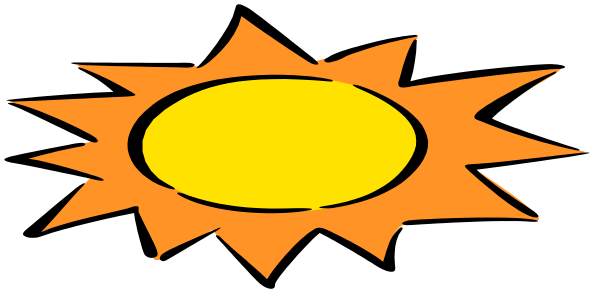


# Vitamin D Deficiency (VDD): Research Experience in Pakistan

Dr Aysha Habib Khan
Assistant Professor & Consultant Pathologist
Department of Pathology & Microbiology
and Medicine
Aga Khan University, Karachi

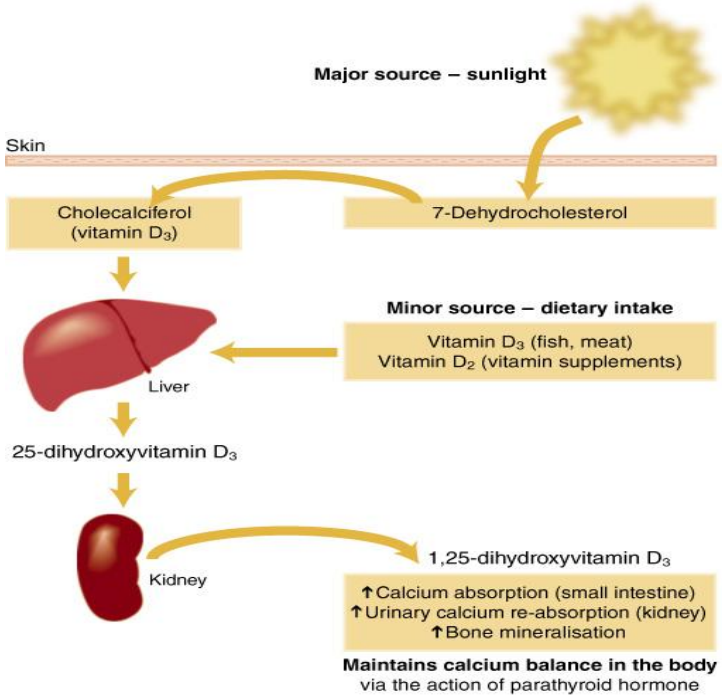
aysha.habib@aku.edu

# Outline

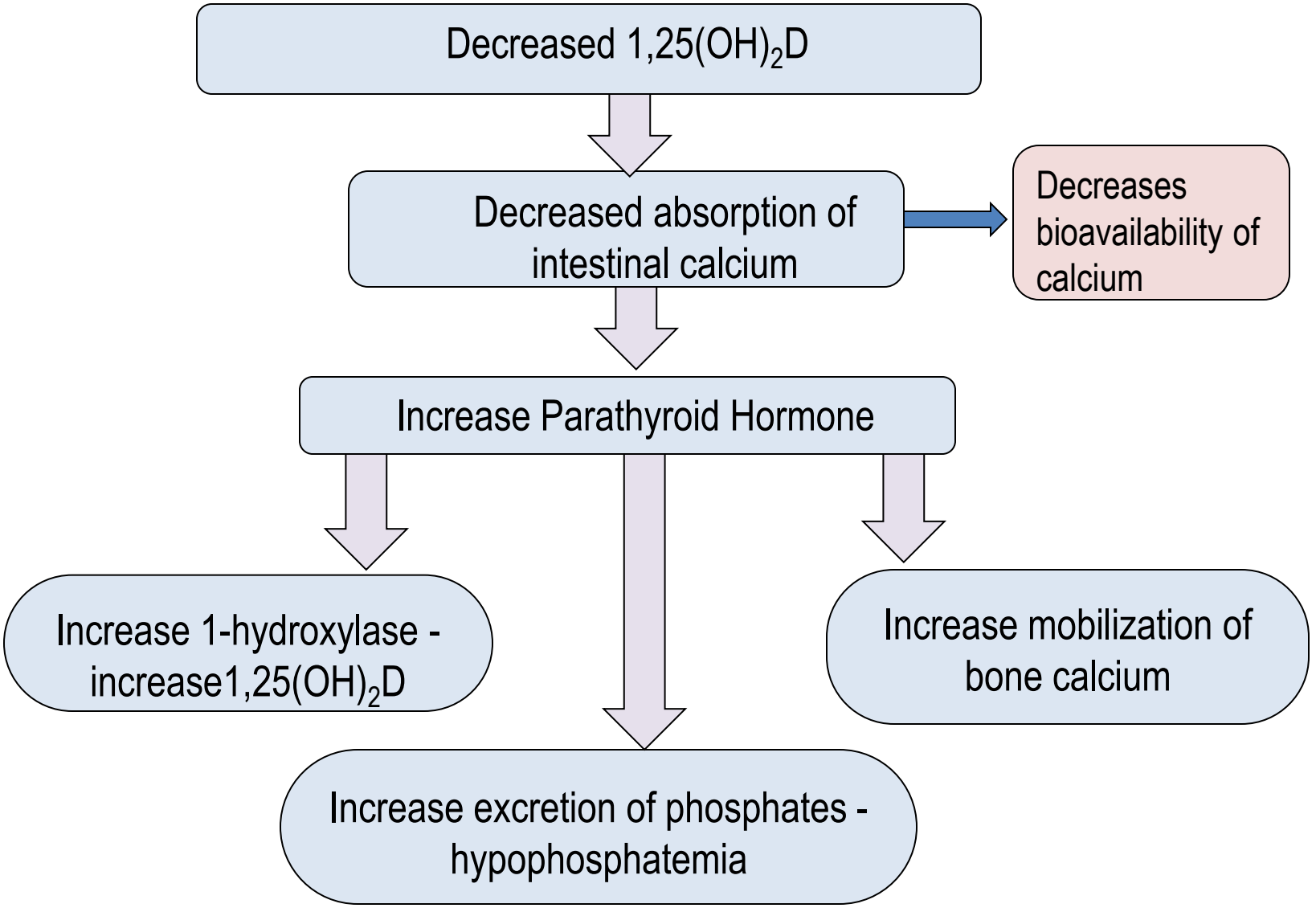
- Salient features of Vitamin D Deficiency
- Evolution of research
- Research findings
- Future directions

# Causes of vitamin D deficiency

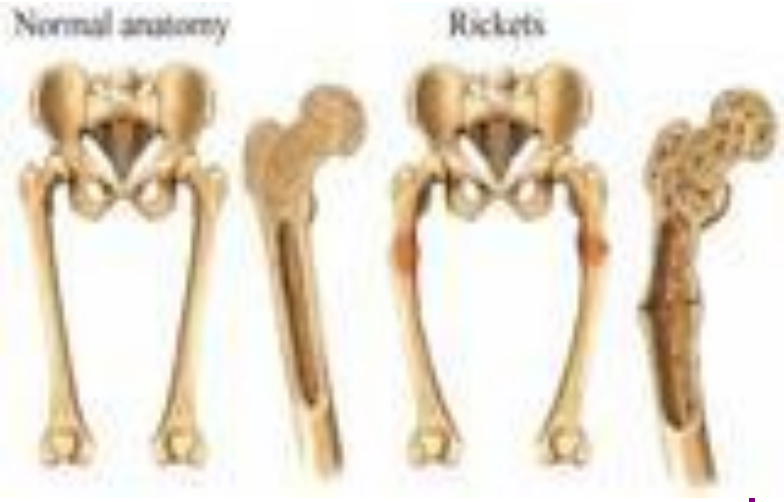
- Primary 25OHD Deficiency:
  - Inadequate sunlight exposure
  - Low dietary intake
- Secondary 25OHD Deficiency
  - Fat malabsorption
  - Liver diseases
  - Kidney disease
- Inherited conditions
  - Type 1: Abnormal or absent 1-hydroxylase enzyme
  - Type II: End-organ resistance



# Vitamin D deficiency (25OHD)



# Vitamin D deficiency osteomalacia




- Osteomalacia means “soft bones”
- Failure of mineralization of remodeled bone
- Bone pains in arms, legs, spine, and pelvis, with actual tenderness of the bones
- Progressive weakness
- Muscle weakness
- Waddling gait & muscle cramps
- High incidence of fracture than expected for age

# Bone & Mineral Research Experience: Background

Year 2002 – 2004

**Evolution of Research**

# Clinical Observation

- Patients at endocrine clinic of AKUH
- Mostly post pubertal females
- Presented with bone pains, muscles aches and proximal myopathy
- Hypophosphatemia
- Most of these were treated with high doses of calcitriol

# Review of Literature

- 1970's:
  - High incidence of VDD in Asians in UK
  - Dietary vitamin D deficiency?
  - Various causes were postulated (low exposure, life style)
  - Several questions remain unanswered

# Pakistani's living elsewhere

- Indian and Pakistani women had lower BMD then their western counterparts
- Lower 25 vitamin D
  - Caucassian
  - Other etnic groups

Osteoporosis International 1999;9(4):327-38

# Local Data

- Maternal D deficiency noted in 48 % mothers and 52% infants in Pakistan.
- 35% of women in Pakistan have low D levels

M Atiq et al. Acta Paediatr 87:737-40. 1998

# Clinical Laboratory Data at AKUH (2002 – 2004) N=3099

| Serum levels of 25 OHD | No of cases N=3099 (%) | Mean levels (ng/ml) |
|---|---|---|
| Vitamin D  Deficiency | 2107 (72) | 8.04 |
| Vitamin D Insufficiency | 572 (18) | 27.6 |
| Optimal | 280 (9) | 61.0 |
| Toxic | 37 (0.1) | 107.9 |

Note: 618 (20.8) cases had levels below 1.5

# Vitamin D deficiency osteomalacia: the continuing challenge

- Immediate action
- Early identification
- Public awareness
- Education of primary care physician
- Nutritional causes and inadequate exposure to sunlight
- Physicians in Pakistan give 1,25 $(OH)_2$ to patients
- There is likely to be significant under diagnosis of Vitamin D deficiency

# Is it Vitamin D deficiency?

- Paucity of data
- Need to exclude Vitamin D deficiency by testing
- Lack of funding/resources
- Management strategies needs to be reviewed

# Research Questions

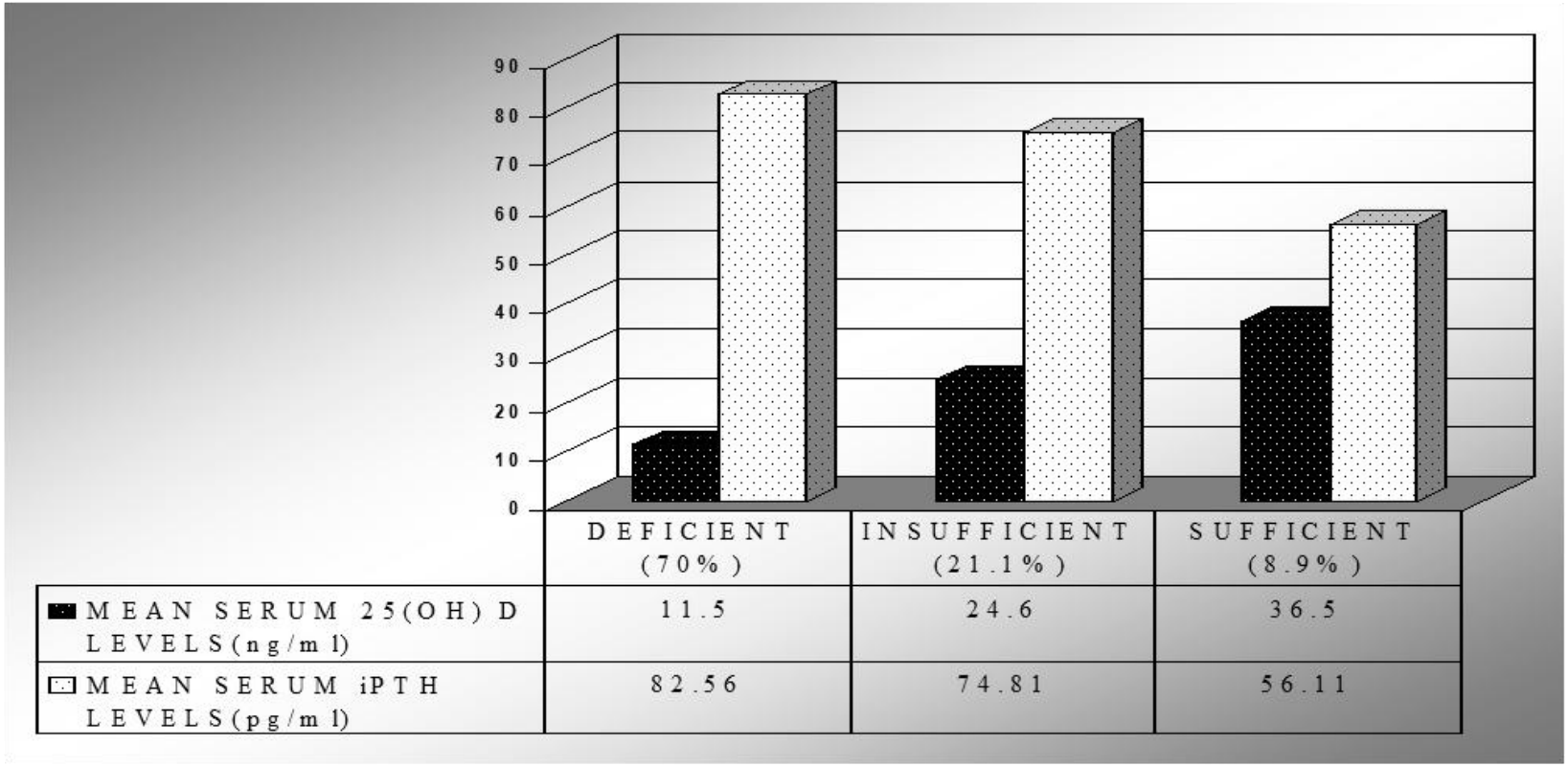
- What is the status in:
  - out-patient?
  - healthy population?
  - in our community?

# High Prevalence of Vitamin D Deficiency in Out-Patients

- 95% had D deficiency
- A low serum calcium and elevated alkaline phosphatase were reflective of severe deficiency
- Elevated iPTH  correlated with mild to moderate deficiency
- Serum calcium, phosphate and alkaline phosphatase are poor markers of moderate to mild deficiency, and cannot be relied upon as a screening tool
- A serum 25 vitamin D level and an iPTH are better biofunctional markers of this deficiency.

Lubna M Z, Aysha HK: Vitamin D Deficiency in Ambulatory Patients: JPMA, 2008

# Healthy Volunteers (n=123, 43% females; 57% males)




| | DEFICIENT (70%) | INSUFFICIENT (21.1%) | SUFFICIENT (8.9%) |
|---|---|---|---|
| MEAN SERUM 25(OH) D LEVELS(ng/ml) | 11.5 | 24.6 | 36.5 |
| MEAN SERUM iPTH LEVELS(pg/ml) | 82.56 | 74.81 | 56.11 |

- **Thirty eight participants (30.89%), have raised PTH (mean 107 ±18.04 pg/ml).**
- **Negative correlation between serum iPTH and Vitamin D levels (P=<0.001, r=0.3).**

Shireen M, Aysha HK et al. Prevalence and significance of vitamin D deficiency in apparently healthy adult volunteers in Karachi Pakistan. Clinical Biochemistry 2010

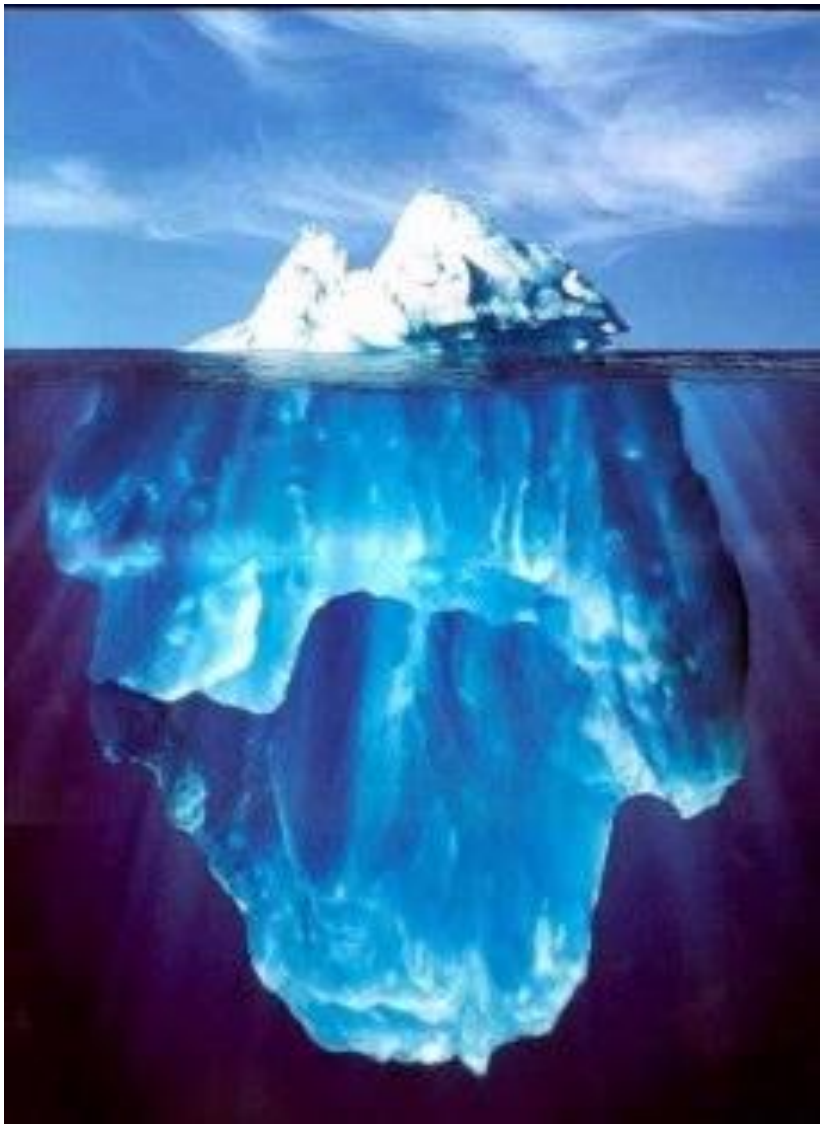
# Assessing vitamin D status in adult premenopausal females in Karachi – A preliminary report from Pakistan (2007 – 2009) n=**174**

- Mean age 29.06**±6.89** (18 – 48 years)
- Mean BMI 23.12±4.58 (13.84 – 41.2) kg/m2
- 92.8% of the females were identified as D deficient,
- 6.1% had insufficient levels
- 1.1% had optimal levels.
- Secondary hyperparathyroidism was present in 25.9% volunteers

Farhan Dar, AH Khan et al: Meeting of American Society of bone and mineral research. Toronto, 2010

# Clinical and subclinical vitamin D deficiency…. It's the tip of the iceberg

Rickets & Clinical Osteomalacia



Asymptomatic Osteomalacia

- Cancers
- Diabetes
- CVS
- Osteoporosis
- Tuberculosis

# Causes of Vitamin D deficiency

- Two main determinants:
  - nutrient intake
  - sunlight exposure
- Issues:
  - Lack of tools for assessment of nutrient intake and sunlight exposure

# Development and validation of a food frequency questionnaire for assessing macronutrient and calcium intake in women residing in Karachi, Pakistan

Romaina I, et al

# Mean daily nutrient intakes estimated by the FFQ and 24 h recalls

| Variables | FFQ | | Mean of 4 24h recalls | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| **Energy (kcal)** | 1643.5 | 703.2 | 1391.8 | 365.3 |
| **Calcium** | 610.7 | 306.4 | 462.1 | 175.7 |

- All of the correlations between mean of 24 hr recalls estimates and FFQ were significant.

# Development and Validation of Sunlight Exposure Measurement Questionnaire (SEM-Q) for use in adult population residing in Pakistan

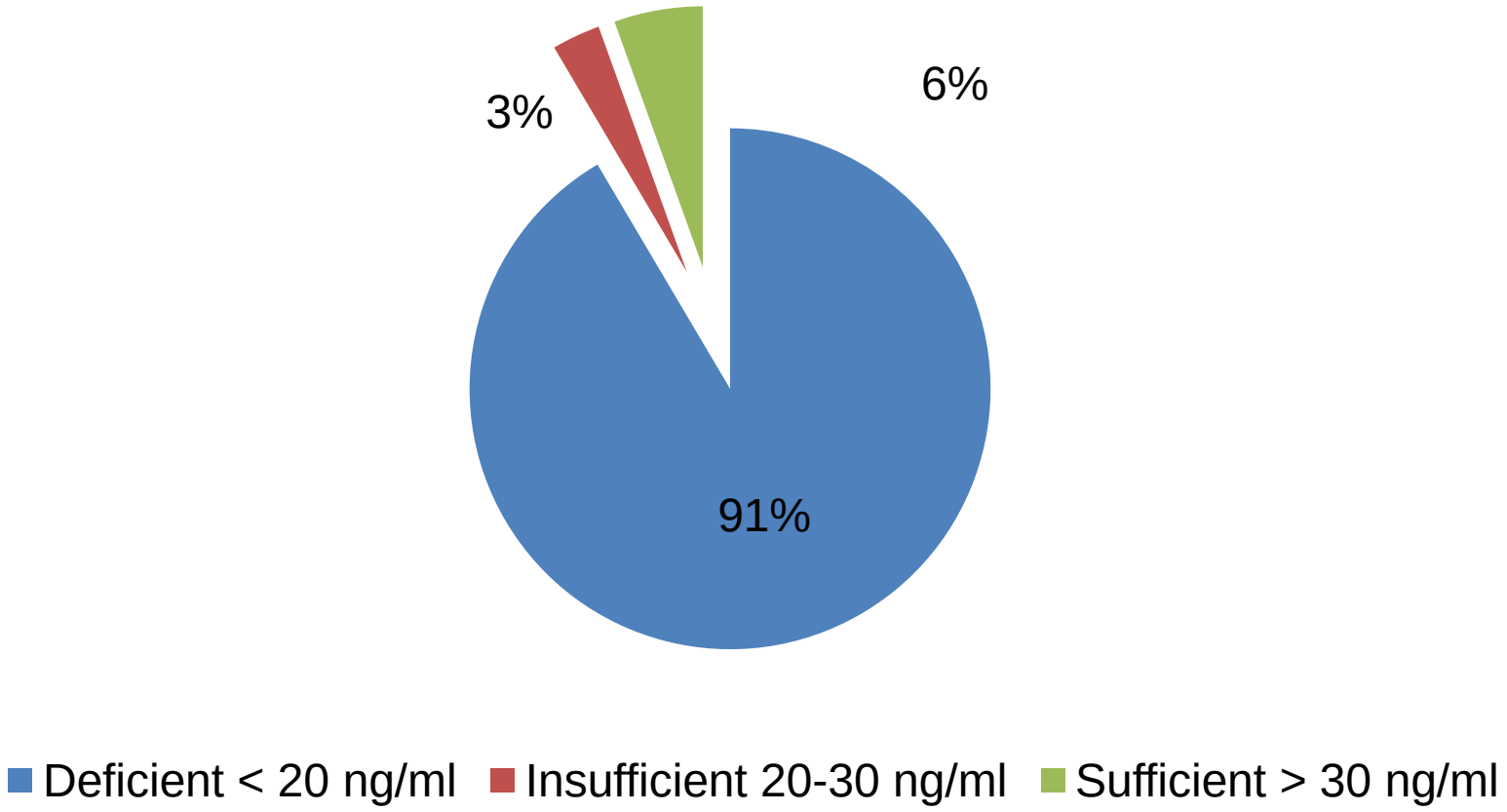
**Quratulain Humayun, Romaina Iqbal et al**

# 25OHD status in premenopausal women from Community in Karachi, Pakistan n=200

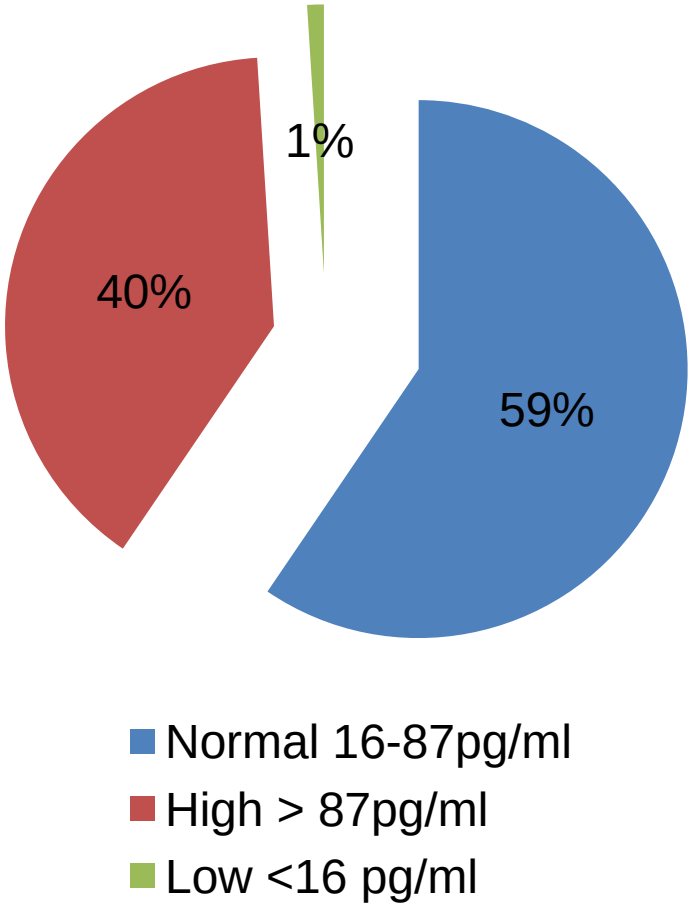
| Biochemical Parameters | Mean ± SD | Saddar | Gulshan |
|---|---|---|---|
| Vitamin D (ng/ml) | 8.5 ± 8.4 | 6.2 ± 5.4 | 10.8 ± 10.4 |
| iPTH (pg/ml) | 92.19 ± 72.53 | 111.8 ± 90.5 | 72.5 ± 40 |
| Calcium (mg/dl) | 8.98 ± 0.49 | 9.0 ± 0.5 | 8.9 ± 0.4 |
| Albumin (g/dl) | 4.05 ± 2.29 | 4.2 ± 3.2 | 3.9 ± 0.3 |

AH. Khan, G. Naureen, F. Dar, R. Iqbal

# Prevalence of vitamin D deficiency in Saddar & Gulshan Town in Karachi n=200

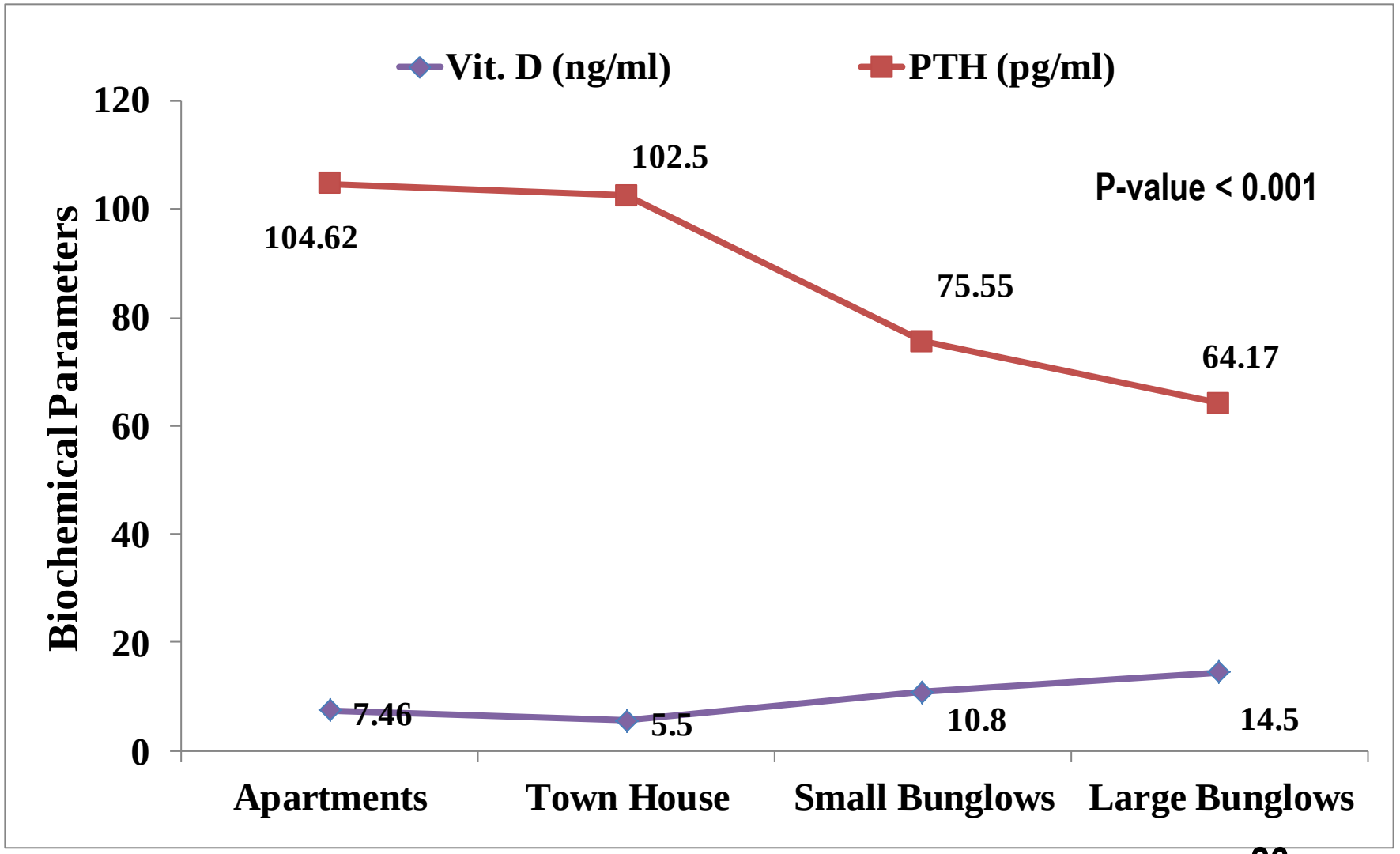


# iPTH status of study participants




| | Mean Vit. D ng/ml |
|---|---|
| Normal iPTH | 9.5 ± 8.1 |
| High iPTH | 6.2 ± 6.2 |

# Relationship of housing structure with vitamin D and iPTH



# Nutrient intake of study participants

| Nutrients | Mean/Day ± SD |
|---|---|
| Total Energy (kcal) | 1870.2 ± 695.7 |
| Total Fat (g) | 55 ± 21g |
| Total Protein (g) | 58 ± 20g |
| Total Calcium (mg) | 686.2 ± 271.4 |

# Highlights of the Research

- Vitamin D deficiency with sHPTH is highly prevalent among females
- Important to address life style variables
- Need to explore other factors such as genetics (Wang et al. 2010)
- Measures for improving the status of vitamin D
- Public Awareness

# Year 2010 Onwards

## Future Directions

# Why is D deficiency so extensive?

1. Genetics
2. What is the optimum level for our population?
3. Are we unable to manufacture D efficiently from sunlight?
4. Are we breaking down active D more rapidly?
5. Is it a difference in expression of Vitamin D receptor and its signaling pathways?