



(REVIEW ARTICLE)



## An audit on the management of patients with chronic hypoparathyroidism in a district general hospital in the UK

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### Abstract

Chronic Hypoparathyroidism is a rare condition but can be responsible for a wide range of co-morbidities including nephrocalcinosis and nephrolithiasis, neuropsychiatric disorders, seizures, brain fog, prolonged QT interval on ECG (from hypocalcemia) and Cardiac Arrhythmias, Dilated Cardiomyopathy and Cataract. The National (UK) Survey for the management of Chronic Hypoparathyroidism is currently ongoing (Year 2020) and our Hospital has participated in it, Therefore, I performed this Audit comparing our performance with the prevalent Guidelines on management of Chronic Hypoparathyroidism

**Keywords:** Hypoparathyroidism; Calcium; Phosphate; Magnesium; Vitamin D

### 1. Introduction

Hypoparathyroidism is a rare endocrine disorder and is listed in NORD (National Organization of Rare Disorders) database. Hypoparathyroidism has the following causes [1]:

- Thyroidectomy, Parathyroidectomy, or other surgical interventions in the central part of the neck. These are the most common causes of hypoparathyroidism.
- Polyglandular Autoimmune syndrome Type 1 is an autosomal recessive syndrome due to mutation of the *AIRE* gene resulting in hypoparathyroidism, hypogonadism, adrenal insufficiency, vitiligo and mucocutaneous candidiasis
- Hemochromatosis
- DiGeorge Syndrome (Chromosome 22q11 microdeletion) with absence or dysfunction of the parathyroid glands, cleft palate, heart problems, hearing loss, kidney problems and infections
- Hypomagnesemia
- Mutation of the *CASR* or *GNA11* gene (Autosomal Dominant)
- Idiopathic or Familial condition called Barakat syndrome or HDR syndrome (Hypoparathyroidism, Sensorineural deafness, and Renal disease)
- Kenny-Caffey Syndrome is an autosomal dominant with skeletal abnormalities and caused by a mutation in *FAM111A*

Hypoparathyroidism is characterized by its hallmark Hypocalcemia, together with Hyperphosphatemia and low PTH (Parathyroid Hormone).

The six goals of management include:

- to ensure that the patients do not have symptoms of hypocalcaemia

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- improve the patient's QoL (Quality of Life)
- maintain serum calcium levels in the low normal range (N: 2.2-2.6 mmol/l)
- to keep serum phosphate within the normal range (N: 0.8-1.45 mmol/l),
- to keep total calcium-phosphate product under 4.4 mmol<sup>2</sup> /l<sup>2</sup> (55 mg<sup>2</sup> /dl<sup>2</sup>)
- to prevent hypercalciuria

Hypocalcemia is an adverse prognostic marker with regards to COVID-19 infection and predicts hospitalization. The Hypoparathyroidism, UK website recognizes these patients as highly vulnerable against COVID-19 infection [2]. Such patients should be encouraged to access and read the contents of the Website or to ring the dedicated Parathyroid UK helpline number on 0044(0)1342316315. The objective of the study was to ensure that the management of Chronic Hypoparathyroidism was being carried out in our hospital in accordance with the existing Guidelines, mainly the one of the ESE (European Society of Endocrinology).

### 1.1. Aims

To find out if patients with Chronic Hypoparathyroidism were managed in our Hospital according to the prevalent Guidelines. As currently there is no NICE (National Institute for Health and Care Excellence), UK guideline available for the management of this condition, the audit was performed comparing our performance mainly with the published European guidelines.

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## 2. Methods

The details of patients with chronic hypoparathyroidism seen at the OPD during the last 1 year till June 2020 were studied for the purpose of the audit. The names of the patients were provided by our Clinical Audit Department and all the Endocrine Consultants in our Hospital.

The Guidelines of the ESE on the management of Chronic Hypoparathyroidism were considered following the 3rd European Symposium on Hypoparathyroidism in Athens, Greece (8-9 Nov 2019) and previous ESE meeting in Oslo, May 2015 [3,4]. The proforma of the National Audit (UK) on management of Hypoparathyroidism, 2020 and The International Guidelines on the management of Chronic Hypoparathyroidism, published in 2016 were also reviewed [5,6].

### 2.1. Criteria/Recommendations of ESE [3,4]

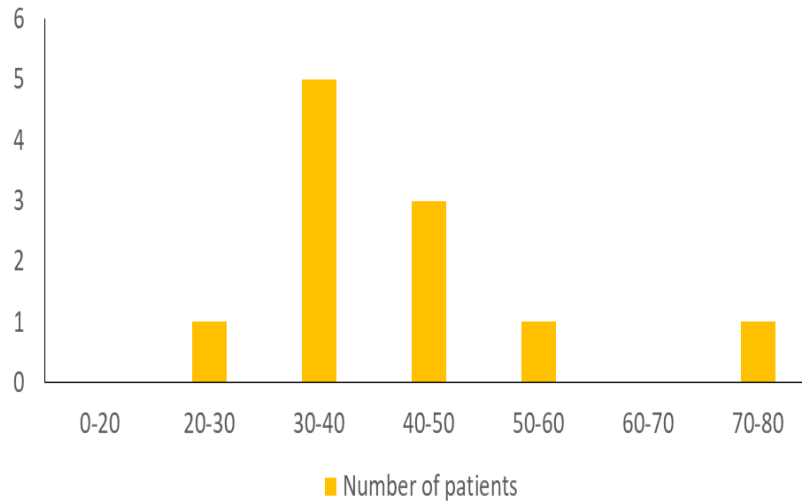
- Documentation of the cause of hypoparathyroidism
- Target for albumin adjusted Calcium documented. Treatment is targeted to maintain calcium level (albumin adjusted total calcium or ionized calcium) in the lower part or slightly below the lower limit of normal with patients being free of symptoms or signs of hypocalcaemia. Target for serum total Calcium is 2.1-2.3 mmol/l and ionized Calcium 1.05-1.15 mmol/l.
- Target for Phosphate documented (serum phosphate levels should be within the reference range: 0.8-4.5 mmol/l)
- Recording of Calcium-Phosphate Product (should be below 4.4 mmol<sup>2</sup> /l<sup>2</sup>).
- Serum Vitamin D should be normal
- Serum Magnesium should be normal
- 24 hours Urinary Calcium should be documented annually, and the aim is to avoid hypercalciuria. In case of hypercalciuria, to use sodium restricted diet (less than 2.9 gm per day) and thiazide diuretics (Bendroflumethiazide 5 mg daily)
- QoL assessed and documented; the recommendation is to use the SF-36 score
- Education is to be provided to the patients regarding the symptoms and complications of hypo and hypercalcaemia (which occur with Vitamin D Analogues)
- Treatment with Vitamin D analogues, Calcium supplements and Cholecalciferol.
- Annual renal imaging particularly if renal stones are suspected or if creatinine rises
- Annual DEXA scan is only part of the National Audit Proforma on management of Hypoparathyroidism (not part of ESE Guidelines). However, it is included in the International Guidelines (2016) together with imaging of the Skull [6]. Hypoparathyroidism results in increased bone mineral density, sclerosis, increased trabecular volume, cortical thickening, and fractures [7].

Recombinant Human Parathyroid Hormone (rhPTH) is still not routinely recommended in European Guidelines for the treatment of Hypoparathyroidism either as once or twice daily injection or in the form of infusion pump. In 2015, the

Food and Drug Administration (FDA) in the USA approved rhPTH for treatment of hypoparathyroidism. In February 2017, the European Medicines Agency (EMA) recommended conditional marketing authorization in the European Union for the use of rhPTH. It may be an important therapeutic option for patients who are not well controlled on conventional treatment [8].

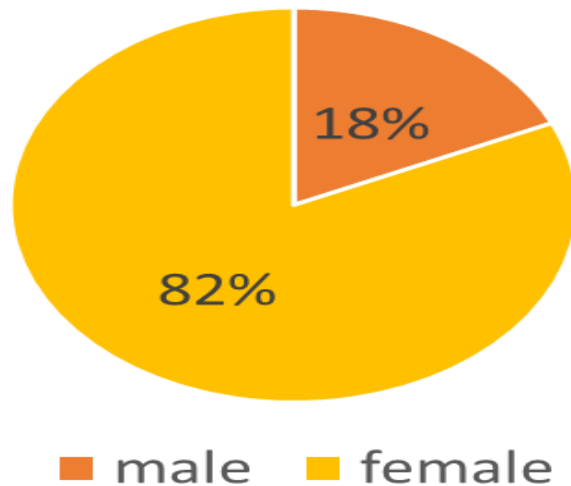
### 3. Results

- Total: 11 Patients
- Age: 20-30 years=1; 30-40 years=5; 40-50 years=3; 50-60 years=1; 70-80 years=1
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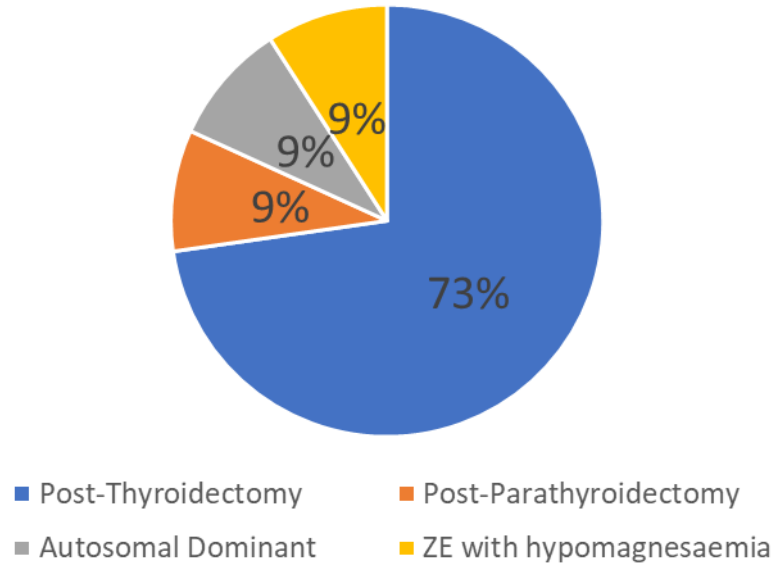
**Figure 1** Age Distribution

- (3) Sex: Male: 2; Female: 9



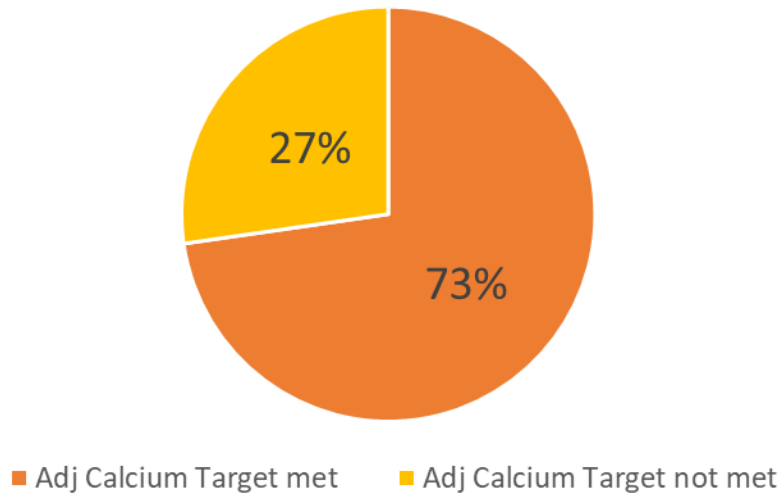
**Figure 2** Gender chart

- (4) Causes of hypoparathyroidism documented: 11/11(100%), causes are: Post Thyroidectomy: 8; Post parathyroidectomy: 1; Autosomal Dominant:1; Zollinger Ellison Syndrome with hypomagnesemia:1.



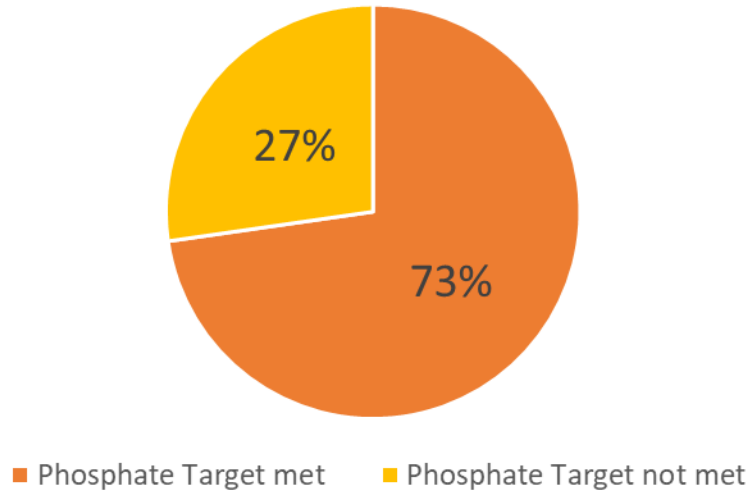
**Figure 3** Causes of Hypoparathyroidism

- Target for albumin adjusted Calcium documented/Achieved, according to European Guidelines: 8/11 or 73% cases (Three exceptions: 1.82 mmol/l, 1.98 mmol/l and 2.47 mmol/l). The target suggested by NHS UK though is 1.8-2.25 mmol/l. By that standard target Calcium was achieved in 10/11 or 91% patients.



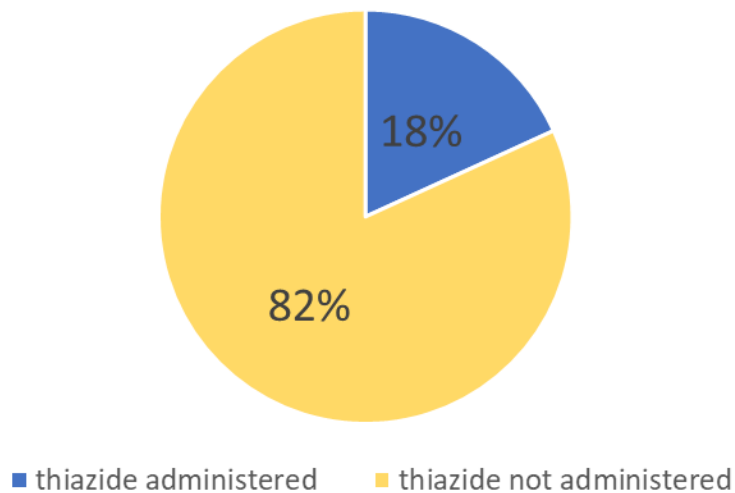
**Figure 4** Targeted Adjusted calcium

- Target for Phosphate documented/achieved: 8/11 or 73% cases (Three exceptions: 1.54 mmol/l, 1.61 mmol/l, and 1.64 mmol/l).



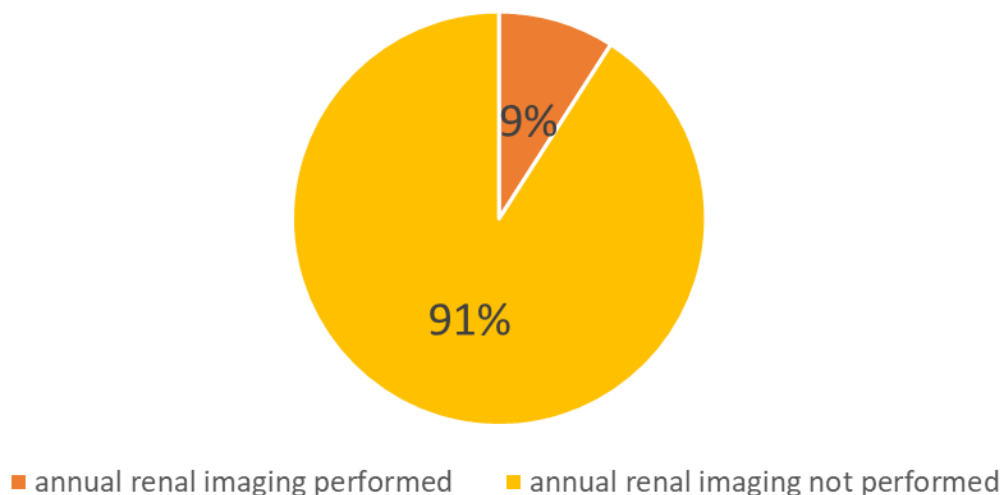
**Figure 5** Targeted Phosphate Level

- Magnesium measured and documented: Measured 11/11 (100%); Normal: 10/11 (91%)
- Vit D measured: 11/11(100%)
- Calcium- Phosphate product (CaPP) recorded: Nil (0%)
- Annual 24 hours Urine Calcium done: 1/11 (9%)
- Treatment with Vitamin D analogues, Calcium supplements and Phosphate binders and Vitamin D3: 11/11 (100%)
- Treatment with Magnesium: 2/11
- Treatment with Thiazide diuretics: 2/11



**Figure 6** Patients on Thiazide diuretics

- Information/Education provided to the patient regarding the symptoms of hypocalcaemia: 9/11 or 82% patients (aware of at least the following symptoms of hypocalcaemia: tingling, numbness, muscle spasms, cramps, fatigue)
- QoL measured: Nil (0%)
- Annual renal imaging done: 1/11 (9%)



- Annual DEXA scan: Nil (0%)

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#### 4. Summary of Results

- Causes of Hypoparathyroidism were documented in 100% cases.
- Target adjusted Calcium (according to European Guidelines) and phosphate were obtained in 73% cases, Magnesium in 91% cases and Vitamin D in 100% cases
- Calcium- Phosphate product was recorded in no patient
- Annual 24 hours urine Calcium was done in 9% cases
- Symptoms of hypocalcaemia were known to 82% patients
- QoL of life was recorded in no patient
- Annual renal imaging was done in 9% patients
- Annual DEXA Scan was recorded in no patient

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#### 5. Discussion and Recommendations

Hypoparathyroidism is not a common Disorder. Also, following Thyroidectomy approximately only 2-5% of the population develop permanent hypocalcemia. Chow, et al suggests that about 2.8% of the patients will develop permanent hypoparathyroidism after 6 months following Thyroid Surgery [9]. Although the number of patients we treat in our hospital overall for chronic Hypoparathyroidism is slightly higher, the audit was performed, considering only those patients (11 in total) who were seen between June 2019 and June 2020. The recommendations at the end of the audit are as follows:

- To try to achieve and maintain target adjusted calcium, phosphate, Magnesium and Vitamin D in all cases
- Calcium- Phosphate Product is to be documented in all cases
- 24 hours Urinary calcium is to be done annually in all cases
- Leaflets documenting the symptoms and complications of hypo and hypercalcaemia are to be provided to all patients
- SF-36 or a different QoL leaflet is to be designed and provided to the patients and they are to be asked to fill it in at various stages of treatment to note the progress or improvement in symptoms
- Renal imaging possibly is to be done annually
- Whether DEXA Scan is to be done annually or every 2 years- will need discussion, as included in the International Guidelines which will be revised in 2021. This is not included in the European (ESE) Guidelines

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#### 6. Conclusion

The audit revealed that with regard to achieving the targeted blood biochemistry, we were successful in most cases; however, there are certain areas where we would need to improve our performance in future and hence would require to perform a re-audit in 1 year. This audit also aims to help the society in understanding the significance of Chronic

Hypoparathyroidism with its hallmark of hypocalcemia and the way forward to managing such patients as mentioned above.

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## Compliance with ethical standards

### *Acknowledgments*

I like to acknowledge all my Endocrine colleagues and the Secretaries for helping me with the data towards preparation of the audit.

### *Disclosure of conflict of interest*

There was no conflict of interest.

### *Statement of informed consent*

For an audit Informed Consent is not required. Informed Consent is required for Research

If studies involve information about any individual e.g. case studies, survey, interview etc., author must write statement of informed consent as “Informed consent was obtained from all individual participants included in the study.”

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