2 (3.6%)	
Causes:			
SA	27 (84.4%)	48 (85.7%)	0.314
DA	1 (3.1%)	5 (8.9%)	
HP	4 (12.5)	3 (5.4%)	
Thyroid FNA	2 (6.25%)	17 (30.4%)	0.008
Surgical Outcome			
Persistence	1 (3.1%)	1 (1.8%)	1
Recurrence	0 (0%)	1 (1.8%)	1

Eighty-seven patients (99%) underwent a preoperative localization images in the form of parathyroid sestamibi scan. One patient with men I was planned for subtotal parathyroidectomy; therefore the surgeon did not order a preoperative localization images. Sestamibi scanning localized the diseased gland in 71 cases (81.6%). In addition, ultrasound neck was performed on 77 patients (87.5%) to evaluate the thyroid gland and confirm the localization. Ultrasound neck localized the diseased gland in 50 cases (64.9%) and among them, a synchronous thyroid nodule(s) were found in 20 patients (40%). Only 8 patients (16%) underwent thyroid surgery: 6 (12%) underwent total thyroidectomy due to thyroid cancer; and 2 (4%) underwent hemithyroidectomy due to Follicular Lesion of Undermined Significance (FLUS) which turned to be benign in the final pathology.

The majority underwent minimally invasive parathyroidectomy: 75 patients (85.2%) and 13 patients (14.8%) underwent bilateral neck exploration. Single adenoma was the major cause of the PHPT in 75 patients (85.2%), followed by hyperplasia in 7 patients (8%) and then double adenoma in 6 patients (6.8%). The mean postoperative serum levels were 2.27 mg/dl ± 0.15 mg/dl for calcium and 79 pg/ml ± 53 pg/ml for PTH. The persistence and recurrence rates were 1.1% and 2.2% respectively.

We compared females vs. males, but there were no statistically significant differences between them in the form respect of age, preoperative levels of calcium and PTH, causes of PHPT, persistence, recurrent rate and presentations. However, we noticed a statistically significant difference in the level of vitamin D preoperatively between two groups of patients (39.7 nmol/L ± 28.6 nmol/L vs. 73.87 nmol/L ± 19.73 nmol/L, p=0.0001, Table 1). In addition, the immediate postoperative calcium level was lower and the immediate postoperatively level of the PTH was higher in females (2.52 mg/dl ± 0.61 mg/dl vs.

2.35 mg/dl \pm 0.22 mg/dl, $p=0.005$ and 88 pg/ml \pm 67 pg/ml vs. 98 pg/ml \pm 108 pg/ml, $p=0.006$, respectively, Table 1).

In addition, we compared the younger patients (<40 years) vs. older patients (>40 years) but there was no statistical difference in respect of gender, serum level of calcium and PTH, presentations and causes, but the younger patients presented with more bone symptoms 22 (68.8%) vs. 28 (50%); however, it was not statistically significant ($p=0.234$). Moreover, patients over 40 years old were found to have more thyroid nodules compared to patients under 40 years old: 2 (6.25%) vs. 17 (30.4%), ($p=0.008$), which could be explained by the age (Table 2).

Finally, we compared those patients who had a single adenoma with those who had a multiple glands disease. There was no statistical difference in respect of age, gender, preoperative serum level of calcium and PTH and presentations, but the immediate postoperative level of calcium was lower among those with SA 2.26 mg/dl \pm 0.13 mg/dl vs. 2.41 mg/dl \pm 0.17 mg/dl ($p=0.0004$). In addition, the recurrence rate was higher among those with a multiple glands disease 0 (0%) vs. 2 (15.4%) ($p=0.020$) younger patient presented with more bone symptoms (Table 3).

Discussion

Percivale et al. [6] and Bilezikian et al. [2] in their recent review reported the annual worldwide incidence of the PHPT to be 20 cases per 100,000 people and the prevalence of the PHPT to be 0.5% to 2% [11,12]. Nevertheless, in the KSA, there is no accurate available data on the incidence or the prevalence of the disease. In our study, we identified 88 cases during a period of 6 years. This study cannot reflect an accurate data of the incidence or the prevalence of the PHPT in the KSA; however, it reflects an increase in the number of the diagnosed cases as compared with the available previous national studies [8,9]. Bismar et al. [9] reported 41 cases from 1992 to 2002, and Malabu et al. [8] reported 46 cases from 2000 to 2006.

In our study, the mean age of the cases was 46 years at the presentation of PHPT, with a male to female ratio of approximately 1:4.5. While we are in agreement with the literature in respect of the male to female ratio which was reported to be from 1:3 to 1:5 [8,9,11-13]. The mean age of our patients was younger than that reported in the western literature [11-14], but older than the age reported by the developed countries [7,14,15] and similar to the age of the PHPT patients in the previous national studies [8,9].

The majority of our patients (57%) presented with bone symptoms, while 28% were asymptomatic and 5% presented with renal stone. However, in the El-Bakry et al. [9] study, 73% of the patients presented with musculoskeletal symptoms, 14.6% patients presented with renal stones and 5% patients were asymptomatic [9] and in the Malabu et al. [8], 45.7% complained of bone symptoms, 23.9% were asymptomatic and 15.2% had renal manifestations [8]. Our findings demonstrate the decline of the renal presentation and the increase of the number of the patients with asymptomatic disease which could be due to the introduction of routine calcium test in Saudi hospitals [8].

In our study, the parathyroid sestamibi scan localized the diseased gland in 81.6% of the cases and ultrasound neck localized the diseased gland in only 64.9% of the cases. This goes along with the previously reported sensitivity of the 99 mTc sestamibi scan and the neck ultrasound; 70% to 90% and 22% to 80%, respectively [16-18].

Table 3: PHPT characteristics based on cause.

Variables	SA	Multiple-gland disease (13)	p Value
(N)	-75		
Age	46 \pm 14	43 \pm 18	0.486
Gender			
Male	12 (16%)	4 (30.8%)	0.243
Female	63 (84%)	9 (69.2%)	
Pre-op Ca mg/dl	2.84 \pm 0.32	2.92 \pm 0.44	0.435
Pre-op PTH pg/ml	397 \pm 489	461 \pm 397	0.654
Presentations:			
Bone	43 (57.3%)	7 (53%)	0.606
Renal	4 (5.3%)	0 (0%)	
Asymptomatic	21 (28%)	4 (30.8%)	
Fatigability	6 (8%)	1 (7.7%)	
Gastric	1 (1.3%)	1 (7.7%)	
Postpone Ca mg/dl	2.26 \pm 0.13	2.41 \pm 0.17	0.0004
Surgical Outcome			
Persistence	0 (0%)	1 (7.7%)	0.147
Recurrence	0 (0%)	2 (15.4%)	0.02

Moreover, the incidence of finding a synchronous thyroid nodule was 40% in our study in which 12% found to have a thyroid cancer. Thus, our results are in agreement with the previous literatures [19].

In regard to the causes of PHPT, our study demonstrates that single adenoma was the cause in 85.2% of the cases which is in agreement with the previous national and international literatures [2,3,8,9,11]. However, 85.2% of our cases underwent minimally invasive parathyroidectomy comparing with 9.8% in the Bismar et al. [9] study and 0% in the Malabu et al. [8] study. That can be explained by the difference in the time of the study. MIP is a relatively new surgical approach which appears to have become the standard operation in KSA nowadays. Moreover, our persistence (1.1%) and recurrence rates (2.2%) are in agreement with previously published national and international figures [8,9,20,21].

In addition, we found that females had a lower preoperative vitamin D level and higher immediate postoperatively PTH level which may indicate a vitamin D deficiency among them. This was in agreement with the Malabu et al. [8] study. Moreover, younger than 40 years old patients presented with more bone symptoms and patients more than 40 years old were found to have more thyroid nodules. Shah et al. [14] found that bone presentation were common in young patients, while renal presentations were common in adults. Finally, the recurrence rate was higher among those with a multiple glands disease which is in agreement with the previously published studies [20-22].

The results of this study should be taken with caution since this study is retrospective study. Detailed information about pre- and postoperative vitamin D levels were missing. Generalizability is limited as well, since the study was carried out on a single, high-volume tertiary hospital and the operations were performed by experienced endocrine surgeons. Thus, further prospective studies on a larger population are needed to validate our findings and to clarify the incidence and the prevalence of PHPT in Saudi Arabia.

Conclusion

Our data suggested that PHPT patients in Saudi Arabia affecting females more than males. Although half of the patients still presented mainly with bone symptoms, one fourth of the patients were asymptomatic. Moreover, one third of the cases are younger than 40 years old.

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