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### Paediatric Respiratory Reviews



Mini-symposium: Interventions to prevent respiratory disease

# Interventions to prevent respiratory diseases - Nutrition and the developing world



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#### **EDUCATIONAL AIMS**

The reader will come to appreciate:

- Nutrition plays a critical role in healthy lung development.
- Nutritional interventions harness great potential in reducing respiratory illness related morbidity and mortality in the developing world.
- Several nutritional interventions (e.g. breast feeding, vitamin D, zinc) have proven to be effective in preventing and ameliorating respiratory illnesses while others lack concrete evidence.

#### ARTICLE INFO

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#### SUMMARY

Malnutrition is a major cause of morbidity and mortality in developing countries and nutrition plays a critical role in both acute and chronic respiratory conditions. Inadequacies in the nutritional requirements of a developing lung in utero and in early life can compromise the respiratory system integrity and result in poor lung function, reduced protection against infections, greater likelihood of acute illnesses in childhood and chronic illness in adulthood. Nutritional interventions harness great potential in reducing respiratory illness related morbidity and mortality in the developing world. In this review we have summarized the findings from published systematic reviews/meta-analysis, experimental and observational studies that looked into different nutritional interventions for preventing respiratory diseases in developing countries.

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#### INTRODUCTION

Malnutrition is one of the leading causes of child mortality, causing 3.5 million deaths annually in low and middle income countries (LMIC) [1]. There is increasing evidence to support that malnutrition is the underlying cause for increased susceptibility to infections, and certain infectious diseases could also lead to malnutrition [2]. For example, malnutrition predisposes children

to pneumonia which is one of the major causes of under-five mortality in LMIC [3]. Globally, an estimated 120 million new episodes of pneumonia are observed annually among children aged less than 5 years, of which 14 million progress to severe episodes and result in the deaths of 1.3 million young children [4]. Children suffering from both severe acute malnutrition and pneumonia are more likely to have treatment failure and endure fatal outcomes thus creating a vicious cycle of malnutrition and pneumonia, occurring more commonly in developing countries [5,6]. A greater proportion of this burden is observed in LMICs possibly due to the variation in demographic, socioeconomic and environmental factors which have been identified as important determinants of nutritional status among children aged less than

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5 years in low resource settings [7,8]. The burden of chronic respiratory diseases, particularly asthma and chronic obstructive pulmonary diseases (COPD) is also a major public health concern globally. An estimated 300 million and 210 million people suffer from asthma and COPD respectively worldwide. It is predicted that COPD will be among the top three causes of mortality by the year 2030 [9]. Studies have postulated early origins and role of nutrition in both acute and chronic respiratory diseases [9].

### INTERACTION BETWEEN NUTRITION AND RESPIRATORY DISEASES

Malnutrition and early lung development

Nutrition plays a critical role in healthy lung development [9]. Inadequacies in the nutritional requirements of a developing lung in utero and in early life can compromise the respiratory system integrity and result in poor lung function, reduced protection against infections, and greater likelihood of development of acute illnesses in childhood and chronic illnesses in adulthood [9]. Moreover, pre and perinatal factors, including maternal malnutrition during pregnancy and micronutrient deficiency, have been linked with abnormal lung function in the form of decreased alveolar number and increase in alveolar size in experimental studies [9].

In early life, malnutrition and the adverse effects of the consequent poor lung development manifests in the form of impaired immunity, resulting in more frequent and more severe respiratory infections. There is a strong body of epidemiological evidence which supports the association between poor nutrition and infections [10]. Although the exact mechanism is unclear, impairment of cell mediated immunity, particularly "T-cell anergy", is one of the most common hypotheses. Moreover, malnutrition might also lead to reduced capacity of the cells of the innate immune system [10].

Several studies have highlighted the early origins of asthma and COPD as far back as the fetal period [9]. The critical role of lung development and the immune system in the modulation of environmental stimuli makes nutrition an important element in the pathophysiology of both acute and chronic respiratory conditions [10] (Figure 1).

Breastfeeding and respiratory diseases

Breast milk is the ideal nutrition for newborns and infants, and suboptimal breastfeeding is associated with greater risk of mortality among children aged less than 2 years [11]. Early and

exclusive breastfeeding plays a vital role in infants' immune systems and substantially lowers the risk of death from infectious diseases including pneumonia [3]. It is believed that breastfeeding enhances antibody response to pneumonia-causing pathogens, pneumococci and haemophilus influenzae [12]. A pooled analysis of the role of breastfeeding in prevention of infant mortality showed that protection provided by breastfeeding infants falls steadily with age [13].

Micronutrients and respiratory diseases

Micronutrient malnutrition increases the susceptibility of infections, delays recovery, and raises the probability of severe illness in childhood. Pregnant women and children are particularly vulnerable to micronutrient malnutrition and some deficiencies are passed on over generations. Hence, maternal deficiencies could manifest as adverse health outcomes of infants [14]. Vitamins A, C, D, zinc, iron and folic acid are important micronutrients and have been investigated for the prevention and treatment of infectious diseases in childhood.

Vitamin A plays an important role in the immunological response to infections [15] and its deficiency substantially contributes to childhood morbidity and mortality [11]. Earlier works of Sommer and colleagues showed that "the risk of respiratory disease and diarrhoea were more closely associated with vitamin A status than with general nutritional status" [16].

Vitamin D has broad immunomodulatory effects within the lungs including increased secretion of antimicrobial peptides, reduced chemokine production, inhibition of dendritic cell activation, and alteration of T-cell activation. These are important for host responses against respiratory infections and also for the development of allergic respiratory diseases like asthma [17].

Adequate dietary vitamin C, iron and zinc, has also been shown to be associated with reduced infectious morbidity, including that of pneumonia, possibly through their vital role in mediating immunological functions and inflammatory response to foreign organisms [14,18].

## BURDEN OF RESPIRATORY DISEASES AMONG MALNOURISHED CHILDREN IN DEVELOPING COUNTRIES

In 2014, it was estimated that globally 159 million children under the age of 5 years were stunted and 50 million were wasted, and lower-income countries bear a disproportionate share of this burden [19]. Although, globally less than half of all children under 5 years of age live in LMIC, two thirds of all stunted children are

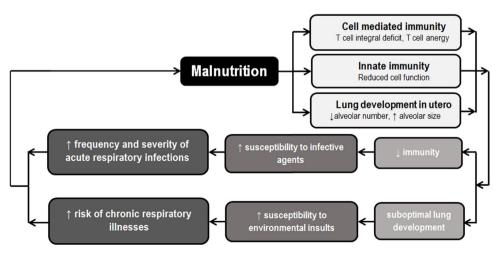


Figure 1. Interaction between nutrition, early lung development and respiratory diseases.

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