

Malnutrition in Asia and Neurological Consequences

*Jagjit S. Chopra**, *Sudesh S. Prabhakar** and *Pratibha D. Singhi***

Departments of Neurology* and Peadiatric Medicine**,

Post Graduate Institute of Medical Education and Research, Chandigarh-160012

ABSTRACT

Prevalence of malnutrition is a global phenomenon but the greatest contribution towards it is from the developing countries. Malnutrition impairs physical growth, cognitive functions of brain, physiological functions, immune response changes. Twenty Seven percent of children under 5 years are malnourished in the developing countries. India contributes to approximately 5.6 million child deaths annually with almost one billion children dying worldwide from the consequences of malnutrition. Malnutrition produces lasting effect on developing brain during the “Brain growth spurt” phase which corresponds to the period from 30 weeks of gestation to two-year of post natal age. In the peripheral nervous system the growth of axons, migration of Schwann cells and onset of myelination starts at 14 to 20 weeks of gestation.

Malnutrition causes muscle wasting, hypotonia and impaired deep tendon reflexes from 30-40% of malnourished children. Deficiency of micronutrients in malnourished can cause myelopathy, peripheral neuropathy, dementia, infantile seizures, infantile tremor syndrome, night blindness, optic neuropathy and spinocerebellar degeneration.

Keywords : Malnutrition, prevalence, central nervous system, peripheral nervous system.

Introduction

According to United Nations statistics about 25% of Indian population particularly children <14 years are undernourished. Nervous System disease due to dietary deprivation appears under circumstances as diverse as famine, extreme poverty, intestinal malabsorption due to disorders such as sprue, chronic infections and administration of metabolic antagonists such as INH, anorexia nervosa and food fads, especially among adolescents. Protein Calorie Malnutrition or Protein Energy Malnutrition (PEM) in children produced by failure of lactation/inadequate food intake is due to poverty.

Epidemiology

Malnutrition is a predominant problem of the tropics due to poverty, over population, illiteracy and socioeconomic disparity. According to UNICEF, Asia pacific is home to 50% of slum population worldwide, with 30% children <5 yrs being underweight. Fifty percent of world's malnourished resides collectively in India, Bangladesh and Pakistan. To an extent of 54% deaths in children in developing countries are due to PEM. 300,000 children <5 yrs die per year in developing countries (WHO).

According to WHO by 2015 malnutrition will decrease by 17.6%. Globally 113.4 million children younger than 5 yrs are affected. Malnutrition decreases educational achievement, labour productivity and economic growth. Under nutrition during pregnancy linked with low birth weight and low brain weight.

National survey 2004-05 in India (1) showed that out of 1.1 billion population 38% are poor and 40% new born are under weight. Northern region which is bread-bowl of India almost 80% infants are anaemic, every 2nd child is stunted, every 3rd child of educated mother is malnourished and 60% children anaemic (2).

In India, according to Economic Survey 2008-2009, 5.6 million children die annually due to malnutrition (3). Forty percent of world's malnourished children are from India. State wise, Madhya Pradesh has highest malnourished children, i.e. 60.3% and with Jharkhand being 2nd with 59.2%. The prevalence of severe PEM in India is 5 million. Countrywise data are illustrated on the startup of underweight children (Fig.1), acute malnutrition (Fig. 2) and malnutrition underweight and stunting in children (Fig. 3).

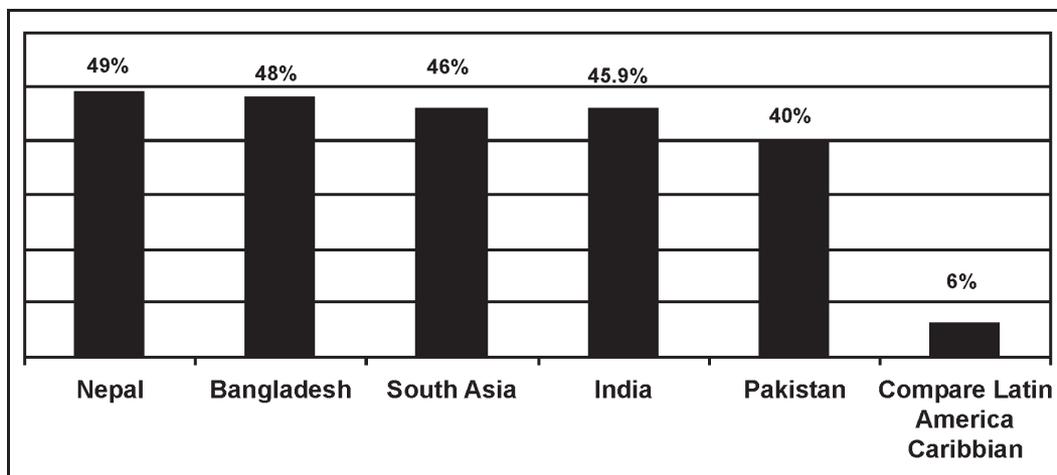


Fig. 1 : Under Weight Children

Millions are malnourished in Bangladesh(48%), 11.7% are wasted, 57.5% are stunted, 60.0% are low weight and height, 70% women are anaemic, 20% goiter and 9% have rickets in this country (4).

In Pakistan 40% children under

5 years are malnourished, 35.2% are undernourished and 32.6% population is below poverty line.

Nepal one of the poorest country of the world has highest (49%) malnutrition in south Asia, its 50%population is stunted, 40% anaemic and 40% with

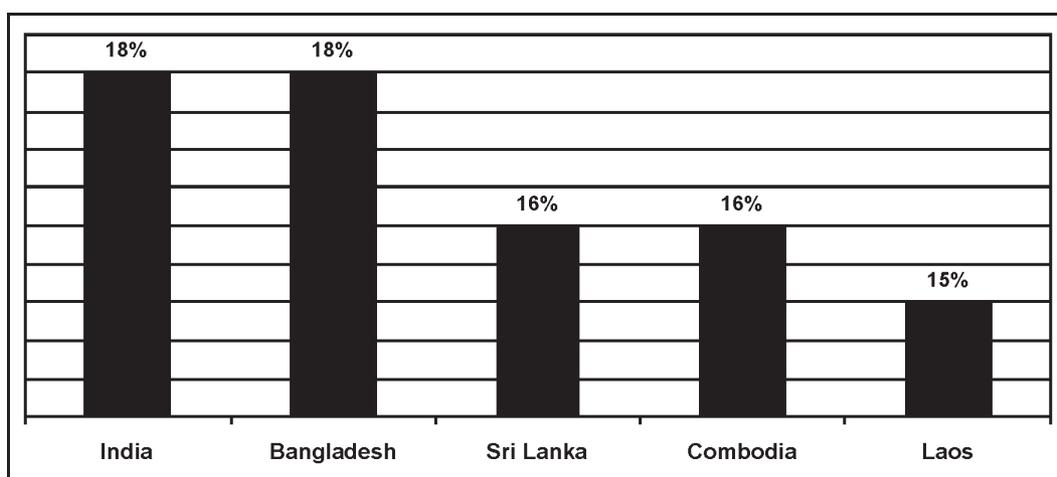


Fig. 2 : Acute Malnutrition

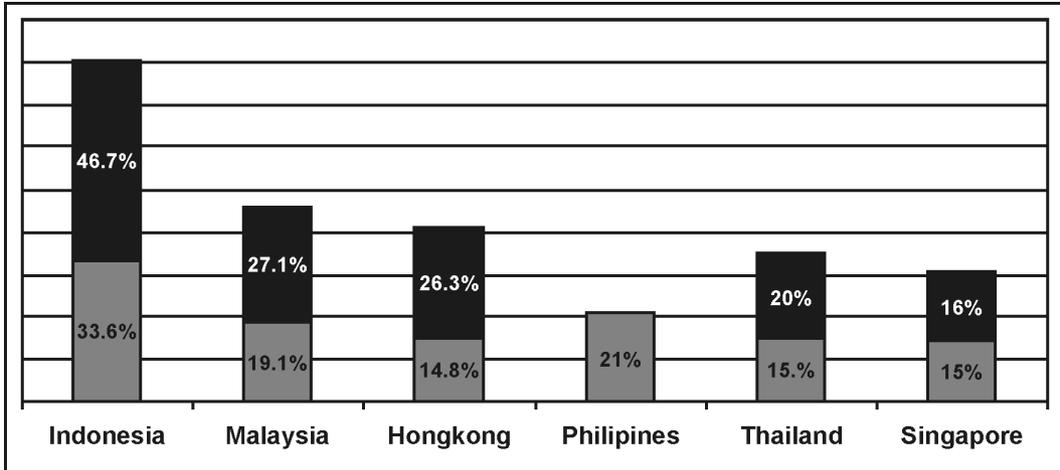


Fig. 3 : Malnutrition, Under-weight, Stunting (UNICEF, UN)

iodine deficiency. Twenty eight percent of its population survive on one US dollar a day. In Myanmar 33% young children suffer from chronic malnutrition and 82% eat damaged rice. In Sri Lanka 22% children are underweight, 18% are stunted and 15% suffer from acute malnutrition. In Jaffna area 24% suffer from acute malnutrition (5).

In Afghanistan a child dies every 3 seconds, 50% live below poverty line, 54% under 5 years are stunted and 72% under 5 years are anaemic. In Cambodia 40% population live below poverty line, 90% are poor in rural areas, 33% population is malnourished and it is highest in South Asia, 45% under 5 years are stunted.

Laos, North Korea, Vietnam and Mangolia, there is also very high level

of malnutrition, 50% children below 5 years, 60% children (6 months to 7 years), 35-45% under 5 years and 13% are malnourished, respectively.

Effects on Developing Nervous System

Human brain growth spurt begins at 13th week gestation and continue till 4th year after birth (6). The neuronal multiplication ends at birth and glial multiplication ends little later. Myelination starts during second half of growth spurt period (7). Cellular proliferation, migration, myelination and synaptogenesis occur in early phase of development. White matter is more vulnerable to PEM than grey matter. If nutritional deficiency occurs during growth spurt, it can cause irreversible

damage to CNS, muscle and peripheral nerves are less affected. Complete recovery occurs if adequate nutrition is started early and recovery is partial if nutritional correction is delayed (8).

Lamination of cord tracts identifiable by 14th week and adult pattern is reached by 30th week. In peripheral nervous system myelination starts by 14-20th week of gestation and continues till 4th postnatal year. Protein calorie malnutrition results in lack lustre scholastic performance, inadequate perception, maladjustment at home and school (9). Further the children show attention deficit, easy distractibility, low IQ, impaired memory and cognition. Abstract abilities are worst hit. Beneficial effects are noted following protein supplementation (9). Malnutrition also impairs physical growth, cognitive and physiological function and impairs immune response.

PEM and Nervous System

Functional deficit were noted in nerve and muscle due to reduced protein synthesis, reduced oxygen uptake, functional impairment of mitochondria, instability of ribosomes and enhanced IGF 1 and 2 binding.

EEG showed nonspecific slowing

with delayed peripheral and central conduction on SEP. BAER is prolonged in 40% Kwashiorkor children (10).

Nutritional deficiency

Classification based on deficient nutrients

1. Protein and/or calories

Primary PEM: - Marasmus
- Kwashiorkor

Secondary PEM:- Marasmus-
kwashiorkor

2. Specific Deficiency

Primary : Vitamin B1, B2, B3, B6,
B12, Folate, C

Vitamin A, D, E, K, and
mixed

Conditional: (dependency states)

Minerals: Calcium, Iron,
Magnesium, Zinc, Iodine, Copper,
Selenium, etc.

Protein deficiency

Kwashiorkor : This type of malnutrition is usually seen in the age group of 2-3 years with edema, hair changes, stunted growth and hypoalbuminemia.

Marasmus is seen usually between 6-18 months with growth retardation, decrease protein calories which can be

mild, moderate or severe.

In PEM muscle wasting is seen in all cases with hypotonia, hyporeflexia and delayed motor milestone in 15-45% cases. Occasionally proximal muscle weakness is noted. Electrophysiology study done showed evidence of sensory motor polyneuropathy. Severity of myelin and axonal loss parallels with severity of PEM (11-12).

Vitamin deficiency and nervous system:

A number of factors in the B group of vitamins are of clinical importance with regards to neurological disease. Although each is considered separately below, in many instances deficiencies of these and other vitamins occur in combination and may lead to complex clinical distribution.

Thiamine (Vitamin B1): Thiamine pyrophosphate serves as a coenzyme in oxidative decarboxylation and cofactor in trans-ketolation. Deficiency of thiamine in animals results in accumulation of lactic acid and reduction in oxygen uptake and depression of trans-ketolase activity especially in brainstem (13). Thiamine deficiency studied in developed countries in chronic alcoholics easily transposed to those in nutritionally depleted non alcoholics.

Two disorders that appear most clearly related to thiamine deficiency are nutritional polyneuropathy and the Wernicke-Korsakoff syndrome.

Nutritional polyneuropathy:

Nutritional polyneuropathy is the most common of all nutritional disorders of nervous system. Clinically, it is symmetrical, mixed sensorimotor neuropathy affecting lower limbs much more than upper limbs. Signs and symptoms of dysfunction of autonomic nervous system are sometimes encountered as well, including vocal cord paralysis with hoarseness, dysphagia, pupillary abnormalities, and hypotension. Hyperhidrosis of hand and feet is common.

Electrophysiological studies reveal findings suggestive of axonal polyneuropathy (11). Pathologically the primary change is segmental demyelination with axonal degeneration, affecting distal portion of the peripheral nerves. In long standing cases, retrograde changes may be found within the spinal cord.

Restoration of a well balanced diet with supplemental of thiamine is the keystone of therapy. Thiamine is given parenterally initially at 50-100mg/day then orally for several days. Symptomatic

treatment with amitriptyline, pregabalin and carbamazepine is required. Recovery is variable depending upon chronicity.

Wernicke-Korsakoff Syndrome:

Traditionally looked on as two distinct entities, they are best regarded as representing simply two aspects of the same disease, separable chronologically into acute (Wernicke's encephalopathy) and chronic (Korsakoff's syndrome) phase (14). Thus the typical mental changes of Korsakoff's syndrome may be present from the early stages of acute Wernicke's encephalopathy. Furthermore examination of patients with classic Korsakoff's psychosis reveals residual features of Wernicke's such as nystagmus and trunkal ataxia.

Wernicke Encephalopathy: Wernicke's disease is an acute or subacutely evolving disorder. Appearing on a background of chronic or severe undernutrition frequently preceded by some additional metabolic stress like trauma or infection. Characteristic clinical features of this disorder include the following

1. Abnormal mental status which include apathetic, restlessness and drowsiness to hallucination, agitation and confusion.
2. Ophthalmoplegia - is the hallmark.

Bilateral sixth nerve palsies are most common but any pattern of restricted ocular motility may be found. Diplopia is characteristically experienced.

3. Nystagmus – typically encountered in both the horizontal and vertical planes.
4. Ataxia- has both trunkal and gait ataxic with occasionally trunkal titubation.

The clinical course is dramatically altered by administration of thiamine (14-15). Within hour of the parenteral thiamine 50 mg, the ophthalmoplegia improves and ocular palsies generally disappear within few days but nystagmus may persist. Trunkal ataxia recovers slowly. Patients are maintained on 50-100 mg of thiamine three times a day for several weeks. The disease can be fatal in 10-20 % cases. The pathology is mainly seen involving brain stem and hypothalamus. Lesions are seen in mamillary bodies, medial dorsal nucleus of thalamus in the periaqueductal gray matter and mesencephalon and in the superior cerebellar vermis. The characteristic lesion is subtotal tissue necrosis and hemorrhage in few involving neurons, axons and myelin to variable degrees.

Korsakoff's syndrome: This is a chronic form of Wernicke-Korsakoff syndrome and is characterized primarily by an amnesic dementia. The core of the defect appears to be an impairment of the ability to acquire new information. The patient tends to confabulate. The outlook for patients with established syndrome is discouraging. However, thiamine administration 50 mg three to four times a day is advised and in few cases though initial improvement may not be seen but over a period of months few show remarkably complete functional recovery. The neuropathological changes are identical to Wernicke's encephalopathy with only noteworthy change being chronic form of glial reaction.

Niacin: Deficiency of niacin causes pellagra seen predominantly in India and South Africa. In its fully developed clinical form, pellagra comprises a host of symptoms referable to the gastrointestinal tract (diarrhoea, anorexia, nausea and vomiting), skin and nervous system. Both central and peripheral nervous systems may be affected.

Central nervous system involvement includes irritability to frank dementia. Occasionally extra pyramidal or

cerebellar features are noted. Niacin deficiency can cause polyneuropathy which has mixed sensory motor involvement. Although it is widely held that the above features are due to niacin deficiency, the neurological changes are remarkably resistant to high dose of niacin even parentally. Associated deficiency of other vitamins like thiamine, vit B12 and pyridoxine may be important.

Pyridoxine (Vitamin B6): Neurological disorder reflecting both pyridoxine deficiency and excess has been recognized. During infancy pyridoxine deficiency results in seizure, excessive irritability, tremulousness and poor psychomotor development.

Deficiency of dietary pyridoxine causes a mixed distal symmetric polyneuropathy. The lack of pyridoxal phosphate as a coenzyme is responsible for neuropathy. Although the minimum daily requirement is only 2 mg, 50 mg or more may be required for successful therapy of deficiency state daily for one week then once a week for 4 weeks and then monthly.

Vitamin B12: Poor dietary intake of vitamin B12 as in malnutrition, extreme vegetarian, fish tapeworm infestation in addition to various other causes may lead

to serious disease involving both central and peripheral nervous systems.

The most widely recognized neurological disorder resulting from vitamin B12 deficiency is subacute combined degeneration of the spinal cord. Clinically presents as tingling paresthesias of the feet subsequently associated with weakness and stiffness of the legs and a spastic gait. It is an important cause for upgoing planters and sluggish or absent ankle reflex. It can present as pure axonal polyneuropathy (16) or pure myelopathy. Occasionally primary optic atrophy may be seen. A variety of mental changes may also be seen ranging from depression to paranoid states and most important progressive dementia.

On MRI, an increased T2-weighted signal, decreased T2-weighted signal and contrast enhancement of the posterior and lateral columns of the spinal cord may be found in the cervical cord (17). Electrophysiological studies done to confirm polyneuropathy show mixed demyelization and axonal neuropathy. Treatment should be early and aggressive. 1,000 mg of cyanocobalamin intramuscularly daily for 1 week and then once a week for 4 weeks, followed by monthly injection.

Folic Acid: Reduced serum folate levels

have long been recognized in patients with subacute combined degeneration of spinal cord. Reversible depression and cognitive decline have frequently been reported in individuals with folate deficiency

Vitamin A (Retinol): A deficiency of vitamin A is remarkably common in many parts of the world, such as southeast Asia, Africa and the Middle-East where extreme poverty and nutritional depletion are endemic (18). Hypovitaminosis A leads most importantly to a variety of ophthalmic disorders, grouped under the rubric xerophthalmia. Early manifestation include night blindness, followed by conjunctival xerosis, Bitot's spots, corneal xerosis and keratomalacia. Hyperkeratosis and growth retardation is noted. Hypovitaminosis A can cause intracranial hypertension similar to hypervitaminosis A.

Vitamin A deficiency should be treated urgently. 200, 000 IU of retinol palmitate orally on two successive days which will reverse the clinical features.

Vitamin D: Deficiency of vitamin D causes rickets in children and osteomalacia in adults. Both rickets and osteomalacia are frequently reported in India. A deficiency in vitamin D has been held responsible, in part for the

weakness, fatiguability and muscular atrophy due to hyperparathyroidism and renal tubular acidosis. Muscle weakness and tetany is seen secondary to hypocalcaemia. Minor myopathic features may be noted histologically.

Vitamin E: There has been growing awareness of the role of acquired vitamin E deficiency in neurological dysfunction (19, 20). A deficiency of vitamin E results in a remarkable constellation of abnormalities referable to both central and peripheral nervous system (21). Features of both spinocerebellar degeneration and polyneuropathy had been noted. In few cases seizures have been recorded. A lack of tocopherol has been demonstrated in peripheral nerves

in vitamin E deficient patients.

Variable improvement in the clinical and electrophysiological parameter were seen after the administration of oral or preferably parenterally (50-100 mg weekly) for several months to years, but may not necessarily reverse the clinical symptomatology (22).

Other Vitamins

Pantothenic acid deficiency is a rare case of predominant sensory neuropathy. Deficiency of biotin can cause dementia, seizures and ataxia.

Trace element deficiency causes various neurological dysfunctions as shown in the Table 1.

Table 1 : Neurological and other manifestation of trace element

Element Deficient	Clinical Features
Iron	Anaemia, poor brain development
Zinc	Microcephaly, psychological disturbance, encephalopathy, congenital malformation
Copper	Anaemia, growth failure, mental deterioration
Cobalt	Features similar to vitamin B12 deficiency
Selenium	Myopathy
Iodine	Cretinism, developmental delay, deaf mutism
Magnesium	Myopathy

Nutritional Recovery Syndrome

During recovery of PEM mainly kwashiorkor following nutritional supplementation, the child develop coarse tremors, myoclonus, bradykinesia, rigidity, trunkal ataxia and up gaze palsy which are self limiting.

Deficiency Disorder of Unknown Origin

Infantile tremor syndrome

This is seen in north, central and north east India usually during Feb to July. This syndrome is exclusively of breast fed children between 6 to 24 months in poor socioeconomic population. Abrupt onset tremors and trunkal dystonia along with mental and physical retardation, pallor, hair and skin pigmentation are noted. This is self limiting entity.

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