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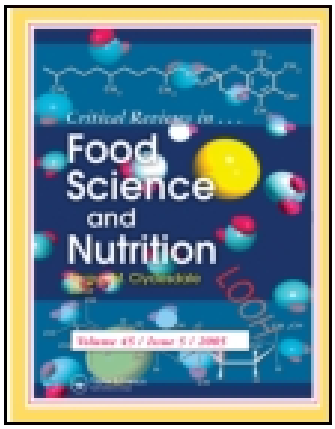

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Protein-Energy Malnutrition: A Risk Factor for Various Ailments

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Protein–Energy Malnutrition: A Risk Factor for Various Ailments

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The wheel of industrialization that spun throughout the last century resulted in urbanization coupled with modifications in lifestyles and dietary habits. However, the communities living in developing economies are facing many problems related to their diet and health. Amongst, the prevalence of nutritional problems especially protein–energy malnutrition (PEM) and micronutrients deficiencies are the rising issues. Moreover, the immunity or susceptibility to infect-parasitic diseases is also directly linked with the nutritional status of the host. Likewise, disease-related malnutrition that includes an inflammatory component is commonly observed in clinical practice thus affecting the quality of life. The PEM is treatable but early detection is a key for its appropriate management. However, controlling the menace of PEM requires an aggressive partnership between the physician and the dietitian. This review mainly attempts to describe the pathophysiology, prevalence and consequences of PEM and aims to highlight the importance of this clinical syndrome and the recent growth in our understanding of the processes behind its development. Some management strategies/remedies to overcome PEM are also the limelight of the article. In the nutshell, early recognition, prompt management, and robust follow up are critical for best outcomes in preventing and treating PEM.

Keywords Protein–energy malnutrition, innovations, developing countries, ailments, remedies

BACKGROUND AND INTRODUCTION

The World Health Organization defines malnutrition as "the cellular disparity amid the supply of energy, nutrients, and the body's demand for them to ascertain maintenance, growth, and specific functions" (Anstead et al., 2001; Dean et al., 2003). For millennia, malnutrition has been reasoned due to a shortage of food. Malnutrition is the condition produced by the intake of a few macronutrients (protein energy under nutrition, vitamin, and mineral deficiency), too many macronutrients (obesity), or inordinate amounts of substances such as alcohol (Pinstrup-Andersen et al., 1993; Brabin and Coulter, 2003).

Malnutrition is associated with both structural and functional pathology of the brain. Structurally malnutrition results in growth retardation, reduction in synapses, disorderly differentiation, tissue damage, delayed myelination, synaptic neurotransmitters, and reduced overall development of dendritic arborization of the developing brain. There are deviations in the temporal sequences of brain maturation, which in turn disturb the formation of neuronal circuits (Muhimbula and Issa-Zacharia, 2010). Long-term alterations in brain function have been reported linked to extend cognitive impairments associated with malnutrition (Kalanda et al., 2006; Dahl and Yamada, 2008).

The axiom protein–energy malnutrition (PEM) pertains to a group of allied disorders that includes kwashiorkor, marasmus, and intermediate states of kwashiorkor-marasmus (Niiya et al., 2007; Tizazu et al., 2009). In 1959, Jelliffe introduced the term "protein calorie malnutrition" which has largely been replaced by "PEM." Patients with PEM are at a higher risk for problems akin to hypoglycemia, hypothermia, serious infection, and electrolyte disturbances. PEM results in premature birth, interrupted breastfeeding, mental disorder, vomiting, infectious tuberculosis, and parasitic diseases for instance; measles, malaria, diarrhea, and whopping cough (De-Mutsert et al., 2008). The term "marasmus" is inferred from the Greek word *marasmus*, correlating wasting or withering. Marasmus involves inadequate intake of protein and calories and is typified by emaciation. Kwashiorkor is taken from the Kwa language of Ghana and entails "the sickness of the weaning." Williams first used the term in 1933, and it adverts to an inadequate protein intake with sane caloric (energy) intake. Edema is distinguishing phase of kwashiorkor that does not exist in marasmus (Dicko et al., 2006). Kwashiorkor represents a maladaptive response to

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starvation while marasmus demonstrates an adaptive response to starvation (Stoltzfus et al., 2004). For the reason, Jelliffe suggested the term protein calorie (energy) malnutrition to include both entities. Patients with PEM may have deficiencies of essential fatty acids, vitamins, and trace elements, all of which may contribute to their dermatosis (Black, 2003).

No clear distinction has yet been made between growth failure (marasmus and under nutrition) and oedematous malnutrition (kwashiorkor and marasmic kwashiorkor) in terms of pathology and clinical conditions. PEM, a consequence of various factors, reasoned to inadequate intake of nutrients, abnormal gastrointestinal assimilation of the diet, and stress response to acute injury or chronic inflammation. Although PEM affects virtually every organ system, but this article primarily rivets on its cutaneous manifestations. PEM is more prone to parasitic infections as it diminishes the immune response to infections. It is associated with various degrees of intestinal malabsorption (Ambrus and Ambrus, 2004; Malafaia, 2009). It is allied with villous atrophy of the jejunal mucosa (Machado-Coelho et al., 2005; Holzmuller et al., 2006) and this may impair drug absorption (Al-Mekhlafi et al., 2011). In Pakistan, 50% infant and child deaths are related to malnutrition. 59.5% of the preschool children are suffering from PEM and only 40.5% of them are above 90% of the standard weight for their age (GOP, 1988, 2010).

MALNUTRITION AND HEALTH STATUS IN DEVELOPING COUNTRIES

Owing to malnutrition, about 13 million infants and children die each year in the developing countries (Briassoulis et al., 2001). About half of the South Asian children are underweight or stunted and malnutrition contributes to an estimated 55% deaths in children (Briassolis et al., 2001). South Asia (India, Bangladesh, and Pakistan) is home to merely 29% of the emerging world's under-five population; restrain 50% of the world's underweight children (Berkman et al., 2002). To an estimate, it has been documented that underweight children in developing world accounts for around 146 million under age of five children. Majority of these deaths are mainly attributed to parasitic and infectious diseases. According to UNICEF estimate, over 220 million children under age five have significantly impaired growth (Savino, 2002). There is convincing evidence that impaired growth is associated with delayed mental development, poor school performance, and reduced intellectual capacity (Getaneh et al., 1998). Malnutrition as an immediate cause of death is not precisely known in poor countries children from birth or soon after is caught in a cycle of infection and malnutrition, and many of them unable to resist (Xavier et al., 2007). Likewise, in Africa, for instance, more than 20% on average do not reach their fifth birthday (Mahgoub et al., 2006).

Malnutrition, with its two constituents of PEM and micronutrient deficiencies, continues to be a major health risk in developing countries. It is globally the most important risk factor for illness and death, with millions of pregnant women and young children particularly affected. Apart from marasmus and kwashiorkor (the two forms of PEM), deficiencies in iron, iodine, vitamin A, and zinc are the other forms of malnutrition. Worldwide, an estimated 852 million people were undernourished in 2000–2002, with most (815 million) living in developing countries (FAO, 2005). China had major reductions in its number of cases of PEM during this period. However, this was balanced by a corresponding increase in the rest of the developing world (FAO, 2005).

In developing countries, a high prevalence of poor diet and infectious disease regularly unites into a vicious circle. Although treatment protocols for severe malnutrition have in recent years become more efficient. Most patients (especially in rural areas) have little or no access to formal health services and are never seen in such settings. Interventions to prevent PEM range from promoting breast-feeding to food supplementation schemes. To be effective, all such interventions require accompanying nutrition-education campaigns and health interventions. To attain the goals pertaining to hunger and malnutrition as mentioned in Millennium Development Goals, we need to address poverty, which is clearly associated with the insecure supply of food and nutrition.

In children, PEM is defined by measurements that fall below 2 standard deviations under the normal weight for age (underweight), height for age (stunting), and weight for height (wasting) (Pinstrup-Andersen et al., 1993). Anthropometric measures such as height, weight, skin fold thickness, and arm circumference with reference to age are considered as important indicators of PEM (Jones, 2004). Muscle harbors a unique functional protein pool that can be clinically measured as an index of overall PEM severity, regardless of the underlying cause of negative energy balance. These measures are closely linked with the fulfillment of basic needs and standard of living of individuals. Thus, these measures not only help in evaluating the health and nutritional status but also provide an indirect measure of the quality of life. Wasting indicates recent weight loss, whereas stunting usually results from chronic weight loss (Bloss et al., 2004). Of all children under the age of 5 years in developing countries, about 31% are underweight, 38% have stunted growth and 9% show wasting (Müller and Krawinkel, 2005). PEM usually manifests early, in children between 6 months and 2 years of age and is associated with early weaning, detained introduction of complementary foods, a low-protein diet and severe or frequent infections (Pelletier et al., 1995; Waterlow, 1996; Kwena et al., 2003; Ahmed et al., 2009) (see Tables 1 and 2).

PROTEIN–ENERGY MALNUTRITION AND CHILDHOOD

PEM is amongst the most serious nutritional discrepancies in infants and young children. It contributes to more than 50% of childhood mortality in developing countries (Walker et al.,

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1990). PEM is responsible, either directly or indirectly, for 54% of the 10.8 million deaths per year in children under 5 and contributes to 53% of deaths associated with infectious diseases in children belonging to this age group in developing countries (Brundtland, 2000).

The prime risk factors of PEM have been diagnosed as ignorance, family size, residence, lack of means to buy food, poor maternal education, poverty, negligence of food, cultural and religious food customs, lack of quality healthcare, inadequate breast feeding, malformations or congenital defects, chronic infections, gender of the child, and incomplete immunization (Nova et al., 2002). Malnutrition affects physical growth, mortality, reproduction, morbidity, cognitive development, and physical work capacity (Mamiro et al., 2005). Malnutrition and infectious ailments are the most widespread troubles affecting infants and young children in economic countries (Ouedraogo et al., 2008). The wallop of intestinal parasitic infections on nutrition, growth and development of children has been studied since the seventies (Terstappen et al., 1990; Kuvibidila et al., 1993). Most of the encouraging evidence relating to parasitic infections and malnutrition demonstrate improvement in children growth after antihelminthic treatment (Dunki-Jacobs et al., 2009).

Breast milk is a sole and sufficient source of nutrition during the first 6 months of infant life. Breast milk encloses all the nutrients and immunological factors that infants require to sustain optimal health and growth (Mariam 2005). Towards the middle of the first year, breast milk becomes insufficient to support growing infants (Mamiro et al., 2005). Therefore, nutritious complementary foods need to be introduced. Inadequate supplementary feeding of infants is an essential factor in the high incidence of child malnutrition (Yewelsew et al., 2006). Infant malnutrition is owing to low energy and nutrient density that might be due to high viscosity or undesirable sensory properties of complementary foods (Thaoge et al., 2003; Kikafunda et al., 2006).

Children with PEM are deficient of total protein and in severe cases the total protein may be reduced to around 50%. The reductions of total serum protein and albumin were more marked in kwashiorkor than in marasmus. In the acute phase of PEM, serum insulin levels are depressed and growth hormone (GH) elevated among kwashiorkor children (Ferdous et al., 2009). GH values are also elevated in the marasmic children but the levels were much lower than those for the kwashiorkor children. While the GH concentration fell gradually, the insulin rose especially among the kwashiorkor children after nutritional rehabilitation (Chowdhury et al., 2008). The adrenal glands of PEM children are atrophic at autopsy but plasma cortisol concentrations were elevated and response to corticotrophin challenge was unaffected (OWOR et al., 2000).

Children with severe PEM have a smaller and thinner heart and a lower stroke volume (Mamoun et al., 2005). The inability of the kidneys to adequately excrete surplus fluid and sodium in kwashiorkor-marasmic and kwashiorkor also unfavorably affects the heart. Thus, the circulation is overloaded more easily than usual. The cell membranes of the heart become leaky because of oxidative damage (Caulfield et al., 2004). The number of Na-K pumps in the cell membrane is reduced so as to conserve energy and the remaining pumps work more slowly. Thus intracellular sodium accumulation and potassium leakages occur, leading to electrolyte and fluid imbalance (Kossmann et al., 2000). Children with PEM have most often urine devoid of glucose, protein, and formed elements such as casts, epithelial cells, and red blood cells. Their blood urea nitrogen and creatinine are normal, indicating that children with PEM do not have an established renal failure (De-Mutsert et al., 2008).

Protein deficiency and lack of immune mediators is responsible for immunologic deficiency in the humoral and cellular subsystem, which predisposes a child with PEM to infections (Yoshino et al., 2006). In addition, urinary and gastrointestinal tracts infections, as well as septicemia may complicate PEM (Fouque et al., 2008). Many of these infections are due to Gram positive and Gram negative organisms and are usually implicated in patients with severe PEM (Qureshi et al., 2002).

Hypoproteinaemia is a common feature of PEM (Kovesdy et al., 2009). In this plasma albumin and fractions of the glycoprotein responsible for binding drugs are decreased (Keith et al., 2004). As a result of this decreased protein binding there may be a substantial increase in the plasma free-drug fractions of highly protein-bound drugs and children with PEM may experience variations in their response to drug treatment or be at risk of increased drug toxicity (Muntner et al., 2005). However, in clinical practice, the decreased plasma protein has not been reported to significantly increase the plasma free-drug fractions in children with PEM.

PROTEIN–ENERGY MALNUTRITION AND OLDER AGES

Malnutrition can adversely influence the well-being of older persons, causing a slump in functional status, induction of bedsores, reduced immune function, and worsening of existing medical problems (Millward and Jackson, 2004). Among community-dwelling elderly, a relation between dietary quality and dependency in activities of daily living has been shown. In hospitalized patients, a decipherable correlation has been shown between the parameters reflecting poor nutrition in-hospital complications, readmissions, and mortality (Stoltzfus et al., 2004).

PEM occurs in about 50% of hospitalized old people. With ageing, especially when associated with PEM, the ability to respond successfully to an inadequate diet or other stressful conditions is reduced. Both qualitative and quantitative changes in circulating amino acid concentrations have been reported in PEM. Factors affecting the concentration and the pattern of plasma amino acids include the amount and composition of dietary protein, muscle protein metabolism, and the labile protein reserves in various tissues, particularly in the liver. In old

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patients, PEM has two main causes, i.e., a decrease in nutrient intake and an increase in catabolic reactions, i.e., a hypermetabolic state). Both these conditions may be present at the same time or may occur successively in a short time as consequences of multiple pathologies (Raja et al., 2004).

Patients with PEM showed low concentrations of ornithine, histidine, glutamine, and glutamic acid (which have intricate pathways), urea cycle amino acids and alanine. The decrease in plasma alanine concentration (33%) may be because of alanine, a transamination product of pyruvate, which is released by muscle before being processed by the liver into gluconeogenesis. This suggests that in elderly patients with PEM, decreases in urea cycle amino acids are of prime importance. Arginine is the precursor of urea and an important factor in albumin synthesis. This relationship between urea cycle amino acids and albumin synthesis may explain the positive correlation found between urea cycle amino acids and albumin concentrations in elderly patients with PEM. It is suggested that phenylalanine hydroxylase activity is reduced in PEM, resulting in decrease in plasma tyrosine relative to plasma phenylalanine. These amino acids are involved in brain neurotransmitter systems, including the synthesis of dopamine, adrenaline, and nor-adrenaline (Raja et al., 2004).

Renal insufficiency is common in older adults (Lee et al., 1993). In non institutionalized adults of 60 years age and over, renal insufficiency was strongly associated with malnutrition. In end-stage renal disease, the prevalence of PEM is high (16–54%), and its presence is a predictor of morbidity (impaired wound healing, susceptibility to infection, fatigue, and poor rehabilitation) and mortality (Raja et al., 2004). Cross-sectional studies in tertiary-care patients with renal insufficiency have documented lower levels of calorie and protein intake in patients with lower glomerular filtration rate (Nordenram et al., 2001), (see Table 3).

PEM AND RELATED AILMENTS

Kwashiorkor

Kwashiorkor is a form of PEM caused by the inadequate intake of protein with reasonable caloric (energy) intake. Kwashiorkor is the most common and far-flung nutritional disorder in developing countries. Kwashiorkor was first reported in children with maize diets and implied that a deficiency of protein was its major cause, even when the energy input was adequate. It mostly occurs in areas of famine or with limited food supply, and particularly in those countries where the diet consists mainly of corn, rice and beans (Edhborg et al., 2000). It is more common in children as compared to adults. The onset in infancy during the weaning or postweaning period is due to insufficient protein intake. Early signs and symptoms of kwashiorkor include fatigue, irritability, and lethargy. As protein deprivation continues the following abnormalities become apparent involving failure to thrive (failure to put on height and weight), loss of muscle mass, generalized swelling (edema), large protuberant belly (pot belly), and fatty liver (Galler et al., 2006).

Physical examination of patients might show an enlarged liver and generalized swelling (edema). Laboratory tests usually show the significant findings in kwashiorkor, i.e., low blood sugar and protein levels, high levels of cortisol and GH, low levels of salts in the blood (especially potassium and magnesium), reduced levels of the waste product urea in urine, iron-deficiency anemia, metabolic acidosis (low pH of blood) (Rahman et al., 2004), reduced hydroxyproline in the urine, reflecting poor growth, and defective wound healing. Other tests include detailed dietary history, growth measurements, body mass index, and complete physical examination. Skin biopsy and hair-pull analysis may also be performed (Anoop et al., 2004).

Treatment should start with correcting fluid and electrolyte imbalances. Any infections should also be treated appropriately. Once the patient is stabilized, usually within 48 h, small amounts of food should be introduced. Food must be reintroduced slowly, carbohydrates first to provide energy, followed by protein foods. Vitamin and mineral supplements may also be given. The reintroduction of food may take over a week by which time the intake rates should approach 175 kcal/kg and 4 g/kg of protein for children and 60 kcal/kg and 2 g/kg of protein for adults (Paulson et al., 2006). The outlook for patients with kwashiorkor is dependent on the stage of the disease at the time it is first treated. Treatment given early in the course of the disease generally produces a good recovery, although growth potential will never be achieved in children who have had kwashiorkor. Treatment in the later stages of the disease generally improves the patient's health but physical and intellectual disabilities are usually irreversible. The disease can be fatal if it is not treated or when treatment is given too late in the course of the condition (Patel et al., 2002).

Marasmus

Marasmus is a chronic disorder that develops over a period of months to years and is caused by an inadequate energy intake (Figure 10.21). It occurs in epidemics due to famine and is endemic in many areas of Africa, Asia and South America, and in patients with long-term illnesses, such as chronic pulmonary disease and anorexia nervosa. Children with marasmus fail to thrive, are emaciated and lack subcutaneous fat. Cachexia, muscle wastage associated with some chronic infections, such as tuberculosis or the severe and prolonged weight loss seen in some cancers (Tomlinson et al., 2005) produces similar clinical features to marasmus but the etiologies are different.

There has been growing evidence showing that malnutrition (e.g., dietary deficiency of protein, selenium, or zinc) gives rise to oxidant stress and cell injury (Smith and Lawrence, 2000). Marasmic children had increased lipid peroxidation and decreased antioxidant enzyme activities and leptin (Lesourd et al., 1995). Marasmic children have an increased oxidative stress and decreased antioxidant defense mechanism compared with

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healthy controls. Increased oxidative stress may result from some deleterious effects of deficient caloric and micronutrient intake. However, lower concentrations of the antioxidants, β carotene, glutathione, and vitamin E are observed in children suffering from kwashiorkor than in those affected by marasmus, both of course have reduced levels compared with healthy children (Henderson and Wachs, 2007; Astor et al., 2008).

Leptin, the Ob gene protein, is an adipocyte-secreted hormone plays a key role in energy homeostasis of the body by controlling food intake. Leptin concentrations correlate with the amount of fat mass, with higher levels in more obese people. The decrease in leptin after energy restriction is a starvation signal to the brain (Schneider and Hebuterne, 2000), which probably has a protective effect. Serum leptin levels are low in patients suffering from PEM (Nishizawa et al., 2003). There is a positive significant correlation between leptin and malondialdehyde (a lipid peroxidation by product) and negative correlations between leptin and antioxidants. Therefore, there is a possible relationship between leptin and oxidation processes in a clinical example of children with nephrotic syndrome (Kilpatrick et al., 2007). In studies related to childhood malnutrition, generally very low leptin levels (Wanner et al., 2005) and increased oxidant stress have been reported (deFilippi et al., 2003).

INFECTIOUS DISORDERS AND IGF-1

The "malnutrition-infection" intimately remains the most prevalent public health problem in the world today. Nutrition and health are linked together but nutritional knowledge remains to be applied to the same extent as those in the field of health. Although understanding of protein energy and micronutrient deficiencies is now well advanced; however, preventing these deficiencies appears still to be problematic. PEM is related to poverty and long-term progress is linked to development, although in the interim effective programmes can be undertaken. Although globally the proportion of people undernourished fell somewhat during the 1970s, probably less so during the 1980s – and actually increased in Africa. The total numbers of people undernourished continue to rise with population growth (Habib, 2008). Along with this, the total numbers of children underweight due to malnutrition and infection are still increasing (Jitta et al., 1992) as described in earlier section of the article.

Insulin-like growth factor-I (IGF-I) is single-chain peptides of 7.5 kilo Daltons (kDas). Its structure is similar to the IGF-II and proinsulin (Daughaday and Rotwein 1989; Humbel, 1990). The liver is believed to be the main source of production of IGF-I, but the highest concentrations of IGF-I are observed in blood (Furlanetto et al., 1977; Thissen et al., 1994). Many factors intervene in the regulation of the IGF-I but the most important are GH, insulin, and nutritional status (Thissen et al., 1994). Nutritional status plays an important role in the regulation of the IGF-I. Adequate food intake is essential for maintaining normal IGF-I and IGFBP-3 circulating rates in the serum (Clemmons et al., 1981; Isley et al., 1984). Indeed, energy and protein restrictions in children lead to a decrease of circulating IGF-I and IGFBP-3 rates (Smith et al., 1995). Low IGF-I values were observed in hospital children suffering from PEM (Zamboni et al., 1996; Bhutta et al., 1999). But values were lower in children suffering from marasmus than in children suffering from kwashiorkor; this suggests that the secretion of IGF-I is closely related to energy consumption than to protein consumption (Zamboni et al., 1996). Smith et al. (1995) observed that the caloric restriction induced a reduction in IGF-I and IGFBP-3 in adults and children. After nutritional rehabilitation, an increase was achieved, but without reaching the initial rates.

The ability of IGF-I to follow variations of nutritional status shows that it is potentially a good clinical marker to follow nutritional rehabilitation in children with PEM. The prognostic interest of IGF-I remains to be demonstrated by the implementation of studies which will measure the impact of IGF-I on the mortality of children with malnutrition in comparison with other markers of nutrition like albumin, pre albumin, and RBP. If the prognostic interest of IGF-I were proved, the use of IGF-I will be recommended. (Kouanda et al., 2009).

BIOCHEMICAL DISTURBANCES IN THE BODY

The study of the electrical cerebral activity is important because it exerts control over a variety of developmental processes, such as: neuronal differentiation, migration, synaptogenesis, neurotransmitter specification, and synaptic plasticity (Weiner et al., 2007). Considering these facts, it is important to study the influence of the nutritional status during development on the electrical cerebral activity in different stages of life. Study of lymphocyte subpopulations in bone marrow in a model of PEM (Panichi et al., 1998).

PEM is known to be associated with many biochemical disturbances in the body. Enzymes being proteins, disturbances in their functions and levels in the body are expected to occur in PEM of any severity (Contreras et al., 2010). Thus enzymes measurement can provide the physician with valuable diagnostic and prognostic clinical evidence.

Menon et al. (2005) found that 20–70% cases of PEM serum ALT and AST level were raised. They suggested that the exaggerated tissue breakdown in PEM is associated with conversion of most pyruvate into alanine by transamination in order to transport ammonia out of tissue breakdown. The increase in levels of serum ALT and AST were maximum in Grade I PEM (Mian et al., 2002). This probably indicates maximum tissue breakdown in early stages of PEM. But present study shows that all grades of PEM are associated with alteration in levels of serum ALT and AST. The enzyme levels both ALT and AST are higher than control. This reflects an effort on the part of the body to maintain homeostasis through protein synthesis from tissue breakdown and amino acid metabolism (Abdalla et al., 2009).

The comparatively smaller increase in activities of serum ALT and AST in case of PEM may be related to the decrease

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Table 1 Different classification of protein–energy malnutrition

Gomez classification of PEM	
Degree of PEM	Percentage of desired body weight for age and sex
Normal	90–100
Grade-I mild malnutrition	75–89
Grade-II moderate malnutrition	60–74
Grade-III severe malnutrition	<60

of liver cell mass and possibly also to low concentration of liver cell enzymes (Hamid et al., 2008). In liver disease, level of ALT usually exceeds as that of AST activity (Borelli1 et al., 2007). But in PEM it is seen that level of AST has exceeded the ALT activity. Therefore, in absence of clinical liver disorder, the increased serum AST and ALT in this study is possibly due to tissue breakdown. It can be concluded that serum enzymes (ALT, AST, and ALP) changed in PEM and these varied according to severity. These results may help physician in early detection of PEM before the clinical features are manifested and it may also help to detect the severity. A definite range of different enzyme levels may be defined as a supportive tool to detect different grades of PEM, mainly mild and moderate PEM, which form the major bulk of the problem.

The pathogenesis of edema and anemia commonly found in children with PEM has been suggested to be caused by an imbalance between the production of toxic radicals and their safe disposal. Protein malnutrition produces alterations in bone marrow that lead to cellular depletion. This, in turn, results in anemia with significant reticulocyte reduction and leucopenia. The weaker leukocyte response to bacterial infections in PEM is due to a reduction in the reserve compartment of the bone marrow. PEM decreased the number of rosette forming T lymphocytes, of T4 positive cells and their ability to provide help to B cells in antibody synthesis. There was a reduction in serum thymic hormone activity and an elevation of leucocyte terminal transferase and plasma cortisol levels. The numerical and functional deficiency of T4+ helper cells may be important in the pathogenesis of some of the clinical and immunological manifestations of PEM (Chandra, 1983).

PEM is one of the main causes of immunodepression (Keusch, 2003), modifying both the adaptive and innate immune system, as well as impairing hemopoiesis by altering T-dependent areas of the lymphoid tissue (Borelli et al., 1995), decreasing phagocytosis (De-la-Fuente and Munoz, 1992), hindering respiratory burst, reducing nitric oxide availability (Fock et al., 2003), and downregulating proinflammatory cytokine production (Fock et al., 2007). It also reduces the number of granulo-monocytic colony forming units (Vaisman et al., 1996) thus leading to DNA damage (Cortes et al., 2001) and to cytogenetic alterations (Olmos et al., 2001).

Table 2 Problem prevalence of children under 5

Population group/problem prevalence (%)	Population group/problem prevalence (%)
Protein energy malnutrition	
Children under 5	
Underweight	42
Stunted	31
Wasted	12
Women	
Women taking calories less than RDA (%)	50

(National Nutrition Survey 2001–2002).

The risk of anastomotic leakage is higher in the colon and rectum than in other sites of the gastrointestinal system, and is associated with the large microorganisms and increased enzyme activity of collagenase (Martens and Hendriks, 1992). It occurs in around 3.4–6% in the colon, increasing to 15% in the rectum. Mortality after anastomotic leakage ranges from 6% to 39.3% (Koruth et al., 1985). Various systemic and local factors such as surgical technique, oxygenation of the anastomotic site, presence of intra-abdominal infection and diabetes mellitus may play a role in the healing of colon anastomoses (Thornton and Barbul, 1997). Malnutrition is one of the most important factors impeding the proper healing of the anastomosis (Ward et al., 1982; Meguid et al., 1986; Law and Ellis, 1990; Kiyama et al., 1999). While long-term PEM leads to impaired wound healing, patients who have lost 30% of their body weights are at greater risk of severe anastomotic complications (Law and Ellis, 1990).

FACTORS EFFECTING PROTEIN–ENERGY MALNUTRITION

PEM is a prevalent problem in older persons. Its relation to increased morbidity and mortality has been well documented. Early recognition of malnutrition allows for a timely intervention. A large proportion of chronic diseases affecting older persons can be either precluded or significantly ameliorated by improving nutrition, which underscores the importance of developing a screening system that can trigger a more comprehensive evaluation when indicated. Screening for malnutrition in older persons can be intricate because of the normal age-related changes in many of the commonly used parameters. A comprehensive nutritional evaluation includes a complete history and physical examination in addition to a more specific nutrition-oriented assessment. Specific nutritional assessment includes estimating food intake, anthropometric measurements, and evaluation of several biochemical parameters commonly affected by changes in nutritional status. In this article, we review the commonly used tools for nutritional assessment in older persons. The goal is to promote disease-free, active, and successful aging (Omran et al., 2000).

Aflatoxins (AFs) are secondary metabolites of fungi *Apergillus flavus* and *Aspergillus parasiticus* and assumed as common contaminants of foodstuff, particularly in the tropical regions (Himmelfarb et al., 2002; Kopple et al., 2002). AF B1 detected in the urine of malnourished children and there seemed to be a link between malnutrition and the presence of AFB_1. Furthermore, it has been suggested that AF reduces the

Table 3 Protein and energy requirement per capita

	1949–50	1979–80	1989–90	1999–00	2003–04	2005–06	2006–07	2007–08	2008–09 (E)	2009–10 (T)
Calories per day	2078	2301	2324	2416	2381	2386	2349	2470	2456	2441
Protein per day	62.8	61.5	67.4	67.5	67.8	69.5	69.0	72	72.5	72.9

(GOP, 2010).

nutritional capacity of food by interfering with metabolic processes (Graham et al., 2006). As a consequence of the known effect of AF on protein synthesis, AF in body fluids of children could be a modulating factor on the rate of recovery from protein malnutrition, although it has not been shown to be responsible for the development of the condition.

Although causes of malnutrition are multifactorial, helminthes infections also have been associated with impaired growth (Stephenson, 1993; Stolzfus et al., 1997) and stunting (Casapía et al., 2006). The most important parasites related to malnutrition are intestinal parasites, especially soil-transmitted helminthes and *Giardia duodenalis*, followed by other parasites such as the coccidian, *Schistosomia sp.*, and malarial parasites. Intestinal parasitic infections, especially severe trichuriasis and giardiasis, were identified as the main predictors of stunting and wasting, respectively (Berkman et al., 2002; Kwena et al., 2003). Even mild to moderate intensity helminthes infections during childhood have been associated with undernutrition and reduced physical fitness (Wilson et al., 1999; Ezeamama et al., 2005). There are several mechanisms by which intestinal parasitism may cause or aggravate malnutrition including impaired nutrient absorption and reduced appetite (Mata et al., 1977; Crompton and Nesheim, 2002). Adult helminthes worms residing in the small intestine also interfere with their hosts, nutrition, and can induce damage to the intestinal mucosa thus reducing the bioavailability of nutrients. Some other health problems arising due to helminthes infections like vomiting, diarrhea, anorexia, abdominal pain, and nausea are also correlated with reduced food intake (Stephenson, 1993; Stephenson et al., 2000).

REMEDIES

Protein from meat and meat products are more concentrated than plant sources thus the communities belonging to below line of poverty are unable to meet protein requirements or eat quality/balanced protein. There is a dire need to improve the status of the protein intake of the whole community through crop breeding selection of high yield and also to explore unconventional food sources to cope these challenges (Khalil, 2007). Following are the suggestion for overcoming the PEM.

Quality and quantity of protein consumed in diet could possibly be improved by incorporating unconventional food sources in the dietary modulations, especially in wheat (Anjum et al., 2005). In this context, exploration of unconventional foods especially rich in protein contents are main focusing tools to overcome malnutrition and related health gap in developing countries (Müller and Krawinkel, 2005; Becker, 2007). Some unconventional sources like oil seeds cake or defatted fractions can be efficiently used as a potent food or protein source to enrich the protein deficient foods. Legumes are one of the cheapest sources of proteins with good nutritional and protein quality. Wild legumes are also analyzed to evaluate their potential as protein substitute (Arshad et al., 2007).

Cereals are the staple food in many parts of the world and more than 60% of the total daily requirement of protein and calories of people are met through wheat especially in Pakistan (Butt et al., 2004). The crude protein in the wheat is 13.95% while lysine contents are in the rage of 2.67%. Data indicated that lysine is the primary limiting amino acid with a deficit of 50–75%. Because of low levels of lysine and tryptophan, the protein quality of cereals is relatively poor that demand blending of protein rich sources various crops for a nutritional point of view (Onwulata and Constance, 2006). Composite flour or blends technology especially mixing of wheat flour with other cereals or legumes is also one of the ways to overcomes there threats (Rehman et al., 2007). In many cases, this implies the partial substitution of wheat flour with others referred as diversifying as well as upgrading the indigenous agricultural food products.

Honey is composed primarily of the sugars glucose and fructose; its third greatest component is water. It contains numerous other types of sugars, as well as acids, proteins, and minerals (Ferdous et al., 2009) with a lot of benefits for nutrition and health (Visvanathan et al., 2004). Patients with PEM have delayed gastric emptying time which may affect nutritional rehabilitation. Honey supplementation can increase gastric emptying time (GET) in PEM patients thus yielding positive effects on the improvement in the anthropometric measurements and serum albumin. The honey delay in GET might be primarily a compensatory phenomenon that can be utilized to modulate the vicious cycle of PEM.

It is the dire need to enhance the level of dietary protein in diet base regimens with special reference to vulnerable group of susceptible group by blending high dietary protein commodities in staple ones. A variety of wheat flour substitutes have been formulated in bakery products, for example, soy flour or defatted soy flour (Junqueira et al., 2008), defatted wheat germ (Arshad et al., 2007), flaxseed (Koca and Anil, 2007), sunflower seed (Skrbic and Filipcev, 2008), and lupin flour (Hall and Johnson, 2004). Sorghum and wheat flour composite up to 10% and 20% resulted in acceptable in bakery products like breads and biscuits (Elkhalifa and El-Tinay, 2002).

Defatted soy flour and grits can be blended with cereals to raise both the quantity and quality of the protein in end products. The quality of the protein is improved in soy-cereal blends

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because soy protein is a rich source of lysine, first limiting essential amino acid in most cereal proteins (Lang et al., 1999). In another research trial, addition of 11.1% defatted soybean and 5.6% soybean isolate in wheat flour, improved nutritional, physical, chemical, and sensorial attributes of wheat flour. Fortified wheat flours were reported to contain 35% more protein and twice the lysine contents (Gonzalez-Agramon and Serna-Saldivar, 2006).

Substitution of barley flour with full fat and defatted soy flour up to 15% has significantly increased the protein contents, total lysine, dietary fiber, and β-glucan in the bread. It was also concluded that bread supplemented with barley and defatted soy flour, are organoleptically and nutritionally more acceptable than nonsupplemented (Dhingra and Jood, 2002). Singh and Mohamed (2007) evaluated that incorporation of protein blends increased the acceptability and quality characteristics of cookies.

The law of complementarity's can be employed to improve the nutritional status of the bakery products by partial replacement of wheat with protein rich flours, e.g., defatted black cumin. Defatted black cumin seed is a good source of crude protein and energy (El-Kady et al., 2001). Add reference of Tauseef Bhai here of *Nigella Sativa.* It can also be used in feed as 25% in soybean meal with no any adverse effect on body physiological function systems (Abdo, 2004).

CONCLUSION

PEM is a common nutritional problem worldwide and commonly occurs in developing economies. PEM decreases resistance to infection by impairing a number of physiological processes, including hematopoiesis. Moreover, it impairs immune response and thus infectious disorders are largely responsible for the very high postneonatal mortality and morbidity in malnourished children. Availability of food is just one environmental factor in the etiology of PEM—many others such as size at birth, infection and culture play a role. Diet needs as careful prescription as any other form of therapy, but in the severely malnourished child it is only one aspect of management. PEM is a global public health problem which should be kept in mind during the evaluation of every patient. There still exists a question unanswered in the diagnosis, treatment and follow-up of this very common problem.

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