

The silent tragic reality of *Hidden Hunger*, anaemia, and neural-tube defects (NTDs) in India

Aśok C. Antony,^{a*} Ravindra M. Vora,^b and Santosh J. Karmarkar^c

^aDivision of Hematology-Oncology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA

^bDepartment of Paediatric Surgery, Paediatric Surgery Centre & Post-Graduate Institute, Implementing The Lancet Commission on Global Surgery in India, Sangli, Maharashtra, India

^cDepartment of Paediatric Surgery, Lilavati Hospital and Research Centre, Mumbai, Maharashtra, India

Summary

Hidden Hunger arising from nutritional iron-, folate-, and vitamin-B₁₂-deficiencies is exceedingly common in India and has profound negative impacts on anaemia, on pregnancy, and on embryonic-foetal neurodevelopment *in utero*, which predisposes to NTDs and psychological-psychiatric manifestations in childhood. Whereas younger-to-middle-aged Indians fail to perform at maximum potential, the elderly are at risk for calamitous neurologic events. However, these micronutrient-deficiencies are eminently correctable through food-fortification. Therefore, the Indian Government can no longer afford the luxury of inaction by either denying or downplaying the gravity of this problem. What is critically needed from India's leaders is an urgent, clear-eyed reappraisal and act of anagnorisis—an often startling self-recognition and discovery of a profoundly serious error and tragic flaw—in failing to confront this problem for decades. Only when closely followed by a metanoia—a transformative change of heart that triggers remedial action—can they help India avoid a catastrophic tryst with destiny.

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“... A moment comes, which comes but rarely in history, when we step out from the old to the new, when an age ends, and when the soul of a nation, long suppressed, finds utterance... Are we brave enough and wise enough to grasp this opportunity and accept the challenge of the future?... The service of India means the service of the millions who suffer... so long as there are tears and suffering, so long our work will not be over...”

—excerpts from Prime Minister Jawaharlal Nehru's speech “Tryst with Destiny” (14 August 1947)

deficiencies of either minerals (like iron, iodine, or zinc) and/or vitamins (like vitamin-A, vitamin-D, folate, and vitamin-B₁₂), which arise from chronic consumption of a relatively monotonous diet that lacks a balanced combination of grains, vegetables, lentils, fruits, and animal-source foods (meats, seafood, dairy-products). As a distinguished UNICEF leader observed: “The ‘hidden hunger’ due to micronutrient deficiency does not produce hunger as we know it. You might not feel it in the belly, but it strikes at the core of your health and vitality.”¹ Indeed, *Hidden Hunger* has struck at the core of India's most precious resource—her women and children—and insidiously left its mark on all Indians.

Introduction

India is in the unenviable position of being a world leader of “*Hidden Hunger*”.¹ The term ‘Hunger’ refers to the compelling desire for food and the distress arising from a lack of it, which is easily resolved by a few mouthfuls of conventional nutriment. By contrast, ‘*Hidden Hunger*’, refers to overt or subtle micronutrient

Inter-generational iron-, folate-, and vitamin-B₁₂-deficiency and its consequences in India

Throughout life, most Indians consume diets that range between ‘barely sufficient’ to ‘frankly inadequate’ in providing daily requirements of iron, folate, and vitamin-B₁₂—key micronutrients that are critically required to optimize erythropoiesis.^{2–7} These micronutrient deficiencies are more acutely felt in women whose requirements increase during menstruation, pregnancy, and

*Corresponding author at: Walther Hall, R3-C321B, 980 West Walnut Street, Indianapolis, Indiana 46202.

E-mail address: aantony@iu.edu (A.C. Antony).

lactation. Because it is not customary in India to intentionally seek to correct each of these deficiencies in adolescent girls, pregnancy triggers a worsening health crisis and further depletes their extant meagre micronutrient stores.

Of note, a nutritional deficiency of either iron, or folate, or vitamin-B₁₂ can independently lead to anaemia.^{6,7} Conversely, all three micronutrients must be given in sufficient amounts to restore normal haemoglobin values.^{6–8} Therefore, full therapeutic ‘replacement doses’ of each depleted or deficient micronutrient is initially indicated to rapidly fill body’s stores^{6–8} before using lower supplemental ‘maintenance doses’ to compensate for ongoing dietary insufficiency. Without this critically important two-step intervention, pregnant women will pass down their borderline-to-deficient micronutrient stores [much like ‘bank-balances’] to their newborn baby girls.⁹ These girls—growing up on an unbalanced diet at home—are destined to limp across childhood into adolescence carrying their burden of low-micronutrient stores. Upon entering pregnancy, just like their mothers did, they will bequeath a depleted quota of micronutrients to their own progeny—thereby vertically propagating this vicious cycle of nutritional poverty down the next generation, *ad infinitum*.⁹

Nutritional anaemia in pregnancy increases the risk for bleeding at delivery, and shock following even mild haemorrhage can be fatal without immediate blood replacement. Because of an inadequate blood-banking infrastructure nationally to support ~26-million pregnancies each year, there is a perpetual paucity of blood transfusions for obstetrical emergencies. In 2018, anaemia contributed to ~25,000-maternal deaths in India,¹⁰ and ‘pregnancy-related complications’ were the commonest cause of death in young Indian women between 15-19 years of age.¹⁰

An underappreciated fact is that deficiency of either iron, or folate, or vitamin-B₁₂ in a pregnant woman can adversely affect *in utero* neurodevelopment of her baby, leading to postnatal neurologic, or psychologic, or psychiatric consequences in childhood (discussed below). So, when all three micronutrients are insufficient during pregnancy—as is often the case in Indian women—one can predict a far worse outcome in their progeny. This issue demands an urgent solution.¹¹

Iron

Iron deficiency anaemia affects well over one-half of all Indian women, and is associated with cognitive impairment, fatigue with low productivity, susceptibility to infection, and serious consequences for both mother and baby, warranting iron replacement and prophylaxis well before menarche.¹² Whenever there is insufficient iron, red blood cell (RBC) precursors in the bone marrow receive first priority of any available iron for haemoglobin synthesis; as a result, dysfunction of other iron-

dependent enzymes/proteins in non-haematological tissues—such as skeletal muscle, heart, and brain—can manifest in muscle fatigue, heart failure, cognitive dysfunction and behavioural changes even before iron deficiency anaemia manifests clinically.^{13–15}

The recommended dietary allowance (RDA) for iron in non-pregnant women (aged 19-50 years) is 18-mg/day, but in pregnancy it is 27-mg/day.¹⁶ Every pregnancy requires an additional 1000-mg iron, warranting supplemental iron. For each 325-mg ferrous sulphate tablet containing 65-mg of elemental iron, ~25-mg can be absorbed and utilized. Although combined iron-folate tablets are distributed by the Indian Government, an intractable and as-yet-unsolved problem is that oral iron has notoriously unpleasant adverse side effects leading to poor compliance in ~75% Indian women^{11,17}; an unintended outcome is that these women do not get their critical quota of folate, which contributes to anaemia, risk of NTDs, and other consequences as discussed below.

During pregnancy, iron deficiency also contributes to maternal morbidity from premature labour, placental abruption and low-birthweight infants,^{18–20} and deficiency of maternal iron *in utero* can severely affect foetal neurodevelopment.²¹ Two-thirds of a newborn baby’s 75-mg iron/kg is in haemoglobin, and 80% of iron is transported from mother-to-foetus in the third-trimester; so, if a mother is iron-deficient during this period, net foetal transfer of iron is compromised. Delayed cord-clamping can significantly improve iron transfer to the baby at the time of delivery,²² but it is unclear how widely this is routinely practiced throughout India. Although iron deficiency is reversible in early infancy, when left untreated it can lead to irreversible neurocognitive problems by school age,¹⁵ manifested by defective intellectual, cognitive, and social development.^{23,24}

Full-term healthy infants of iron-replete mothers who are exclusively breastfed usually have sufficient iron only for the first 4-months of life, after which they become increasingly at risk for developing iron deficiency. For this reason, in USA it is recommended that all exclusively breastfed babies be supplemented with oral iron after this time, until they start consuming age-appropriate iron-containing foods.²⁵ And for those iron-replete mothers who deliver prematurely, their infants are endowed with a relatively lower amount of iron at birth; so, depending on the extent of prematurity, guidelines exist for administration of either enteral or intravenous iron.²⁶ By contrast, in India, where maternal iron deficiency is common in the third-trimester, these full-term newborn babies are also at high risk for iron deficiency, which warrants rapid iron replacement. However, there is a dearth of information on whether such mothers and their infants are optimally managed throughout India. Without affordable and easily available iron preparations, millions of Indian infants of iron-deficient mothers are destined to develop adverse

neurological sequelae from inadequately treated iron deficiency every year.^{23,24,27}

Vitamin-B₁₂

Intracellular vitamin-B₁₂ deficiency results in a functional folate deficiency and profoundly perturbs both haematopoiesis and the nervous system.⁷ Humans primarily receive vitamin-B₁₂ from animal-source foods^{28,29} and although the RDA for vitamin-B₁₂ is 2.4-µg/day, ~6-7-µg/day is likely more optimal.³⁰ Because vegetarian diets provide ~0.5-µg/day of vitamin-B₁₂, all vegetarians are at risk for vitamin-B₁₂ deficiency and must be supplemented.⁵ Of related significance, most Indians who indicate they are 'non-vegetarians' actually consume a 'near-vegetarian' diet,^{5,31} containing relatively small quantities of meat only once or twice a week, which cannot sustain optimum vitamin-B₁₂ balance—(compare such a diet to the daily non-vegetarian diet in the West that is replete with animal-source foods). Not surprisingly, ~75% adults in the Indian subcontinent have nutritional vitamin-B₁₂ deficiency, a fact we confirmed last year among women of reproductive age.¹⁷ However, there are no robust programs designed to improve the vitamin-B₁₂ status of children, adolescent girls, or women of childbearing-age in India. Even the *Anemia Mukht Bharat* programme of India's Ministry of Health and Family Welfare³² has not been optimized since it fails to include vitamin-B₁₂ replacement—despite numerous studies pointing to low-vitamin-B₁₂ status among Indian women.^{17,33,34} Since vitamin-B₁₂ is also not routinely replaced during pregnancy, the developing foetus is deprived of sufficient maternal-vitamin-B₁₂, which is essential for growth. Following delivery, women with low-vitamin-B₁₂ stores have a low-vitamin-B₁₂ content in breast-milk that is grossly insufficient for their infants,³⁵ which can impair their reasoning, abstract thinking, and learning.³⁶ When such infants are weaned to a traditional Indian diet that is intrinsically low in vitamin-B₁₂,^{4,5,37} this chronic low-vitamin-B₁₂ status is perpetuated in young girls through childhood into adulthood, and then into their own reproductive cycles. This warrants urgent attention among tens of millions of Indian mothers and their babies.

Folate

Folate is critically required during pregnancy for growth of maternal-and-foetal tissues, and after birth throughout all stages of life. The RDA for folic acid is 400-µg/day.¹⁶ The Indian diet is intrinsically low in folate as a result of a meagre consumption of fresh green salads, vegetables, and fruits. In addition, cooking of vegetables, lentils, or beans often extends beyond 30-minutes, which destroys the folate content of these foods.⁷ As a consequence, folate deficiency is widely prevalent in

India at all ages, especially among women of reproductive age.^{4,7,17,38,39}

Recently, a dangerous myth propagated in the contemporary medical literature—which maintains that folate deficiency is uncommon across India and Africa—was traced to its origin and unmasked.³⁹ As background: RBCs have a 30-fold higher folate content than that present in serum; therefore, haemolysis from any cause—(such as malaria, sepsis, haemoglobinopathies)—predictably raises the serum folate level into the normal range, even in subjects with severe nutritional folate deficiency.³⁹ Likewise, during vitamin-B₁₂ deficiency, the vitamin-B₁₂-dependent intracellular enzyme, methionine synthase,⁷ cannot process the folate which enters cells; as a result, this cellular folate leaks out back into serum, resulting in higher-than-baseline serum folate levels and thereby masking even severe folate deficiency.^{7,39} Despite this long-established knowledge, a grave diagnostic-and-therapeutic error was perpetrated when investigators mistakenly used serum folate levels as a biomarker for folate deficiency among severely undernourished children in Africa with malaria; and on finding a normal serum folate, they withheld critically needed folate supplements. Later, a similar error occurred in India among women [and children] with nutritional vitamin-B₁₂ deficiency who also had normal serum folate levels despite very low dietary folate intake. The upshot is that hundreds of millions of women and children with dietary histories pointing to severely restricted dietary folate intake have been deprived of desperately needed folate replacements.³⁹ Thus, any assertion that folate deficiency is rare in resource-limited countries is patently false.³⁹

Chronically raised maternal plasma/serum total homocysteine, which is usually due to folate- and/or vitamin-B₁₂-deficiency, is associated with various pregnancy complications. These include preeclampsia and spontaneous pregnancy loss,⁴⁰ placental abruption,⁴¹ recurrent pregnancy loss, foetal growth restriction,⁴² preterm birth,⁴³ and stillbirth.⁴² Normalization of maternal plasma/serum homocysteine by folate and vitamin-B₁₂ supplementation improves pregnancy outcomes for some complications,⁴¹ suggesting these risks may be reduced by optimizing intake of these micronutrients.

Inverse Relationship of Maternal Folate Status and Risk of NTD

Embryonic neural-tube closure, which is completed by the 28th day of conception, is directly dependent on sufficient provision of maternal folate. This was shown when periconceptional folate supplements (administered at least a month before conception and continued up until the date of the second missed menstrual period) led to significant reduction in first occurrence of NTDs.⁴⁴ A subsequent massive China-US collaboration

demonstrated that periconceptional supplementation using 0.4-mg of folic acid daily led to a reduction of NTD risk by as much as 81%.⁴⁵ Such information led to the implementation of folic acid-fortified wheat flour (140-µg folic acid/100-gram flour) to prevent NTDs in USA.^{7,46} This improved the serum folate concentration,⁴⁷ reduced first-occurrence of NTDs,⁴⁸ and prompted over 80 countries to adopt this practice to reduce NTDs.⁴⁹

Two important follow up studies^{50,51} have established the minimum required levels of RBC and serum/plasma folate levels to prevent NTDs—i.e., they provide the threshold nutrient levels to aim beyond for women of childbearing-age to prevent NTDs. Briefly, among women without anaemia, a population-based, randomized trial of folic acid supplementation determined that a population-level RBC folate concentration below the threshold of 400-ng/mL (i.e., 906-nmol/L)—which corresponds to a plasma folate level of 11.3-ng/ml (i.e., 25.5-nmol/L)—is insufficient and suboptimal for NTD-prevention.^{50,51} This implies that for the minority of Indian women with normal vitamin-B₁₂ status, those with plasma folate levels less than 11.3-ng/ml remain at significant risk for having babies with folate-responsive NTDs. However, for most Indian women who have combined low-folate and low-vitamin-B₁₂ status,^{17,33,34} those with an even [falsely]-higher basal plasma folate value of up to 15.3-ng/ml (i.e., 34.6-nmol/L)⁵¹ continue to remain at risk for having a baby with a folate-responsive NTD.

The practical significance of these data is that an “apparently normal” serum/plasma folate concentration (i.e., with values from the lower-limit of normal up to 15.3-ng/ml) in an Indian woman with low-vitamin-B₁₂ status, can lead an uninformed physician to conclude that she is protected from the risk of having a baby with a NTD, when in actuality, her risk remains high. In all recent studies^{17,33,34} the supermajority of Indian women would be at risk. The implication and challenge for Indian public health policy makers is to ensure that the dose of folate and vitamin-B₁₂ used for food-fortification achieves this mid-to-high normal serum folate concentration [and normal vitamin-B₁₂ levels] as rapidly as possible among all Indians.

Scenario of NTDs in India

India does not have a robust active surveillance system for birth defects; this has resulted in wide variation in the reported prevalence estimates of NTDs, which have primarily been from tertiary referral centres. The overall prevalence of birth defects in India is 60-70-cases/1000-live births.⁵² A conservative estimate from a meta-analysis also suggested 4.1-NTDs/1000-live births.⁵³ This translates to well over 100,000 babies born with NTDs each year in India—not accounting for stillbirths with NTDs (Figures 1–4). However, other population-based studies—carried out a decade apart in the largest

Indian state of Uttar Pradesh (U.P.)—range from 7.48- to 8.2-babies with NTD per 1000-live births.^{54,55} The fact that there are an additional 168 districts with similar deficits in health-, social- and economic-development [as in U.P.^{54,55}] suggests NTDs may be widespread across India.¹¹ Extrapolation of data from China-US studies^{45,50} projects that for Indian women with a high prevalence of folate and vitamin-B₁₂ deficiency,^{17,33,34} reduction of NTDs by vitamin supplements via food-fortification would be closer to 90%—i.e., resulting in the prevention of 115,000 Indian babies born with NTDs each year.⁵⁶ In spite of these data, India has not taken appropriate steps to protect women from these devastating complications during pregnancy.

Thus, NTDs continue to remain a ‘silent endemic tragedy’ arising from the intersection of the deafening silence from a culpable Ministry of Health charged with the responsibility of ensuring the health and welfare of Indian women and children, an inexplicably nescient Indian news media on this important topic, and a dearth of champions to advocate on behalf of India’s forgotten children with NTD.¹¹ In this context, we provide two reasons for a deliberate semantic change in referring to the silent tragedy of NTDs in India as a ‘endemic’ problem—rather than the more scientifically precise term ‘epidemic’. First, to highlight the unexplained fact that the Indian Government has not even acknowledged the seriousness of the problem of NTDs—i.e., of well over 3-million babies born with NTDs in India over the past three decades. Indeed, as outlined recently,¹¹ it appears as if the Indian Ministry of Health has relegated the high incidence of NTD in India to the level of a “nondescript entity”, one that is even lower in priority to other endemic diseases in India (like mosquito-borne and human-to-human or water-borne [diarrheal] illnesses) that are at least documented in the official record. Second, to urge the Government of India to take a more proactive stance against the problem of vitamin-preventable NTDs—‘on a war footing’—in the same way a highly commendable nationwide effort was recently mobilized in vaccination against poliomyelitis to prevent an impending epidemic.

The stark reality of children living with NTDs in india

The spectrum of presentations of NTDs—(see examples in Figures 1–4)—range from the most severe anencephaly with complete rachischisis or anencephaly alone, to encephalocele, to spina bifida with neural plaque, to lipomyelomeningocele, to myelomeningocele, to diastematomyelia, to meningocele, to tethered cord, and spina bifida occulta. Depending on the severity and level of the lesion there will be varying degrees of neural deficits with resultant hydrocephalus, motor and sensory loss in lower limbs, loss of bladder and/or bowel control, and lower limb deformities, including club foot. And in a few, there will be associated congenital



Figure 1. Neural-tube defects among Indian babies. (*Upper Row*): Multiple views of a baby with anencephaly with complete rachischisis (Reproduced from Ref. 7, with permission). (*Lower Left*): Large encephalocele. This encephalocele contained a very large portion of the brain floating in cerebrospinal fluid, which precluded neurosurgical repair. (*Lower Right*): Small occipital encephalocele. This encephalocele was amenable to neurosurgical repair. (Reproduced from Ref. 11, with permission).

anomalies involving other systems, further adding to the profound misery of children with NTDs.

Despite formidable obstacles, most Indian parents struggle and strive their utmost to care for their babies with NTD. Most of these children will require 5-7 major corrective operations; however, with costs borne by their parents, this predicts an eventual downward economic spiral into abject poverty. Because of bladder-and/or-bowel incontinence and wheelchair-inaccessible toilets, and the need for frequent change of diapers [anticipating the inevitable ostracism], formal education in any Indian school is a near-impossibility. Indeed, only those fortunate few born into privileged families who receive a private education can consider pursuing an independent professional career. Despite these challenges against

formal education, there are rare instances of children gaining proficiency in the arts or sports or even as an artisan contributing financially to the family. However, the appalling reality and fate of most children with NTDs in India is to be forced to live lonely lives of suffering and despair at home. Eventually, most of these children will be forced to rely on society for basic sustenance. . .

Insufficient maternal folate for the foetal brain and postnatal behaviour

The foetal brain also critically depends on sufficient provision of maternal folate throughout development *in utero*. Our experimental studies on folate deficiency in pregnant mice⁵⁷—[using one-third of optimum dietary



Figure 2. Neural-tube defects (spina bifida cystica) among Indian babies. (*Upper Left*) Lumbar meningocele. (*Upper Right*) Lumbar meningocele. (*Lower Frames*) Various grades of lumbar meningocele.

folate, similar to the dietary availability of folate among women in North India³⁸—resulted in abnormal changes in the brains of foetal mice when assessed just prior to birth; this included cortical cell loss by 20% and perturbed axonal development.⁵⁷ Surprisingly, despite postnatal folate replenishment, mice that experienced folate deficiency *in utero* exhibited anxiety in young adulthood.⁵⁸

Within 5-years of these murine studies,^{57,58} investigators from the U.K. Medical Research Council⁵⁹ confirmed that lower maternal folate status early in pregnancy profoundly affects the foetal human brain and predisposes affected children to psychological-neuropsychiatric disorders in early childhood.⁵⁹ Subsequent confirmatory studies from Norway, Sweden, and even India, then observed a spectrum of abnormal behaviour in affected children: these included hyperactivity-inattention and peer problems,⁵⁹ and learning deficits; children were either emotionally-reactive, anxious or depressed, had somatic complaints, and were either withdrawn or aggressive.^{21,60–63} Conversely, women who took folic acid in early pregnancy provided an *in utero* environment that impacted positively on the child's intellect, emotional intelligence, cognition, language, and academic performance.^{21,61,64}

Therefore, an insufficient maternal folate level has the potential to result in several psychological-neuropsychiatric manifestations in childhood. Collectively, these animal and human studies are consistent with the Barker Hypothesis on developmental origins of disease.⁶⁵

Low iron-, folate-, and vitamin-B₁₂-status in childhood, middle-aged and elderly Indians

In childhood, these micronutrient deficiencies contribute to poor growth,⁶⁶ sub-optimal intellectual development, and impaired gross motor and problem-solving skills.⁶⁷ Given the magnitude of a combined low iron-, folate-, and vitamin-B₁₂-status in Indian women,¹⁷ it is likely that many among the ~26-million babies born each year have such problems that remain untreated, leading to serious underperformance persisting into adulthood.

Folate and vitamin-B₁₂ deficiency pervades every strata of Indian society; thus, slum dwellers living adjacent to wealthy individuals in Haryana State have similar levels of hyperhomocysteinaemia (which is usually due to low-folate and/or low-vitamin-B₁₂ status).³⁸ Indeed, chronic hyperhomocysteinaemia, which affects



Figure 3. Neural-tube defect leading to primary hydrocephalus. A stenosis of the aqueduct of Sylvius [between third and fourth ventricles], which caused primary hydrocephalus was managed by placement of a ventriculoperitoneal shunt. (Courtesy of Dr. Sudhakar Jadhav, Paediatric Surgery Centre & Post-Graduate Institute, Sangli, Maharashtra).

a majority of middle-aged and elderly Indian men and women⁴ is well-established as a major risk factor in occlusive vascular diseases—particularly with increased small-vessel cerebrovascular disease—related strokes,⁶⁸ dementia, and Alzheimer disease.^{69–71} Moreover, accelerated brain atrophy is often a characteristic among those with mild cognitive impairment who go on to develop Alzheimer disease.^{69–71} Fortunately, homocysteine-lowering therapy even in elderly patients can slow accelerated rate of brain atrophy and improve cognition.^{69–71} A recent international consensus statement has concluded that elevated plasma total homocysteine is a modifiable risk factor for development of cognitive decline, dementia, and Alzheimer’s disease in older persons.⁷² This statement is a clarion call to India’s aging leaders.

Counting the cost of NTDs, anaemia, and cognitive dysfunction in India

An estimate of the lifetime costs incurred in taking care of a single baby with NTD in USA is \$791,900—or \$577,000 excluding caregiving costs.⁷³ While there are no comparable studies from India, it is evident that the costs for caring for an additional 115,000-babies with

NTDs every year will be substantial. What cannot ever be assigned a monetary value, particularly in the Indian context, are other intangible costs incurred by each baby with NTDs and the parents—in terms of physical-, mental-, emotional-, psychological-, spiritual-, and social-suffering.

Likewise, (i) the cumulative costs of untreated anaemia and its contribution to maternal morbidity and mortality; (ii) maternal-to-foetal transmission of risk of micronutrient deficiency predisposing to neuropsychiatric disorders and sub-optimal intellectual development; and (iii)—the cost of strokes, cognitive dysfunction, and Alzheimer’s disease, all of which collectively threaten the health and well-being of several hundreds of millions of Indians, will be several orders of magnitude higher than the cost of inexpensive micronutrients added to fortify foods.^{11,73}

A contextual-appropriate solution for India

The ideal scenario of ‘preparation for pregnancy’—also known as preconception or pre-pregnancy care—is rare among Indian women of childbearing-age (Figure 4). The identification of a common food-vehicle that can be fortified with folate and vitamin-B₁₂ and which is



Figure 4. A tale of two Indian women. (*Left Frame*) This woman holding her newborn baby with a NTD was not offered advice about ‘preparation for pregnancy’ and did not use any micronutrient supplement(s) prior to, or during, pregnancy. Her baby, born at term, had lumbosacral spina bifida with exposed neural plaque and cerebrospinal fluid leak, paraparesis, incontinence, and hydrocephalus. Although the delivery took place at a Maharashtra State Government Primary Health Centre, it was left to the parents to transport their baby to a paediatric surgical centre 70-km away, where they were expected to cover all costs for surgical repair. Because of their crippled financial situation, the parents were able to arrange for travel only 8-days later, using public transportation. The baby underwent repair of the open lesion on day 9, but unfortunately succumbed to overwhelming septicaemia. (*Right Frame*) This woman holding her newborn baby practiced all principles of ‘preparation for pregnancy’. She consumed a well-balanced near-vegetarian Indian diet, exercised every day, and used daily supplemental folate (1-mg), vitamin-B₁₂ (1-mg), and iron (ferrous sulphate 325-mg) initially for 6-months to fill her micronutrient stores a full year before conception. She then substituted daily prenatal vitamins 6-months prior to conception and continued these throughout pregnancy. She delivered a healthy baby at term and continued to use prenatal vitamins in anticipation of another pregnancy.

acceptable to all Indian women of every geographic-, social-, economic-, cultural-, and ethnic- distinction—whose diet is dictated by these very differences—has been elusive and a formidable hurdle to progress. We recently identified that a daily cup of tea—[a beverage consumed by most Indians every day]—that is fortified with folate-and-vitamin-B₁₂ can easily eliminate both folate and vitamin-B₁₂ deficiency among Indian women.^{11,17} Following confirmatory studies leading to widespread implementation in India, vitamin-fortified tea promises to dramatically improve the folate- and vitamin-B₁₂-status of women, optimize vitamin-dependent embryonic-foetal neurodevelopment *in utero*, reduce complications of pregnancy and delivery, allow well over 100,000 babies to develop normally [without NTDs] each year, and positively impact the mental and physical health of children, middle-aged and elderly Indians.

One final point warrants repetition: clinical studies consistently point to the fact that over 500-million Indian women with a low-folate status remain at risk for having babies with NTDs and/or psychological-psychiatric abnormalities. Several articles in the Indian

literature also point to the plausible suggestion that low-vitamin-B₁₂ status, which is exceedingly common among Indian women of reproductive-age, can interfere with proper functioning of folate within cells and predispose to NTDs. Therefore, the primary focus of the Government of India ought to be in first rapidly replenishing both folate and vitamin-B₁₂ (as for a clinically significant vitamin deficiency); this will be in keeping with classic principles and practice of nutrition, internal medicine, and haematology.^{6–8,74} By contrast, any unorthodox approach—such as using either physiological or subtherapeutic-doses of both vitamins to achieve a slow reversal of the low-vitamin status among a large population of Indian women over several months [approaching a year]—is ethically problematic. This is because each month’s delay in optimization of vitamin status continues to place millions of women at ongoing risk for [vitamin-responsive] anaemia, while tens of thousands of children remain at risk of being born with [vitamin-preventable] NTDs or neuropsychiatric disorders every month until optimum vitamin status is achieved. Therefore, only after complete replenishment of these vitamins in the shortest possible time is it

reasonable to institute lower supplemental doses of vitamin-fortified food to compensate for ongoing dietary insufficiency (that led to these vitamin deficiencies in the first place). Thus, we suggest two strengths of vitamin-fortified tea¹¹ (or equivalent alternative food-vehicle) be made available in India—a full therapeutic dose of vitamin-fortified tea/food-vehicle for rapid reversal of low-vitamin status, and a lower-maintenance dose of vitamin-fortified tea/food-vehicle for the long term.

From an economic and practical standpoint, the cost of optimizing folate and vitamin-B₁₂ status is relatively small compared to most enterprises aimed at improving societal well-being. Industrial-scale production of vitamin-B₁₂ is achieved using bacteria (*Propionobacterium shermanii* or *Pseudomonas denitrificans*) to efficiently generate the complex molecule, whereas folic acid is chemically synthesised. The cost for 1-gram each of pure—(Indian Pharmaceutical Grade)—folic acid and vitamin-B₁₂ is Rs.13 and Rs.185, respectively (Personal Communication: Meyer Organics, Mumbai, India). Therefore, the cost of adding 1-mg folic acid and 1-mg vitamin-B₁₂ to a daily cup of tea for full therapeutic replacement of low-vitamin status is only Rs.0.2 per day. Assuming a daily cup of vitamin-fortified tea is required for 90-days to restore optimum folate-and-vitamin-B₁₂ status, this translates to a total cost of vitamins per person of Rs.18. Parenthetically, this approximates the cost of a single cup of tea from most tea-stalls across India. Moreover, the annual cost of adding folic acid [0.5-mg] and vitamin-B₁₂ [100-µg] to a daily cup of tea to supplement an Indian diet intrinsically low in these vitamins will cost less than Rs.10-per-person.

While an oral iron preparation without unpleasant side effects remains elusive, this fact alone should stimulate urgent search for a contextually appropriate and scientifically validated solution for children and adolescents before they reach sexual maturity. Fortified flour, rice and salt⁴⁹ are under consideration for fortification with all three micronutrients, but each of these vehicles have very real intrinsic limitations in widespread distribution [and acceptability] in India—particularly for the poorest-of-the-poor who comprise several hundred-million Indians.^{11,17} In addition, a uniform approach to normalize a low-iron status in all women at the earliest stages of pregnancy will significantly reduce obstetric complications and optimize *in utero* and post-natal neurodevelopment in their newborn babies.

Conclusion

India must strive to ensure that all her adolescent girls and women of childbearing-age receive sufficient iron, vitamin-B₁₂, and folate to fully replenish their low-to-deficient micronutrient stores as soon as possible. With the advent of a quintessentially Indian beverage that easily reaches all Indians every day,^{11,17} [and any equivalent alternatives], there is now an ethical imperative to

rapidly replenish all Indians with vitamin-fortified food to reduce several life-threatening complications. Therefore, developing a comprehensive strategy should be an urgent national priority, and warrants bringing this problem to the forefront of all Governmental policy-making discussions. Success in eliminating *Hidden Hunger* involving these three micronutrients would be a major step forward for India as she turned 75-years old as an Independent Nation.

These challenges to improving the health of women and children are not unique to India; up to 90% of the world's women in resource-limited countries do not receive sufficient dietary folate.^{39,75} A major obstacle remains the formidable plethora of more powerful competing interests that entice politicians to banish most initiatives that are designed to benefit women and children to the realm of neglect, while keeping them submerged under a plenitude of political oratory. To these politicians we proclaim: “The time for equivocation—(use of ambiguous or deliberately evasive statements to avoid telling the truth)—and prevarication—(use of statements known to be untrue and made in order to deceive)—is over. Simple pragmatic solutions for widespread implementation of fortification are already available, and even now the children of the world cry out for champions to their cause. Here is that once-in-a-lifetime challenge and opportunity [*for you*] to do great things for humanity.”

Contributors

A.C.A. conceived the idea for writing this viewpoint, wrote the original draft, incorporated suggestions by the co-authors for revision, provided some of the photographs used in the figures, re-edited several drafts, and approved the final version of the paper.

R.M.V. provided valuable suggestions for revision of the original and subsequent drafts, added some photographs used in the figures, and approved the final draft of the paper.

S.J.K. provided ideas for revision of the original draft, added some photographs used in the figures, and approved the final draft of the paper.

Declaration of interests

The authors declare no conflicts of interests with regards to the present study. Authors did not receive any external funding for the study.

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