

CHAPTER 1

INTRODUCTION

Undernutrition is still rampant in majority of Indian states [Som *et al.*, 2006] including Gujarat. Ironically, India has celebrated it's 69th Independence Day this year with almost half of it's future holders being undernourished. Although, India has made substantial progress in human development since 1947, the manifestations of malnutrition are at unacceptable level [Mehrotra *et al.*, 2011].

Undernutrition is defined as the outcome of insufficient food intake and repeated infectious diseases. It includes being underweight for one's age, too short for one's age (stunted), dangerously thin for one's height (wasted) and deficient in vitamins and minerals (micronutrient malnutrition) [UNICEF, 2006]. Malnutrition is a serious public-health problem that has been linked to a substantial increase in the risk of mortality and morbidity. Women and **young children** bear the brunt of the disease burden associated with malnutrition [WHO, 2005].

Even foreign authors roused the issue saying that the Indian subcontinent has the most severe problem with undernutrition, with half of children (86 million in that subcontinent) undernourished [Black *et al.*, 2008; Petri *et al.*, 2008]. Undernutrition commonly affects all groups in a community, but infants and **young children** are the most vulnerable because of their high nutritional requirements for growth and development.

Undernutrition remains one of the primary causes of ill-health among children in developing countries like India [Nandy *et al.*, 2005].

India is a home to more than one billion people, of which 42 percent are children [Mehrotra *et al.*, 2011]. Children are considered the most important natural resource and biggest human investment for development in every community [Kaushik *et al.*, 2012]. School children form 20% of total population of India which is vulnerable than rest of population for infection and malnutrition [Park, 2009]. Children belonging to 5-12 years age group are vulnerable because of their rapid growth rate. They need more attention and care for the physical and mental development. Physical growth, development, and well being are directly related to the nutritional status [Manna *et al.*, 2011]. There is growing evidence of considerable burden of morbidity and mortality due to infectious diseases and undernutrition in school children [Das *et al.*, 2013].

Undernutrition may not be considered as specific disease but it's certainly known to be a mother of lot of acute and chronic diseases such as **diarrhea** and **acute respiratory infections or common colds**.

Infectious diseases like **diarrhea, acute respiratory infections**, malaria and whooping cough have been found to be the world's leading cause of morbidity and premature death especially in children in developing countries [Ujwala and Dhruv, 2012].

Diarrhea is a condition of having three or more loose or liquid bowel movement per day [WHO, 2008]. Reports in the literature indicate that in 2009

diarrhea was estimated to have caused 1.1 million deaths in people aged 5 years and over [Galadima and Kolo, 2014]. It is more prevalent in immuno-compromised children and a substantial cause of undernutrition. Diarrhea is the most common cause of gastroenteritis both in children and adult [Galadima and Kolo, 2014].

Acute upper respiratory tract infections (URTIs), which include the **common cold**, is a major cause of morbidity, especially in children and the elderly [Duijvestijn *et al.*, 2009; Kassel *et al.*, 2010; Liberati *et al.*, 2004], 6.9% of deaths in children were attributed to respiratory infections [Lakshmi *et al.*, 2005].

There are multiple mechanisms of action that relate to undernutrition and susceptibility to bacterial infections diseases. The mucosal barrier immunity is impaired in the undernourished host in the gastrointestinal tract due to the altered architecture and composition of the intestinal mucosal tissues which includes flattened hypotrophic microvilli, reduced lymphocyte counts in Peyer's patches, or reduced IgA secretion [McCracken, 2001]. The Gastrointestinal Associated Lymphoid Tissues (GALT) comprises a secondary lymphoid tissue where effect or immune responses directed gastrointestinal pathogens occur. Under nutrition in young children causes atrophy of the thymus with reduced cell numbers and subsequently ill-developed peripheral lymphoid organs, i.e. lymph nodes and spleen. These children show diminished functional T cell counts, increased undifferentiated lymphocyte numbers and reduced gut microflora [McCracken, 2001].

Activation and sustenance of immune responses during infection requires increased energy consumption [Schaible and Kaufmann, 2007]. Stimulation of an immune response by infection increases the demand for metabolically derived anabolic energy and associated substrates, leading to a synergistic vicious cycle of adverse nutritional status and increased susceptibility to infection [Schaible and Kaufmann, 2007]. Clinical and epidemiologic data point to a causal inter-relationship between nutritional deficiency and infectious illness. Both are major contributors to childhood morbidity and mortality, particularly in underprivileged population groups [Mandal, 2009]. Infection per se results in nutrient losses, either actual or by sequestration, and produce immunosuppression. The correction of postnatal nutritional deficits and/or infection is associated with reversal of immunological functions to normal.

Severe malnutrition leads to an immunodeficiency state known as Nutritionally Acquired Immune Dysfunctions (NAIDs), [Issac, 1990]. Neumann *et al.*, (1975) also stated the significant association between the parameters of PCM (low total serum protein and albumin and/or markedly decreased anthropometric measurements for age) and decreased cellular immunity.

Serum IgA is considered one of the important aspect of cell mediated immunity, as it is the predominant antibody in the secretions that bathe mucosal surfaces such as the gastrointestinal, respiratory, and genito-urinary tracts and in external secretion such as colostrums, milk, tears, and saliva. IgA

represents by far the largest area of contact between the immune system and the environment and can be considered as an important point of exposure to inhaled and ingested pathogens [Kaetzel, 2007].

Healthy intestinal microflora is a positive health asset that crucially influences the normal structural and functional development of the mucosal immune system. An improved understanding of this hidden organ will reveal secrets that are relevant to human health and to several infectious, inflammatory and neoplastic disease processes.

Gut flora have a continuous and dynamic effect on the host's gut and systemic immune systems. Gut microbiome is the key in promoting the early development of the gut's mucosal immune system both in terms of its physical components and function and continue to play a role later in life in its operation [McCracken, 2001].

Friendly bacteria stimulate the lymphoid tissue associated with the gut mucosa, to produce antibodies against pathogens. The immune system recognizes and fights harmful bacteria, but spares the helpful species alone, a tolerance developed in infancy [Isolauri *et al.*, 1991].

The microflora of the human gut is believed to be the major part of one's immune system and there is a growing interest in the role diet plays in the microbial composition of the intestinal tract and the related health benefits. *Bifidobacteria* and *Lactic acid bacteria* (LAB) colonized in the human colon are known to aid digestion, boost immunity, and lower the incidence of allergies [Bengt *et al.*, 2001]. In addition, an increased proportion of *Bifidobacteria* in the

gut may crowd out undesirable pathogenic bacteria such *E.coli* thus reducing the chance of diarrhea and infection [Gibson and Roberfroid, 1995; Walker, 2000].

There is increasing evidence that fermentable dietary fibers and the newly described prebiotics can modulate various properties of the immune system, including those of the Gut-Associated Lymphoid Tissues (GALT) [Schley, 2002]. “A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health”[Roberfroid, 2007].The prebiotic effect includes a significant change of gut microbiota composition, especially an increase of fecal concentrations of *Bifidobacteria*. This concomitantly improves stool quality (pH, Short Chain Fatty Acid/SCFA, frequency and consistency), reduces the risk of gastroenteritis and infections, and improves general well-being [Roberfroid *et al.*, 2010].

In the recent years, some data is generated on the prebiotics and its role in improving gut immunity, however these studies should be substantiated with more research to establish its role in improving health in undernourished children.

The potential mechanism of prebiotics induced immunomodulation proposed by Watzl and Seifert, (2007) are selective increase/decrease in specific intestinal bacteria that modulate local cytokines and antibody production; increase in intestinal Short Chain Fatty Acid (SCFA) production and enhanced binding of SCFA to G-coupled protein receptors on leucocytes;

interaction with carbohydrate receptors on intestinal epithelial cells and immune cells.

Fructooligosaccharides (FOS), are one such authentic prebiotics that has shown beneficial health effects in reducing obesity and diabetes and improving oral health and immunity [Sheth and Gupta, 2014; Mahendra and Sheth, 2014; Lotankar and Sheth, 2014; Mandali and Sheth, 2011].

Fructooligosaccharide supplementation has shown to enhance the selective friendly microflora such as *Lactic acid bacteria* and *Bifidobacteria* growth in human gut and thus FOS has a potential to boost immunity through the mentioned mechanism in children who are the most vulnerable age group of the society and therefore it should be tested for its impact on the said parameters of Indian children.

To rectify the age old unchanged status of undernutrition, India gravely needs some strong approach for it and present study in one such step towards that direction. Authors of the present research intends to integrate a substantially different perspective of Undernutrition and validate the potentials of FOS in terms of its bifidogenecity, reduction in diarrheal, common cold incidences and its association with serum IgA levels and nutritional status in young school going children of urban Vadodara, Gujarat.