

Endocrinologists of Indian Origin: A Global Force that can (and should) Collaborate

Wise are those who learn from History

When we left India in the mid-1960s, there were only a few clinical units with a special interest in Endocrinology in the country but no recognized Endocrinology training programs. Therefore, for those of us who wanted to obtain further training in Endocrinology, leaving the country was a necessity. Since then, we have come a long way. The first recognized certificate in the subspecialty of Endocrinology, Doctor of Medicine (DM) in Endocrinology, was started in 1969 at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, and the first recipient of DM in Endocrinology was Radharaman Jivan Dash, who subsequently became the head of the Endocrine Department at the same institution; unfortunately, Professor Dash passed away recently (Aug 21, 2021). There are now about 30–40 programs that award DM in Endocrinology, with approximately 100 individuals receiving this distinction annually.

The Endocrine Society of India (ESI) was established in 1971. The ESI is probably one of the first, if not the first, sub-specialty societies in India, which now has more than 1000 members. The Research Society for the Study of Diabetes of India (RSSDI), the second in our specialty, was established in 1972 and has more than 9000 members. This contrasts with a membership of 4998 endocrinologists in the American Association of Endocrinologists in the USA. The total number of endocrinologists (Endocrinology, diabetes, and metabolism) in the USA is estimated to be 8377.

Most of the medical knowledge that we have acquired has come from the textbooks that were authored by Western physicians. However, it is well known that the etiology, as well as the presentation of various diseases, may be quite different based on the ethnicity and geographical area of the patients, besides other factors. Therefore, the management of these diseases needs to be different. Specific to the specialty of endocrinology, the management of diabetes is a good example. The prevalence of diabetes in India is about 8.9%, about 77 million, and one in six adults with diabetes in the world comes from India.^[1] There are more than 2 million persons of Indian origin currently residing in the USA, and it is one of the fastest-growing immigrant groups in the United States. According to the Center for Disease Control and Prevention (CDC) prevalence of diabetes among Asian Indians in the USA is estimated to be 12.6%.^[2] It is believed that the prevalence of diabetes and cardiovascular disease risk factors may be higher among South Asians (India, Pakistan, Sri Lanka, or Bangladesh) compared to other ethnic groups.^[3] A meta-analysis performed by a group of investigators concluded that despite modest

changes for adiposity, lifestyle modification in the high-risk South Asian population resulted in a clinically important 35% relative reduction in diabetes incidence.^[4] The effects of acculturation have also been studied in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. The prevalence of diabetes was studied in three different groups: Separation (preference for South Asian culture), Assimilation (preference for the US culture), and Integration (similar preference for both cultures). The integration class had the lowest prevalence of diabetes, pre-diabetes, fasting, and 2-hour glucose compared to the women in the Separation class.^[5] Finally, it has been described that the adoption of the “Western/non-vegetarian” dietary habits is associated with an adverse cardiometabolic profile in Asian Indians.^[6] Endocrinologists of Indian origin have made major contributions to these studies.

Besides diabetes, obesity is a common worldwide health problem. The World Health Organization (WHO) defines overweight and obesity as a BMI of ≥ 25 and ≥ 30 respectively. A 2000 expert panel of the WHO proposed BMI criterion for overweight as 23–24.9 kg/m² and that for obesity as ≥ 25 kg/m² for people residing in the Asia-Pacific region,^[7] and later added the cut-off points of 23 kg/m² and >27.5 kg/m² as the critical points for moderate-risk and high-risk public health action.^[8] Finally, in 2009, more than 100 Indian medical experts representing reputed medical institutions, hospitals, government-funded research institutions, and policy-making bodies participated in developing Asian Indian-specific guidelines for defining and managing overweight and obesity. The consensus guidelines defined overweight as those with BMI between 23.0–24.9 kg/m² and obesity as those having BMI ≥ 25.0 kg/m².^[9] However, despite these efforts, different criteria to define overweight and obesity continue to be applied in recent studies. Visaria and Lo, for instance, defined normal weight as BMI <23 kg/m², overweight as BMI 23–27 kg/m², and Obese as BMI ≥ 27 kg/m² in their recent study.^[10] In another study, Luhar *et al.*^[11] predicted that the prevalence of overweight will more than double among Asian Indian adults aged 20–69 years between 2010 and 2040, while the prevalence of obesity will triple during the same time periods. However, they used the WHO definitions of overweight and obesity (Overweight BMI 25.0–29.9 kg/m² and Obesity BMI >29.9 Kg/m²). It is apparent that these predictions would be very different if the definitions for overweight and obesity specific for the Indian population were applied.

Since the last consensus conference to develop Asian Indian specific guidelines for overweight and obesity guidelines was

held in 2009, it may be time to have another meeting to review and update these criteria by involving Endocrinologists of Indian origin living in India and abroad.

It is well established that good control of diabetes is beneficial in the prevention and management of chronic complications of diabetes. Measurement of the proportion of glycated hemoglobin (HbA1c) is now routinely applied not only to estimate the degree of control of diabetes but also for the diagnosis of diabetes and pre-diabetes. Although it has been known for some time that there are differences in HbA1c based on race and ethnicity, this factor is not often considered when using HbA1c as a diagnostic measure or as an indicator of the degree of control of diabetes. Various studies have shown that the HbA1c values are higher among Asians without diabetes^[12] and with impaired glucose tolerance^[13] compared to their White counterparts. It has been hypothesized that ethnic differences may be due to multiple factors, including differences in glycation, the life span of erythrocytes, biological differences, type of lifestyle, or socioeconomic factors. Genetic studies also indicate that there may be a significant genetic contribution. Some of the differences between different countries may be explained by rates of hemoglobinopathies (e.g., higher rates of Thalassemia among Southeast Asians) and nutritional iron deficiency (Higher rates in East Indians).^[14] The ethnic variations of HbA1c have obvious diagnostic and therapeutic implications. Some studies have evaluated the diagnostic utility of HbA1c among Indians living in India and those living in the USA^[15] and concluded that in Asian Indians, the use of HbA1c for diagnosis of type 2 diabetes could result in a higher prevalence and that HbA1c may identify a subset of individuals with milder glucose tolerance. More detailed studies of the HbA1c among Indians and their influence on the diagnosis and control of diabetes and pre-diabetes are warranted. Once again, the Endocrinologists of Indian origin globally will have the unique ability and perspective to play a major role and contribute significantly to these studies.

Unlike the evolution of the ESI, the bone and mineral field evolved more insidiously in India, but the seminal works started much earlier. The initial emphasis was on understanding the pathogenesis of rickets and osteomalacia despite plenty of sunshine, the so-called sunshine paradox, and fluorosis that was (and still continues to be) endemic. The seminal works of Jolly, Rizvi, Vaishnava, and Teotia^[16-19] are often cited in relation to nutritional rickets and osteomalacia, and endemic fluorosis. In fact, the observed osteosclerosis and the lack of fragility fractures in patients with endemic fluorosis led to the concept of using sodium fluoride as a potential anabolic therapy for age-related osteoporosis in later randomized clinical trials. In addition, it was proposed that a major contributor to age-related osteoporosis was due to co-existent nutritional osteomalacia due to poor dietary calcium and vitamin D intake, the so-called “osteomalacia”, although not uniformly accepted. The contemporary adoption of supplemental calcium and vitamin D in the management of osteoporosis has its origins from earlier work from India

and other countries with similar nutritional challenges. The next wave of contributions by the Indian clinical investigators centered around the differential phenotypic expression of primary hyperparathyroidism in comparison to the West,^[20,21] an enigma even still to be solved. In fact, it was often stated that primary hyperparathyroidism (PHPT) does not exist in India and that all HPT is secondary to chronic vitamin D deficiency. It was not uncommon to encounter rickets and/or osteomalacia in association with PHPT.^[22] Much of these seminal works were carried out in a few select centers, and the works were largely outside the domain of ESI for a number of years.

The more organized collaborative research in the bone and mineral field took off with the formal formation of the Indian Society for Bone and Mineral Research (ISBMR) in 1997 under the visionary leadership of Dr. Ambrish Mithal, an endocrinologist from Sanjay Gandhi Post Graduate Institute (SGPGI), and Dr. Ajay Gupta, a nephrologist from Henry Ford Hospital, Detroit, MI, USA (visit www.ISBMR.org). Although the ISBMR mission and vision was conceived during an ESI meeting in 1984, it took another decade for the inaugural ceremony of ISBMR at SGPGI Lucknow in 1997. The organization gave a forum and intellectual support in India and initially in the USA to support the collaborative research enterprise. The global collaborative efforts led to the development of guidelines specific to Asian Indians with respect to calcium and vitamin D intakes,^[23] country-specific bone mineral density (BMD) thresholds for the detection and diagnosis of osteopenia and osteoporosis,^[24,25] the role of vitamin D in the pathogenesis and disease expression of PHPT,^[26] and more recently the molecular basis for parathyroid adenoma formation.^[27,28] The recent publication of the CUBES results will have far-reaching clinical implications for the diagnosis and treatment of osteoporosis.^[24] The CUBES study and similar other studies, including the multicenter Indian Council of Medical Research (ICMR) funded study, highlighted the challenges the patients and health care providers face when applying the non-Indian databases in making clinical decisions for long term treatments. Similarly, studies linking vitamin D nutrition and the clinical expression of parathyroid disease eventually could eliminate bone disease and osteitis fibrosa cystica in PHPT,^[20,21,26] just as iodination of salt eliminated endemic goiter. Several ISBMR researchers contributed immensely to our understanding of the similarities and differences in disease expression between countries and within India.^[20,21,26,29,30] This was truly a global collaboration and must continue so we can deliver ethnic-specific based personalized care.

From a broader perspective, these three major organizations (ESI, RSSDI, and ISBMR) have really propelled advances in research, clinical care, and public health measures. But the time is now right for this collaborative network to expand. Besides India, there is a large number of Endocrinologists of Indian origin, at least in the US and perhaps in other countries as well. Like the history of ESI, RSSDI, and ISBMR, the history of AEIOU (Association of Endocrinologists of

Indian origin in the USA) is a long one. It was started back in 1991 when Dr. Prakash Kansal (Professor of Medicine at the University of Alabama) established the organization. For reasons that are not clear, it became dormant for many years but has recently been reactivated. It is now registered as a nonprofit organization in the state of Michigan (USA). In the recent past, it has sponsored several webinars in which the Endocrinologists from USA and India have presented their research and clinical findings, and a few from the UK, UAE, and Africa have attended. Perhaps this could serve as the focal point of this worldwide collaboration of Endocrinologists of Indian Origin. We hope that this collaboration will continue for a long time for the benefit of all and will lead to the recognition of Endocrinologists of Indian Origin as a truly global force.

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