

# Infant Health at Birth

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## **Abstract**

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This paper takes the view that poor health is both a dimension and a cause of poverty. This vicious circle begins in-utero and manifests itself as sub-optimal health at birth. Improving Infant Health at Birth could present a means of breaking this vicious circle.

In chapter 2, health at birth is defined both in terms of mortality and in terms of the qualitative aspects of survival. Low Birth Weight (birth weight less than 2500 g) emerges as a significant factor impacting both survival and later development and health. Approximately a third of all babies born in India are Low Birth Weight. Of these roughly 70% are Low Birth Weight because of growth retardation during fetal development (Intra-uterine Growth Retardation—IUGR). Chapter 3 sharpens focus within Low Birth Weight on IUGR, its prevalence in India and its implications for survival, physical and cognitive development and adulthood disease.

The emphasis in chapters 4 and 5 shifts from arguing for the importance of IUGR as a public health issue, to a broad concern with the body of knowledge on its prevention. Chapter 4 surveys available literature on the etiology (causes) of IUGR, and the resultant implications for preventing IUGR. Chapter 5 takes this further to review evidence from nutritional studies. The chapter identifies key maternal nutritional deficiencies causally linked to LBW and gaps that need further research.

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## **ABBREVIATIONS**

BMI: Body Mass Index  
CHD: Coronary Heart Disease  
IHB: Infant Health at Birth  
IMR: Infant Mortality Rate  
IUGR: Intra-uterine Growth Retardation  
LBW: Low Birth Weight  
NMR: Neonatal Mortality Rate  
PI: Ponderal Index  
PMR: Post neonatal Mortality Rate  
WHO: World Health Organisation

## Preface

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This paper is an attempt by the authors to identify a strategic health focus capable of impacting poverty in India. In the paper, health is understood as a state of complete physical, mental and social well being and not merely as the absence of disease or infirmity<sup>1</sup>. The chosen focus is on optimising infant health at birth, understood in terms of birth weight. This focus has been arrived at based on the prevalence and impact of Low Birth Weight on survival, physical and cognitive development and on long-term health. The paper tries to explore the causes of the Low Birth Weight problem and to identify significant research gaps in the Indian context that impede the development of interventions for its prevention.

Postulated medical cause is the definition of 'cause' adopted. This is not to suggest that the social and economic factors that result in poor female nutrition are not important. However, addressing these factors is not within the scope of this paper, which seeks to understand the root physiological causes. The rationale for this is to facilitate a clearer definition of the nutritional goals for action and physiological risk factors. Defining the precise nutritional goals will ultimately facilitate the design and implementation of more effective action (which could be non-nutritional, e.g. Behaviour Change Communication). A better understanding of the physiological risk factors in turn will facilitate a sharper definition of the groups to focus on, and also of the point/s of intervention.

The paper also needs to be distinguished clearly from a strategy paper. The emphasis on maternal nutrition does not imply that the authors view feeding programmes for girls and women as the only or the most appropriate solution.

Discussions presented in the paper are based on available scientific literature. The objective is to stimulate further debate and discussion on the problem of Low Birth Weight in India.

### 1. Why Health?

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Poverty encompasses two dimensions: (a) poverty as a state of basic deprivation, and (b) poverty as a lack of real opportunity to choose other types of livings<sup>2</sup>. In this understanding, the factors mediating the ability to make and exercise livelihood related choices are crucial bottlenecks in poverty reduction. Arguably, health is one such factor.

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<sup>1</sup> World Health Organisation: <<http://www.who.int/aboutwho/en/definition.html>>

<sup>2</sup> Sen, A. & Dreze, J., 1995

## **1.1 Health as a capacity**

Intuitively speaking, poor health<sup>3</sup> clearly erodes the most fundamental capital that the poorest have — the ability to engage in manual work. This erosion is both a direct result of morbidity<sup>4</sup> and, also a result of sub-optimal functioning in the absence of morbidity. This ultimately impacts poverty.

Sub-optimal functioning is related to two sets of health-related factors:

- a) Morbidity
- b) General nutritional status

The sharp boundary drawn between these two sets of factors is artificial. Nutritional status influences the ability of an individual to resist infection. In turn, frequent illness impinges on nutritional status creating a vicious cycle<sup>5</sup>. While malnutrition is not necessarily a result of poverty, poverty is strongly associated with malnutrition. This association could be a result of too little food, high bulk low nutritive value food, frequent illness and sub-optimal feeding practices, e.g. weaning practices.

## **1.2 Achieved potential: the hidden costs of sub-optimal health**

Malnutrition in early life has an impact greater than the direct results of morbidity. There is an increasing body of evidence on the impact of malnutrition in early life (in-utero and in the first three to five years) on achieved physical growth and cognitive potential.

The fetal period and the 0 to 3 years stage are the most growth-intensive stages in the lifecycle. Nutrition during these stages has a critical bearing on development of the immune system, physical growth and cognitive development. Malnutrition leads to growth failure, which cannot be compensated for after age 3<sup>6</sup>. Maturation delays may allow time for compensatory growth. However, the maturational delays commonly seen in developing countries allow adequate catch-up growth for only a small proportion of malnourished children<sup>7</sup>.

Malnutrition in early life and malnutrition that endures the first few years adversely impacts learning achievement, and worker productivity<sup>8</sup>. One of the few studies that quantified the impact on cognitive development suggests that iron deficiency alone results in an IQ deficit of 8 points or half a standard deviation among anaemic 5 to 6 years olds<sup>9</sup>. In general, micronutrient deficiencies tend to co-exist, multiplying the effect of iron deficiency on IQ. An

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<sup>3</sup> Health is understood as “a state of complete physical, mental and social well being and not merely the absence of disease or infirmity”. WHO: <<http://www.who.int/aboutwho/en/definition.html>>

<sup>4</sup> Illness or sickness.

<sup>5</sup> The UNICEF model of malnutrition, which gives equal importance to food, health and care, is based on this insight.

<sup>6</sup> Martorell, R., 1997

<sup>7</sup> Martorell, M., Kettel, K. & Schroeder, 1994

<sup>8</sup> Barker, D. J. P., 1998, Micronutrient Initiative, 1998

<sup>9</sup> Seshadri & Gopaldas, 1989

inability to stay in school and poor learning achievement can, at least in part, be attributed to poor cognitive development<sup>10</sup>. Good nutrition is a critical input for cognitive development. The growth, health potential and educability of half of all Indian children born is diminished by malnutrition<sup>11</sup>.

Alderman et al.<sup>12</sup> linked poor cognitive and physical development with adult productivity. They found that an increase in cognitive skills of one standard deviation was associated with an increase in wages ranging from 10% to 12% in rural Pakistan<sup>13</sup>. There is evidence that correcting anaemia alone is associated with a 5% increase in productivity in all blue-collar work, and a 17% productivity increase for heavy manual work<sup>14</sup>. Putting this in a larger perspective, one estimate suggests that malnutrition reduced India's GDP by between 3 and 9 percent in 1996<sup>15</sup>. Another study estimates that iron deficiency anaemia alone results in a loss equivalent to 1.27% of the GDP<sup>16</sup>.

### **1.3 Morbidity: the visible costs of sub-optimal health**

Over and above this is the welfare and economic cost of morbidity. In India, 75% of all health spending is out-of-pocket expenditure by households<sup>17</sup>. Given the higher relative susceptibility of the poor to illness, this translates into a disproportionate burden on poor households as a whole. Household rationing of health care expenditure according to perceived priority is an inevitable response, implying a large unmet demand for health care among poor households<sup>18</sup>. Within poor households, women and children, whose health needs are perceived as low priority, are particularly affected<sup>19</sup>. Moreover, dependence on out-of-pocket expenditure makes the cost of medical treatment a significant cause of indebtedness among the poor. Over 40% of hospitalisation episodes are met either by sale of assets or by taking loans<sup>20</sup>.

### **1.4 Summing up**

Poor health perpetuates poverty: (a) through its impact on physical and cognitive capacity, and therefore future productivity, and (b) through direct expenditure on curative care. Moreover, as good health is desirable in itself, the effects of ill health are a dimension of poverty in a broader

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<sup>10</sup> One study in rural Maharashtra showed that 80% of 172 school dropouts had some degree of learning disability. There are other supporting studies. Patel, V. & De Souza, N., 2000

<sup>11</sup> Chatterjee, M. et al., 1998

<sup>12</sup> Alderman et al., 1996

<sup>13</sup> The latter estimate allowed for simultaneity and selectivity.

<sup>14</sup> Ross, J. & Horton, S., 1998

<sup>15</sup> Administrative Staff College of India, 1996, as cited in Chatterjee, M. & Measham, A. R., 1999

<sup>16</sup> Ross, J., & Horton, S., 1998

<sup>17</sup> The private sector accounts for 78.8% of overall health spending in India, of which households account for 75%. By comparison, in OECD countries (excepting USA), the public sector accounts for 65 to 90% of all health expenditures. Naylor, D. et al., 1999

<sup>18</sup> IIHMR, The Policy Project, 2000

<sup>19</sup> Madhiwala, N. & Deosthali, P., 2001

<sup>20</sup> Shukla, A., 2001

sense. This vicious circle begins in-utero, resulting in sub-optimal health at birth. Sub-optimal health at birth has cumulative effects on infant and child survival, development and health, ultimately impacting on adult productivity. A feasible way of arresting this vicious circle is to optimise birth outcomes i.e., to ensure good Infant Health at Birth.

## **2. Defining Infant Health At Birth**

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This paper understands Infant Health at Birth in terms of:

- Survival beyond birth, or conversely, preventing disproportionate mortality at birth.
- Qualitative aspects of survival, including the potential to resist morbidity and achieve optimal physical and cognitive development.

### **2.1 Survival beyond birth**

Failure to survive till birth or mortality at birth is measured by the perinatal mortality rate (PMR) and also indicated by the neonatal mortality rate (NMR).

The perinatal mortality rate is the number of deaths for every 1000 births in the period from 22 completed weeks of gestation<sup>21</sup> to the first 7 days of life. It includes both fetal deaths such as stillbirths and miscarriages as well as deaths after birth.

The neonatal mortality rate is the number of deaths for every 1000 live births in the first four weeks of life.

The perinatal and the neonatal periods overlap. They represent a biological continuum during which the causes and the determinants of death are substantially the same.

India has a perinatal mortality rate of 65 per 1000 and a neonatal mortality rate of 50 per 1000. This is considerably higher than 25 and 20 for Sri Lanka, 45 and 35 for Egypt, 45 and 30 for Brazil and comparable to 65 and 40 for Rwanda respectively<sup>22</sup>. Low Birth Weight (LBW) is probably the single most important factor that affects neonatal mortality. In addition, LBW is a significant determinant of post neonatal mortality and of infant and childhood morbidity<sup>23</sup>. Compared to normal birth weight babies, those born LBW (a birth weight of less than 2500 grams) are 4 times as likely to die in the neonatal period<sup>24</sup> and twice as likely to die in the post-neonatal period<sup>25</sup>. In their study on neonatal mortality and birthweight Kaushik et al. found that LBW contributed to 79.5% of the neonatal deaths<sup>26</sup>. Recent National Neonatology Forum data

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<sup>21</sup> Fetal deaths before 22 weeks of gestation are considered to be abortions. WHO, 1996

<sup>22</sup> WHO, 1995

<sup>23</sup> McCormick, M. C., 1985

<sup>24</sup> The first four weeks after birth.

<sup>25</sup> Fuchs, G. J., 1999

<sup>26</sup> Kaushik et al., 1987

documents this inverse relationship between birth weight and infant mortality even in secondary and tertiary care settings<sup>27</sup>.

In a very fundamental sense, survival is a pre-requisite to enjoying good health at birth and beyond.

## **2.2 Optimal physical and cognitive development**

Physical and cognitive development of the infant can be viewed as achieved genetic potential. This achievement is mediated significantly by the environment. Environmental influence begins in-utero.

The interaction between genetic potential and certain in-utero (predominantly nutritional) influences translates into LBW incidence. LBW, in itself and through further interaction with the environment negatively impacts physical and cognitive development.

LBW has been associated with impaired immune function in infancy and also beyond. LBW infants are twice to four times more likely to develop acute diarrhoea than their normal weight counterparts. Their risk of contracting pneumonia or acute lower respiratory infections is almost double that of normal weight babies or three times greater if they weigh less than 2000g<sup>28</sup>.

Increasing episodes of illness during early childhood can cause malnutrition and affect growth. Growth failure occurs almost exclusively during intra-uterine life and the first few years of life. Catch up growth is possible only when there are maturational delays prolonging the growth period. However, such delays are usually of less than two years in developing countries. In most cases this does not provide a large enough window for adequate growth compensation. Follow up studies of subjects with growth failure either in intra-uterine life or early childhood who continue in the same socio-economic setting in early life revealed little or no catch up growth in later life<sup>29</sup>. Moreover, as a study of LBW infants adopted in early infancy by wealthy Swedish families shows, the mean attained adult height of the adopted Indian girls was only 1 cm higher than their poor counterparts in India. Their mean attained adult height was also significantly lower than that of girls born in wealthy Indian families<sup>30</sup>. This indicates that the impact of growth failure in intra-uterine and early life is not entirely reversible.

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<sup>27</sup> NNF, 1997, as cited in Sachdev, H. P. S., 2001

<sup>28</sup> Bukenya et al., 1991; Ittiravivongs et al., 1991; Victora et al., 1991; Victora et al., 1990; Cerqueiro et al., 1990; Fonseca et al., 1996; Chandra, 1999; Chandra, 1997; Victora et al., 1988 as cited in ACC/SCN, 2000

<sup>29</sup> Beaton 1989; Beaton et al., 1990; Martorell, Kettel Khan, and Schroeder 1994 as cited in Martorell, R., 1997

<sup>30</sup> Proos et al., 1992

### **2.3 Prevalence of Low Birth Weight (LBW)**

Estimates of LBW vary by region, ranging from 16% for Sub-Saharan Africa to 34% for South Asia including India, Bangladesh, Nepal and Pakistan. At 50%, Bangladesh<sup>31</sup> has the highest percentage of LBW infants. Within South Asia, Sri Lanka has an LBW incidence of 25%. In sharp contrast, Thailand has an LBW incidence of 6%<sup>32</sup>.

Widely accepted estimates for India suggest that LBW prevalence in India is second only to that in Bangladesh.

The majority of deliveries in India take place within the community<sup>33</sup>. Recording birth weight reliably in the community requires rigorous training and accurate equipment. Most studies derive their birth weight data on the basis of institutional deliveries. Given these issues, estimates of LBW prevalence available for India are better viewed as broad indicators of its magnitude.

District based data generated through the Child Survival and Safe Motherhood (CSSM) programme estimates LBW prevalence to be 18.4%<sup>34</sup>. These figures, however, are considered to be clear underestimates in light of the consistently higher prevalence identified by other studies<sup>35</sup>.

UNICEF estimates that 33% of all infants born in India are LBW<sup>36</sup>. National Neonatology Forum data suggests an LBW prevalence of approximately 32.8%<sup>37</sup>. Other studies identify a prevalence range of between 24% and 40%<sup>38</sup>

Assuming an LBW prevalence of 33%, a birth rate of 48 per minute implies that approximately 8 million LBW infants are born in India every year.

In India the mean birth weight ranges from 2493 to 2970 g. It has not changed much since 1993 when the mean birth weight was estimated at  $2633 \pm 417$ .<sup>39</sup>

Available evidence suggests that rural and urban slum populations consistently record the highest prevalence of LBW across regions<sup>40</sup>. One study found a sharp prevalence disparity

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<sup>31</sup> The prevalence identified by other studies on Bangladesh ranges from 23% to 60%. Sachdev, H. P. S., 2001

<sup>32</sup> UNICEF, 2000

<sup>33</sup> Sachdev, H. P. S., 2001

<sup>34</sup> Ramji, S. as cited in Sachdev, H. P. S., 2001. This data is also of centre based deliveries.

<sup>35</sup> Sachdev, H. P. S., 2001

<sup>36</sup> UNICEF, State of the World's Children- 2000

<sup>37</sup> NNF, 1995 as cited in Sachdev, H. P. S., 2001. The data pertains to births in institutions.

<sup>38</sup> Srikantia, 1989; UNDP, 1996; NNF, 1997; Sachdev, 1997; UNICEF, 1997 as cited in Sachdev, H. P. S., 2001

<sup>39</sup> Gopalan, C., 1994. This observation is debatable. A similar observation of little change in birth weight between the 1960s and late 1980s has been criticised by Sachdev. He suggests that this was based on a comparison of data from disparate settings at various points. Sachdev, H. P. S., 2001

<sup>40</sup> Sachdev, H. P. S., 2001

between socio-economic strata—10% among higher socio-economic strata and 56% among urban slum dwellers<sup>41</sup>.

## 2.4 *Summing up*

Optimising Infant Health at Birth could be approached in terms of two main dimensions in the Indian context:

Survival beyond birth: This is measured in terms of neonatal and infant mortality. Survival is both a fundamental pre-requisite to enjoying good Infant Health at Birth, and an indicator of quality of health at birth. Babies born LBW are much more likely to die during infancy than normal weight babies.

Quality of health at birth: This could be understood in terms of birth weight, a sensitive indicator of in-utero health. It is a factor impinging on achievable physical and cognitive development. It is also a determinant of morbidity.

Reducing LBW incidence in India is a pre-requisite to optimise Infant Health at Birth. The overall level of incidence clearly defines its significance as a public health priority in India. Babies born in poor socio-economic strata are far more likely to be LBW. Given its implications for survival, morbidity and physical and cognitive development, a focus on LBW represents a poverty-centered health focus.

## **3. Sharpening Focus: Intra-Uterine Growth Retardation**

### 3.1 *Unpacking “Low Birth Weight”*

The World Health Organisation has defined a birth weight of less than 2500 g as low.

Birth weight, however, is also a function of gestational age. As the fetus grows it acquires mass with the weight gain being most rapid towards the latter part of gestation. A full term baby is one that has completed 37 to 42 weeks of gestation. If the baby is born before 37 weeks of gestation, its weight will be lower relative to that of babies that have completed the gestational period. A gestational age of less than 37 weeks is defined as prematurity<sup>42</sup>. A birth weight of less than 2500 g at a gestational age of 37 weeks, on the other hand is generally an indication of intra-uterine growth failure or intra-uterine growth retardation (IUGR)<sup>43</sup>. In summary, two major processes govern birth weight:

1. Duration of gestation
2. Intra-uterine growth rate

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<sup>41</sup> Bhargava, S. K., 1997; Nahar, N., 1997; Roy, S. K., 1997 and Bhargava, S. K. et al., 1990 as cited in Sachdev, H. P. S., 2001

<sup>42</sup> WHO, 1996

<sup>43</sup> Babies that weigh less than 2500 g at birth despite having completed 37 weeks could also be Small for Gestational Age (SGA). While IUGR and SGA tend to be used synonymously, there is a technical difference between the two.

LBW may be caused by either of these processes independently or in interaction. Intra-Uterine Growth Retardation (IUGR) is defined as either birth weight less than the 10<sup>th</sup> or 5<sup>th</sup> percentile for gestational age or as birth weight less than 2 standard deviations below the mean value for gestational age. Evidence suggests that IUGR implies fetal undernutrition<sup>44</sup>.

IUGR can be sub-divided into two categories:

- a. Disproportional/Asymmetric or wasted IUGR: this is characterised by a normal height and head circumference (approximates to brain growth) and low weight for height and skin fold measurements. The ponderal index<sup>45</sup> (PI) for such babies is less than 2. This kind of IUGR is generally assumed to be the result of poor fetal nutrition later rather than earlier in pregnancy.
- b. Proportional/ Symmetric or stunted IUGR: this is characterised by proportionally low weight, height and head circumference. The PI for such babies is approximately 2-2.5. This is more likely to occur if the nutritional insult<sup>46</sup> occurs earlier in gestation.

Most studies, in their examination of the impact of IUGR on growth, have not distinguished between wasted IUGR and stunted IUGR. While there are some studies that have looked at the differential impact of the two subtypes of IUGR, this is an area that requires further research.

The two types of IUGR differ substantially in their characteristics, etiology and implications for survival, morbidity and physical and cognitive development.

### **3.2 Implications of Low Birth Weight**

Premature babies face immediate problems because their organ systems are immature and stores (e.g. glycogen and brown fat) are low at birth. This is a result of insufficient time to build organ systems and stores. An inadequately developed immune system also contributes to the problems faced by premature babies.

Such babies have ill-developed vascular beds around their ventricles, making them more prone to intra-cerebral bleeds. They suffer from metabolic<sup>47</sup> problems such as hypoglycemia<sup>48</sup>, hypocalcemia<sup>49</sup>, metabolic acidosis<sup>50</sup> and hyperbilirubinemia<sup>51</sup>. An ill

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<sup>44</sup> Gillespie S, 1997

<sup>45</sup> Weight in grams/ height in cm<sup>3</sup>. A Ponderal Index of 2 to 2.5 is considered to be within the normal range.

<sup>46</sup> Undernutrition.

<sup>47</sup> Relating to metabolism, the whole range of biochemical processes that occur within us (or any living organism). Metabolism consists of anabolism (the buildup of substances) and catabolism (the breakdown of substances). [www.medterms.com](http://www.medterms.com)

<sup>48</sup> Low level of sugar in the blood.

<sup>49</sup> Low level of calcium in the blood.

<sup>50</sup> The accumulation of acids harmful to the body as a result of substrate (e.g. glucose) utilisation in an oxygen poor environment.

<sup>51</sup> Jaundice.

developed immune system results in a higher incidence of neonatal sepsis<sup>52</sup> among premature babies. They tend to suffer from asphyxia<sup>53</sup> due to hyaline membrane disease<sup>54</sup>.

Being weak, premature babies find it difficult to suck and therefore need artificial feeding. This further worsens their already compromised nutritional status<sup>55</sup>.

All these factors lead to an increased likelihood of mortality. Premature babies who do survive are more prone to develop long-term morbidities such as chronic lung disease, cerebral palsy<sup>56</sup>, cognitive and developmental defects etc. However, if premature babies survive their immediate major problems, they exhibit good catch-up growth.

### **IUGR infants**

On the other hand, growth-retarded babies face problems not of immaturity, but of in-utero hypoxia, poor nutrition and the resultant stress. There is a substantial overlap between their problems and those that premature babies face<sup>57</sup>. The effects of this disadvantageous start, however, tend to persist. IUGR babies exhibit poor catch-up growth and impaired cognitive and neuro-behavioural development. In addition, emerging evidence<sup>58</sup> suggests that they are also more likely than normal weight babies to suffer from degenerative diseases like hypertension, diabetes and cardiovascular diseases in adulthood.

### **3.3 Prevalence of IUGR**

Very few studies in developing countries distinguish between the sub- types of LBW<sup>59</sup>.

Villar and Belizan<sup>60</sup> have estimated that 55% of LBW in developed countries is due to prematurity on the basis of an analysis of data from 11 different regions in developed countries and 25 areas in developing countries. In developing countries they estimate that approximately 70% of the low birth weight is due to IUGR.

Other studies arrive at similar estimates for India. Recent multicentric data (37000 live births) suggests that 67.2% of all LBW babies in India are IUGR<sup>61</sup>. Another estimate suggested that

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<sup>52</sup> A serious blood bacterial infection in an infant less than 4 weeks of age.

<sup>53</sup> Impaired or impeded breathing.

<sup>54</sup> Respiratory disease of the newborn in which a membrane lines the air sacs in the lungs making gas exchange difficult or impossible.

<sup>55</sup> This is both a result of being denied the benefits of best milk, and also of the effects of inadequate hygiene and infections it may cause. In poor families where mothers have to go back to work, mothers often have less time to breast feed premature babies that can suck for short stretches of time.

<sup>56</sup> A syndrome of weakness, spasticity, poor coordination of the limbs and other muscles, impaired sensory perception, and sometimes impaired intelligence. The cause of cerebral palsy is not always known, although many cases are linked with lack of oxygen during birth. <[www.medterms.com](http://www.medterms.com)>

<sup>57</sup> For instance, metabolic problems such as hypoglycemia, hypocalcemia; higher likelihood of developing asphyxia or neonatal sepsis.

<sup>58</sup> Barker, D. J. P., 1998

<sup>59</sup> Kramer, M., 1987; Sachdev, H. P. S., 2001

<sup>60</sup> Villar et al., 1982

<sup>61</sup> Reddy, V. et al., 1999 as cited in Sachdev, H. P. S., 2001

55% to 70% of babies in the 1501 to 2000 g category and 85% to 87% in the 2000 to 2500 g category are IUGR<sup>62</sup>. According to de Onis et al. approximately 20% of all Indian babies born are IUGR. This is more than two-thirds of the total LBW incidence<sup>63</sup>.

All of these estimates are likely to be fairly conservative since home deliveries tend to get left out of such enumerations. 65.4% of deliveries in India take place at home<sup>64</sup>.

### **3.4 Implications of IUGR**

#### **3.4.1 IUGR and mortality and morbidity**

Ashworth<sup>65</sup> reviewed 29 data sets to assess the risks of mortality and morbidity associated with IUGR. He estimated that for term infants<sup>66</sup> weighing between 2000 and 2499 g the risk of neonatal death is four times higher than that for infants weighing between 2500 and 2999 g. Infants weighing between 2000 and 2499 g have a ten times higher risk of dying in the neonatal period than those weighing between 3000 and 3499 g.

Ashworth presents data from 9 studies substantiating the observation that IUGR infants are more susceptible to diarrhoeal diseases and respiratory tract infections. The studies indicate that IUGR infants are between 1.2 and 3.6 times more likely to develop these infections<sup>67</sup>.

#### **3.4.2 IUGR and physical development**

IUGR infants are found to be much more likely to exhibit growth deficiencies<sup>68</sup>, which appear to be permanent<sup>69</sup>. A study in Guatemala compared development at age 3 for children born with disproportional IUGR, proportional IUGR and those born normal (control). The study found that the group with disproportional IUGR recuperated from thinness within the first few months. However infants with proportional IUGR remained lighter and shorter and had a smaller head circumference than the infants in the other two groups<sup>70</sup>.

An Indian study by Bhargava et al.<sup>71</sup> followed up small for date infants with a birthweight of 2000 g for 6 years and found significant growth retardation<sup>72</sup> in comparison with children of the same age born with normal weight. They also displayed delayed skeletal growth and maturation between 6-10 years of age and impaired immunocompetence<sup>73</sup>.

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<sup>62</sup> Bhargava, S.K. et al., 1987 as cited in Sachdev, H. P. S., 2001

<sup>63</sup> de Onis et al., 1998

<sup>64</sup> NFHS-2. These are NFHS-2 estimates for the 3 year period preceding 1998- 99. Only 33.9% of urban women as compared to 74.3% of rural women delivered at home.

<sup>65</sup> Ashworth, 1998

<sup>66</sup> Infants who have completed the gestational period and are not premature.

<sup>67</sup> Ashworth, 1998

<sup>68</sup> Hofvander, Y., 1982 as cited in Kramer, M.S., 1987

<sup>69</sup> West wood, M. et al., 1983, as cited in Martorell, 1997

<sup>70</sup> Villar et al., 1984

<sup>71</sup> Bhargava et al., 1984

<sup>72</sup> Growth retardation was reflected as lower body weight, height and head circumference.

<sup>73</sup> Ability to develop an immune response.

However, the low socio-economic status of these children and the resultant lack of stimulation and opportunity to learn could have confounded these results. To avoid such a bias, Proos et al.<sup>74</sup> studied growth and development of Indian children adopted in Sweden. 81% of these children, adopted in early infancy, were IUGR. They found significant differences with respect to height for age and weight for age at 2 years<sup>75</sup> between children < 2000 g at birth and those > 2000 g at birth. This indicates that the effects of IUGR cannot be reversed by an ideal environment and postnatal nutrition.

Strauss and Dietz<sup>76</sup> also found a significant growth difference in terms of height and weight in their study. Strauss and Dietz compared 220 IUGR children with their normal birth weight siblings, thereby controlling for confounders like genetic potential and environmental factors. While IUGR infants as a group tend to be shorter than their appropriate birth weight counterparts, they do exhibit partial catch up growth during the first two years of life<sup>77</sup>. The patterns of catch up growth tend to differ across IUGR sub-types. In conditions of optimal early nutrition, asymmetric IUGR babies exhibit catch up weight gain. In similar conditions the catch up growth potential of babies with symmetrical IUGR is limited and translates as an increase in height only in the first few months<sup>78</sup>. These babies tend to grow into stunted adults.

### **3.4.3 IUGR and cognitive development**

Subtle neurocognitive deficiencies are found to be common in IUGR babies. Evidence from the Child Development Centre, Kerala<sup>79</sup> shows that for IUGR babies, every 500g decrease in birth weight is associated with a corresponding decrease in the developmental status at one, two and five years of age. In the Guatemalan study, described above, Villar et al.<sup>80</sup> found that children born with proportional IUGR obtained a lower IQ score at 3 years on the Composite Infant Scale as compared to children with disproportional IUGR who in turn scored lower than the control group. For the same study group at the age of 3-5 years Gorman and Pollit<sup>81</sup> found that postnatal growth retardation and socio-economic status influences behavioural performance only in children that were born with IUGR.

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<sup>74</sup> Proos et al., 1992

<sup>75</sup> The window for catch up growth post birth are the first two years of life.

<sup>76</sup> Strauss et al., 1999

<sup>77</sup> ACC/SCN, 2000

<sup>78</sup> Dewey et al., 1999, as cited in ACC/SCN, 2000

<sup>79</sup> Nair, M. K. C., 2001

<sup>80</sup> Villar et al., 1984

<sup>81</sup> Gorman & Pollit, 1992, as cited in Martorell, 1997

#### **3.4.4 IUGR and adult morbidity: The Fetal Origins of Adult Disease**

The "Barker Hypothesis"<sup>82</sup> states that many degenerative diseases in adults, such as Coronary Heart Disease (CHD), hypertension, stroke and Non Insulin Dependant Diabetes Mellitus (NIDDM) are induced by the effects of undernutrition in fetal life and infancy, reflected as Low Birth Weight. This is explained by the effect of fetal "programming". Fetal programming refers to the process wherein in-utero exposure to undernutrition leads to permanent changes in metabolic and hormonal regulation systems in the body<sup>83</sup>.

Various authors have criticised Barker's hypothesis at different levels ranging from statistical interpretation<sup>84</sup> to the lack of consistency in the associations drawn between LBW and chronic adult disease<sup>85</sup>. As Jane Harding points out, birth weight is not a reliable indicator of the nature of in-utero events that may programme the fetus adversely. Insults at different points in gestation or of differing severity could in different fetuses result in the same birth weight at term.

Nevertheless, at the end of the First World Congress<sup>86</sup> a BMJ editorial<sup>87</sup> commented that the evidence looked convincing, especially for the association between IUGR and blood pressure and non insulin dependent diabetes mellitus. The combined evidence therefore predicts that more heart disease and impaired glucose tolerance will be seen in India.

#### **3.5 Focusing on IUGR**

Given the immediate and long-term implications of IUGR and its high prevalence in India, a focus on IUGR is both rational and strategic from a public health perspective. A 20% approximate prevalence of IUGR in India implies that it is a significant public health problem.<sup>88</sup> IUGR is strategic from the point of view of neonatal and infant mortality and adulthood morbidity.

IUGR's close connection with maternal and fetal undernutrition is an indicator of its interlinkages with poverty. Data enabling precise estimates of its prevalence by socio-economic class are not available in the Indian context. Nevertheless, the figures that are available and the relationship of IUGR with maternal undernutrition imply that the poor are

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<sup>82</sup> The Barker hypothesis has its origins in an extensive epidemiological analysis of diligently kept records in a Hertfordshire hospital suggested links between IUGR and an increased incidence of Coronary Heart Disease and stroke in adults. Barker, D. J. P., 1998

<sup>83</sup> The concept of "programming" (i.e. the idea that insults or stimuli during critical or sensitive periods in early life have permanent consequences in later life.) is well established in developmental biology. Many such examples exist. For instance, the eggs of the American Alligator if incubated at 30 degrees centigrade result in a female off-springs, and if incubated at 33 degrees centigrade result in male off-springs.

<sup>84</sup> Lucas et al., 1999

<sup>85</sup> See for instance, Kramer et al., 1996

<sup>86</sup> First World Congress on the Fetal Origins of Adult Disease, Mumbai, February, 2- 4, 2001

<sup>87</sup> BMJ Editorial, 2001, Vol. 322

<sup>88</sup> de Onis et al., 1998. A prevalence of or greater than 15% for LBW and 20% for IUGR are considered to be public health problems.

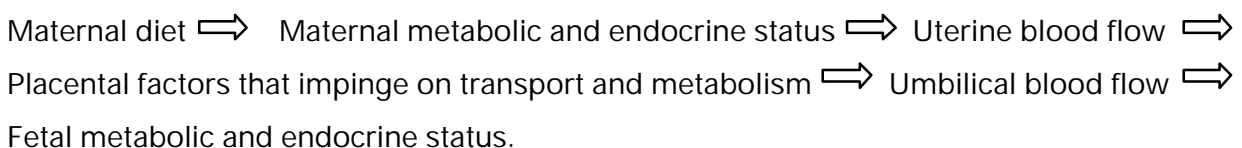
more likely to have IUGR babies. The potential impact that IUGR has on physical and cognitive development clearly indicates its impact on the achievable potential of the poor. Henceforth the paper deals exclusively with possible causes of IUGR to review implications for intervention.

#### **4. The Etiology of Intra-Uterine Growth Retardation (IUGR) Implications for Intervention**

Fetal development is the product of the interaction between genetic potential and the uterine environment. The nature of this interaction is such that the achievement of inherited genetic potential is essentially mediated by the intra-uterine environment<sup>89</sup>. Evidence for the mediating role of the maternal environment comes from kinship studies. An analysis of birth weights found that 62% of the variation between related individuals was the result of the intra-uterine environment; maternal genes caused 20% while fetal genes accounted for the remaining 18% of the variation<sup>90</sup>.

The uterine environment is influenced by maternal nutritional, hormonal and metabolic factors. These factors interact to impinge on the supply of nutrients and oxygen to the fetus. The nutrients and oxygen received by the fetus are significant determinants of fetal growth<sup>91</sup>. At this point, it may be crucial to distinguish between maternal nutrition and fetal nutrition<sup>92</sup>.

According to Jane Harding, fetal nutrition is the end result of a precarious supply chain, of which maternal nutrition and intake during pregnancy is only the starting point. This chain can be synthesised as:



Fetal nutrition is clearly not a simple function of maternal dietary intake during pregnancy, but is influenced by every link in the supply chain. All factors impinging on one or more of these links could impact fetal growth by ultimately impacting fetal metabolic and endocrine status. Given a constant level of maternal nutrition, the degree of efficiency with which the fetal supply line transfers nutrients to the fetus determines fetal growth.

<sup>89</sup> Kline et al., 1989

<sup>90</sup> Penrose, 1954

<sup>91</sup> Gluckman et al., 1990 as cited in Barker, D. J. P., 1998

<sup>92</sup> Harding, J., 2001

The mechanism by which fetal undernutrition impacts fetal development is known as fetal 'programming'. There is a critical period during development when a system is plastic. An environmental influence at this point pushes the system to develop in a certain direction. This leads to a particular effect known as 'programming'. These critical periods are typically more likely to be in the early stages of fetal development and at times of rapid cell replication. These programming influences thus set off further development, in a direction towards degenerative processes, rather than growth. This makes the individual likely to be born LBW and more prone to morbidity and mortality throughout the lifecycle.

The set of factors that could potentially influence the fetal supply line may be classified into:

(a) Maternal nutritional factors: maternal nutritional status can be proxied by several variables across the female lifecycle. These proxies include maternal height, pre-pregnancy weight and gestational weight gain.

(b) Maternal non-nutritional factors: these include parity, maternal morbidity during pregnancy including malaria and episodic illness and toxic exposures to tobacco and alcohol.

The selection of the above set of factors from the overall maternal environment is based on a large meta-analysis of 895 studies conducted by Kramer which established the independent causal effect of each factor<sup>93</sup>. The factors have been identified on the basis of (a) the strength of available evidence (b) prevalence of the risk factor in the context of developing countries and (c) modifiability in the short and long term. They are applicable to a developing country context and do not include other factors like medical complications of pregnancy, which may lead to IUGR<sup>94</sup>.

#### **4.1 Maternal height**

Evidence for the independent causal effect of maternal height on IUGR comes from Kramer's meta-analysis<sup>95</sup>. The meta-analysis estimated a sample size weighted effect of 7.8 g on birth weight for every centimetre of maternal height. It calculated a relative risk<sup>96</sup> (RR) of 1.27 for IUGR associated with a maternal height of less than 157.5-158 cm.

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<sup>93</sup> Kramer, M.S., 1987

<sup>94</sup> Sachdev, H.P.S., 2001

<sup>95</sup> Kramer, M.S., 1987

<sup>96</sup> A relative risk is a measure of association used in comparative studies to quantify the relationship between an exposure and a health outcome. It is typically calculated for prospective studies, where individuals are followed up and the risks of their developing the condition of interest are computed.

For the Indian population with a mean maternal height of 152 cm<sup>97</sup> and therefore an 84% prevalence of women less than 158 cm in height, the above findings imply that a maternal height of less than 158 cm may be responsible for 18% of the IUGR<sup>98</sup>.

The influence of maternal height on IUGR may be through a genetic mechanism or due to the physical limitations imposed on the growth of the uterus, placenta and the fetus. Maternal height is itself a function of the interaction between inherited genetic potential and the intra and extra-uterine environment. Malnutrition during uterine growth and the first two to three years of life leads to the onset of stunting<sup>99</sup> which is not completely reversed even with long term exposure to good nutrition<sup>100</sup>. In a study that followed up LBW Indian children adopted into wealthy Swedish families, it was found that the mean final (adult) height attained by the adopted Indian girls was 154 cm. This attained height was only 1 cm more than their poor counterparts in India and significantly less than the mean height of 159.2 cm attained by affluent Indian girls<sup>101</sup>. The LBW baby girl is likely to be a stunted adult woman, who in turn is likely to give birth to LBW babies, thereby perpetuating a vicious cycle through generations<sup>102</sup>.

The prevention of maternal stunting appears to be a necessary element of the package of interventions required to reduce IUGR. Intervening to prevent maternal stunting would require a focus on both intra-uterine growth and development during the first two years of life. Improvement in maternal height through these interventions is essentially possible only in the long term.

#### **4.2 Maternal pre-pregnancy weight**

Maternal pre-pregnancy weight has been identified as one of the best predictors of potential IUGR<sup>103</sup>. Kramer's meta-analysis found a sample size weighted independent effect of 9.5 g on birth weight for every 1 kg of maternal pre-pregnancy weight. It estimated an odds ratio<sup>104</sup> (OR) of 1.84 for IUGR associated with a pre-pregnancy weight of less than 49.5 kg for developed countries<sup>105</sup>.

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<sup>97</sup> Approximated from NFHS-2 data on the mean height of women. (15-49 yr.)

<sup>98</sup> The estimated attribution to maternal height is indicative only. It is based on the assumption of constant relative risks.

<sup>99</sup> Stunting is height expressed as a percentage of the expected height-for-age.

<sup>100</sup> Seshadri et al., 1989

<sup>101</sup> Proos, L. A, 1992 as cited in Gopalan, C., 1994

<sup>102</sup> Sachdev, H.P.S., 2001

<sup>103</sup> Hirve et al., 1994 as cited in Sachdev, H.P.S., 2001

<sup>104</sup> An odds ratio is a measure of association used in comparative studies to quantify the relationship between an exposure and a health outcome. It is typically calculated for retrospective and case-control studies where, after a medical condition is observed, the odds of individuals with or without the condition having been exposed to particular factors are calculated.

<sup>105</sup> Kramer, M.S., 1987

For the Indian context there is some controversy about the threshold of pre-pregnancy weight below which the relative risk for IUGR is greater than 1. An Indian Council of Medical Research multicentric study recorded a pre-pregnancy weight of less than 40 kg as an influencing determinant<sup>106</sup> while Viller et al. found a pre-pregnancy weight of less than 45 kg as significant<sup>107</sup>. The mean weight of Indian women in the reproductive age group (15-49) is 46.4kg<sup>108</sup>.

The postulated mechanism through which pre-pregnancy weight is believed to impact IUGR is linked to the determination of the intra-uterine growth rate. The intra-uterine growth rate is set on the basis of cell allocation between the placenta and the fetus<sup>109</sup>, which in turn is influenced by maternal nutritional and hormonal status. Better periconceptual<sup>110</sup> nutrition is believed to raise the growth trajectory and to increase the demand for nutrients in late gestation<sup>111</sup>. However, the evidence linking fetal growth limitation with maternal undernutrition at a distinct point in time or period either periconceptual or postconceptual is mixed. Instead, it has been proposed that female undernutrition across the lifecycle could harm fetal growth through its effects on maternal metabolic and endocrine status<sup>112</sup>. This ultimately impacts the fetus's access to nutrients.

The above evidence points to the potential importance of ensuring adequate pre-pregnancy weight in the process of reducing IUGR incidence. Interventions to improve pre-pregnancy weight would imply a focus on the nutrient intake of women of the reproductive age group, with an emphasis on the period of the adolescent growth spurt.

### **4.3 Gestational weight gain**

Gestational weight gain refers to maternal weight gain across the period of pregnancy. This can be understood either in aggregate terms or in terms of unit of weight gain per week or across the first, second and third trimesters. A WHO multi-centric study identified attained (maternal and fetal) weight at 20 weeks and at 36 weeks of gestation as a good predictor of IUGR<sup>113</sup>.

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<sup>106</sup> Bhargava et al., 1990

<sup>107</sup> Viller et al., 1986

<sup>108</sup> Estimated from mean height and mean body mass index for Indian women in the age group 15-49, National Family Health Survey-2, 1998-99

<sup>109</sup> Early in fetal development, the embryo consists of two groups of cells. The inner cell mass becomes the fetus and the outer cell mass the placenta.

<sup>110</sup> Around the point of conception.

<sup>111</sup> Barker D.J.P., 1998

<sup>112</sup> Harding J.E., 2001

<sup>113</sup> WHO, 1995

Kramer's classic meta-analysis<sup>114</sup> reported a positive relationship between gestational weight gain and gestational-age-adjusted birth weight. Strauss et al.<sup>115</sup> in their literature review<sup>116</sup> and analysis of two cohorts present substantial evidence on the importance of adequate weight gain during the second trimester of pregnancy<sup>117</sup>. This remains true even when overall weight gain was adequate during pregnancy. Low weight gain in the second or third trimesters was associated with approximately double the risk of IUGR. 73% to 82% of all patients with inadequate weight gain in the second and third trimesters had normal weight gain overall. A study by Scholl et al.<sup>118</sup> highlights a two-fold increase in IUGR when weight gain is low in the second trimester.

Gestational weight gain is found to interact very closely with pre-pregnancy weight gain. Miller et al.<sup>119</sup> reported that IUGR rates increased among women with low gestational weight gain as their pre-pregnancy weight for height decreased. This implies that in developing countries with a low pre-pregnancy weight and gestational weight gain of less than 7 kg, the relative risk of poor gestational weight gain for IUGR is much higher.

The exact mechanism by which gestational weight gain affects fetal growth is not clear and it has been used largely as a rough indicator of fetal growth. Gestational weight gain is a function of (a) the physiological process of pregnancy and fetal growth i.e. plasma volume and amniotic fluid expansion, growth of uterine tissue, of the fetus and placenta etc, and (b) the laying down of fat stores. The fat stores laid down ultimately impact fetal growth rate but do not indicate the growth rate at a particular point in time.

Ensuring adequate gestational weight gain among at-risk mothers seems to be a potentially useful intervention to reduce IUGR incidence. The general consensus is that weight gain of at least 1 kg per month is necessary if IUGR is to be avoided, particularly among undernourished women. Nutritional interventions during pregnancy could hold the potential to improve gestational weight gain.

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<sup>114</sup> Kramer, M. S., 1987

<sup>115</sup> Strauss, R. S. & Dietz, W. H., 1999

<sup>116</sup> Studies analysed include Abrams & Selvin, 1995, Hickey et al., 1996, Lawton et al., 1988, Scholl et al., 1990

<sup>117</sup> Adequate gestational weight gain is taken to mean a weight gain greater than the defined low gestational weight gain. Low gestational weight gain in this study is defined as 0.3 kg/ week in the second and third trimesters. Low gestational weight gain overall is defined as less than 6.8 kgs. (Institute of Medicine norms)

<sup>118</sup> Scholl et al., 2000

<sup>119</sup> Miller et al., 1979 as cited in Kramer, M.S., 1987.

#### **4.4 Age & Parity**

Parity refers to the number of live births borne by a woman<sup>120</sup>. It is correlated with birth weight such that higher parity is accompanied by an increase in mean birth weight. Kramer's meta-analysis<sup>121</sup> found a sample size weighted effect of 43.3 g on birth weight per birth associated with parity. It estimated a relative risk of 1.23 for IUGR associated with primiparity<sup>122</sup>.

Parity interacts with age, such that multiparity<sup>123</sup> increases the risk of LBW for women aged less than 20, has little effect on women aged 20-34 and substantially decreases the risk of LBW for women more than 35 years in age. Thus the risk group from the standpoint of parity-age interaction is young multiparae<sup>124</sup>.

In the Indian context, according to the NFHS-2 an estimated 29% of births are first order births<sup>125</sup>. This is indicative of the proportion of all births exposed to the risk of IUGR associated with primiparity. As a pointer to the risk that young multiparity poses for IUGR, 26% of births to women of age group 15-19 were of a birth order greater than 1<sup>126</sup>. However, births to 15-19 year old women constitute only 11% of the total births<sup>127</sup>.

Parity can function as a predictor of IUGR but is unlikely to be modifiable at the individual case level. However, the risk that the grand multipara faces has relevance in a public health context in which the risk for IUGR may be reduced through advocacy for and adherence to a 'small family' norm.

#### **4.5 Maternal morbidity**

Maternal morbidity in terms of general episodic illnesses and malaria has been found to have a significant impact on the incidence of IUGR. According to Kramer's analysis<sup>128</sup> conditions such as anorexia, headache and diarrhoea in rural developing country populations may reduce birth weight by an average of 45 g. The mechanisms by which bouts of such illnesses could impact the incidence of IUGR may be: reduction of food intake, metabolic cost of the illness and reduction in uterine blood flow.

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<sup>120</sup> Draft Dictionary of Demographic and Reproductive Health Terminology, United Nations, 1999

<sup>121</sup> Kramer M.S., 1987

<sup>122</sup> The state of a woman who has given birth to her first, only child. (Draft Dictionary of Demographic and Reproductive Health Terminology, United Nations, 1999)

<sup>123</sup> The state of a woman who has given birth to more than one child. (Draft Dictionary of Demographic and Reproductive Health Terminology, United Nations, 1999)

<sup>124</sup> Kramer M.S., 1987

<sup>125</sup> National Family Health Survey-2, 1998-99. The births referred to occurred in the three years preceding the survey.

<sup>126</sup> Ibid.

<sup>127</sup> Ibid.

<sup>128</sup> Kramer M.S., 1987

Evidence for the influence of malaria on the incidence of IUGR comes from retrospective studies due to ethical reasons. Macgregor et al.<sup>129</sup>, found that in the Solomon Islands with the spraying of DDT the mean birth weight increased by 165 g and the rate of LBW decreased from 20.5 % to 11.8%. In a related study Macgregor found a 170 g decrease in birth weight in a larger sample for women with placental malaria.

Pregnant women are more likely to become infected with malaria because pregnancy inhibits anti malarial immunity. Besides the metabolic and physiological consequences of malaria, the malarial parasite tends to infect the placenta, which may affect the uterine blood flow leading to growth retardation.

The significance of maternal morbidity during pregnancy for the incidence of IUGR emphasizes the need for customised and early antenatal care for at risk populations and greater public health measures to prevent vector-borne diseases in developing countries in general.

In India the most commonly reported health problem during pregnancy is excessive fatigue. According to the NFHS-2, 43% of the respondents experienced excessive fatigue during pregnancy. This may be linked to the fact that 35.8% of women in the reproductive age group have a body mass index of less than 18.5 kg/m<sup>2</sup>, which is indicative of chronic energy deficiency<sup>130</sup>. However, malaria as a problem has seen a resurgence in India and according to the WHO, 90% of the population living in moderate to high risk of malaria lives in India, Indonesia, Myanmar and Thailand<sup>131</sup>. National data on the incidence of malaria during pregnancy is not available but the impact of malaria on IUGR incidence in India needs to be explored.

#### **4.6 Toxic exposures**

Maternal toxic exposures through smoking or tobacco consumption and alcohol intake are found to have deleterious effects on fetal growth.

Studies are unanimous regarding the effects of smoking on fetal growth. Kramer's meta-analysis<sup>132</sup> found an average decrease of 11.1 g in birth weight per cigarette. It estimated a relative risk of 2.42 for IUGR associated with smoking. Cigarette smoking can affect intra-uterine growth through the effects of carbonmonoxide and nicotine. Carbonmonoxide affects

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<sup>129</sup> Macgregor et al., 1974 as cited in Kramer, M.S., 1987

<sup>130</sup> National Family Health Survey-2, 1998-99

<sup>131</sup> World Health Organisation: <<http://w3.who.org/malaria/problem1.htm>>

<sup>132</sup> Kramer M.S., 1987

the supply of oxygen to the fetus while nicotine is an appetite suppressant and constricts uterine blood vessels. The effect of smoking on birth weight is more marked for the last trimester.

For India, the prevalence rates for the use of smokeless tobacco by women in general vary from 0.2 % in the state of Punjab to 33.2 % in Arunachal Pradesh to 60.7% in Mizoram. However, overall prevalence of smoking and use of smokeless tobacco among women is approximately 3% and 12.4% respectively<sup>133</sup>.

Alcohol consumption impacts IUGR by causing fetal hypoxia or decreasing the incorporation of amino acids from protein. Kramer found that consumption of 2 drinks or more per day decreases birth weight by 155 g. The relative risk for IUGR associated with the consumption of 2 or more drinks per day was 1.78<sup>134</sup>. Exposure to absolute alcohol in the latter stages of pregnancy is found to have a relatively greater impact.

Consumption of alcohol by women (above 15 yr.) in India also varies by state but at a national level is 2.2% in general and 4.4% for women of a low socio-economic status<sup>135</sup>.

#### **4.7 Implications for intervention: a lifecycle approach**

The etiology of IUGR is complex and multi-factoral. Deriving directions for intervention to reduce IUGR incidence from an examination of the etiological evidence is therefore not an easy task. In principle, the significance of a causal factor in a given population depends upon the interaction between the magnitude of its effect and its prevalence in that particular population. In addition, the determination of any intervention is guided by the understanding that a focus on a few critical and related causes yields greater impact at the level of public health in the short and long term than a scattered attempt to address every cause.

Applying this approach to the causality of IUGR in the Indian context, the risk factors that assume significance are the maternal nutritional factors as manifested in maternal height, pre-pregnancy weight and gestational weight gain<sup>136</sup>.

The prevalence and effect magnitude of the factors examined in this section in the Indian context may be roughly summarised as follows:

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<sup>133</sup> NFHS-2, 1998-99

<sup>134</sup> Kramer M.S., 1987

<sup>135</sup> NFHS-2, 1998-99

<sup>136</sup> The authors recognise that more accurate—with reference to IUGR—indicators of female/ maternal nutritional status need to be identified/ developed. Exploring this issue, however, is beyond the scope of this paper.

Table no. 1: Risks factors for IUGR and their prevalence in India

S. No	Factors	Effect magnitude in terms of relative risk/odds ratio for IUGR <sup>137</sup>	Prevalence in India <sup>138</sup>
1.	Maternal height	RR: 1.27 for a maternal height of less than 157.5-158 cm	84%
2.	Pre-pregnancy weight	OR: 1.84 for a pre-pregnancy weight of less than 49.5 kg	The mean weight of Indian women in the 15-49 age group is 46.4 kg
3.	Gestational weight gain	RR: 1.98 for a weight gain of less than 7 kg.	Not Available
4.	Parity	RR: 1.23 for primiparity	29% first order births
5.	Maternal morbidity	Malaria control increased birth weight by 165 g	90% of the population at moderate to high risk of malaria lives in India, Indonesia, Myanmar and Thailand <sup>139</sup>
6.	Toxic exposures	RR: 2.42 for smoking RR: 1.78 for consumption of more than 2 drinks per day	3% of women smoke and 12.4% use smokeless tobacco. Consumption of alcohol by women nationally is 2.2%

While each of the above factors has been found to independently affect IUGR, in interaction with each other the effects of these factors may well be greater than their independent effects. Based on the above analysis, this paper takes the view that the maternal nutritional causes of IUGR incidence in India require urgent attention in view of their significance and complexity.

## 5. Defining Intervention

### 5.1 Debates regarding nutritional interventions

The previous chapter argued that maternal undernutrition is a key cause of IUGR in the Indian context. However, paradoxically enough, whether nutritional interventions to reduce IUGR are more harmful than beneficial for the baby is a point of serious debate.

Yajnik<sup>140</sup> presents a paradoxical observation that is the starting point of this debate. He points out that the prevalence of Coronary Heart Disease (CHD) and diabetes is at least four times as common in urban than in rural India. This is despite the fact that maternal malnutrition is more widespread (and possibly more severe) in rural India. He suggests that this apparent paradox can be explained if adult body size is factored in. While urban adults are 109% larger than their rural counterparts at birth, they outgrow their rural counterparts by 130% in adulthood. Urban

<sup>137</sup> The relative risks/odds ratios quoted are from M.S. Kramer's 1987 meta-analysis which is largely based on data from developed countries.

<sup>138</sup> The figures are drawn from the National Family Health Survey- 2 data (1998-99)

<sup>139</sup> <http://w3.who.org/malaria/problem1.htm>

<sup>140</sup> Yajnik, C. S., 2001

adults have a mean BMI of 20 kg/m<sup>2</sup>, compared to a mean BMI of 19 kg/m<sup>2</sup> for rural adults. Babies most likely to develop CHD or diabetes in adulthood were those who were born small but who had grown big in later life<sup>141</sup>.

Evidence from Mysore, India, brings to light the possibility that retarded intra-uterine growth lowers the nutritional threshold for risk of obesity in adulthood. The highest prevalence of CHD at 45 years of age was found in individuals who had lower weight, head circumference or height at birth but 'normal' weight as adults<sup>142</sup>. 'Normal' adult weight for IUGR babies may be the outcome of a substantial upward movement during postnatal growth. Populations with a high prevalence of IUGR (and LBW) face an increased risk of developing cardio-vascular disease and diabetes at a lower BMI threshold than populations without a high prevalence of IUGR (and LBW)<sup>143</sup>.

This implies that post-natal 'catch-up growth' has its own set of problems. The endocrine and metabolic adaptations that the fetus makes in response to in-utero malnutrition programme the pathways of nutrient utilisation in later life<sup>144</sup>. When post-natal improvements in nutrition result in a positive energy balance, the individual ('programmed' to be 'thrifty' in-utero) tends to deposit fat, especially in 'central' depots<sup>145</sup>.

A recent study conducted by Rao et al.<sup>146</sup> in Pune involving increased Green Leafy Vegetable pre-natal intake by mothers found that babies had better birthweights but were also "fat-fat" and "muscle-thin"<sup>147</sup>. While this has benefits for neonatal survival, it also increases long term risk of developing cardiovascular disease. Even prenatal supplementation could have deleterious consequences—for a few transitional generations at least.

The debate is a complex one. At a very basic level, survival is a pre-requisite to leading a healthy life. Tangible benefits for perinatal, neonatal and infant mortality are likely if the birth weight distribution shifts to the right through improvements in maternal nutrition. The birth weight range associated with the lowest infant mortality is 3500 to 4000 g<sup>148</sup>. Given that 33% of Indian babies weigh less than 2500 g, there is considerable room for improvement. Higher birthweight—even if "fat-fat" and "muscle-thin"—is likely to have benefits for neonatal and infant mortality. Moreover, the cohort supplemented in the Pune study<sup>149</sup> is being followed up. Additional information on the likely implications of 'muscle-thin' and 'fat-fat' increase in birth weight will be available in the near future.

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<sup>141</sup> Ibid.

<sup>142</sup> Stein et al., 1996

<sup>143</sup> Yajnik, C. S., 2001

<sup>144</sup> Ibid.

<sup>145</sup> This manifests itself in increased waist to hip ratio.

<sup>146</sup> Rao et al., 2001

<sup>147</sup> Yajnik, C. S.: presentation at the First World Congress on Fetal origins of Adult Disease, 2001, Mumbai.

<sup>148</sup> This is true for UK, USA and Norway. McCormick, M. C., 1985, Ashworth, A., 1982

<sup>149</sup> Rao et al., 2001

Improving nutritional status and eliminating micronutrient deficiencies will have a positive impact on cognitive development with consequent positive spin-offs for achievable potential among the poorest.

Finally, the nutritional transition is an inevitability. Urban India is in the throes of this transition. Rural-urban migration is an established phenomenon. It could be argued that optimal nutrition allowing for the “thriftness” programmed in-utero would imply the need to keep Indians at low levels of nutritional intakes. This is neither feasible nor optimal in the long run. Poor nutrition also carries its own set of survival and health risks.

The paper takes the view that improving maternal nutrition and reducing IUGR incidence is desirable from an ethical and public health point of view.

## **5.2 *Defining the precise nutritional goals for intervention***

Defining the precise set of nutritional factors that are causally linked to IUGR is the starting point for defining the nature of intervention required. Given the need for a preventive focus, addressing risk factors that indicate the likelihood of an IUGR outcome is critical. Strategies to reduce IUGR incidence typically include a package of interventions addressing risk factors across the lifecycle<sup>150</sup>. The impact of these interventions across two or more generations is expected to break the IUGR vicious cycle. The cumulative impact of the package may be greater than the sum of the impact of each individual intervention.

Assessing the impact of lifecycle based strategies is difficult because of the paucity of accurate information on impact and (in the case of NGO intervention areas) the history that individual NGOs have in their field areas. This section attempts to review the evidence for impact achievable by addressing individual risk factors, which are modifiable over the short term. In the Indian context, this would include: inadequate gestational weight gain, macronutrient<sup>151</sup> and micronutrient<sup>152</sup> deficiencies during pregnancy and low pre-pregnancy weight<sup>153</sup>. These risk factors essentially mirror female undernutrition across the lifecycle. There could be an overlap in the physiological pathways through which these risk factors impact IUGR.

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<sup>150</sup> The general consensus is that lifecycle based interventions are the most feasible way to break the IUGR vicious circle. This consensus has been endorsed at “The International Symposium and Workshop on LBW”, Dhaka, 1999 and “The Short and Long term consequences of LBW”, New York, 2000.

<sup>151</sup> A food substance mainly important for the calories it provides, such as carbohydrates, proteins or fats.

<sup>152</sup> A food substance that is consumed in small portions and is needed for physiological processes.

<sup>153</sup> The authors have not found adequate information on interventions to increase pre-pregnancy weight. The chapter therefore does not review pre-pregnancy weight.

### **5.2.1 Improving gestational weight gain**

As chapter 4 indicates, gestational weight gain (in terms of overall maternal weight gain during pregnancy) is both an outcome and determinant of fetal growth. It is possible that gestational weight gain mediates the impact of identified risk factors on birth weight.

How to increase gestational weight gain—with a view to increasing fetal growth—is a matter of debate. Both macronutrients and micronutrients may have a role to play. This chapter seeks to explore the evidence for the impact that sub-optimal macronutrient and micronutrient status before and during pregnancy may have on IUGR. Whether this impact is necessarily reflected in better gestational weight gain (i.e. in overall maternal weight gain) is not entirely clear.

### **5.2.2 Improving macronutrient intake**

Improving macronutrient intake during pregnancy presents a means of improving gestational weight gain among women at nutritional risk. The average daily dietary intake is 2153 kcal in rural India and 2071 kcal in urban India<sup>154</sup>—below the 2400 kcal recommended. Intra-household distributional factors are likely to distribute food away from women in the family. Average figures of caloric intake are therefore very likely to be over-estimates of women's (and pregnant women's) daily intake. ICMR has recommended that dietary allowances for pregnant women should be 300 kcal and 10 to 15 g of protein daily, over and above the corresponding requirement for non-pregnant women of matched weight and height. This would imply a recommended average caloric intake of at least 2700 kcal per day.

These requirements are well above the average caloric intake in 9 major states in India. In the absence of comprehensive figures, BMI data provided by NFHS-2 are indicative of inadequate caloric intake by pregnant women<sup>155</sup>.

Existing evidence from studies, however, is not entirely consistent regarding an association between increased intake<sup>156</sup> and improved birth weight. The strength of association obtained is also not entirely consistent across studies. Data from some studies<sup>157</sup> in developing countries suggests that caloric supplementation during pregnancy leads to significant weight gain across pregnancy but only modest increases in birth weight among women at nutritional risk.

Kramer's 1987 meta-analysis of caloric supplementation studies<sup>158</sup> indicated a significant impact of maternal caloric intake on birth weight, provided the mother is not well nourished prior to pregnancy. The impact, however, varies according to maternal nutritional status.

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<sup>154</sup> NSS 1993- 94 estimates

<sup>155</sup> Mean BMI for India is 21.3 kg/m<sup>2</sup>. 38.8%, 41.8% and 35.8% of married women in the 15-19, 20-24 and 15-49 age groups respectively have a BMI less than 18.5 kg/m<sup>2</sup>- NFHS- 2

<sup>156</sup> The reference throughout is to women at nutritional risk.

<sup>157</sup> Mardones-Santander et al., 1988; Tontisirin et al., 1986; Lechtig et al., 1975

<sup>158</sup> An important factor that needs to be controlled for to determine relationship with gestational weight gain and birth weight would be caloric expenditure.

Working with the simplifying assumption that calories taken at any time have the same impact on birth weight, Kramer calculates a sample size weighted average birth weight gain of 99.7 g/100 kcal of intake per day among women who have a BMI of less than 20 kg/m<sup>2</sup>. This analysis did not correlate these findings with gestational weight gain across pregnancy.

### ***Evidence from balanced protein-energy supplementation studies***

Subsequent meta-analyses<sup>159</sup> of balanced protein-energy supplementation<sup>160</sup> randomised controlled trials identify only a modest increase in maternal weight gain and fetal growth, even among under-nourished women. In their meta-analyses, de Onis et al.<sup>161</sup> and Kramer<sup>162</sup> point out that the improvements in fetal growth were lower among the more under-nourished women. While poor compliance could be one explanation, another more disturbing explanation is that chronically malnourished women do not respond readily to acute increases in intake<sup>163</sup>. Fetal growth for chronically undernourished mothers could be improved with more long term improvements in intake as demonstrated by Villar et al.<sup>164</sup>. Improving pre-pregnancy BMI by improving pre-pregnancy macronutrient status may be more efficacious.

On the other hand, it could also be that the modest improvements in fetal growth achieved through balanced protein-energy supplementation are despite the common pitfalls in supplementation studies—poor compliance and dietary replacement<sup>165</sup>. It can be argued that the apparently modest effect is indicative of the larger potential that protein-energy supplementation holds for reducing IUGR incidence.

### ***High energy supplementation-evidence from the Gambia study***

A five-year randomised controlled trial in rural Gambia by Ceesay et al.<sup>166</sup> found that the supplementation of chronically undernourished Gambian women<sup>167</sup> with high energy biscuits (4.3 MJ/ day) produced a significant increase in birth weight. Maternal weight gain was also substantially greater in supplemented villages as compared to the control villages. The increase in birth weight varied by level of nutritional deprivation. The average birth weight increase in supplemented villages was greatest—201g—during the ‘hungry season’ when workload is the highest. In comparison, the average birth weight increase in supplemented villages during the harvest season was approximately 94 g.

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<sup>159</sup> Kramer, M. S., 1993; Kramer, M. S., 2002, Gulmezoglu, 1997

<sup>160</sup> A supplement wherein protein accounts for less than 25% of the total energy content.

<sup>161</sup> de Onis et al., 1998

<sup>162</sup> Kramer, M. S., 1993

<sup>163</sup> Ibid.

<sup>164</sup> Villar et al., 1988 as cited in de Onis et al., 1998

<sup>165</sup> de Onis et al., 1998

<sup>166</sup> Ceesay et al., 1997

<sup>167</sup> Gambian women gain about 60% of the optimal weight gain during pregnancy and also lose fat stores during pregnancy.

The impact achieved in the Gambia intervention by Ceesay et al. is greater than the modest gains observed in other macronutrient supplementation studies. Whether this large difference in impact can be attributed entirely to compliance and study design problems is a valid question.

### ***Evidence from high protein supplementation studies***

A high protein content in supplements has been found to have a deleterious impact on fetal growth. The Mardones-Santander<sup>168</sup> trial in Chile found an increased risk of IUGR births for a supplement with higher protein content than for one with normal protein content<sup>169</sup>. Two other high protein supplementation trials reviewed by de Onis et al.<sup>170</sup> also suggest the possibility of an increase in IUGR. Kramer observes that protein supplementation does not appear to confer any benefits and may even impair fetal growth<sup>171</sup>

### **5.2.3 Micronutrient deficiencies**

Micronutrients—vitamins and minerals—play a significant part in the metabolism of macronutrients (protein and energy) and in maintaining tissues at an optimal level of activity<sup>172</sup>. The specific facilitation function performed by each micronutrient varies, as does the daily intake requirement<sup>173</sup>.

While recent evidence suggests that micronutrient deficiencies may be a significant cause of IUGR<sup>174</sup>, the question of which micronutrients are 'limiting' factors leading to IUGR may have a context sensitive answer. Most randomised controlled trials have been conducted in developed countries where populations tend not to suffer from micronutrient deficiencies. This and other study design problems render these study findings inconclusive.

A number of micronutrients have been implicated as factors causing IUGR either independently or because of their effects on other micronutrients that may cause IUGR. The paper however restricts itself to iron for its independent impact on IUGR.

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<sup>168</sup> Mardones- Santander et al., 1988

<sup>169</sup> The supplement with normal protein content also contained higher concentrations of vitamins, iron and other micronutrients than that with higher protein content.

<sup>170</sup> Rush et al., 1980 and Iyengar, 1967

<sup>171</sup> Kramer, M. S., 1993

<sup>172</sup> Sethi, G. R., 1994 in Gopalan C. (Eds.) Nutrition in Children: developing country concerns.

<sup>173</sup> This is a function of the intake quantum required to maintain all processes affected by that micronutrient at an optimal level.

<sup>174</sup> Ramakrishnan et al., 1999

## Iron

Iron deficiency anaemia is defined as a haemoglobin concentration that is more than 2 standard deviations below the mean for healthy individuals of the same age, sex and stage of pregnancy.

The WHO criteria for anaemia in women is:

- Adult women (non-pregnant): 12 g/dl
- Adult women (pregnant): 11g/dl<sup>175</sup>

The prevalence of iron deficiency anaemia in India among pregnant women has been found to be almost 87% with 10% of the women suffering from severe anaemia (Hb < 8 g/dl)<sup>176</sup>.

Iron deficiency anaemia signifies a stage of severe iron deficiency<sup>177</sup>. By the time a woman becomes anaemic, her iron stores have been depleted and biochemical processes affected<sup>178</sup>. If a woman begins pregnancy with anaemia, she has effectively no iron stores to meet the increased requirements of iron during pregnancy. Iron deficiency anaemia has long been implicated in the causation of IUGR. That there is a strong association between iron deficiency anaemia during pregnancy and IUGR is undisputed and established by several observational studies<sup>179</sup>. Given this, an 87% prevalence of anaemia among pregnant women in India is a matter of serious concern and requires further investigation.

However, whether iron deficiency anaemia is causally linked to IUGR is a matter of debate. The paucity of *causal* evidence either way is mainly a result of study design problems, and also of ethical problems with conducting randomised controlled trials. It is also seriously confounded by measurement issues, especially during pregnancy.

Exploring whether or not a causal relationship between iron deficiency anaemia and IUGR exists is interesting for two main reasons:

- Most evidence points in the direction of a strong relationship. The only study without major study design defects identified in Rasmussen's review<sup>180</sup> provided evidence of a statistically significant positive effect of iron supplementation on birth weight. Those studies that have negative findings have serious study design problems that bias them<sup>181</sup>.
- The extent of anaemia prevalence among pregnant Indian women.

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<sup>175</sup> The cut off below which a woman is likely to be anaemic is lower for pregnant women as compared to non-pregnant women to account for the expansion in blood plasma volume that occurs in pregnant women in the last two trimesters. The disproportionate increase in plasma volume during pregnancy leads to a drop in haemoglobin concentration of approximately 1g/dl (Bothwell, 2000).

<sup>176</sup> ICMR Bulletin, 2000

<sup>177</sup> Iron deficiency anaemia is the third stage in the progressive development of iron deficiency- namely iron stores depletion, impaired haemoglobin production, and finally, iron deficiency anaemia.

<sup>178</sup> The implications of this for bodily functioning are a matter of debate. There are those such as Viteri who suggest that even sub-clinical iron deficiency has deleterious consequences and is therefore a matter of concern. On the other hand, there are others who suggest that only severe anaemia should be regarded as an issue.

<sup>179</sup> Rasmussen, K., 2001

<sup>180</sup> Rasmussen, K., 2001

<sup>181</sup> Ibid.

A positive finding would further heighten the need to understand and address the various programmatic issues in the National Nutritional Anaemia Prophylaxis Programme. Some of the significant programmatic issues relate to sub-optimal absorption of iron due to other dietary factors<sup>182</sup> and micronutrient interactions.

### ***Micronutrient Interactions***

In practice, multiple micronutrient deficiencies tend to co-exist<sup>183</sup>. Vitamin A deficiency, for instance, interferes with iron absorption<sup>184</sup>. Vitamin C enhances iron absorption<sup>185</sup>. High doses of zinc, on the other hand, interfere with iron absorption. The few RCTs available have not been designed to test the relative benefit of multiple micronutrient supplementation programmes over selective supplementation<sup>186</sup>. Addressing a single micronutrient deficiency pharmacologically in this context may not achieve much impact on IUGR. There is a strong case for addressing multiple micronutrient deficiencies simultaneously.

Pill based supplementation brings with it the various problems mentioned above. These issues do not apply to micronutrient intake through foods—fortified or non-fortified. Some micronutrients can also present toxicity concerns<sup>187</sup> when taken as pills. Cost presents another dimension of concern.

### ***Micronutrient Rich Foods—Green Leafy Vegetables, milk and fruits***

Given these issues, both multiple micronutrient fortification and increasing consumption of micronutrient rich foods are generating considerable interest.

Recent research suggests that Green Leafy Vegetables (GLV) may play a significant role in reducing IUGR incidence<sup>188</sup>. The Pune Maternal Nutrition Study sought to observe the relationship between GLV, milk and fruit intake and size at birth among 797 women near Pune. Approximately thirty-one percent of these women had a body mass index of less than 17 kg/m<sup>2</sup>—indicative of chronic energy deficiency<sup>189</sup>. The study adjusted for gestational age at delivery, the baby's sex and maternal parity.

The study found a significant relationship between milk, fruits and GLV consumption and size at birth.

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<sup>182</sup> See for instance, ICMR, 2000

<sup>183</sup> Ramakrishnan et al., 1999

<sup>184</sup> Kolsteren et al., 1999

<sup>185</sup> Sandstorm, B., 2001

<sup>186</sup> Black, R. E., 2001

<sup>187</sup> Such as Vitamin A.

<sup>188</sup> Rao et al., 2001

<sup>189</sup> World Health Organisation, 1995

- GLVs: GLV consumption<sup>190</sup> was associated with an increase of 19 g in birth weight. This trend was the strongest among the lightest mothers. An average increase in birth weight of approximately 90 g was achieved among the lightest mothers in this study consuming GLV most frequently<sup>191</sup>. The odds for delivering a Low Birth Weight baby was 0.43 among those mothers consuming GLVs as opposed to 1.0 among mothers who never consumed them.
- Fruits: The frequency of fruit consumption at 28 weeks of gestation was related to birth weight, birth length and head circumference. Again, the relationship was the strongest among the lightest mothers. A 15 g increase was achieved among women with a pre-pregnancy weight of less than 40 kgs. The sample average increase was 4 g.
- Milk products<sup>192</sup>: After adjusting for all of the above factors, the frequency of milk consumption at 18 weeks gestation was related to birth weight, birth length, mid-upper arm circumference, head circumference and placental weight.

Rao et al. conclude that micronutrient deficiencies may be critical factors leading to IUGR among undernourished women. They also suggest that the observed differential impact of nutrients at different points in gestation may indicate the varied nutritional needs of different developing tissues. The precise causal pathway through which GLVs, fruit and milk impact birth weight in combination is not clear as yet.

The implications of these findings for intervention are far-reaching. However, as this was an observational study, the women consuming GLV, fruit and milk most frequently were those from higher socio-economic strata and had a higher pre-pregnancy body mass. Further research on this subject may be needed.

### **5.3 Summing up**

Maternal macronutrient and micronutrient status has a bearing on IUGR incidence. The relative significance of the two or the causal pathway through which either macronutrient or micronutrient deficiencies impact IUGR is not entirely clear. Several studies do, however, document the effects of macronutrient and micronutrient/s (food and pill based) supplementation on birth weight.

This chapter explored the impact of different kinds of nutritional supplementation on birth weight—balanced protein-energy, high energy, high protein and single (iron) and multiple (food-based) micronutrient supplementation.

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<sup>190</sup> This is after adjusting for the relevant variables.

<sup>191</sup> Those with a pre-pregnancy weight below 40 kg. Those consuming GLVs 'most frequently' consumed GLV 'greater than or equal to every alternate day'. Rao et al., 2001

<sup>192</sup> Milk consumption is strongly associated with socio-economic status.

Balanced protein-energy supplementation studies: Study design problems in existing studies do not permit conclusive inferences about the possible benefits of balanced protein-energy supplementation during pregnancy. While only modest benefits are apparent, further research is necessary before ruling out its potential to reduce IUGR.

High energy supplementation—the Gambia study: A community-based trial in Gambia showed that high energy supplementation during pregnancy improved birthweight, especially during the hungry season. In the Gambian context there were clear seasonal variations in gestational weight gain and birth weight. The efficacy of high energy food supplementation in terms of an impact on birth weight needs to be validated in the Indian context.

High protein supplementation studies: these have found a problematic impact of high protein supplements on birthweight.

Pre-pregnancy BMI: Improving pre-pregnancy body mass index (BMI) by improving pre-pregnancy macronutrient status is an area that may be worth exploring further through well-designed intervention research. The pre-pregnancy BMI threshold(s) that results in an increased risk of IUGR at the population level for the Indian context remains unidentified.

Micronutrient supplementation studies: The role of micronutrients in reducing IUGR has gained significance relatively recently. Many studies have been carried out on the impact of micronutrient deficiencies on birth outcomes. Most of these, however, have been conducted in populations where micronutrient deficiencies are not a problem. Drawing conclusions from this body of research is not easy.

India has an 87% anaemia prevalence among pregnant women. Available literature documents a strong association between iron deficiency anaemia and LBW. However, whether this linkage is causal i.e. whether curing anaemia will reduce LBW/ IUGR incidence is unclear. Conducting randomised controlled trials to clarify this point is difficult because of ethical concerns. A significant point of interest within the question of causality is whether improving pre-pregnancy iron status is the most effective way of improving birth weight.

Most micronutrient studies test the impact of a single micronutrient on birth outcomes when, in practice, multiple micronutrient deficiencies tend to exist. Interactions between micronutrients consumed in pill form create additional problems in making inferences from the body of available knowledge. A strong case therefore exists for addressing multiple micronutrient deficiencies simultaneously through food rather than pharmacologically.

A recent observational study in Pune has found a strong correlation between milk, fruit and GLV consumption during pregnancy and size at birth. The effects of increased consumption were stronger among the more undernourished women. However, a higher consumption of milk, fruit and GLV was apparent among women from a higher socio-economic class. Further

research in terms of a randomised controlled trial may be required to establish impact on fetal growth and birth weight.

## Glossary

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**Amniotic fluid:** The fluid bathing the fetus and serving as a shock absorber.

**Anemia:** The condition of having less than the normal number of red blood cells or less than the normal quantity of haemoglobin in the blood. The oxygen-carrying capacity of the blood is, therefore, decreased.

**Anorexia:** Poor appetite.

**Asphyxia:** Inadequate supply of oxygen to tissues of the body.

**Asymptomatic bacteriuria:** The presence of bacteria in the urine without producing symptoms of urine infection.

**Body mass index (BMI):** A key index for relating body weight to height. The BMI is a person's weight in kilograms (kg) divided by their height in meters (m) squared.

**Cardiovascular disease:** Disease affecting the heart or blood vessels.

**Catecholamines:** Vasoactive amines secreted by the adrenal glands, which circulate in the blood and are active in stress responses, e.g. adrenaline.

**Coronary heart disease:** A major cause of illness and death, coronary heart disease (CHD) begins when hard cholesterol substances (plaques) are deposited within a coronary artery.

**Etiology (adj: etiologic):** The word "etiology" is mainly used in medicine, where it is the science that deals with the causes or origin of disease, the factors which produce or predispose toward a certain disease or disorder.

**Ferritin:** The major iron storage protein. The blood level of ferritin serves as an indicator of the amount of iron stored in the body.

**Gestation:** Period from conception upto birth.

**Hyaline membrane disease:** A respiratory disease of the newborn, especially the premature infant, in which a membrane composed of proteins and dead cells lines the alveoli (the tiny air sacs in the lung), making gas exchange difficult or impossible. The word "hyaline" comes from the Greek word "hyalos" meaning "glass or transparent stone such as crystal." The membrane in hyaline membrane disease looks glassy.

**Hyperbilirubinemia:** An elevated level of the pigment bilirubin in the blood. A sufficient elevation will produce jaundice. Some degree of hyperbilirubinemia is very common in babies right after birth, especially preemies.

**Hypocalcemia:** Lower-than-normal blood calcium.

**Hypoglycemia:** Low sugar glucose in the blood, usually a complication of diabetes, in which the body does not produce enough insulin to fully metabolize glucose.

**Hypothermia:** Abnormally low body temperature. Someone who falls asleep in a snowbank may become hypothermic. Hypothermia is intentionally produced to slow the metabolism during some types of surgery.

**Hypoxia:** Concentration of oxygen in arterial blood that is less than normal. Anoxia refers to complete lack of oxygen.

**Immunocompetent:** Ability to develop an immune response. The opposite of immunodeficient.

**In-utero:** The period spent inside the uterus.

**Infant mortality rate:** The number of children dying under a year of age divided by the number of live births that year. The infant mortality rate is also called the infant death rate.

**Low Birth Weight:** Birth weight of below 2500 grams.

**Macronutrient:** A food substance mainly important for the calories it provides such as carbohydrates, proteins or fats.

**Meconium Aspiration Syndrome:** A condition which newborn babies suffer from when they pass meconium (a thick green- black viscid material secreted from the anal passage) while still in-utero , and which gets aspirated into the lungs at the first breath. This causes them to have respiratory difficulties.

**Micronutrient:** A food substance that is consumed in small portions and is needed for physiological processes.

**Multipara:** Pregnant for more than the first time.

**Neonatal mortality rate (NMR):** Number of deaths that occur from birth to one month of life divided per 1000 live births.

**Obstetric:** The art and science of managing pregnancy, labor and the puerperium (the time after delivery).

**Odds Ratio (OR):** is a measure of association used in comparative studies to quantify the relationship between an exposure and a health outcome. Odds ratios are typically calculated for retrospective and case-control studies where, after a medical condition is observed, the odds of individuals with or without the condition having been exposed to particular factors are calculated. Consider a case-control study comparing Low Birth Weight (LBW) infants with normal infants, and attempting to understand the association that maternal stature has on birth weight. Individual odds of LBW and normal children having had mothers of height less than 158 cm can be calculated. Thereafter the odds ratio is the ratio of the odds for the two groups. An odds ratio greater than one indicates that low birth weight children are more likely to have had mothers of height less than 158 cm.

**Parity:** Tells us the number of pregnancies the woman has had.

**Perinatal mortality rate (PMR):** The number of deaths that occur from the age of viability (22 weeks of gestation) plus those till seven days of age divided per 1000 live births.

**Placenta:** A temporary organ joining the mother and fetus, the placenta transfers oxygen and nutrients from the mother to the fetus, and permits the release of carbon dioxide and waste products from the fetus.

**Polycythemia:** The presence of too many red blood cells. Polycythemia formally exists when the haemoglobin, red blood cell (RBC) count and total RBC volume are both above normal.

**Ponderal index:** Weight in grams divided by length in centimetres cubed. It indicates the nutritional status of a newborn.

**Post neonatal mortality rate (PNMR):** number of deaths that occur one month of age to one year of age divided by 1000 live births.

**Prematurity:** The current World Health Organization definition of prematurity is a baby born before 37 weeks of gestation, counting from the first day of the Last Menstrual Period (LMP).

**Phenotype:** The appearance of an individual, which results from the interaction of the person's genetic makeup and his or her environment. By contrast, the genotype is merely the genetic constitution (genome) of an individual.

**Primipara:** Term denoting somebody who is pregnant for the first time.

**Pulmonary hemorrhage:** life threatening bleeding that occurs in the tissues of the lung.

**Relative Risk (RR):** is a measure of association used in comparative studies to quantify the relationship between an exposure and a health outcome. It is typically calculated for prospective studies, where individuals are followed up and the risks of their developing the condition of interest are computed.

**Stroke:** The sudden death of some brain cells due to a lack of oxygen when the blood flow to the brain is impaired by blockage or rupture of an artery to the brain. A stroke is also called a cerebrovascular accident or, for short, a CVA.

**Vasoconstriction:** Narrowing of the blood vessels resulting from contracting of the muscular wall of the vessels. The opposite of vasodilation.

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## Notes

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