BEST PUBLICATIONS OF Prof Dr. C V HARINARAYAN

His research work has provided

1. New perspectives in diagnosing and treating metabolic bone diseases in India.
2. Documentation of low serum 25 hydroxy vitamin D levels and low dietary calcium intake as the cause of bone disease in primary hyperparathyroidism and large parathyroid adenomas. His work on primary hyperparathyroidism is quoted in many textbooks on metabolic bone disease. Improvement in vitamin D status and dietary calcium intake in the general population has led to a reduction of bone disease and a smaller size of parathyroid adenomas.
3. Documentation of the low vitamin D levels in urban and rural (agricultural workers) subjects through population survey. The impact of his research work led to remedial measures in society – Revision of Recommended Dietary Allowances (RDA) for calcium and Vitamin D for the Indian population has been changed (by ICMR) and various National food fortification programs are initiated in the country to address the problem of vitamin D and dietary calcium deficiency in India.
4. Developed the first national guidelines for the treatment of vitamin D deficiency in sun-drenched country-India.
5. Documented by in vitro studies on the ampoule model of previtamin D synthesis have shown that we as Indians can synthesize enough vitamin D on exposure to sunlight from 11 am to 2 pm, by exposing 10 to 15% of body surface area for 15 to 30 minutes.
6. Documentation of renal tubular damage as the cause of bone disease in fluorosis. (Ranked top 10 publications – the year 2006 by Internet).
7. Indigenously develop intact IRMA radioimmunoassay for parathyroid hormone in India along with BARC Mumbai. – MAKE IN INDIA CONCEPT.
8. Development of "Clinical Practice Guidelines on the management of Postmenopausal osteoporosis (2012-13) – Executive summary and Recommendations" for Indian Menopause Society.
9. Documented that correction of vitamin D deficiency can improve the pancreatic beta cell secretory function.
10. Given a road map for the country to address the problem of Twin nutrient deficiency - Vitamin D and dietary calcium deficiency.

VITAMIN D STATUS IN INDIA AND ITS IMPACT ON VARIOUS DISEASE STATES

His work demonstrated low serum 25OH Vitamin D levels and low dietary calcium intake as the predominant cause for radiological bone changes and large size of parathyroid adenomas in patients with Primary Hyperparathyroidism (PHPT) in India. THIS IS THE FIRST PUBLICATION IN THE COUNTRY TO DOCUMENT LOW DIETARY CALCIUM INTAKE AND VITAMIN D DEFICIENCY IN INDIA. This striking observation contradicted the then-existing impression of normal Vitamin D status in Indians – a tropical Country with plenty of sunshine. This observation has now been confirmed countrywide and has established Vitamin D deficiency, as an important public health problem in India.

He documented low vitamin D status and low dietary calcium intake in the south Indian population both in rural (agricultural workers) and urban subjects – by population studies in Andhra Pradesh. This is the first population survey (and only large survey so far) in the country on dietary calcium and serum 25OHD levels of rural and urban south Indians. He was the first to document the dietary calcium intake of rural, urban, and metro subjects in India, which co-exists with low vitamin D levels The **impact of his research work led to** the revision of national guidelines of Recommended Dietary Allowances for calcium and vitamin D by the ICMR.

By in-vitro "Ampoule Model" studies by exposing 7- Dehydrocholesterol to sunlight on an hourly basis the whole day and in various seasons all-round the year he demonstrated that exposure of 15 – 20% of body surface area to mid-day sun for 30 minutes a day will produce enough vitamin D from the skin. His work on the ampoule model of pre-vitamin D synthesis has shown that we as Indians can synthesize enough vitamin D on exposure to sunlight from 11 am to 2 pm, by exposing 10 to 15% of body surface area for 15 to 30 minutes

He pointed out that vitamin D deficiency coexists with low BMD in the Indian population and serum 25OHD needs to be documented in women having low BMD. Calcium and vitamin D need to be supplemented as part of therapy in postmenopausal women. His studies also pointed out the efficacy and safety of cholecalciferol supplementation in vitamin D-deficient subjects based on Endocrine Society Clinical Practice Guidelines. With his wide experience, he has given the guidelines on how to vitamin D deficiency in sundrenched India. His expertise was utilized in the formulation of clinical practice guidelines for post-menopausal osteoporosis.

With food fortification and widespread supplementation of calcium and vitamin D, the bone disease in primary hyperparathyroidism is reduced (not seen in plain x-rays by can only be picked up by subtle tests such as bone densitometry) with the reduction in size of adenomas from grams to milligrams. The

presentation of primary hyperparathyroidism had changed from hypercalcemic to Normocalcemic presentation. This is again documented by his study of the same disease three decades later.
With his vast experience and expertise in the field, he has reviewed the vitamin D status and dietary calcium intake of the country in the past half a century and given a roadmap for remedial measures in his publications.

- Harinarayan CV, Gupta N, Kochupillai N. Vitamin D status in primary Hyperparathyroidism in Northern India. Clinical Endocrinology 1995;43:351-358.
- Harinarayan CV, Ashok H, Munigoti SP, Tandon S, Sarma KVS, Tandon A, et al. Vitamin D status in primary hyperparathyroidism in 1990 and thence – Emergence of normocalcaemic presentation and diagnostic challenges – Utility of parathyroid function index. J Clin Sci Res 2022;11:167-74.
- Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PVLN, Sarma KVS, Kumar EGTV. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy South Indians. Am J Clin Nutr 2007;85:1062-67.
- Harinarayan CV, Holick MF, Prasad UV, Sreevani P and Himabindu.G. Vitamin D status and sun exposure in India. Dermato Endocrinology 2013;5(1):130-141.
  http://dx.doi.org/10.4161/derm.23873
  http://www.landesbioscience.com/journals/dermatoendocrinology/article/23873.
- Harinarayan CV. How to treat Vitamin D deficiency in sun-drenched India - guidelines. J Clin Sci Res 2018;7:131-40.
- Harinarayan CV and Akhila H. Modern India and the tale of twin nutrient deficiency–calcium and vitamin D–nutrition trend data 50 years-retrospect, introspect and prospect. Front. Endocrinol., 09 August 2019 | https://doi.org/10.3389/fendo.2019.00493.
- Harinarayan CV, Akhila H, Shanthi Sree E. Modern India and dietary calcium deficiency – half a century nutrition data – retrospect-introspect and the road ahead. Front. Endocrinol. https://www.frontiersin.org/articles/10.3389/fendo.2021.583654/abstract. Front. Endocrinol. 12:583654.doi: 10.3389/fendo.2021.583654.

- First to document the improvement in pancreatic β-cell function with vitamin D and calcium supplementation in vitamin D-deficient nondiabetic subjects.
- First to document that the serum 25OHD levels fall in patients with epilepsy therapy irrespective of the antiepileptic drug used even at therapeutic concentrations of the drugs.
- He documented the impact of low vitamin D levels in thyrotoxicosis and its impact on bone.
- A Collaborative study with AIIMS, New Delhi showed that Vitamin D Receptor gene polymorphisms and hypovitaminosis D might predispose to multidrug-resistant tuberculosis (MDR-TB). Lower serum 25OHD may increase the time to MDR-TB sputum smear negativity.

- Harinarayan CV, Arvind S, Joshi.S, Thennarasu K, Vedavyas V and Baindur A. Improvement in pancreatic β-cell function with vitamin D and calcium supplementation in vitamin D-deficient non-diabetic subjects. Endocr Pract.2014;20(2):129-38.
- Menon B, Harinarayan CV. The effect of anti-epileptic drug therapy on serum 25-hydroxyvitamin D and calcium and bone metabolism parameters – a longitudinal study. Seizure. 2010 Apr;19(3):153-8. Epub 2010 Feb 7.
- Rathored J, Sharma SK, Singh B, Banavaliker JN, Sreenivas V, Srivastava AK, Mohan A, Sachan A, Harinarayan CV, Goswami R. Risk and outcome of multidrug-resistant tuberculosis: vitamin D receptor polymorphisms and serum 25(OH)D. Int J Tuberc Lung Dis. 2012;16(11): 1522-8

First to characterize that bone disease in fluorosis is primarily due to renal tubular damage and is amplified due to low vitamin D levels in the Indian population. His **original research work** has shown the pivotal link played by the kidney in the causation of flurotoxic bone disease. It was his astuteness in the bedside investigation of the patients under his care that led to this original observation of the study.

- Harinarayan CV, Kochupillai N, Madhu V, Gupta N and Meunier PJ. Endemic Skeletal Fluorosis in India. Flurotoxic metabolic bone disease: an osteo-renal syndrome caused by excess fluoride ingestion in the tropics. Bone 2006;39:907-14. (RANKED AS ONE OF THE TOP TEN SCIENTIFIC DEVELOPMENTS FOR THE YEAR 2006 BY FLUORIDE ACTION NETWORK. http://www.fluoridealert.org/top-10.htm BY FLUORIDE ACTION NETWORK – INTERNET).

ORIGINAL TECHNOLOGY DEVELOPMENT:

Development of 2nd generation parathormone assay indigenously, by raising antibodies along with Radiopharmaceuticals division, BARC, Mumbai. An indigenous parathormone IRMA assay methodology has been developed and submitted to BARC. The work was carried on along with the radiopharmaceutical division of BARC, Mumbai (BRNS grant). **The kit can be taken up for commercialization after clearance of logistics like transport, shelf life, etc. (MAKE IN INDIA CONCEPT)**

- Prasad. U.V., Krishna Mohan. R., Grace Samuel, **Harinarayan CV**., Sivaprasad. N and Venkatesh.M. Standardization of a two-site PTH immunoradiometric assay using various solid phase formats. Indian J Med Res. 2012;136(6):963-70.