

**hyperparathyroidism :**  
**pathophysiology, clinical**  
**features and evaluation**

# Clinical features and complication of primary Hyperparathyroidism (1)

## I. Related to hypercalcemia per se

### Central nervous system

lethargy  
drowsiness  
depression  
stupor  
coma

### Neuromuscular

fatigue  
weakness  
proximal myopathy  
hypotonia

### Cardiovascular

hypertension  
bradycardia  
short Q-T interval  
potentiation of digitalis  
intoxication

### Renal

polyuria  
calcium nephropathy-  
nephrocalcinosis

### Gastrointestinal

nausea  
vomiting  
constipation  
dyspepsia  
possibly increased peptic ulcer  
pancreatitis

Metastatic calcification (usually  
requires P to be elevated  
as well)

band keratopathy  
pruritus

# **Clinical features and complication of primary Hyperparathyroidism (2)**

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## **II. Related to hypercalciuria**

**Kidney stone diathesis (10 per cent)**

## **III. Related to PTH effect on bone and joints**

**Bone pain from osteitis fibrosa cystica**

**Bone cysts-rarely with fracture**

**Epulis-abrown tumor (osteoclastic) of the jaw**

**Arthralgias**

**Increased incidence of gout and pseudogout**

# Clinical Presentations of Primary Hyperparathyroidism

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Asymptomatic hypercalcemia

**Bone or stone disease**

Other recognized complications (neuromuscular, gastrointestinal, articular, hematologic, central nervous system)

Acute primary hyperparathyroidism

**Parathyroid carcinoma**

Familial primary hyperparathyroidism

Familial cystic parathyroid adenomatosis

**Neonatal hyperparathyroidism**

Multiple endocrine neoplasia, type 1 or 2

# MODE OF PRESENTATION OF PRIMARY HYPERPARATHYROIDISM

|  | Current study | previous                                       |                                 |                               |                            |
|--|---------------|--|---------------------------------|-------------------------------|----------------------------|
|  |               | Hellstrom and Ivemark (Sweden)<br>138 patients | Mc Geown (U.K.)<br>177 patients | Watson (U.K.)<br>100 patients | Wang (USA)<br>431 patients |
|  | 111 patients  |  |                                 |                               |                            |
|  | %             | %  | %                               | %                             | %                          |
| Accidental (no symptoms)                             | 57            | -  | 3                               | 14                            | 1                          |
| Renal (stones or nephrocalcinosis)                   | 7             | 79   | 72                              | 47                            | 55                         |
| Bone disease   | -             | 20   | 17                              | 13                            | 21                         |
| Psychiatric disorder                                 | 5             | -  | -                               | 2                             | 1                          |
| Acute hypercalcemic syndrome                         | 14            | -  | 2                               | -                             | 2                          |
| Gastrointestinal syndromes                           | 4             | -  | 4                               | 12                            | 12                         |
| Symptoms of hypercalcemic (lethargy, polyuria, & c.) | 8             | -  | 2                               | 8                             | 4                          |
| Hypertension   | 5             | 1  | -                               | 4                             | 1                          |

## Changing Profile of Primary Hyperparathyroidism

| Symptomatology       | Study                 |                               |                                  |                                    |
|----------------------|-----------------------|-------------------------------|----------------------------------|------------------------------------|
|                      | Cope<br>(1930 – 1965) | Heath et al.<br>(1965 – 1974) | Mallette et al.<br>(1965 – 1972) | Silverberg et al.<br>(1984 – 1999) |
| Nephrolithiasis (%)  | 57                    | 51                            | 37                               | 17                                 |
| Skeletal disease (%) | 23                    | 10                            | 14                               | 1.4                                |
| Asymptomatic (%)     | 0.6                   | 18                            | 22                               | 80                                 |

## **Frequency of clinical symptoms of primary hyperparathyroidism in 62 subjects**

| <b>Manifestation</b>  | <b>Patients (No.)</b> | <b>Frequency (%)</b> |
|---|-----------------------|----------------------|
| <b>Skeletal symptoms (pain, fracture, tumor, and deformity)</b> | <b>58</b>             | <b>93.5</b>          |
| <b>Fatigue and weakness</b>                                     | <b>54</b>             | <b>87</b>            |
| <b>Arthralgia</b>   | <b>48</b>             | <b>77.5</b>          |
| <b>Gastrointestinal complaints</b>                              | <b>39</b>             | <b>63</b>            |
| <b>Polyuria</b>   | <b>28</b>             | <b>45</b>            |
| <b>Muscle weakness</b>  | <b>21</b>             | <b>34</b>            |
| <b>Weight loss</b>  | <b>21</b>             | <b>34</b>            |
| <b>Slow mentation</b>   | <b>16</b>             | <b>26</b>            |
| <b>Depression</b>   | <b>14</b>             | <b>22.5</b>          |
| <b>Hypertension</b>   | <b>13</b>             | <b>21</b>            |
| <b>Renal colic</b>  | <b>4</b>              | <b>6.5</b>           |
| <b>Generalized pruritus</b>                                     | <b>2</b>              | <b>3</b>             |
| <b>Acute pancreatitis</b>                                       | <b>1</b>              | <b>1.5</b>           |
| <b>No symptoms</b>  | <b>0</b>              | <b>0</b>             |

## Biochemical profile in 62 individuals with primary hyperparathyroidism

|                                     | Mean $\pm$ SD  | Range      | % of patients with abnormal result |
|-------------------------------------|----------------|------------|------------------------------------|
| Serum calcium (mg/dL)               | 11.2 $\pm$ 1.1 | 9.3 – 15.6 | 92                                 |
| Serum phosphorus (mg/dL)            | 2.1 $\pm$ 0.2  | 1.4 – 3.6  | 79                                 |
| Serum alkaline phosphatase (IU/L)   | 657 $\pm$ 116  | 84 – 3150  | 90                                 |
| Serum PTH * (pg/mL)                 | 184 $\pm$ 41   | 76 – 1300  | 100                                |
| 24 hour urinary calcium excretion** | 162 $\pm$ 23   | 58 – 291   | 0                                  |

\* PTH was measured in 29 subjects

\*\* 24 hour urinary calcium was determined in 34 patients



**frequency and sites of pathological fractures in 62 patients with primary hyperparathyroidism**

| <b>Fracture site</b>                   | <b>Frequency* (%)</b> |
|--|-----------------------|
| <b>Femoral and pelvic bones</b>        | <b>18 (29)</b>        |
| <b>Tibia and fibula</b>                | <b>8 (13)</b>         |
| <b>Long bones of arms and forearms</b> | <b>9 (14.5)</b>       |
| <b>Metatarsal bones</b>                | <b>4 (6.5)</b>        |
| <b>Metacarpal bones</b>                | <b>3 (5)</b>          |
| <b>Vertebral bones</b>                 | <b>3 (5)</b>          |
| <b>Ribs and scapula</b>                | <b>2 (3)</b>          |

**\* In some patients there was more than one site of fracture**

## **frequency of radiologic changes in 62 patients with primary hyperparathyroidism**

| <b>Abnormal radiologic finding</b>               | <b>No. of patients</b> | <b>Frequency (%)</b> |
|--|------------------------|----------------------|
| <b>Subperiosteal bone resorption</b>             | <b>48</b>              | <b>77.5</b>          |
| <b>Salt and pepper appearance of skull</b>       | <b>39</b>              | <b>63</b>            |
| <b>Brown tumor including jaw tumors (epulis)</b> | <b>37</b>              | <b>60</b>            |
| <b>Pathologic fractures</b>                      | <b>32</b>              | <b>51.5</b>          |
| <b>Loss of lamina dura of the teeth</b>          | <b>25</b>              | <b>40</b>            |
| <b>Nephrolithiasis</b>                           | <b>7</b>               | <b>11</b>            |
| <b>nephrocalcinosis</b>                          | <b>2</b>               | <b>3</b>             |
| <b>Chondrocalcinosis</b>                         | <b>1</b>               | <b>1.5</b>           |

## Results of this study in comparison with reported results from western countries

| Parameter                           | Present study | Western countries |                            |
|-------------------------------------|---------------|-------------------|----------------------------|
|                                     |               | Before 1970s      | After 1970s                |
| Female to male ratio                | 5:1           | 2:1               | 3 – 4: 1                   |
| Mean age of patients (y)            | 38.6          | 52.4              | 53.7                       |
| Most common pattern of presentation | Bone disease  | Renal disease     | Asymptomatic hypercalcemia |
| Bone disease (%)                    | 93.5%         | %15 – 20          | Rare                       |
| Renal disease (%)                   | 14.5%         | %50 – 70          | %7 – 10                    |
| Asymptomatic hypercalcemia (%)      | 0             | %3 - 5            | %50 - 60                   |

**Results of this study in comparison with reported results from other developing countries**

| <b>Parameter</b>                        | <b>Present study</b> | <b>Bhansali North India</b> | <b>Atefi Iran</b> | <b>Harinarayan India</b> | <b>Cheung Hong Kong Chinese</b> |
|---|----------------------|-----------------------------|-------------------|--------------------------|---------------------------------|
| <b>Female to male ratio</b>             | <b>5:1</b>           | <b>3.3:1</b>                | <b>9:1</b>        | <b>2:1</b>               | <b>1.5:1</b>                    |
| <b>Mean age of patients (y)</b>         | <b>38.6</b>          | <b>36.3</b>                 | <b>34</b>         | <b>38</b>                | <b>42</b>                       |
| <b>Most common form of presentation</b> | <b>skeletal</b>      | <b>skeletal</b>             | <b>skeletal</b>   | <b>skeletal</b>          | <b>skeletal</b>                 |
| <b>Bone disease (%)</b>                 | <b>93.5%</b>         | <b>86.5%</b>                | <b>100%</b>       | <b>90%</b>               | <b>74%</b>                      |
| <b>Renal disease (%)</b>                | <b>14.5%</b>         | <b>70%</b>                  | <b>22.5%</b>      | <b>50%</b>               | <b>39%</b>                      |
| <b>Asymptomatic hypercalcemia (%)</b>   | <b>0</b>             | <b>0</b>                    | <b>0</b>          | <b>0</b>                 | <b>0</b>                        |

# Primary Reasons for Initial Evaluation in Hyperparathyroidism (566 Operated Cases, 1953-1984)

| Reason for Evaluation                      | Number, of patients |
|--|---------------------|
| Asymptomatic hypercalcemia                 | 311                 |
| Renal calculi                              | 128                 |
| Secondary hyperplasia                      | 28                  |
| Incidental during thyroid operations       | 24                  |
| Gastrointestinal (ulcer, pancreatitis)     | 19                  |
| Skeletal manifestations                    | 17                  |
| Neurologic or psychotic symptoms           | 10                  |
| Coma                                       | 8                   |
| Minimal symptoms (e.g., fatigue, polyuria) | 8                   |
| Tertiary hyperparathyroidism               | 8                   |
| MEN-I                                      | 4                   |
| MEN-II                                     | 1                   |

# **Clinical Situations Deserving Investigation for Hyperparathyroidism**

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## **Renal Disease**

**Nephrolithiasis (kidney stones)**

**Nephrocalcinosis**

**Unexplained impaired renal failure**

## **Bone Disease**

**Diffuse (Metabolic) bone disease, regardless of supposed type**

**Solitary bone cyst or tumors**

**Hypercalcemia, regardless of supposed cause**

**Symptoms of Hypercalcemia**

**Gastrointestinal disease**

**Peptic ulcer**

**Pancreatitis**

# **Clinical Situations Deserving Investigation for Hyperparathyroidism**

## **Multiple Endocrine Neoplasia**

**MEN type 1 or 2**

**Zollinger-Ellison syndrome**

**Insulinoma**

**Pheochromocytoma**

**Medullary thyroid carcinoma**

**Watery diarrhea syndrome**

## **Family History**

**MEN type 1 or 2**

**Hyperparathyroidism**

## **Others**

**Mothers of infants with neonatal tetany**

**Band keratopathy**

**Unexplained myopathy**

**Severe depression**

**Hypertension**



