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Diabetes epidemic in India- Why and what can be done?

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Introduction

Diabetes poses a major health problem globally and has become one of the top five leading causes of death in most developed countries. A substantial body of evidence suggests that it could reach epidemic proportions particularly in developing and newly industrialized countries. Nowhere is the diabetes epidemic more pronounced than in India. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be over 50 million in India in the year 2010 and this is further set to rise to 87 million by the year 2030[1].

Effective preventive programmes need to be urgently implemented to stem the tide. However, numerous questions still need to be answered. eg: Is this increase in diabetes merely a reflection of the population increase, or is there a true increase in prevalence rate of diabetes? What is the burden due to diabetes complications? Is there an ethnic susceptibility to diabetes among Indians, and if yes, why so? Can diabetes prevention programmes be effectively implemented through community empowerment? This article will try to answer some of these questions based on our work at the Madras Diabetes Research Foundation, Chennai.

Prevalence of diabetes in India during the last three decades

Starting from the early 1960's, there have been over 60 studies which have reported on the prevalence of diabetes[2]. These studies are characterized by several limitations: they are regional, have small sample sizes and low response rates, use varied diagnostic criteria and sample designs, and lack standardization, thereby leading to measurement errors and incomplete reporting of results. To date, surveys have not managed to capture standardized measures of diet and physical activity, health service utilization, health care costs, and glycaemic control. In addition, a disproportionately large number of studies have examined the prevalence of diabetes in urban settings, to the exclusion of the rural areas, where almost 70% of India's population resides.

Despite these limitations, a steady increase in the prevalence of type 2 diabetes has undoubtedly been noted during the last three decades. In the 1970's, a systematic collaborative study on diabetes in six different parts of the country was conducted by the Indian Council of Medical Research (ICMR)[3] which reported an urban prevalence of around 2.0% and a rural prevalence of 1.0%. The National Urban Diabetes Survey (NUDS) conducted in six large cities (metros) in 2001, reported that the age-standardized prevalence of type 2 diabetes was 12.1%[4]. In order to see whether there is a true increase in prevalence, serial studies need to be done in the same region, using a similar methodology. Chennai is one city for which data from such studies are available. In 1989, the age-standardized prevalence of diabetes in Chennai was 8.3%; this rose to 11.6% in 1995 and to 13.5% in 2000, while in the Chennai Urban Rural Epidemiology Study (CURES) (2003–2004), it was 14.3%. Thus, within a span of 14 years, the prevalence of diabetes in Chennai had increased by 72.3%[5]. There also appears to be a temporal shift in the age at diagnosis of type 2 diabetes to younger ages.

Till date, however, there has been no national representative study of the prevalence of diabetes in India. The ICMR- India Diabetes [ICMR- INDIAB] study is designed as a cross-sectional, door-to-door survey to estimate the prevalence of diabetes and pre-diabetes in individuals aged 20 years and above from all 28 states of India, National Capital Territory of Delhi and two union territories in India. Its objective is to determine the national prevalence of diabetes mellitus and impaired fasting glucose (IFG) / Impaired glucose tolerance (IGT) in India, by estimating the state-wise prevalence of the same, and also to compare the prevalence of diabetes and pre-diabetes in urban and rural areas across India. The first phase of the study involving Tamil Nadu, Maharashtra, Jharkhand and the Union territory of Chandigarh has been completed and shows a huge increase in diabetes prevalence in India, especially in rural India.

The explosion of diabetes in India also

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increases the propensity for developing complications of diabetes. The Chennai Urban Population Study (CUPS) and CURES studies done by us provided the first population-based data on the prevalence of diabetic complications in Indians. Thus, the prevalence of coronary artery disease (CAD) was found to be 21.4%[6], peripheral vascular disease (PVD) 6.3%[7], diabetic retinopathy (DR) 17.6%[8], microalbuminuria (diabetic nephropathy) 26.9%[9] and diabetic neuropathy 26.1%[10]. This translates to millions of people in India who are prone to develop morbidity and mortality due to diabetes.

Why are Indians more prone to Type 2 diabetes?

Despite the diversity within India, a number of common themes can be found with regard to the patterns of diabetes and rising prevalence rates. The probable reasons for the escalation in diabetes in Indians are increased insulin resistance, stronger genetic factors and environmental factors particularly associated with urbanization. One of the important factors contributing to increased type 2 diabetes in Asian Indians is the fact that they have a greater degree of insulin resistance as compared to Caucasians. Mohan *et al.*[11] first demonstrated that Asian Indians have higher insulin levels to a glucose load than Europeans (hyperinsulinemia). Studies by Yajnik *et al.*[12,13] demonstrated that low birth weight is a contributor to insulin resistance among Indians. Genetic susceptibility and familial aggregation play important roles in the occurrence of type 2 diabetes. Environmental and lifestyle changes resulting from industrialization and migration to urban environments from rural settings may be responsible, to a large extent, for the epidemic of type 2 diabetes in Indians. Obesity, especially central obesity and increased visceral fat due to physical inactivity, and consumption of high-calorie/high-fat and high sugar diets are other major contributing factors[14].

Role of genetic factors

We recently reported on several genetic associations with diabetes in South Indians. The plasma cell glycoprotein 1 (PC-1) gene impairs insulin signalling at the insulin receptor level. The plasma cell glycoprotein 1 (PC-2) gene K121Q polymorphism was associated with diabetes both in Indians and in Europeans[15]. However, the PPAR gamma gene Pro12 Ala polymorphism which protects Europeans against diabetes does not appear to protect Indians[16].

With respect to the PGC-1α gene, the Thr394Thr polymorphism was associated not only with type 2 diabetes[17] but also with metabolic syndrome and visceral fat in south Indians[18]. This was recently reported in two north Indian populations as well[19].

Another important and recently-discovered type 2 diabetes susceptibility gene with strong evidence for a role in insulin secretion is the transcription factor 7-like 2 gene (TCF7L2)[20]. Current evidence supports the idea that TCF7L2 dysfunction results in impairment of insulin secretion leading to the development of type 2 diabetes. TCF7L2 gene variants have been consistently associated with type 2 diabetes in populations of different ethnic descents. This has been shown to be strongly associated with diabetes in South Indians[21] and also in western India[22].

Recent genome-wide association studies have identified several new gene variants associated with type 2 diabetes mellitus (T2D) mostly in European populations[23-25]. We studied a total of 45 single nucleotide polymorphisms (SNPs) from 15 genes and 13 unannotated loci identified from recent genome-wide association T2D studies were genotyped. However, only 6 of 45 SNPs studied were replicated in South Indians[26] and several others in North Indians[27]. Genome-wide association studies may throw new light on novel diabetes-related genes in Indians.

Epidemiological transition

Currently, India is undergoing a rapid epidemiological, demographical transition with increasing urbanization and industrialization, increasing income levels, and changing life styles, values and culture. This leads to increased intake of calories (glycaemic load) and decreased physical activity. We undertook studies to look at the environmental factors contributing to the risk of diabetes in Indians.

Risk of type 2 diabetes by dietary glycaemic load (white rice intake)

Although genetic causes and sedentary lifestyle have been shown to contribute to the so-called Asian Indian phenotype, there is paucity of data on the role of dietary factors and their association with the risk of type 2 diabetes and other components of metabolic syndrome in this ethnic group. In India, marked changes have occurred in food consumption patterns, changing from 'traditional' to 'western' due to rapid nutritional transition. Diet has long been linked to the development of obesity, diabetes and cardiovascular disease and dietary modification is one of the cornerstones of prevention and management of chronic diseases.

The association of dietary carbohydrates and glycaemic load with the risk of type 2 diabetes among an urban adult Asian Indian population was examined by us recently[28]. Adult subjects aged 20 years and above (n=1843) were randomly selected from the Chennai Urban Rural Epidemiology Study, in Chennai. Dietary carbohydrates, glycaemic load and food groups were assessed, using food frequency questionnaire (FFQ). The intake of refined grains (white rice) was positively associated with the risk of type 2 diabetes [OR 5·31 (95% CI 2·98, 9·45); P<0·001]. In the multivariate model, after adjustment for potential confounders, total carbohydrate [OR 4·98 (95% CI 2·69, 9·19), P<0·001], glycaemic load (OR 4·25 (95% CI 2·33, 7·77); P<0·001) and glycaemic index (OR 2·51 (95% CI 1·42, 4·43); P=0·006) were associated with type 2 diabetes. Dietary fibre intake was inversely associated with diabetes [OR 0·31 (95% CI 0·15, 0·62); P<0·001]. Thus, in urban south Indians, total dietary carbohydrate and glycaemic load (mainly due to the high intake of polished white rice) are associated with increased risk of type 2 diabetes, whereas dietary fibre is associated with decreased risk[29].

We also studied the influence of physical activity on the prevalence of diabetes in an urban south Indian population in Chennai[30]. The prevalence of diabetes was significantly higher among subjects with light-grade activity (17.0%) as compared to those with moderate-grade (9.7%) and heavy-grade activity (5.6%)[30].

Prevention of Diabetes

Studies in the western countries and in India have shown that diabetes is preventable by lifestyle modification, mainly in terms of increased physical activity[31-33]. However, several questions remain unanswered: Are such approaches possible at the community level and in a real-life setting? Can these

simple approaches benefit the community? How will the community respond to such approaches? Finally, are such community-level lifestyle changes possible in India? We present below some of our experiences in India, which are very encouraging.

Our experience at Chennai shows that community-level intervention programmes are not only feasible but are also welcomed by the community. In 1996, we took up a population-based study called the Chennai Urban Population Study (CUPS) involving two residential areas, Asiad colony in *Tirumangalam* and *Bharathi Nagar* in *T.Nagar*, representing the middle and lower income groups in Chennai. The age-standardized prevalence rates of diabetes were significantly higher in the middle-income group (Asiad Colony-12.4%) as compared to the low-income group colony studied (6.5%)[34]. The results of the study clearly demonstrated that, with affluence, which was invariably associated with decreased physical activity, there was a marked increase in the prevalence rate of diabetes.

After the CUPS results were published in 2001, the residents of Asiad Colony were motivated by our team to increase their physical activity. This led to the people themselves raising money to build a beautiful park and also to maintain it through a modest annual contribution. The construction of the park was completed in 2002, with bushes, trees, fountains and a play area for children. There was lot of coverage in the local press and media about this project. This led to several more parks being developed in Chennai entirely through public effort. This led to the local bodies taking up the construction or renovation of several parks. According to a recent report, there are now more than 245 parks in Chennai city. Similar activities have been started in other parts of the state and country. This is a demonstration of the power of community empowerment and has been highlighted in the WHO publication 'Preventing Chronic Disease—a vital investment' in the section on 'Improving the built environment in India' and this has been showcased as a model for developing countries[35].

A follow-up survey demonstrated that the construction of the park led to a 300% increase in the number of people in this community who exercised[36]. Further studies have shown that this is already having an impact on the prevention of diabetes and obesity in the colony. If this model can be replicated, it could lead to prevention of not just diabetes, but of non-communicable diseases (NCD's) in general.

Diabetes care in rural India

The epidemic of diabetes is increasing not only in urban areas but also in rural areas. The number of people with diabetes in India is actually higher in rural areas (~23.0 million) as compared to urban areas (~17.9 million), because 72% of India's population lives in rural areas. However, it is a paradox that nearly all diabetes prevention and control efforts in India are currently focused in urban areas and there are virtually no ongoing diabetes prevention or awareness activities in rural areas.

Hence, to track the burden of diabetes in rural India and to make health care "available, accessible, affordable and *acceptable*" in the rural population, we launched the 'Madras Diabetes Research Foundation-World Diabetes Foundation (MDRF-WDF) *Chunampet* Rural Diabetes Project' with the support of the WDF, Denmark. The *Chunampet* model is an example of inter-sectoral collaboration involving areas of health, agriculture and the economy. This community-based programme serves as a model to screen for diabetes and its complications in low-resource rural settings. In addition, this project is the first of its kind to tackle the problem of diabetes in rural India by addressing prevention of diabetes at all three levels, i.e. focusing on primary, secondary and tertiary diabetes prevention. The use of telemedicine facility 'to reach the unreached' leads to a greater understanding of the problems associated with the complications of diabetes. This doorstep delivery of diabetes care has helped to improve compliance among rural people who had no access to such facilities. This has reduced the cost to patients, thus helping in improving their quality of life. Eventually, this approach could help reduce the economic costs due to diabetes and associated complications.

Conclusion

The 'diabetes epidemic' currently threatening the health of developing nations like India needs local solutions with active community participation, backed by government initiatives. Only then will the emerging health threat due to diabetes be effectively tackled. The time for action is NOW!

The author is Chairman and Chief Diabetologist, Dr Mohan's Diabetes Specialities Centre, Chennai, who delivered the C Ramachandran Memorial Lecture 2010.

References

1. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In: Gan D, editor. Diabetes Atlas. International Diabetes Federation. 4th ed. Belgium: International Diabetes Federation; 1-105.2009.

2. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian Scenario. Indian Journal of Medical Research. 125:217-230.2007.

3. Ahuja MMS. Epidemiological studies on diabetes mellitus in India. In: Ahuja MMS, editor. Epidemiology of diabetes in developing countries. New Delhi: Interprint; p. 29-38.1979.

4. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, et al. Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia ; 44 : 1094-101.2001.

5. Mohan V, Deepa M, Deepa R, Shanthirani CS, Farooq S, Ganesan A, Datta M. Secular trends in the prevalence of diabetes and impaired glucose tolerance in urban south India – the Chennai Urban Rural Epidemiology Study (CURES-17). Diabetologia. 49:1175-1178.2006.

6. Mohan V, Deepa R, Rani SS, Premalatha G; Chennai Urban Population Study (CUPS No.5). Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: The Chennai Urban Population Study (CUPS No. 5). J Am Coll Cardiol ; 38:682-687.2001.

7. Premalatha G, Shanthirani CS, Deepa R, Markovitz J, Mohan V.Prevalence and risk factors of peripheral vascular disease in a selected south Indian population – The Chennai Urban Population Study (CUPS). Diabetes Care. 23:1295-1300.2000.

8. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of Diabetic Retinopathy in Urban India: The Chennai Urban Rural Epidemiology Study (CURES) Eye Study-I. Invest Ophthalmol Vis Sci ; 46: 2328-2333. 2005.

9. Unnikrishnan RI, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, Mohan V.Prevalence and risk factors of diabetic nephropathy in an urban South Indian population: the Chennai Urban Rural Epidemiology Study (CURES 45).Diabetes Care. 30:2019-2024. 2007.

10. Pradeepa R, Rema M, Vignesh J, Deepa M, Deepa R, Mohan V . Prevalence and risk factors for diabetic neuropathy in an urban south Indian population– The Chennai Urban Rural Epidemiology Study (CURES- 55), Diabetic Medicine,25:407-412. 2008.

11. Mohan V, Sharp PS, Cloke HR, et al. Serum immunoreactive insulin responses to a glucose load in Asian Indian and European Type 2 (non insulin dependent) diabetic patients and control

subjects. Diabetologia . 29: 235- 237.1986.
12. Yajnik CS. The insulin resistance epidemic in India: Fetal origins, later lifestyle, or both? Nutr Rev; 59:1-9. 2001.

13. Yajnik CS, Lubree HG, Rege SS, et al. Adiposity and hyperinsulinemia in Indians are present at birth. J Clin Endocrinol Metab; 87:5575 - 5580.2002.

14. Deepa R, Sandeep S, Mohan V. Abdominal obesity, visceral fat and Type 2 diabetes - "Asian Indian Phenotype". In: Type 2 Diabetes in South Asians : Epidemiology, Risk Factors and Prevention. Mohan V, Gundu HR Rao (Eds), Under the Aegis of SASAT. Jaypee Brothers Medical Publishers. p.138-152.2006.

15. Abate N, Chandalia M, Satija P, Adams-Huet B, Grundy SM, Sandeep S, Radha V, Deepa R, Mohan V. ENPP1/PC-1 K1 21Q Polymorphism and genetic susceptibility to Type 2 diabetes. (CURES - 11). Diabetes. 54:1207-1213. 2005.

16. Radha V, Vimaleswaran KS, Babu HNS, Abate N, Chandalia M, Satija P, Grundy SM, Ghosh S, Majumder PP, Deepa R, Rao SMR, Mohan V. Role of genetic polymorphism peroxisome proliferator – Activated Receptor – 2 Pro 12Ala on ethnic susceptibility to diabetes in south Asian and caucasian subjects (CURES-5). Diabetes Care. 29: 1046-1051.2006.

17. Vimaleswaran KS, Radha V, Ghosh S, Majumder PP, Deepa R, Babu HNS, Rao MRS, Mohan V. Peroxisome proliferators-activated receptor- co-activator -1 (PGC-1) gene polymorphisms and their relationship to Type 2 diabetes in Asian Indians (CURES-14). Diabetic Medicine. 22:1516-1521.2005.

18. Vimaleswaran KS, Radha V, Anjana M, Deepa R, Ghosh S, Majumder PP, Rao MRS, Mohan V. Effect of polymorphisms in the PPARGC1A gene on body fat in Asian Indians. (CURES-20). International Journal of Obesity. 30:884-891.2006.

19. Bhat A, Koul A, Rai E, Sharma S, Dhar MK, Bamezai RN. PGC-1alpha Thr394Thr and Gly482Ser variants are significantly associated with T2DM in two North Indian populations: a replicate case-control study. Hum Genet. 121:609-614. 2007.

20. Grant SF, Thorleifsson G, Reynisdottir I, Benediktsson R, Manolescu A, Sainz J, Helgason A, et al. Variant of transcription factor 7-like 2 (TCF7L2) gene confers risk of type 2 diabetes. Nat Genet. 38:320-323. 2006.

21. Bodhini D, Radha V, Monalisa Dhar, Narayani N, Mohan V. The rs12255372 (G/T) and rs7903146(C/t) polymorphisms of the TCF7L2 gene are associated with type 2 diabetes mellitus in Asian Indians. (CURES-42). Metabolism Clinical and Experimental. 56:1174-1178. 2007.

22. Chandak GR, Janipalli CS, Bhaskar S, Kulkarni SR, Mohankrishna P, Hattersley AT, Frayling TM, Yajnik CS. Common variants in the TCF7L2 gene are strongly associated with type 2 diabetes mellitus in the Indian population. Diabetologia. 50 :63 –67.2007.

23. Sladek R, Rocheleau G, Rung J, Dina C, Shen L, Serre D, et al. A genome-wide association study identifies novel risk loci for type 2 diabetes. Nature ;445:881-885. 2007.

24. Scott LJ, Mohlke KL, Bonnycastle LL, Willer CJ, Li Y, Duren WL, et al. A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants. Science ;316:1341-1345. 2007

25. Saxena R, Voight BF, Lyssenko V, Burtt NP, de Bakker PI, Chen H, et al. Genome- wide association analysis identifies loci for type 2 diabetes and triglyceride levels. Science ;316:1331-1336.2007.

26. Chidambaram M, Radha V, Mohan V. Replication of recently described type 2 diabetes gene variants in a South Indian population. Metabolism, 2010;59: 1760 – 1766.2007.

27. Chauhan G, Spurgeon CJ, Tabassum R, Bhaskar S, Kulkarni SR, Mahajan A, et al. Impactof common variants of PPARG, KCNJ11, TCF7L2, SLC30A8, HHEX, CDKN2A, IGF2BP2, and CDKAL1 on the risk of type 2 diabetes in 5,164 Indians. Dabetes. 59:2068-74. 2010.

28. Mohan V, Radhika G, Sathya RM, Tamil SR, Ganesan A, Sudha V. Dietary carbohydrates, glycaemic load, food groups and newly detected type 2 diabetes among urban Asian Indian population in Chennai, India (Chennai Urban Rural Epidemiology Study 59). British Journal of Nutrition. 102: 1498-1506. 2009.

29. Mohan V, Radhika G, Vijayalakshmi P, Sudha V. Can the diabetes / cardiovascular disease epidemic in India be explained, at least in part, by excess refined grain (rice) intake?. Indian Journal of Medical Research. 131:369-474.2010.

30. Mohan V, Gokulakrishnan R, Deepa R, Shanthirani CS, Datta M. Association of physical inactivity with components of metabolic syndrome and coronary artery disease – the Chennai Urban Population Study (CUPS 15). Diabetic Medicine.22:1206-1211. 2005.

31. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med :18:1343-1350. 2001.

32. The Diabetes Prevention Program: baseline characteristics of the randomized cohort. The Diabetes Prevention Program Research Group. Diabetes Care ;11:1619-1629.2000.

33. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V; Indian Diabetes Prevention Programme (IDPP). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia. 49:289-97.2006.

34. Mohan V, Shanthi Rani S, Deepa R, Premalatha G, Sastry NG, Saroja R. Intra urban differences in the prevalence of the metabolic syndrome in southern India – the Chennai Urban Population Study (CUPS-.4). Diabetic Medicine. 18:280-287.2001.

35. Improving the built environment in India. Preventing chronic disease a vital investment World Health Organization Bulletin , p 136,2005.

36. Mohan V, Shanthirani CS, Deepa M et al. Community empowerment –A successful Model for prevention of non-communicable dioseases in India-The Chennai Urban Population Study (CUPS-17). J Assoc Physicians India;54: 858-862.2006.

NUTRITION NEWS

The 42nd Annual meeting of the Nutrition Society of India (NSI) was held on 18-20th November 2010 in Mumbai. The theme of the conference was "Wholesome Nutrition: Challenges, Scope and Management". Under this theme, two symposia were organized in the meeting:

I) Challenges of under- and over-nutrition: economic, sociological and psychological burden

ii) Approaches to wholesome nutrition

Dr Prema Ramachandran (Director, NFI) made a presentation on " Overnutrition and non- communicable diseases in the symposium on "Challenges of under- and over- nutrition"

A pre-conference workshop was conducted on the 18th November 2010 to update the knowledge of student delegates. The topics were "Instrumentation in Food Analysis – An Update" and "Guidelines for Preparation of Manuscript for Publication".

The 34th Gopalan Oration was delivered by Prof. DJP Barker, (MRC Environmental Epidemiology Unit, University of Southampton, UK) on "Nutrition in the womb".

The 22nd Srikantia Memorial Lecture was delivered by Dr.B.Sivakumar, (Former Director, National Institute of Nutrition, Hyderabad) on "Carotene conversion to vitamin A is not inefficient".

The first Dr. Rajammal P. Devadas Memorial Lecture Award was delivered by Dr. Mahtab S. Bamji, (INSA Hon. Scientist, Dangoria Charitable Trust, Hyderabad & Director Grade Scientist (Retd.), National Institute of Nutrition, Hyderabad) on "Striving for village level nutrition security – challenges and opportunities".

Lifetime Achievement Award (Science in Tradition) was conferred by NSI Mumbai Chapter to Dr G Subbulakshmi (Nutrition Consultant; Former Director, DPGSR in HSc., SNDT Women's University, Mumbai).

Reviews and Comments

Vitamin A supplements and morbidity in children: A conundrum unanswered?

Michael C. Latham

Introduction

A long unanswered conundrum for those who both support widespread mega dose vitamin A supplements for young children, and who also believe that this reduces childhood mortality, is "why these supplements do not reduce morbidity except from measles?" A debate rages again on the issue of whether massive dose vitamin A supplements provided every 4 to 6 months in grossly unphysiologic doses actually reduces mortality[1, 2]. This topic has been reviewed many times. I have from the outset, like Dr. Gopalan[3] and his colleagues, been critical of some of the mortality studies, and have for many reasons not been an advocate of high dose vitamin A supplementation, especially in areas where serious cases of xerophthalmia and keratomalacia are now relatively rare. I have also, for decades, favored food-based approaches as being the best and most sustainable means of improving vitamin A nutritional status. Here I wish mainly to discuss the scientific evidence, which is rather consistent, in showing that other than with measles, vitamin A supplementation has no impact on morbidity, especially from diarrhea and respiratory infections. These are two leading causes of death in children 6-60 months of age in underprivileged populations.

Currently very large programmes exist to provide vitamin A supplements, usually in megadoses, to hundreds of millions of children in dozens of countries (including India) at a cost of millions of dollars. This vitamin A supplementation appears to have the support of WHO, UNICEF, The World Bank, the Gates Foundation, many large NGO's, the pharmaceutical industry and apparently is also supported (or at least "accepted") by the governments of many countries, including India. None of these "players" seem very much to consider the conundrum that death in children is usually preceded by morbidity. So even if these "players" have somehow been led to believe that vitamin A supplements markedly reduce young child mortality, the research shows no reduction in the incidence, nor the morbidity, of diseases that mainly cause these deaths. So on these grounds alone large dose vitamin A supplements are not justified. I have been a strong proponent of universal measles immunization. I believe that funds (including those now spent on vitamin A supplementation programs) would be better spent on total eradication of measles[4].

The mortality studies

By far the most influential study showing a major reduction in child mortality following vitamin A supplementation was that conducted in Indonesia[5]. The conclusions that children even without ocular clinical signs of xerophthalmia may be at an increased risk of death and that vitamin A supplements may decrease mortality by as much as 34 percent, was clearly important, if proved to be true. In the *Lancet* we immediately raised serious questions about this study[6]. We stated that randomization was not all done at the time of the baseline examination; that no placebos were used; and that despite randomization the control group at baseline had more clinical signs of vitamin A deficiency and poorer growth than the supplemented children. We pointed out that the units of randomization are villages but the data are presented for the point sampling units (children). We went on to point out that "no information is provided on cause of death." We concluded in the *Lancet*, "until the questions raised by us, and others, are resolved it would be premature to rush to action with vitamin A dosing in the belief that it will reduce young child mortality."

After the Indonesian research, the next most influential study showing a reduction in child mortality due to vitamin A supplementation was that done in India[7]. This helped stimulate a rush to the wide use of non-physiological high dose vitamin A supplements to whole populations. In the *New England Journal of Nutrition* we raised a note of caution stating that the problem is how best to ensure increased intakes of carotene and vitamin A to children at risk. This may be achieved by fortifying a suitable food and preferably in conjunction with better health care, nutrition education and horticultural activities to increase the availability of carotene-rich foods[8]. We stated: "Our major worry is that governments and international agencies may, as a result of recent research, only use vitamin A supplementation programs as a magic bullet to reduce childhood mortality, divorcing such programs from other efforts to improve nutrition and reduce morbidity. We cannot afford to ignore the underlying causes of malnutrition and infections, which may include poverty and associated inadequate diets, unsatisfactory sanitation and water supplies, and uncontrolled infections. Attractive-sounding and well-motivated programs that are not sustainable must be avoided"

Only two vitamin A mortality studies were conducted in Africa. The first was by the Harvard University group in the Sudan. This showed no difference in child mortality between children receiving vitamin A compared with those not receiving it[9]. The second study was conducted in Ghana on a large population of children. There were 88 fewer deaths in the control population of children than in the vitamin A supplemented children. This was not a large difference, but was highly significant[10]. A piece in the *Lancet*[11] examined the findings and raised the still relevant question of whether the difference, in mortality might be due to measles. It is well known that measles presents with high fever, respiratory symptoms, and there is frequently diarrhea. As the causes of deaths in this study were "established by verbal autopsy (a wonderful oxymoron)" from mothers or relatives sometimes months after the actual death of the child, it is entirely feasible that many of the deaths recorded as due to a respiratory infection, diarrhea or fever (malaria) were in fact measles deaths. For example 23 percent of deaths were recorded as due to malaria, presumably based on a history of fever. Malaria can only be definitively diagnosed by identifying plasmodia in blood. So the fever could well have been due to measles not malaria. Similarly 26 percent of deaths in this Ghana study were recorded as due to "gastro-enteritis" presumably a history of diarrhea prior to death. Diarrhea is also a very common feature in measles; and measles presents with respiratory signs and symptoms.

A trial conducted recently in India compared death rates over a period of five years among nearly a million children, half of whom received high dose vitamin A supplements and half no supplementation. There was no significant difference in the death rates of those receiving the supplement compared with those not receiving it[2, 12].

In India, the Ministry of Health is stated to provide vitamin A supplements to about 55 million young children annually presumably on the questionable assumption that this would markedly reduce childhood mortality: an assumption which has been strongly questioned over many years [13].

Vitamin A supplementation and morbidity

A detailed review was published in 1993 of eight major studies on the impact of vitamin A supplementation on young child mortality and this has had enormous influence[14]. It stated, "These studies together suggested that vitamin A supplementation resulted in an average reduction of 23 percent in mortality rates in children between 6 and 60 months of age." That single statement has had an enormous influence in moving UN agencies, The World Bank, international NGO's, and governments themselves, to implement programs to supplement young children with vitamin A. This "Beaton" report also stated: "In contrast to the very clear effect of vitamin A on mortality, we were forced to conclude that improvement of vitamin A status cannot be expected to impact on incidence, duration or prevalence of diarrheal and respiratory infections." The Beaton paper went on to state "one aspect of the morbidity analysis that has direct relevance to field programs was the fact that vitamin A intervention after the onset of measles impacted favorably upon the development of severe complications and reduced the case fatality rate." So in reviews of these vitamin A supplementation studies in two African and several Asian countries, showed no impact on morbidity from diarrhea or respiratory infections, but markedly reduced the severity of the illness in measles, and lowered case fatality rates.

The obvious question to ask is if medicinal high dose vitamin A supplements reduce child mortality by 20-35 percent, then to what extent is this due to reduction in morbidity from diarrhea and respiratory infection (other than measles). Diarrhea according to WHO contributes to 32% and respiratory infections to 36% of child mortality (a total of 68%) in developing countries. Accordingly, we initiated studies in two countries to answer this very important question. These were conducted in Tanzania[15] and in India[16]. It is worth noting that (unlike most of the mortality studies reviewed by Beaton) our studies in Tanzania and India were true double blind placebo controlled clinical trials, and importantly we assured that all children were immunized (including against measles); we did not include seriously malnourished children, and all study children had access to reasonable health care. In neither study did regular vitamin A supplementation reduce morbidity from either diarrhea or respiratory infections. For the Indian study it was written "The differences in respiratory and diarrheal morbidity between the two groups were not statistically significant, and these findings remained unaltered after multivariate analysis"[16].

There have been many studies done on vitamin A supplementation and morbidity. Almost all have shown no reduction in morbidity from diarrhea or respiratory infections as a result of vitamin A supplementation. Some have shown vitamin A supplementation increased morbidity from respiratory infections. In contrast several good studies have clearly demonstrated that vitamin A supplementation greatly reduces the severity of measles complications, signs of morbidity and case fatality rates from this important disease[17,18].

One of the more recent morbidity studies was conducted in Mexico to evaluate the impact of vitamin A and zinc supplementation on overall rates of childhood diarrheal disease and respiratory tract infections[19] This was a double blind, randomized placebo controlled trial which included 736 children aged 6-15 months in periurban Mexico City. The subjects were assigned randomly to one of four groups namely

- vitamin A every two months,
- zinc daily,
- vitamin A and zinc, and
- placebo.

The children were followed for 12 months. The results showed that vitamin A supplementation in the four group analysis, was associated with a 27% increase in diarrheal disease and a 23% increase in cough with fever. Zinc decreased diarrhea in children under some circumstances. They concluded in quote "vitamin A increases diarrheal disease and respiratory tract infections in young children in periurban Mexico City."

A double blind randomized placebo controlled field trial was conducted in New Delhi in India to assess the impact of vitamin A supplementation on "morbidity from acute respiratory tract infections and diarrhea"[20]. In this study 900 children aged 9-60 months were studied. The conclusions were: "The study found the incidence and average number of days with acute lower respiratory tract infections to be similar in both groups. The incidence of diarrhea was also similar." The paper goes on to state that "the incidence of measles was significantly reduced in the vitamin A supplemented group" when compared with those children receiving a placebo.

A WHO/CHD multicountry study published in the Lancet[21] looked at 9,424 mother infant pairs in Ghana, India and Peru. Fifty percent of mothers received 200,000 IU of vitamin A and their children received 25,000 IU of vitamin A at times of standard immunizations. The 50% in the control group received immunizations without vitamin A supplements. The conclusion was that the vitamin A intervention "had no effect on anthropometric status, or on overall, or severe, morbidity."

Research in Indonesia[22] was conducted to evaluate the effect of simultaneous vitamin A supplementation on the immune response to measles immunization at 6 months of age. This was a randomized double blind placebo controlled clinical trial. It was found that "vitamin A administration reduced the likelihood of seroconversion to measles (after controlling for maternal antibody titers). The authors conclude "these results suggest that simultaneous high-dose vitamin A may thwart seroconversion to live measles vaccine in infants with maternal antibodies." There are numerous other studies, almost all of which show that vitamin A supplements do not reduce morbidity, but the exception is that vitamin A does have an important role in reducing measles morbidity and mortality[23].

Conclusions

Reviewing the data relating vitamin A supplementation and its impact on morbidity and mortality, I can only draw one evidence-based conclusion: Vitamin A supplements reduce morbidity and mortality from measles. And clearly increasing vitamin A, or carotene intakes, will help prevent xerophthalmia. But despite the very dubious data showing that vitamin A supplements reduce childhood mortality, and the very conclusive evidence that it has no impact on morbidity from diarrhea and respiratory infections (with the exception of measles) we still see, in 2008 huge sums expended on vitamin A supplements. Why is this so? I have to conclude that many nutritionists, physicians and other players have been

very uncritical. They have allowed one group of scientists, with one point of view, to set the agenda and to stifle other views. There is no need here to provide names. These "experts" took control of the International Vitamin A Consultative Group (IVACG) almost from its founding. The IVACG committee was appointed and run in a very undemocratic fashion. Some nutritionists labeled it this Group, "International Vitamin A Capsule Group." As a result of this dominance of the field food based approaches to control vitamin A deficiency have received too little attention, as have general measures to reduce hunger, to control infections, to improve health care and to prevent widening inequity almost everywhere. And we still have not assured that children receive their rights to be immunized against measles, let alone put in place measures to totally eradicate measles from planet earth

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References

1. Mudur GS. Sheen goes off vitamin A effect on child deaths. *The Telegraph*, Kolkalta, India 2-3, 2008.

2. Anonymous. www.ctsu.ox.ac.uk/projects/devta/istanbul-vit-a-lecture,ppt. 2008.

3. Gopalan C. Child-mortality reduction with vitamin A now the "Bellagio Declaration"! *NFI Bulletin* 13 (3), 1992.

4. Latham MC. Global action against worm infections, measles and malaria. In: *Global Obligations for the Right to Food*, G. Kent (ed.). Bowman and Littlefield, Lanham, Maryland, USA, pp 145-160, 2008.

5. Sommer A, Djunaedi E, Loeden AA, Tarwotjo I, Jr, WKP, Tilden R. Impact of vitamin A supplementation on childhood mortality. *Lancet* 1: 1169-73, 1986.

6. Martinez H, Shekar M, Latham M. Vitamin A Supplementation and Child Mortality. *Lancet* 11: 451, 1986.

7. Rahmathullah L, Underwood BA, Thulasiraj RD, Milton RC, Ramaswamy K, Rahmathullah R, Babu G. Reduced mortality among children in India receiving a weekly dose of vitamin A. *New Engl J Med* 323: 929-935, 1990.

8. Latham MC, Habicht JP. Vitamin A and Childhood Mortality. *New Engl J Med* 324(10): 694-695, 1991.

9. Herrera MG, Nestel P, Amin AE, Fawzi WW, Mohamed KA, Weld L. Vitamin A supplementation and child survival. *The Lancet* 340:267-271, 1992.

10. Ghana VAST Study Team. Vitamin A supplementation in northern Ghana: effects on clinic attendances, hospital admissions and child mortality. *Lancet* 342: 7-12, 1993.

11. Latham MC. Vitamin A and Childhood Mortality. *The Lancet* 342: 549, 1993.

12. Gopalan C. Vitamin A deficiency—Overkill. *NFI Bulletin*, 2008.

13. Gopalan C. Vitamin A deficiency and child mortality. *NFI Bulletin* 7(3), 1986.

14. Beaton GH, Martorell R, Aronson KJ, Edmonston B, Ross AC, Harvey B, McCabe G. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. Toronto, Canadian International Development Agency, Dic 1993. 120 p. tab. (Nutrition Policy Discussion Paper, 13), 1993.

15. Ndossi GD, Latham MC, Roe DA, Miller DD, Stephenson LS. Impact of Vitamin A Supplementation in Preschool Children in Iringa, Tanzania. *V International Vitamin A Consultative Group Meeting*. Arusha, Tanzania: 8-12, 1993.

16. Ramakrishnan U, Latham MC, Abel R, Frongillo Jr EA. Vitamin A Supplementation and Morbidity Among Preschool Children in South India. *Am J Clin Nutr* 61: 1295-1303, 1995.

17. Barclay AJG, Foster A, Sommer A. Vitamin A supplements and mortality related to measles: a randomized clinical trial. *BMJ* 294: 294-296, 1987.

18. Hussey GD, Klein M. A randomized, controlled trial of vitamin A supplementation in children with severe measles. *New England Journal of Medicine* **323**: 160-164, 1990.

19. Long KZ, Montoya Y, Hertzmark E, Santos JI, Rosado JL. A double-blind, randomized, clinical trial of the effect of vitamin A and zinc supplementation on diarrheal disease and respiratory tract infections in children in Mexico City, Mexico. *Am J Clin Nutr* 54: 568-577, 2006.

20. Bhandari N, Bhan MK, Sazawal S. Impact of massive dose of vitamin A given to preschool children with acute diarrhoea on subsequent respiratory and diarrhoeal morbidity. *Br Med J* 309: 1404-1407, 1994.

21. WHO/CHD. Immunisation-Linked Vitamin A Supplementation Study Group. Randomised trial to assess benefits and safety of vitamin A supplementation linked to immunization in early infancy. *Lancet* 352: 1257-1263, 1998.

22. Semba RD, Munasir Z, Beeler J, Akib A, Huhilal, Audet S, Sommer A. Reduced seroconversion to measles in infants given vitamin A with measles vaccination. *Lancet* 345: 1330-1332, 1995.

23. Stephenson LS, Latham MC, Ottesen EA. Global malnutrition. *Parasitology* 121: S5-S22, 2000.

FOUNDATION NEWS

- Dr C Gopalan was the Guest of Honour at the Inaugural Meeting of the Indian Council of Medical Research Centenary Celebration on 15th November 2010 and delivered the Key Note Address on "Nutrition Security".

- The first meeting of the Prime Minister's National Council on India's Nutrition Challenges was held on 24th Nov. 2010.Dr Gopalan and Dr Prema Ramachandran are members of the Council.

Dr Gopalan had sent a note on addressing India's nutrition concerns. Dr Prema Ramachandran attended the meeting.

- **C Ramachandran Memorial Lecture**

The Annual Foundation Day of NFI was held on 29th November 2010. Dr V Mohan (Chairman and Chief Diabetologist, Dr Mohan's Diabetes Specialities Centre, Chennai) delivered the Tenth C Ramachandran Memorial Lecture on "The diabetes epidemic in India: Why? What can be done?"

- **Study Circle Lecture**

Dr Prema Ramachandran (Director, NFI) delivered a lecture on "Integrated health, nutrition and population surveys: way forward" on 27th October 2010.

- **Technical consultation on Hospital Nutrition Practices in South-East Asia**

Appropriate nutrition support to patients in the hospital setting is increasingly being seen globally as part of overall holistic patient management to ensure good health outcomes. In developed countries, nutrition support systems have seen major advances in recent times, and hospitals have put in place fine-tuned protocols. They have the latest access devices, a range of readily available formulations, and adequate expertise in appropriate intervention techniques.

In secondary and tertiary care hospitals in the South-East Asian countries, on the other hand, nutrition intervention is by and large ad hoc, with only a few of the hospitals having meticulous protocols and record-keeping in this regard. Many of the hospitals do not have dedicated nutrition interventionists on their staff. There are also issues regarding ready availability of some of the nutritional formulations, and affordability of some of the more sophisticated devices. All these issues need to be addressed urgently in this region, because adequate, timely and appropriate nutrition support can save lives, shorten hospital stay, save costs, and help in the quicker restoration of the patient to total health.

NFI in collaboration with WHO SEARO organized a technical consultation on Hospital Nutrition Practices in South-East Asia on 30th November – 1st December 2010. The consultation, brought together experts from the countries of the region with their vast experience and insights, to discuss knowledge gaps, specific problem areas, bottlenecks in the processes and come up with recommendations on strategies to correct these. The summary of these is being published in the CRNSS update .

XXXXII Annual Meeting of the Nutrition Society of India

Message to the members

C Gopalan, Founder President

Friends, I am glad to send you my warmest greetings on the occasion of the Forty-Second National Conference of our Society.

It is through your enthusiasm and regular participation every year that our Society has grown in strength.

Today, nutrition is no longer considered to be a peripheral issue. Our policy makers have now come to recognize that achieving the nutritional well-being of all our people is important not only for health promotion but for overall improvement of our human resources and for national development.

I am glad that the theme of this Conference is 'Wholesome Nutrition'. As you are all aware, there are currently several projects designed to combat poverty and promote food and nutrition security. The success of these programmes will naturally depend upon the efficiency with which they are implemented at the grassroots level. In the ultimate analysis, the nutritional status of our population will improve only when the habitual diets in millions of homes in our countryside are of good nutritional value.

We also know that, through a judicious combination of locally available foods, balanced diets are possible, even among the one-fourth of the population living below the poverty line. Universal nutrition security can be brought about only through the informed and enthusiastic participation of the community. Governments can launch and support projects, but it is the community that must bring about the required changes that can make the difference.

Today we have a great deal of knowledge regarding the nutritive value of Indian foods. I am glad that the information in this regard is being continuously updated by the National Institute of Nutrition and the ICMR. However, if this knowledge is confined to laboratories and research institutions it is not likely to improve the nutritional quality of home diets. This valuable information should be widely disseminated, especially to the middle- and low-income groups.

There are more than 400 Home Science colleges in the country. In each region, food and nutrition departments of the Home Science colleges should identify low-cost, food items on the basis of their nutritive values. They should then formulate appropriate regional menus featuring these food items, and help to popularize them among the community. Perhaps these can be introduced in the Mid Day Meal menus and ICDS cooked food programmes. ASHAs, Anganwadi workers and ANMs can play a major role in communicating these nutrition messages to the women during the village health and nutrition days. In a country as diverse as ours, this will involve a massive programme of intensive nutrition education. In such a programme, emphasis must also be laid on the importance of personal hygiene such as hand-washing and care in the handling of food. A considerable part of the undernutrition in our children is on account of poor absorption of nutrients, due to infections arising from unhygienic environments and contaminated food.

The school system is a potentially valuable entry point for widespread nutrition education. Nutrition and health education imparted in schools not only makes the children more aware of these important issues, but uses them as agents of change who will carry the message to their homes and to the community.

While India is yet to overcome under-nutrition and micronutrient deficiencies, it is increasingly facing problems of over-nutrition and obesity to varying degrees in different segments of the population. Research carried out in India and elsewhere has highlighted the fact that children who are stunted in early childhood because of malnutrition, and who subsequently improve their nutritional intake, may be more vulnerable to overweight and obesity in adulthood, with the attendant risks of the so-called 'lifestyle diseases' such as diabetes and hypertension. On the other hand, overweight children are also at greater risk of growing up to be obese adults, and face the very same set of risks. In India, the increasing obesity rates are attributable mainly to the steep reduction in physical activity over the past two decades, brought about by labour-saving household appliances, mechanised transport and electronic entertainment media. This rapid paradigm shift in lifestyles within just a few decades is probably the prime reason for India earning the dubious distinction of being the 'diabetes capital of the world', with cardiovascular diseases also precipitously rising. Indians are reported to manifest these problems a decade earlier in their lives, on average, than their developed-country counterparts. Making physical exercise and fitness a habit early in life will pay rich dividends throughout the lifespan. This too is an important message that must reach every Indian.

Therefore, friends, we certainly have CHALLENGES.....more than enough to keep all of us in the field of nutrition busy for the foreseeable future. This is because the SCOPE for nutrition research in India is vast and becoming vaster as new problem areas emerge. Ultimately, it is a question of MANAGEMENT. How can we weld together our strengths in various seemingly different areas of activity....nutrition research, food research, dietetics, nutrition education, social work... and even modern communication techniques, policy planning and economics to deliver solutions for the nutritional challenges facing our nation?

Some have predicted that the Twenty first century will be the century of India. The very basic requirement for that to happen must be that every man, woman and child in every Indian home should have nutrition security, summed up in terms of the three A's....availability, accessibility and absorbability of good, wholesome nutritious food. It is a difficult challenge to face, but the rewards of success will be great.

I wish the Conference all success.

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