Clinical Burden of Patients with Hypoparathyroidism in the United States: A Claims Data Analysis

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INTRODUCTION

- The clinical burden of hypoparathyroidism (HP) remains poorly described due to the rarity of this condition.
- The goal of this study was to further investigate the clinical characteristics of patients with chronic hypoparathyroidism (cHP) using patients with transient post-surgical hypoparathyroidism (tHP) as a reference.

METHODS

- **Study Design:** Non-interventional retrospective claims data analysis
- **Data Source:** HealthVerity closed payer claim medical and pharmacy database (Private Source 20) with 130 million covered lives.
- **Study Period:** October 1, 2014 - December 31, 2019
- **Study Population:** Incident and prevalent patients identified with HP. Eligibility criteria were adapted from a study by Powers et al. (1) and defined under the guidance of clinicians experienced in treating patients with cHP. Patients were continuously enrolled ≥1 year pre- and post-index.

Incident tHP (reference group)

- Patients having a claim for parathyroidectomy, complete or partial thyroidectomy, or neck dissection followed by a claim with a diagnosis of HP within 6 months of the procedure, with no HP diagnosis claim before the procedure and 6 months after the procedure
- Index date: Date of the last HP diagnosis claim following the procedure

Incident cHP

- Patients having a claim for parathyroidectomy, complete or partial thyroidectomy, or neck dissection followed by a claim with an HP diagnosis 6-15 months later, and a second HP diagnosis claim at any subsequent time point
- Index date: Date of the first qualifying HP diagnosis claim

Prevalent cHP

- Patients having ≥2 claims for HP that were 6-15 months apart and that had a prescription claim for either active vitamin D, calcium, PTH or thyroid replacement therapy between the first qualifying HP claim and within 30 days of the second HP claim
- Index date: Date of the first of two qualifying HP diagnosis claims

- **Analysis:** All outcomes were assessed up to one year from the index date. Baseline characteristics and outcomes were compared using descriptive statistics.

Abbreviations: cHP: Chronic Hypoparathyroidism; CKD: Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; ESRD: End-Stage Renal Disease; HP: Hypoparathyroidism; Pt: Patient; SD: Standard Deviation; tHP: Transient Hypoparathyroidism; 1,25(OH)2D: 1,25-dihydroxyvitamin D; 25OHD:25-hydroxyvitamin D

RESULTS

- Of the 43,640 patients with a diagnosis claim for HP in the claims database during the study period, a total of 6,297 individuals met the inclusion criteria of the study and were further divided into three cohorts: incident tHP (N=773), incident cHP (N=1,406), and prevalent cHP (N=4,118) (**Table 1**).
- The time between surgery and HP claim that qualified the patient for eligibility was 2.0 (1.7) months for the incident tHP cohort and 8.7 (2.3) months for the incident cHP cohort. In prevalent cHP cohort, only 3.4% had a record of neck surgery in the year before the index.

Table 1. Baseline Characteristics

	Incident tHP N=773	Incident cHP N=1,406	Prevalent cHP N=4,118
Female, n (%)	624 (81.2%)	1,170 (83.2%)	3,146 (76.4%)
Age (Years), Mean (SD)	53.5 (14.9)	52.1 (16.4)	56.5 (18.6)
Insurance type, n (%)			
Commercial	452 (58.5%)	743 (52.8%)	1,591 (38.6%)
Medicaid	204 (26.4%)	397 (28.3%)	1,307 (31.7%)
Medicare Advantage	87 (11.3%)	220 (15.7%)	1,067 (25.9%)
Unknown	30 (3.0%)	42 (2.9%)	152 (3.7%)
Procedures, n (%)			
Parathyroidectomy	286 (37.0%)	368 (26.2%)	139 (3.4%)
Neck dissection	39 (5.1%)	332 (23.6%)	
Thyroidectomy	448 (57.9%)	706 (50.2%)	

Treatment Patterns

- Calcitriol was the most frequently used prescription vitamin D therapy, and PTH replacement therapy was prescribed for less than 5% of patients (**Table 2**).

Table 2. Treatment Patterns

	Incident tHP Follow-up 1-2y N=575	Incident cHP Follow-up 1-2y N=726	Prevalent cHP Follow-up 1-2y N=3,346
Calcitriol	106 (18.4%)	383 (52.8%)	2,072 (61.9%)
Vitamin D*	103 (13.8%)	103 (14.3%)	502 (15.0%)
PTH (Natpara®)	0 (0.0%)	34 (4.7%)	126 (3.6%)
Teriparatide (Forteo®)	1 (0.2%)	1 (0.1%)	11 (0.3%)

**Vitamin D includes ergocalciferol and cholecalciferol.*
Note: Over the counter vitamin D use is not available in claims databases

Table 3. Comorbidities

	Incident tHP		Incident cHP		Prevalent cHP	
	Before Surgery (1 year) N=715	Follow-up 1-2 year N=575	Before Surgery (1 year) N=1,069	Follow-up 1-2 year N=726	Before Index (1 year) N=4,118	Follow-up 1-2 year N=3,346
Cardiovascular and metabolic disorders						
Arrhythmias	113 (15.8%)	55 (9.6%)	195 (18.2%)	120 (16.5%)	551 (13.4%)	529 (15.8%)
Congestive heart failure	33 (4.6%)	29 (5.0%)	60 (5.6%)	52 (7.2%)	321 (7.8%)	326 (9.7%)
Diabetes	175 (24.5%)	127 (22.1%)	225 (21.0%)	154 (21.2%)	1,052 (25.5%)	958 (28.6%)
Hypertension	331 (46.3%)	246 (42.8%)	485 (45.4%)	325 (44.8%)	2,052 (49.8%)	1,817 (54.3%)
Central Nervous System						
Basal ganglia calcification	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (0.3%)	14 (0.4%)
Peripheral Neuropathy	9 (1.3%)	6 (1.0%)	25 (2.3%)	11 (1.5%)	112 (2.7%)	65 (1.9%)
Seizures and convulsions	10 (1.4%)	14 (2.4%)	21 (2.0%)	28 (3.9%)	121 (2.9%)	146 (4.4%)
Laboratory Imbalances						
Hypercalcemia	144 (20.1%)	25 (4.4%)	142 (13.3%)	39 (5.4%)	232 (5.6%)	190 (5.7%)
Hypercalciuria	5 (0.7%)	1 (0.2%)	9 (0.8%)	6 (0.8%)	60 (1.5%)	47 (1.4%)
Hypocalcemia	8 (1.1%)	67 (11.7%)	77 (7.2%)	258 (35.5%)	1,247 (30.3%)	1,041 (31.1%)
Malignancy						
Any Malignancy	265 (37.1%)	217 (37.7%)	457 (42.8%)	347 (47.8%)	1,063 (25.8%)	947 (28.3%)
Thyroid Cancer	212 (29.7%)	189 (32.9%)	379 (35.5%)	310 (42.7%)	832 (20.2%)	750 (22.4%)
Musculoskeletal						
Fractures	19 (2.7%)	13 (2.3%)	32 (3.0%)	22 (3.0%)	113 (2.7%)	116 (3.5%)
Osteoporosis	50 (7.0%)	35 (6.1%)	95 (8.9%)	63 (8.7%)	317 (7.7%)	298 (8.9%)
Neuropsychiatric						
Anxiety	165 (23.1%)	111 (19.3%)	236 (22.1%)	168 (23.1%)	700 (17.0%)	683 (20.4%)
Cognitive impairment	15 (2.1%)	13 (2.3%)	27 (2.5%)	20 (2.8%)	110 (2.7%)	96 (2.9%)
Dementia	6 (0.8%)	9 (1.6%)	10 (0.9%)	3 (0.4%)	75 (1.8%)	84 (2.5%)
Depressive disorders	135 (18.9%)	101 (17.6%)	202 (18.9%)	149 (20.5%)	730 (17.7%)	716 (21.4%)
Sleep-wake disorders	115 (16.1%)	98 (17.0%)	190 (17.8%)	151 (20.8%)	632 (15.3%)	620 (18.5%)
Other						
Cataract formation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	2 (0.1%)
Tetany	1 (0.1%)	0 (0.0%)	2 (0.2%)	4 (0.6%)	23 (0.6%)	9 (0.3%)
Renal Disease						
CKD (Stage 1-4, unspecified)	54 (7.6%)	47 (8.2%)	87 (8.1%)	67 (9.2%)	629 (15.3%)	644 (19.2%)
CKD Stage 5, ESRD and failure	31 (4.3%)	17 (3.0%)	44 (4.1%)	23 (3.2%)	162 (3.9%)	140 (4.2%)
Diabetic Nephropathy	59 (8.3%)	46 (8.0%)	87 (8.1%)	61 (8.4%)	365 (8.9%)	390 (11.7%)
Nephrolithiasis/renal stones	54 (7.6%)	22 (3.8%)	65 (6.1%)	46 (6.3%)	214 (5.2%)	212 (6.3%)

Comorbidities

- Before surgery, ≥5% differences between the incident cHP and tHP cohorts were observed for the following conditions: hyper- and hypocalcemia, any malignancies, and in particular thyroid cancer (**Table 3**).
- As expected, in the 1 to 2 years following an incident diagnosis, there was a decrease in the rate of hypercalcemia and an increase in the rate of hypocalcemia compared to baseline, and in line with rates observed in the prevalent cHP cohort.
- While cHP patients have, on average, an increased bone mineral density (7), it is interesting to note that cHP patients are not immune to osteoporosis, as about 9% of them are diagnosed with osteoporosis.
- The prevalence of CKD Stages 1-4 was approximately greater than two-fold higher in the prevalent cHP cohort during the study period compared to the incident tHP and cHP cohorts.

Monitoring Patterns

- Serum calcium and 25OHD were assessed in more patients with cHP compared to those with tHP (**Table 4**).
- Consistent with the understanding that cHP and its treatments are associated with renal disease (2), eGFR was monitored in 80% of patients in both cHP cohorts with each patient undergoing an average of four tests annually.

Table 4. Monitoring Patterns

	Incident tHP Follow-up 1-2 year N=575		Incident cHP Follow-up 1-2 year N=726		Prevalent cHP Follow-up 1-2 year N=3,346	
	Patient n (%)	Tests/pt mean (SD)	Patient n (%)	Tests/pt mean (SD)	Patient n (%)	Tests/pt mean (SD)
Serum Calcium	388 (67.5%)	3.1 (3.3)	610 (84.0%)	4.3 (6.3)	2,813 (84.1%)	4.3 (8.5)
Parathyroid hormone intact	104 (18.15%)	1.6 (1.5)	311 (42.8%)	1.7 (1.4)	1,050 (31.4%)	1.8 (2.6)
eGFR	380 (66.1%)	3.0 (3.3)	575 (79.2%)	3.8 (4.4)	2,682 (80.2%)	4.2 (8.6)
25OHD	225 (39.1%)	1.6 (0.9)	426 (58.7%)	1.8 (1.3)	1,736 (51.9%)	1.8 (1.9)
1,25(OH)2D	16 (2.8%)	1.2 (0.4)	58 (8.0%)	1.5 (1.1)	233 (7.0%)	1.4 (1.1)

CONCLUSIONS

- This study provides insights into the natural history of HP and demonstrates cHP is associated with increased disease burden and medical needs in contrast to patients with tHP.
- The cHP patient characteristics were consistent with previous reports (1, 3-6) in that the majority of cHP patients were female with mean age consistent with peri- or post-menopause and treated in line with current treatment guidelines.
- During the follow up periods, cHP cohorts had a higher incidence of hypocalcemia and cardiac arrhythmia compared to the tHP cohort.
- While hypoparathyroidism is associated with increases in bone mineral density, almost 10% of patients in this cohort were diagnosed with osteoporosis.
- Given the noted increased burden of and monitoring for renal disease in the prevalent cHP cohort, this could be considered a key target organ for therapeutic intervention.
- The strength of this study lies in the inclusiveness of the US HP patient population and the rigorous eligibility criteria for the identification of cHP patients. Limitations that are common among claims analysis studies also apply to the present study.
- Future studies could examine the costs associated with HP and its complications.

REFERENCES

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DISCLOSURES

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