

Intestinal Parasitic Infections and Micronutrient Deficiency: A Review

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Summary

Malnutrition including vitamin A and iron deficiency and parasitic diseases have a strikingly similar geographical distribution with the same people experiencing both insults together for much of their lives. Parasitic infections are thought to contribute to child malnutrition and micronutrient deficiency through subtle reduction in digestion and absorption, chronic inflammation and loss of nutrients. Parasites may affect the intake of food, its subsequent digestion and absorption, metabolism and the maintenance of nutrient pools. The most important parasites related to nutritional status are intestinal parasites especially soil transmitted helminthes, *Giardia duodenalis*, *Entamoeba histolytica*, followed by other parasites such as the coccidia, *Schistosoma* sp. and malarial parasites.

Key Words: Intestinal Parasitic Infections, Protein-calorie Malnutrition, Micronutrient Deficiency, Vitamin A Deficiency, Iron Deficiency Anaemia

Introduction

Micronutrient malnutrition is a serious threat to the health and productivity of more than 2 billion people worldwide. The three-micronutrient deficiencies of current greatest public health significance are iron, vitamin A and iodine, although zinc is receiving increasing attention¹.

The World Health Organization² considers vitamin A deficiency (VAD) to be a public health problem in 118 countries, putting at risks the lives and eyesight of an estimated 250 million preschool children. It is the single most important cause of blindness in children in developing countries particularly in tropical and subtropical countries. An estimated 250,000 to 500,000 VAD children become blind every year, and about half of them die within a year. Vitamin A deficiency leading to nutritional blindness or active xerophthalmia is a significant public health problem in India, Pakistan,

Bangladesh, Indonesia and Philippines^{3,4}. A study in Yemen⁵ reported a very low prevalence of ocular manifestation of VAD among children aged 1-5 years. The latest study in Nepal reported that the prevalence of night-blindness was 5% among women and over 1% among school-aged children⁶. In Malaysia, ocular changes related to vitamin A deficiency were first documented by Viswalingam⁷. Following that many studies have been reported on the occurrence of ocular changes related to VAD, and the latest study indicates that 82.2% of Orang Asli children had ocular manifestations of vitamin A deficiency ranging from history of night blindness to corneal scars⁸.

Iron deficiency anemia (IDA) is reported to be the most common nutritional deficiency in the world⁹. It affects 20% to 50% of the world's population¹⁰ and it is common in young children¹¹. Prevalence of iron deficiency anemia has been reported as being as high as 22% among East-Asian children of school age¹² and

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60% among children less than 5 years of age². In Malaysia, documentation of anemia amongst Malaysian children was available from around the 1950's. Since then many studies have been reported on the prevalence of anemia amongst children, pregnant women, laborers and industrial workers in Malaysia. Most of the anemic cases were thought to be due to iron deficiency.

Although many studies concluded that the main cause of mineral and vitamin deficiencies is due to low dietary intake of these elements^{13,14,15}, many studies showed that other factors such as childhood illness, parasitic infections and demographic factors also play an important role as predictors of these deficiencies^{13,16,17}.

Intestinal parasitic infections affect over 1800 million people particularly children in developing countries of Africa, Asia and Latin America¹⁸. A study in Yemen¹⁹ showed that the prevalence of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm infections in Sana'a City, the capital, were 15.9%, 17.6% and 1.0%, respectively. Recent studies showed that the prevalence of infections with soil-transmitted helminthes (STH), *Giardia duodenalis* and *Schistosoma mansoni* in Yemen was relatively high particularly in rural areas^{20,21}. In Malaysia, studies on children in underprivileged communities showed a high prevalence of *A. lumbricoides*, *T. trichiura*, hookworm, *E. histolytica* and *G. duodenalis* infections^{22,23,24,25}.

The main impact of intestinal parasitic infections is its relation to VAD and IDA, which may have effects at the community level as regards work and productivity in adults, and learning and school performance in children. Children who have suffered these deficiencies may give less attention to education and social skills irrespective of intelligence quotient (IQ)^{11,22,26,27,28}.

Intestinal Parasitic Infections

Parasitic infections have a worldwide distribution and constitute considerable public health problems especially in developing countries, and may be considered as 'the cancers of developing nations'¹⁶. Intestinal helminthic infections affect over 1800 million people particularly children in developing countries¹⁸. World Health Organization²⁹ reported that intestinal helminthic infections are prevalent where poverty prevails, where sanitation is inadequate or non-existent and where more health awareness and care are

needed, and all these factors are present in most developing countries, particularly in rural communities. About 100 species of helminthes have been reported from the human alimentary tract, and of these the nematodes *A. lumbricoides*, hookworm and *T. trichiura* are the most common with prevalence values of about 1000, 900 and 500 million cases per year, respectively²⁶. Giardiasis is endemic in many countries and children are more frequently infected than adults particularly those who are malnourished^{30,31}. Intestinal coccidiosis and microsporidiosis have been shown to be prevalent worldwide and cause serious illnesses in immunocompromised individuals particularly AIDS patients³².

Malaysia is a developing country with a range of parasitic infections. Indeed, intestinal parasitic infections, in particular soil-transmitted helminthiasis, giardiasis, amebiasis and malaria continue to have a significant impact on public health in Malaysia. Several studies have demonstrated a high prevalence of *A. lumbricoides*, *T. trichiura*, hookworm infections particularly *Necator americanus* and giardiasis in Orang Asli children, where the prevalence's range between 30.2 – 69.0%, 15.8 – 91.7% and 6 – 51.0%, respectively^{22,23,24,25}.

Malnutrition and Micronutrient Deficiency

Malnutrition results from various combinations of factors, including inadequate intake or abnormal gastrointestinal assimilation of the diet, stress response to acute injury or chronic inflammation, and abnormal nutrient metabolism. Protein-calorie malnutrition (PCM) that impairs the growth and development of children is probably the world's major public health problem with iron deficiency anemia (IDA), and vitamin A deficiency (VAD) being other outstanding afflictions²⁶. An estimated 182 million children under 5 years of age, representing 32.5% of all preschool children in developing countries, are malnourished and over two-third of them live in Asia especially southern Asia². Micronutrient malnutrition is a serious threat to the health and productivity of more than 2 billion people worldwide¹.

A first paper to highlight the prevalence of PCM in Malaysia was published by Will³³. Following that many studies have been carried out on the prevalence and determinant factors of PCM in Malaysia^{14,34,35,36,37}. Studies on the prevalence of malnutrition in Malaysia showed that mild and moderate malnutrition is common among

rural and urban preschool and primary school children in which primary school children in rural areas had significantly higher prevalence of malnutrition than those in urban areas^{35,36,37}. These studies have also showed that the prevalence of malnutrition is still high despite much control and prevention has taken place especially in rural communities.

Inadequate production or shortage of food is no longer thought to be the usual causes of malnutrition. Instead the problem develops from, and are maintained by, a complex network of socio-economic and health determinants²⁶. A number of studies in developing countries have investigated the variables that are associated with, and possible determinants of, child growth. Studies have shown that in developing countries the nutritional status of children has a significant inverse relationship with household income^{14,36,37,38}. Other socioeconomic factors such as education level of parents, distribution of food in the family^{13,38,39,40}, demographic data, immunization status and childhood illness⁴⁰, intestinal parasitoses^{16,22}, and childhood nutrition^{13,22,41,42} also have significant association with the nutritional status of children.

A study of malnutrition and its risk factors among rural Malaysian children³⁷ reported that the overall prevalence of underweight, stunting and wasting among these children were 46.2%, 18.1% and 30.3%, respectively. A study of socio-economic determinants of malnutrition status among 208 children aged 0-9 years in Perak, Malaysia, showed that the prevalence of stunting, underweight and wasting were 26.0%, 31.5% and 3.8%, respectively¹⁴ and these levels were relatively lower than the findings in other studies^{23,43}. In a study of nutritional status of women and children in Malaysian rural populations reported that the Orang Asli in rural areas suffered from malnutrition in which the prevalence of stunting was 66.7% in one area and 80.0% in another area²².

Studies of interactions among micronutrient deficiencies and undernutrition concluded that there is apparently an interaction between anaemia and VAD and PCM^{44,45,46}. For example, vitamin A needs proteins for transport in which retinol is slowly released from liver stores to meet metabolic requirements and circulates in conjunction of a binding protein (Retinol Binding Protein, RBP)⁴⁷. In Malaysia, ocular changes related to vitamin A deficiency were first documented in 1928⁷. Following that many studies have been reported on the occurrence of ocular changes related to

VAD. The latest study among 213 Orang Asli children under 15 years old showed that 82.2% of children had ocular manifestations of vitamin A deficiency ranging from history of night blindness to corneal scar, in which the prevalence was significantly higher in school age children (81.4%) compared to pre-school children (47.4%)⁸.

Biochemical determinations of VAD have also been carried out since the sixties. Thompson et al.⁴⁸ found that 25% of women at delivery have serum vitamin A levels below 20µg/dl. Large scales nutrition survey carried out among all age groups in Malaysia showed that low serum vitamin A levels (10-19 µg/dl) were seen in children aged 5-14 years old (males and females) and females aged more than 45 years old. VAD (< 10 µg/dl) was seen in females in all age groups⁴⁹. Following that many studies have been reported on the biochemical status of vitamin A^{50,51,52} in Malaysia.

Iron deficiency anemia (IDA) is reported to be the most common nutritional deficiency in the world⁹. It affects 20% to 50% of the world's population¹⁰ and it is common in young children¹¹. Prevalence of iron deficiency anemia has been reported as being as high as 22% among East-Asian children of school age¹², and 60% among children less than 5 years of age². In Malaysia, documentation of anemia amongst Malaysian children is available from around the 1950's. An ICCND⁴⁹ study reported that 36% of children less than 5 years old and 13% in the age group of 5-14 years were anemic (Hb < 2g/dl). The same results were also reported in a nutritional study among children living in poverty villages in Malaysia^{21,52}. A hospital-based study by Lie-Injo³³ showed that 13% of the children had very low hemoglobin levels of 8g/dl. Most of the anemic cases in children were thought to be due to iron deficiency. Anemia amongst pregnant women, laborers and industrial workers has also been studied extensively since the 1940's^{54,55,56,57,58}. Anemia in pregnant women is mostly related to iron and to a lesser extent, folate deficiency.

The relationship of intestinal parasitic infections and malnutrition

Malnutrition and parasitic diseases have a strikingly similar geographical distribution with the same people experiencing both insults together for much of their lives²⁶. Parasitic infections are thought to contribute to

child malnutrition through subtle reduction in digestion and absorption, chronic inflammation and loss of nutrients. Parasites may affect the intake of food; it's subsequent digestion and absorption, metabolism and the maintenance of nutrient pools⁵⁹. The most important parasites related to nutritional status are intestinal parasites especially soil transmitted helminthes and *Giardia duodenalis*, followed by other parasites such as the coccidia, *Schistosoma* sp. and malarial parasites.

For soil-transmitted helminthes, the intensity of infection remains the key factor for the pathological changes, e.g. heavy infections of *A.lumbricoides* are often associated with kwashiorkor, stunted growth and vitaminoses. Heavy infections with the hookworm *Ancylostoma duodenale* is known to drain nearly 50 ml of blood per a day when the egg per gram (EPG) is about 250 eggs/gm feces thereby decreasing the blood cell count, hemoglobin and serum proteins¹⁸. *T.trichiura* and *Entamoeba histolytica* invade the mucosa of the large intestine, causing bleeding and dysentery. *G. duodenalis* causes derangement of the normal villous architecture, with shortening of villi and inflammatory foci in the crypts and lamina propria, resulting in malabsorption⁵⁹. Intracellular parasites such as intestinal coccidians and microsporidians infect enterocytes of the duodenum and jejunum. Infections result in damage of enterocytes, malabsorption, villous atrophy (blunting), crypt hyperplasia and mononuclear cell infiltration. Another nutritional interaction between hosts and their intestinal helminthes is the exploitation by the parasites of the feeding behavior and food of their hosts to facilitate and ensure transmission and survival²⁶.

The effect of *A. lumbricoides* infection on nutritional status has been studied with varieties in results. Severe ascariasis, trichuriasis and hookworm infections result in growth retardation in children, and this has been proven by many studies carried out worldwide^{60,61,62}. Severe roundworm infections result in malabsorption and atrophy of the villus^{63,64}, indigestion of lactose⁶⁵, reduced absorption of vitamin A and albumin⁶⁶ and poor intake of food¹⁶.

Although many studies have reported positive association between intestinal parasitic infections and malnutrition, a study of malnutrition and its risk factors among children 1 – 7 years old in rural Malaysian communities reported that worm infections had no significant association with malnutrition³⁷. This result

has been reflected in the low prevalence of soil transmitted helminthes infections in the communities studied. A similar study among primary school children in Malaysia also reported similar findings⁶⁷. These results are in agreement with the results of a study among Bangladeshi children aged 2 – 5 years⁵⁹.

Intestinal Parasitic Infections and Vitamin A

The effect of parasitic infections on vitamin A has been studied with variable results. A longitudinal study in 4600 rural preschool-aged children from six Javanese villages found that children with stable vitamin A deficiency are at risk of getting both respiratory diseases and diarrhea. Children with mild xerophthalmia suffered a much higher mortality than children with normal eyes⁶⁸. It is suggested that the association between parasitic infections and vitamin A is diphasic in which poor vitamin A status could increase susceptibility to parasitic infections and vice versa¹³.

Although the malabsorption detected during intestinal parasitic infections is not easily explained or investigated because over 50 conditions are known during which chronic malabsorption may arise²⁶, the mechanisms of malabsorption in patients have been suggested to be a mechanical barrier to absorption, injury to the intestinal mucosa without invasion, mucosal invasion by parasites or bacterial overgrowth in the upper small bowel. The malabsorption of vitamin A may be caused by any of the above pathological factors or the combination of them⁶⁹.

A study of vitamin A absorption in children with ascariasis concluded that in populations with marginal intake of vitamin A, is an important contributing factor in producing clinical vitamin A deficiency⁷⁰. This study also showed that stool egg counts for *A. lumbricoides* were not related to the degree of vitamin A malabsorption. The second stage of this study showed that immediately after deworming and expulsion of the worms, vitamin A absorption improved in 13 out of 14 patients⁷¹. This study also found that there was an association between ascariasis and giardiasis and vitamin A deficiency. Eradication of *A. lumbricoides* and *G. duodenalis* in infected children promptly led to a significant improvement in vitamin A absorption and restored it to normal. Some studies have shown the opposite results. A study in 854 school and preschool Kenyan children to assess the effect of parasites on

serum retinol, suggested that there was no such association¹⁷. Ahmed et al. did a study on the effect of ascariasis on vitamin A in 24 children aged 4 – 10 years from a slum area of Dhaka City, Bangladesh and concluded that there was no association between ascariasis and malabsorption of vitamin A⁷². This study also showed that there was no correlation between the serum retinol concentration and the worm burden of *A. lumbricoides*⁷². By giving an oral dose of retinol (41.8 µmol/L) to 10 children with varying severity of *A. lumbricoides* infection, less than 1% of the supplement could be recovered in the stools collected over the following 48 hours. Retinol content of *A. lumbricoides* worms was negative⁷². A study in Nepal concluded that low serum retinol among preschool children was associated with young age, rural location, wasting, presence of night blindness and Bitot's spots⁶.

Giardiasis has been reported to be the cause of malabsorption both in children and adults and may lead to vitamin A deficiency even though clinical vitamin A deficiency in patients with giardiasis has not been reported. A study in 57 patients, less than 12 years of age in Bangkok, Thailand showed that 35% of patients with giardiasis and 22.6% of normal children showed vitamin A concentrations lower than 20 µg/dl and the children with giardiasis are more prone than normal children to develop vitamin A deficiency⁶⁹. This study also suggested that besides anti-giardiasis agent, supplementary vitamin A should be considered in the treatment of patients with giardiasis to prevent vitamin A deficiency and the administration of vitamin A should be continued for several months⁶⁹. However a study in Bangladesh reported that there was no relationship between the number of hookworm eggs or the number of *T. trichiura* eggs and serum retinol concentration⁷².

Intestinal Parasitic Infections and Iron

T. trichiura and hookworm infections are closely related to iron deficiency anemia. Hookworm infections cause mucosal damage resulting in endogenous losses of iron and other trace micronutrients. Parasitic infections resulting in bleeding (e.g. hookworm infection and schistosomiasis) or in dysentery (e.g. *T. trichiura* and *E. histolytica*) are known to be predictors for iron deficiency anemia.

A study on 427 Thai children to determine the effect of hemoglobin and serum ferritin on cognitive function showed that there was a significant association

between cognitive function and hemoglobin. This study showed that IQ, Thai language scores and mathematics scores in children with low serum ferritin were at the lowest level and increased with increasing of hemoglobin with a significant dose-response relationship. This study also concluded that the adverse effect of iron deficiency on cognitive function might be explained by diminished synthesis, packaging, uptake and degradation of neurotransmitters¹¹.

A study of association between intestinal parasites and nutritional status in northeastern Thailand among 343 rural and urban 3 – 8 year-old children showed that anemia was found more frequently among the infected children (59%) and giardiasis-infected children (61%) than among non-infected children (42%). Daily iron intake as well as the mean hemoglobin, hematocrit, and serum ferritin levels of the infected children was significantly lower than those of the non-infected children. There was also a significant decrease in hemoglobin, packed cell volume as well as serum ferritin with increasing number of parasites per child¹⁶. This study also suggested that a major part of the anemia encountered among the children with multiple infections is caused by iron loss due to parasitic infections.

The association between infection by *T. trichiura* and hookworm and iron deficiency anemia has been shown clearly through several studies. A study among 658 primary school children in Panama showed that blood hemoglobin concentration was significantly lower in children with severe trichuriasis. Children with concomitant *T. trichiura* and hookworm infection were also significantly more likely to have low hemoglobin concentration than children who were uninfected or have single infection with either of these helminthes⁶². A study to determine the relationship of varying intensities of trichuriasis and iron status among 409 Jamaican children, reported that the prevalence of anemia (Hb < 11.0 g/dl) amongst heavily infected children (33%) was significantly higher (p<0.05) than the rest of the sample (11%). In addition, these differences remained significant after controlling for confounding variables including socio-economic status, age, gender, area of residence and the presence of *A. lumbricoides* infection. This study also suggested that in the Jamaican children, iron deficiency anemia is associated with severe trichuriasis⁷³. Severe trichuriasis was also reported as an associate factor of IDA and anaemia in other population⁷⁴. In Malaysia, a study in

Hospital Kuala Lumpur in 1973 reported that severe trichuriasis in children produces chronic dysentery and, together with malnutrition and multiple parasitic infections, contributes to severe anemia and growth retardation⁷⁵.

Studies, which were carried out in high prevalence of hookworm infection, observed that hookworm infection was a strong predictor of IDA and anaemia in school-age children^{76,77,78,79}. Anaemia was significantly worst in children with heavy hookworm infection⁷⁸. Furthermore, it has been reported that children from high prevalence of *Ancylostoma duodenale* areas had significantly worse iron deficiency and anaemia than children from low prevalence areas⁸⁰. A large-scale school-based study in Tanzania suggested that hookworm was responsible for 6% of anaemia cases in this population⁸¹.

From the extensive literature, it can be concluded that parasitic infections and malnutrition including

micronutrient malnutrition are 'the cancers of developing nations', with intestinal helminthic infections affecting almost 2 billion people particularly children in developing countries. Deworming programmes should be included in public health strategies for the control and prevention of protein-energy malnutrition, VAD and anaemia particularly IDA in children from developing countries. This grim health scenario in the third world will not improve unless interventions are carried out on a grand scale, involving the WHO and nations. To do this, each affected nation needs to address the root cause of the problem (poverty) and generate a more concrete database regarding the epidemiology and effective control strategies of intestinal parasitic infections, which can only be realised if due importance is given to these problems in the form of a good general education system, effective health education programs and research grants which should not be marginalised in favor of high-tech research.

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Intestinal Parasitic Infections and Micronutrient Deficiency: A Review

Multiple Choice Questions (MCQs)

1. Predictors of vitamin A deficiencies include
 - A. low socioeconomic status.
 - B. parasitic infections.
 - C. childhood illness.
 - D. gender.
 - E. low educational level.

2. The following intestinal parasitic infections are associated with vitamin A deficiency:
 - A. Giardiasis
 - B. Intestinal coccidian infections
 - C. Amebiasis
 - D. Ascariasis
 - E. Enterobiasis

3. Parasitic infections that can cause iron deficiency anemia include
 - A. hookworm infection
 - B. malaria
 - C. trichuriasis
 - D. schistosomiasis
 - E. amebiasis

4. The possible mechanisms of malabsorption in intestinal parasitic infections include
 - A. mechanical barrier by *Giardia duodenalis* trophozoites in the duodenum.
 - B. injury of enterocytes by intestinal coccidian.
 - C. mucosal invasion of the large intestine by *Entamoeba histolytica*.
 - D. injury of the intestinal mucosa without invasion by hookworm.
 - E. atrophy of the villi.

5. Severe trichuriasis result in
 - A. indigestion of lactose
 - B. reduced absorption of albumin
 - C. poor food intake
 - D. low cognitive functions
 - E. chronic bleeding of the large intestine