Chapter 2

Review of Literature

2.1 Fetal nutrition

The demonstration that normal variations in fetal size and proportions at birth have implications for health throughout life has prompted a re-evaluation of the regulation of fetal growth and development. Though the fetal genome determines growth potential in uterus, the weight of evidence suggests that it plays a subordinate role in determining the growth that is actually achieved (Snow MHL 1989). Rather it seems that the dominant determinant of fetal growth is the nutritional and hormonal milieu in which the fetus develops, and in particular the nutrient and oxygen supply (Keith M Godfrey 2001).

Animal experiments suggest that fetal under-nutrition in early gestation produces small but normally proportioned offspring, where under-nutrition in late gestation may alter body proportions but have less effect on birth weight (Barker DJP 1998).

2.2 Maternal influences on fetal nutrition

Size at birth reflects the product of the fetus's trajectory of growth, set at an early stage in development, and the materno-placental capacity to supply sufficient nutrients to maintain that trajectory. Failure of the materno-placental supply line to satisfy fetal nutrient requirements results in a range of fetal adaptations and developmental changes. In Western communities, randomized controlled trials of maternal macronutrient
supplementation have had relatively small effects on birth weight (Kramer MS 1993). These have led to the view that regulatory mechanisms in the maternal and placental systems act to ensure that human fetal growth and development is little influenced by normal variations in maternal nutrient intake, and that there is a simple relationship between a woman's body composition and the growth of her fetus. Recent experimental studies in animals and observational data in humans challenge these concepts (Barker DJP 1998). These suggest that a mother's own fetal growth and her dietary intakes and body composition can exert major effects on the balance between the fetal demand for nutrients and the materno-placental capacity to meet that demand.

2.3 The fetal growth trajectory

A rapid trajectory of growth increases the fetus's demand for nutrients. This reflects effects on both maintenance requirements, greater in fetuses that have achieved a larger size as a result of a faster growth trajectory, and on requirements for future growth. Though the fetal demand for nutrients is greatest late in pregnancy, the magnitude of this demand is thought to be primarily determined by genetic and environmental effects on the trajectory of fetal growth set at an early stage in development. Experimental studies of pregnant ewes have shown that, although a fast growth trajectory is generally associated with larger fetal size and improved neonatal survival, it does render the fetus more vulnerable to a reduced materno-placental supply of nutrients in late gestation. Thus, maternal under-nutrition during the last trimester adversely affected the development of rapidly growing fetuses with high requirements, while having little effect on those growing more slowly (Harding JE 1992). Rapidly growing fetuses were found to make a series of adaptations in order to survive, including fetal wasting and placental oxidation of fetal amino acids to maintain lactate output to the foetus (Harding
JE 1992). The trajectory of foetal growth is thought to increase with improvements in peri-conceptional nutrition, and is faster in male fetuses.

### 2.4 Maternal dietary balance and body composition

Indications that the balance of macronutrients in the mother's diet can have important short and long-term effects on the offspring has come from experimental studies in pregnant rats. These have found that maternal diets with a low ratio of protein to carbohydrate and fat alter fetal and placental growth, and result in lifelong elevation of blood pressure in the offspring (Langley-Evans SC 1994). A follow-up study of 40 year old men and women in Aberdeen, UK suggested that alterations in the maternal macronutrient balance during pregnancy could have similar adverse effects on the offspring (Campbell DM 1996), the relations with maternal diet were, however, complex and studies to replicate them are in progress. Among women with low intakes of animal protein, a higher carbohydrate intake was associated with a higher adult blood pressure in the offspring; among those with high animal protein intakes, a lower carbohydrate intake was associated with higher blood pressure. These increases in blood pressure were associated with decreased placental size, (Campbell DM 1996).

Support for the thesis that alterations in fetal and placental development may result from a low ratio of animal protein to carbohydrate comes from observational studies of maternal nutrition in pregnancy (Godfrey K1996). Support for adverse effects of a high ratio of animal protein to carbohydrate comes from a review of 16 trials of protein supplementation showing that supplements with a high protein density were consistently associated with lower birth weight (Rush D 1989).
Evidence that maternal body composition has important effects on the offspring have come from studies showing that extremes of body composition in pregnancy are associated with adverse long-term outcomes in the offspring. Follow-up of a group of Jamaican children showed that those whose mothers had thin skin fold thicknesses and a low weight gain in pregnancy had higher blood pressure at the age of 11 years (Godfery KM 1994). Studies in India have found that a low maternal weight in pregnancy is associated with an increased risk of coronary heart disease in the offspring in adult life (Stein CE 1996).

2.5 Maternal nutrition and pregnancy outcomes

In rodents, low protein intake during gestation can result in low birth weight and subsequently leads to various metabolic disturbances in adulthood, such as high blood pressure, impaired glucose tolerance and insulin resistance. The few controlled studies conducted in animals suggest that high protein or energy intake during gestation leads to low birth weights. Observational studies in humans have been inconclusive in establishing a relationship between dietary protein intake in pregnancy and effects on birth weight and adiposity of the offspring later in life (Cornelia C. Metges 2001).

Over the past decade, epidemiological studies in several countries have shown that size at birth and/or placental weight is related to adult health and disease (Hales C. N.1992, Holness M. J.2000, Godfrey K 2000) but the association between low birth weight and greater risk of fatness has not been observed in all studies (Martorell R.2001). That maternal or fetal nutrition has the potential to cause adverse fetal growth and long-term health problems have been met with much skepticism.

Results from rodent studies suggest that low protein intake during gestation (i.e., 80–100 g protein/kg diet vs. 200 g protein/kg diet) can result in low birth weight or thinness
at birth and, subsequently, the development of metabolic disturbances in adult life, such as high blood pressure, impaired glucose tolerance and insulin resistance (Lucas A1998). By contrast, there is some evidence, albeit limited, that high protein or energy intake during gestation can lead to reduced birth weight (Daenzer M.2000, Robinson J.S.1994, Rush D.1989). Indeed, over-nutrition in adolescent sheep throughout pregnancy results in a major restriction in placental mass and a significant reduction in birth weight relative to moderately fed adolescents of equivalent gynecological age, (Wallace J.M.2000). Whether the same or different mechanisms occur during human fetal development has not been resolved.

Epidemiological investigations have recently examined whether low protein intake during pregnancy might be a risk factor for women to give birth to small infants or to have children with metabolic disturbances in later life (Godfrey K.1996) reported that low protein intake in late pregnancy was associated with lower placental and birth weights, whereas a prospective study by (Mathews F.1999) failed to establish a relationship between macronutrient intake and birth weight. In that study, vitamin C was the only nutrient predictive of changes in placental and birth weights. Interestingly, both studies identified higher birth weights when protein intake was lowest in early pregnancy (Godfrey K.1996, Mathews F.1999). There is insufficient evidence that the intake of isocaloric protein supplements during pregnancy may result in a decrease or an insignificant increase in maternal weight gain, a decreased mean birth weight and an increased risk of small for gestational age births (Kramer M.S. 2000).

A prospective observational study conducted to assess how nutrient intakes of mothers in early and late pregnancy influence placental and fetal growth and concluded that mother who had high carbohydrate intakes in early pregnancy had babies with lower
placental and birth weights. Low maternal intakes of dairy and meat protein in late pregnancy were also associated with lower placental and birth weight (K Godfrey 1996). In contrast in a prospective cohort study they stated that, milk intake in pregnancy was associated with higher birth weight for gestational age, lower risk of small for gestational age (SGA), and higher risk of large for gestational age (LGA), (Sjurdur F Olsen 2007). However, the result from another prospective cohort study, indicated that a diet in pregnancy, based on red and processed meat and high fat dairy, was associated with increased risk for SGA (V K Knudsen 2008).

An adequate amount of dietary fat is essential for health, particularly for pregnancy and lactation. Essential fatty acids play a major role during pregnancy. They provide the precursors for prostaglandins and leucotrienes and are present mainly in highly specialised membranes (retina and synapses). The consumption of essential fatty acids is deemed important for normal growth and development in infants. The interest in essential fatty acids in relation to pregnancy stems from both epidemiological observations (Oslen SF 1991, Harper V 1991, Oslen SF 1989, Oslen SF 1990, Oslen SF 1993, AI MD 2000, Oslen SF 2006) and intervention studies (Oslen SF & Secher NJ 1990, Oslen SF 1992). They showed longer gestation, larger babies and, in some cases, reduced numbers of pregnancy complications such as intra-uterine growth retardation, pregnancy-induced hypertension and pre-delivery in association with higher marine fatty acid (long-chain PUFA or n-3 fatty acids), fish or fish oil intake.

Several mechanisms have been suggested for explaining these associations. The first one is a delayed spontaneous delivery, resulting from altered balance between the prostaglandins involved in the initiation of the labour (Hansen HS 1988, Oslen SF 1986). The second one is an increased fetal growth rate, resulting from improved
placental blood flow due to a lowered thromboxane: prostacyclin ratio (Andersen HJ 1989) and blood viscosity (Oslen SF 1990). Moreover, marine fat could reduce the risk of preterm delivery (Oslen SF 2000, Oslen SF 2002) and of intrauterine growth retardation (Rogers I 2004).

However, results in the literature are not consistent. Indeed, in one study (Oslen SF 1995) could not detect any association between the length of gestation, birth weight and length on one hand and on the other hand the intake of n-3 fatty acids in the second trimester of pregnancy, whether the intake was quantified by a validated questionnaire or biochemical measurements. More importantly, another randomized controlled trial in pregnant women failed to detect effects of n-3 and n-6 fatty acid supplementation on gestational length, birth weight and length, head circumference or placental weight (Helland IB 2001). Nevertheless, several studies in both animals and human subjects have shown that deficiency of dietary n-3 PUFA is associated with biochemical changes in the brain and with disturbances in vision and other neurological parameters (Mc Cann Jc 2005). The most vulnerable period of neural development is during embryonic and fetal growth. Essential fatty acids, especially DHA, are required for fetal brain, nervous system and retinal growth in late pregnancy. The maternal plasma concentration of individual fatty acids, and hence the composition of the maternal diet, may have large effects on long-chain PUFA delivery to the foetus (Peggy Drouillet 2009).

2.6 Maternal milk consumption during pregnancy and infant birth weight

In many cultures, milk is an important source of energy for both the pregnant woman and the foetus. Non-randomized and randomized trials alike suggest that protein/energy
supplementation may affect birth weight and reduce the risk of IUGR (Prentice AM 1983, Prentice AM 1987, de Onis M 1998). Data from Great Britain indicate that low intake of dairy proteins affects placental growth (Godfrey K 1996). However, birth weight per se may be more closely related to meat protein intake than to the intake of dairy protein (Godfrey K 1996). In a study in Wales, mothers who had received milk tokens gave birth to infants with a slightly higher birth weight than controls (statistical significance not reported), (Elwood PC 1981). Milk is also an important source of calcium. One hundred milliliters of milk, Swedish milk, Arla Ltd., 3% fat (Arlaforum SE) supplies the pregnant woman about 13% of the recommended daily intake of calcium (Nordic council of Ministers 1996). Calcium may be involved in foetal growth, although the results of active calcium supplementation with respect to birth weight have hitherto been inconsistent. In a placebo-controlled study of calcium supplementation, supplemented infants were 189 g heavier than controls ($p = 0.06$) and less seldom had LBW ($p = 0.03$), (Nillary 1990. Koo WW 1999), who focused on foetal bone mineral content, reported a similar increase in birth weight among infants of supplemented women (3183 vs 3062 g), although the difference was not statistically significant. While (Lopez-Jaramillo P 1989) showed an increase in birth weight among Andean infants of women receiving calcium supplementation. Several other studies focusing on hypertensive disorders during pregnancy failed to show such a relationship (Levine RJ 1997, Sanchez-Ramos L 1994). But there are also data indicating a link between milk consumption and the female reproductive system (Cramer DW 1994, Cramer DW 1989, Yanagis 1994).

Milk is an important source of energy. Although few recent data support a correlation between milk intake and IUGR, there are several studies pointing towards a correlation
between balanced protein/energy supplementation (protein 25 % of the total energy content of the supplement) in pregnancy and infant growth (de Onis M 1998,Kramer MS 2000). Milk is not a balanced protein/energy supplement but rather a high protein supplement. One of the few trials with high protein supplementation during pregnancy indicated a beneficial effect on maternal weight gain, but a more complex effect on intrauterine growth (Rush D 1980). In the Rush D 1980 study, mean infant birth weight was lower in supplemented women giving birth prematurely, while the opposite was seen in infants born after 37 wk (non-significant differences). It may be that milk, although providing more than 25% of the total energy in dairy protein, mediates a specific effect on foetal and placental growth (Godfrey K 1996, Godfrey KM 1997). In the study by Godfrey K 1996, no association was seen between intake of dairy protein and birth weight.

The correlation between milk intake and birth weight seen in study by (JF Ludvigsson 2004), may also be explained by the supply of micronutrients. A recent study on fish intake among Danish women suggests that even small increases in a food containing critical micronutrients may suffice to affect pregnancy outcome (Olsen SF 2002). In most cases, a lower intake of calcium will follow a low milk intake. Pregnant women have an increased need for calcium (Nordic Council of Ministers 1996). Calcium supplementation will increase foetal bone mineral content in subgroups of women (Koo WW 1999), but its effect on birth weight is uncertain (Villar J 1990, Koo WW 1999,Lopez-Jaramillo P 1989,Levine RJ 1997,Sanchez-Ramos L 1994,Rao S 2001).

2.7 Importance of Calcium Intake

The effect of calcium intake in pregnancy is less certain because there have been few studies of it. Pregnancy-associated alterations in calcium and bone metabolism,
however, are evident even in women with very high calcium intakes, and calcium supplements appear to have little effect (Cross NA, 1995, King JC 1992). In addition, the changes in calcium absorption that occur during pregnancy suggest that the physiologic adjustments are likely to cover the increased requirements of the mother without a need for her to increase her calcium intake. However, there is some evidence that mothers with a customarily low calcium intake may benefit from higher calcium intakes during pregnancy. These include the observation that the bone mineral contents of neonates born to Indian women from poor social class backgrounds would be higher if the mothers had received a calcium supplement during pregnancy (Raman L 1978), and that breast-milk calcium concentration, and hence the calcium intake of the breast-fed infant, may be influenced by maternal calcium intake during the preceding pregnancy (Prentice A 1994).

Three studies conducted in pregnant women in Gambia, in Malawi and Nigeria assessed the calcium intake by weighing the food (Nyambose J 2002, Persson V 2001, Oguntona CR 2002).

The authors reported a low intake of calcium in Gambia (404 mg/d) which was explained by the diet being based on cereals, groundnuts and leaves which are very low in calcium (Nyambose J, 2002). In Malawi the mean intake of calcium was 813 mg/d in the 2nd trimester and 640 mg/d in the 3rd trimester. This difference was explained by the seasonal influence: pregnant women used to eat more during prepares and harvest (Persson V, 2001). In a study in Nigeria measuring the calcium intake in adolescents, the median intake was 659.1 mg/d (Oguntona CR 2002). In Asia, the studies showed the lowest calcium intake. In India (Mohapatra P 1990) calcium intake was the lowest amongst all the studies (250 mg/d). The explanation could be that the participants were
rural workers who based theirs meals on grains and vegetables and also described that these women ate only after everybody at home had eaten their share. Whereas included in another study where intake averaged 500 mg/d (Marya RK 1987). In Indonesian women (Prentice A 1993) the intake of calcium was 316 mg/d with very low variation between trimesters of pregnancy. In Brazil (Lopez-Jaramillo P 1989) the authors of these cross sectional study obtained a median intake of calcium in pregnant women of 500mg/d. In Ecuador there were great differences. In the first study (Lopez-Jaramillo P 1989) in 1989 the authors extracted data from another survey conducted in that country without mentioning the method used to measure the intake. The results were lower (mean of 292mg/d) than in the last study (Lopez-Jaramillo P 1997) which measured calcium intake by 24h-recall in an adolescent population and obtained a mean of 605mg/d in the placebo group and 628 mg/d in the supplemented group.

In Guatemala (Fitzgerald SL 1993) a mean of 727mg/d of calcium intake by 24-h recall was measured. In this population diet was predominantly lacto-ovo-vegetarian which could explain that deficit. In Peru (Sacco L 2003) the authors reported (personal communication) a calcium intake among pregnant women of 430mg/d. Three studies were conducted in developed countries like Canada (Waiters B 1999). In this cross sectional study the calcium intake was low, but this was more evident in the native population (Indian: mean 750mg/d, Inuit: mean 670mg/d) than in the Caucasian population (mean: 1256mg/d). An explanation would be that the native women lived in remote communities where calcium fortified foods were not affordable or available.

Studies in experimental animals show that the administration of a calcium-deficient diet during pregnancy or lactation exacerbates the adjustments in intestinal calcium absorption or bone demineralization (Garel 1987).
2.8 Calcium supplementation during pregnancy

Numerous clinical trials of pregnant women have been conducted to assess the effects of calcium supplementation on PIH and pregnancy outcome. There have been few studies that have examined whether calcium metabolism during pregnancy is affected by calcium intake and those studies that have been reported involved American women on relatively high calcium diets. A calcium supplement (750 mg/d) given to pregnant women with a calcium intake of 1200 to 2600 mg/d, had little effect on indices of calcium and bone metabolism (King J.C 1992). In supplementation study involving a small number of pregnant mothers with a calcium intake of around 1100 mg/d, an additional 1000 mg/d calcium did not affect calcium absorption or indices of calcium and bone metabolism (Cross N.A. 1995).

The majority of trials supplementing pregnant women have been conducted with the aim of reducing hypertensive disorders in pregnancy (Carroli G 1994). With the exception of one recent study (Levine RJ, 1997) RCTs (randomized control trials) have shown beneficial effect of calcium supplementation (at least 1 g daily) on the incidence of high blood pressure, particularly among women with low dietary calcium intakes and those at high risk of gestational hypertension. There is weak evidence to support an effect of calcium supplementation on fetal growth (de Onis M 1998). Follow up of calcium supplemented pregnancies (2 g daily) recently showed the 7-year old offspring to have reduced levels of blood pressure (Belizan JM 1997). It is not known whether there are benefits of lower levels of calcium supplementation.
2.9 Gestational weight gain and optimal pregnancy outcome

Appropriate nutrient intake and weight gain during pregnancy are considered as 2 of the most important modifiable behaviors for improved maternal and infant outcomes, (IOM 1990). The WHO Collaborative Study on Maternal Anthropometry and Pregnancy Outcomes (WHO, 1995a; Kelly et al., 1996) reviewed information on 110 000 births from 20 countries to determine anthropometric indicators associated with poor foetal outcomes, such as low birth weight (LBW), intrauterine growth retardation (IUGR) and pre-term birth, and with poor maternal outcomes, such as pre-eclampsia, eclampsia, need for assisted delivery, and postpartum haemorrhage. Attained maternal weight (pre-pregnancy weight plus weight gain) was the most significant predictor of LBW and IUGR (with odds ratios of 2.5 and 3.1, respectively). Low pre-pregnancy weight and BMI, and weight gain between 20 and 28 weeks of gestation were moderate predictors of pre-term delivery (odds ratios of 1.3 and 1.4, respectively), and low maternal height (e.g. 146 compared with 160 cm) was a moderate predictor of caesarean delivery (odds ratio: 1.6) (Merchant, Villar and Kestler, 2001).

Women with short stature, especially in developing countries with inadequate health care systems and high prevalence of impaired growth during childhood, are also at high risk of LBW and pre-term delivery, and of obstetric complications during labour and delivery (WHO 1995a, Martorell et al., 1981). A study of healthy women with uncomplicated pregnancies in the United States showed a positive association between maternal height and birth weight among white, black and Asian women, but not Hispanic women (Picket, Abrams and Selvin, 2000).
An association between low birth weight and raised blood pressure in later life has been reported in >50 published studies (Huxley RR 2000, Whincup PH 1997, Leon DA 1999).

2.10  Pregnancy and under-nutrition

A large number of women in many parts of the world enter pregnancy at suboptimal weight and/or height. An analysis of studies in 20 countries (Kelly et al., 1996) showed that in ten countries many women had pre-pregnancy weights of < 50 kg and heights of < 150 cm. These cut-off points were associated with increased risks of maternal complications. In addition, weight below 45 kg or height below 148 cm was associated with poor foetal outcomes. The linear relationship between gestational weight gain and birth weight is influenced by maternal pre-pregnancy BMI, such that women with a BMI < 18.5 must gain more weight than those with a normal BMI in order to have babies with adequate birth weight. It is then particularly important that underweight women increase their energy intake to gain the prescribed 10 to 14 kg during pregnancy; depending on their height (e.g. taller women should strive for a weight gain of 14 kg). Gestational weight gains as high as 18 kg have been suggested for undernourished women (Institute of Medicine/Food and Nutrition Board, 1992).

The association of short stature with increased risk of either delivering a low birth weight infant or requiring special assistance during delivery owing to cephalo-pelvic disproportion (Merchant, Villar and Kestler, 2001) indicates the importance for such women to have adequate prenatal attention and access to appropriate care during labour and delivery. This also reinforces the recommendations for good nutrition and measures to prevent repeated infections during childhood, which may result in stunting and in pregnancy-related problems at a later age.
2.11 Pregnancy and obesity

Maternal obesity is also associated with a higher risk of maternal and foetal complications. As for under-nutrition, the relative risks of neural tube defects, congenital malformations and pre-term delivery are higher in overweight and obese women (March of Dimes, 2002). Incidences of hypertension, gestational diabetes and the need for caesarean section operations are also higher than in women with normal weight.

Women with a pre-pregnancy BMI > 25 tend to have babies with high birth weights, even when the women have relatively low gestational weight gains (Institute of Medicine/Food and Nutrition Board, 1992; Shapiro, Sutija and Bush, 2000). As this may lead to problems during delivery, it is likely that such women will be better off gaining weight at, or somewhat below, the lower limit of the 10 to 14 kg range recommended for women with normal BMI. It has been suggested that weight gain should be as low as 7 kg for women who enter pregnancy with BMI > 26 (Institute of Medicine/Food and Nutrition Board, 1992).

2.12 Desirable birth weight and gestational weight gain

Weight gain during pregnancy comprises the products of conception (foetus, placenta, and amniotic fluid), the growth of various maternal tissues (uterus, breasts) and the increase in blood, extracellular fluid and maternal fat stores. The desirable amount of weight to be gained is that which is associated with optimal outcome for the mother, in terms of preventing maternal mortality and complications of pregnancy, labour and delivery, and allowing adequate postpartum body weight and lactation performance; and with optimal outcome for the infant, in terms of allowing adequate foetal growth and
maturation, and in the prevention of gestational and perinatal morbidity and mortality. The WHO Collaborative Study on Maternal Anthropometry and Pregnancy Outcomes showed that birth weights between 3.1 and 3.6 kg, with a mean of 3.3 kg, were associated with the optimal ratio of good foetal and maternal outcomes (WHO, 1995a, Kelly et al., 1996). The range of maternal gestational weight gains associated with such birth weights was between 10 and 14 kg, with a mean of 12 kg. This is in agreement with earlier estimates that healthy women in developing countries, who eat in accordance with appetite, gain 10 to 12 kg (Institute of Medicine 1992). An analysis of gestational weight gains associated with optimal outcomes and full-term delivery of 3- to 4-kg infants in the United States gave a similar although somewhat higher range (11.5 to 16.0 kg) for women with pre-pregnancy BMI between 19.8 and 26.0 (Institute of Medicine/Food and Nutrition Board, 1990; Abrams, Altman and Pickett, 2000).

This consultation endorsed the WHO recommendation that healthy, well-nourished women should gain 10 to 14 kg during pregnancy, with an average of 12 kg, in order to increase the probability of delivering full-term infants with an average birth weight of 3.3 kg, and to reduce the risk of foetal and maternal complications.

2.13 Maternal Pre-pregnancy BMI, birth weight and micronutrient intakes

Maternal nutritional status both before and during pregnancy is a well-recognized determinant of birth outcomes (Osrin, D.2000). Only two indicators of maternal nutritional status during pregnancy have shown consistent positive association with infant birth weight: maternal pre-pregnancy weight for height and weight gain during pregnancy (Neggers, Y.1995). Body mass index (BMI), defined as wt/ht2, is a simple,
useful index for evaluating pre-pregnancy nutritional status in clinical settings. In 1990 the United States Institute of Medicine established new weight gain recommendations for women during pregnancy using BMI as the preferred way to classify women into pre-pregnancy weight categories, Institute of Medicine 1990. Although pre-pregnancy BMI has a genetic as well as nutritional component, a low pre-pregnancy BMI is considered a marker for minimal tissue nutrient reserves (Schieve, L.A.2000). Women with low pre-pregnancy weight for height or BMI are at increased risk for a number of adverse pregnancy outcomes, including preterm birth and intrauterine growth retardation (IUGR) (Siega-Riz, A.M.1994).

In developed countries an interaction between pre-pregnancy weight and weight gain during pregnancy has been reported: underweight women with weight gain in excess of 12 kg and overweight women with weight gains limited to 6–11 kg tend to have the best pregnancy outcome (Abrams, B.1995. Spinillo, A.1998) reported a pre-pregnancy BMI < 19.5 and a second and third trimester weight gain <0.37 kg/wk to be associated with a significantly increased risk of spontaneous preterm delivery. Similarly (Schieve, L.A. 2000) reported that women with low pre-pregnancy BMI were at increased risk of preterm delivery only if they failed to gain weight at an adequate rate during pregnancy. However, low pre-pregnancy BMI alone has also been independently implicated as a risk factor for preterm delivery.

Considerable evidence suggests a role for micronutrients in pregnancy outcomes, (Seshadri, S.2001, Bendich, A. 2001). Even in a developed country like the United States, a substantial proportion of women of childbearing age consume diets that provide less than the recommended amounts of micronutrients, particularly, zinc, folate, calcium and iron (Scholl, T.O.1997, Block, G. 1993). In South Asia, iron deficiency
anemia affects 50% or more of pregnant women. The prevalence of folic acid deficiency may be up to 30–50% and zinc deficiency is likely to be widespread (Seshadri, S.2001). However, nutrition intervention studies have not provided unequivocal evidence of an association between micronutrient intakes and pregnancy outcomes such as birth weight, IUGR, preterm delivery and pregnancy-induced hypertension (Onis, M.1998, Ramakrishnam, U. 1999).

The mechanisms of association between pre-pregnancy BMI and IUGR and preterm delivery are not clear, but throughout the literature there is an assumption that the relationship between a low pre-pregnancy BMI and adverse pregnancy outcomes is mediated by protein-energy availability. However, there are reasons to believe protein-energy malnutrition may not provide the full explanation (Rosso, P.1992, Rosso, P. 1994). For example, the effect of reduced pre-pregnancy weight on fetal growth was still present when underweight women were able to gain weight at a normal rate throughout pregnancy (Rosso P.1985, Abrams B.F.1986). It is likely that a normal gestational weight gain indicates a positive energy balance. If maternal energy intake directly affects fetal growth, then it is hard to explain why similar weight gains result in larger infants in women with a normal pre-pregnancy weight than in women with a low pre-pregnancy weight. One explanation for the lower mean infant birth weight in women with low pre-pregnancy weight may be that the fetus was prevented from receiving an adequate supply of nutrients from the mother because of changes in maternal hemodynamic status (Rosso P.1994).

In a study comparing the plasma volume in underweight, normal-weight and overweight women with similar weight gains during pregnancy, underweight women had smaller total plasma volume than did normal and overweight women both early and late in
pregnancy (Rosso P.1994). As expected, the mean birth weight of infants of underweight women was significantly lower than those of the other two groups. During pregnancy no differences in plasma volume expansion were observed between underweight and normal-weight women. It was concluded that because weight gain was similar in all groups, maternal weight and plasma volume increased proportionately.

The authors suggest that this supports a key role for maternal plasma volume in fetal growth. Based on the results of their clinical studies (Rosso P 1994) proposed that in underweight women, a low plasma volume during early pregnancy will result in a proportionately reduced cardiac output. A lower cardiac output would result in a lower utero-placental blood flow and hence a decrease in transfer of nutrients to the fetus and a reduction in fetal growth.

Some evidences show that in underweight women, micronutrient intake during pregnancy may be associated with maternal plasma volume and infant birth weight. In a supplementation study conducted in Chile by (Mardones-Santander F. 1988) in underweight women, infant birth weight was significantly higher in the group that received energy (milk powder) and a micronutrient supplement than the group that received energy supplement alone.

In a recent prospective study conducted in India in underweight women, increased infant birth weight was strongly associated with consumption of foods rich in micronutrients (vitamins A and C, folacin, calcium and iron) whereas energy and protein intakes were not associated with birth size (Rao,S.2001). Women who consumed green leafy vegetables, fruits or milk products 3–4 times/wk compared with women who consumed these foods,1 time/wk had infants with a significantly higher mean birth weight (green leafy vegetables: 2742 vs. 2601 g, fruits: 2721 vs. 2598 g,
milk products: 2704 vs. 2618 g). Because the mean birth weight in this study was low, an increase in birth weight of 139, 122 and 86 g with increased consumption of micronutrient-rich green leafy vegetables, fruits and milk products, respectively, is of biological significance. Thus, in undernourished women with low pre-pregnancy BMI, a lack of association of birth weight with energy and protein intakes but a strong association with micronutrient intakes suggests that micronutrients may be one of the limiting factors for fetal growth.

It can be concluded that in developed countries, pre-pregnancy BMI is a significant predictor of fetal growth. In developing countries, where deficiencies of multiple micronutrients are common, some evidence indicates that increasing micronutrient intakes, either by supplementation or by increased consumption of micronutrient-rich foods, is associated with significant increase in birth size and a reduction of IUGR in women with a low pre-pregnancy BMI. It is plausible that in these undernourished women both low pre-pregnancy BMI and a low plasma volume may be associated with poor micronutrient status. This combination may thus result in a decreased transfer of nutrients from mother to fetus and may have an adverse effect on fetal growth (Yasmin Neggers and Robert L. Goldenber 2003).

### 2.14 Effect of dietary balance

Experimental studies in pregnant rats have shown that feeding the mother on a diet with a low protien: carbohydrate and fat value alters fetal and placental growth and results in lifelong elevation of blood pressure in the offspring (Langley & Jackson, 1994). Follow-up of 40 years-old men and women whose mothers had taken part in a study of nutrition in pregnancy found that at the extreme of the balance of maternal animal-protien: carbohydrate intakes the offspring had both alterations in placental weight at birth and
raised blood pressure in adult life (Campbell et al. 1996). The adverse effect on fetal and placental development may result from a low animal-protein: carbohydrate intake and the offspring had alteration in placental weight at birth and raised blood pressure in adult life (Campbell et al 1996).

The adverse effects on fetal and placental development may result from a low animal-protein: carbohydrate value comes from a study of 538 full term deliveries in Southampton UK (Godfrey et al. 1996c).

### 2.15 Birth Weight & Maternal Dairy product Intake

In humans, few studies have examined the possibility of maternal nutrition during pregnancy having tissue specific effects on the fetus, leading to greater alterations in neonatal proportions than in birth weight. They have found that women with low dairy protein intakes in late pregnancy tended to have babies that were thinner at birth (Godfrey KM 1997) maternal dairy protein intakes were not however related to birth weight (Godfrey K 1996). Furthermore, a recent follow-up study of children whose mothers took part in a randomized controlled trial of calcium supplementation in pregnancy found that while maternal supplementation was associated with lowering of the offspring's blood pressure in childhood, this effect was not associated with any change in birth weight (Belizan JM 1997).

### 2.16 Factors associated with birth weight

The ideal outcome of pregnancy is the delivery of a full term healthy infant with a birth weight of 3.1–3.6 kg. This birth weight range is associated with optimal maternal outcomes in terms of the prevention of maternal mortality and complications of pregnancy, labour and delivery, and optimal fetal outcomes in terms of preventing pre-
and perinatal morbidity and mortality, and allowing adequate fetal growth and
development (WHO 1995). Macrosomia (birth weight > 4.5 kg) is associated with
obstetric complications, birth trauma and higher rates of neonatal morbidity and
mortality. LBW (birth weight < 2.5 kg) is also associated with an increased risk of
neonatal morbidity and mortality. LBW is a leading cause of infant mortality; it is
associated with deficits in later growth and cognitive development, as well as
pulmonary disease, diabetes and heart disease (C. S. Williamson 2006).

In the latest Health Survey for England, the mean reported birth weight was 3.32 kg,
(Sproston & Primasteta 2003). No significant difference was found between the birth
weights of male (3.34 kg) and female (3.31 kg) newborns. The proportion of LBW
infants was 7%, which is in line with the 1998 figure (Macfarlane et al 2000). This
percentage has in fact remained constant in the UK over the past two decades, and is
marginally higher than the average for Western Europe of 6.7% (UNICEF/WHO 2004).
Studies of firstborn children of mothers and daughters suggest that genetic factors play
only a small part in determining birth weight (Carr-Hill et al. 1987).

2.17 Fruit and vegetable intake during pregnancy

Fruit and vegetable intake has frequently been inversely related to the risk of chronic
diseases (World Health Organization 2004) Nutrition and diet for healthy lifestyles in
Europe 2001 (Hu FB 2002). Fruit and vegetables are important sources of antioxidant
nutrients and consumption has been positively correlated with serum vitamin C and
known to be powerful antioxidant nutrients. Via their antioxidant functions of protecting
organisms against free radical damage, vitamin C and β-carotene may play a helpful
role in the prevention of diseases initiated or promoted by oxygen radicals, such as cardiovascular diseases and cancers (Hercberg S 1998).

One of the relevant nutritional factors during pregnancy is the intake of specific micronutrients such as folate, vitamin C, and carotenoids. These are plentiful in fruits and vegetables and have been associated with increased birth size within the full birth weight and birth length range in developed countries, where under-nutrition is uncommon (Mathews F 1999, Laglou P 2005). Focusing on consumption of fruit and vegetables instead of the known specific micronutrients provided by them will enable other possible bioactive constitute of plants, such as phytochemicals, to be considered and will be valuable for nutritional counseling purpose. To our knowledge, only two studies, in totally different populations of pregnant women, one from a rural area in India and the other in the general population in Denmark, have assessed the association of the intake fruit and vegetables as a food group with birth size (Rao S 2001, Mikkelson 2006). Both studies found a small significant increase in birth weight with higher consumption of fruit and vegetables after adjustment for covariates.

2.18 The relationship between maternal physical activity during pregnancy and birth weight

In developing countries like India, women are responsible for a wide range of household work and childcare duties, as well as work outside the home. These women are also the women at highest risk for a poor birth outcome (Launer LJ 1990).

Women from developing countries are at higher risk of poor birth outcomes, including low birth weight, abortions, still births and pre-term deliveries. Maternal and neonatal morbidity are also high in developing countries like India (Sommer A 1986, Shetty PS 1994, De Onis M 1998). An association between birth weight and maternal factors such
as age, parity, and access to primary health, maternal pre-pregnant nutritional status including maternal weight and dietary intake has been demonstrated in some earlier Indian studies (Vijaylakshmi 1985, Trivedi CR 1986, and Rao S 2001).

An important additional effect on birth weight could be the daily physical activity which is an important and variable factor in the antenatal period, since women have variable physical activities at work outside the house and with domestic household chores. The importance of this is highlighted in studies which have demonstrated that manual physical activity during pregnancy is associated with small for gestation age (SGA) babies and lower birth weights and pregnancy weight gain, particularly when energy intake is sub-optimal (Tafari N 1980).

Similarly, strenuous physical work during pregnancy has also been associated with increased rates of abortion and pre-term delivery (Teitelmann AM 1990). Increased household chores have been related to preterm birth (Cavalli AS 2001) while the evidence for leisure time physical activity suggests that participation in moderate to vigorous activity throughout pregnancy may enhance birth weight, with more intense physical activity regimens resulting in the opposite effect (Pivarnik JM 1998). In India, studies have demonstrated an inverse relationship between daily physical activity and birth weight in a cohort of rural women, the majority of whom had high levels of physical activity related to agricultural and domestic activities (Rao S 2003).

In one cohort study that was conducted among urban Indian pregnant women (Pratibha Dwarkanath, 2007) to assess the relationship between maternal physical activities in different domains either at home or at the work place as well as of the aggregate physical activity level (PAL) in all trimesters of pregnancy, with birth weight, in a cohort of urban Indian women from a wide range of socio-economic backgrounds. The
effect of maternal physical activity on other birth outcomes such as baby length, head circumference and mid upper arm circumference was also examined. They reported that, Multivariate logistic regression adjusting for maternal characteristics as well as birth weight of the baby showed that in the first trimester of pregnancy, the odds of having a baby with a smaller head circumference (lowest tertile of head circumference) increased with increasing level of PA and was significantly so for the highest tertile of PAL as compared to the lowest tertile of PAL (OR: 1.89, 95% CI: 1.07-3.34, p=0.028).

In the same study, women who had moderate/heavy physical activity in the 1st trimester of pregnancy were significantly prone to giving birth to low birth weight babies as compared to women who had sedentary physical activity.

Few studies have shown association of work in the third trimester and preterm births and low birth weight. In one study, a 150g – 400 g decrease in birth weight occurred in women who continued to work outside the home during the third trimester compared with those who remained at home during pregnancy (Naeye RL 1982).

Reports from Africa also show that hard physical work by women during pregnancy can retard fetal growth and increase fetal/neonatal mortality (Tafari N 1980, Prentice AM 1980).

In the domain of household chores, earlier studies have shown correlations between activity in this domain and preterm births. Mothers who did half or less of their household chores delivered 9.4 % of the preterm babies compared with the 4.9 % delivered by the mothers who completed all chores (Cavalli AS 2001).

The proportion of women employed during pregnancy has increased constantly during the previous four decades, and women are working in a broader range of occupations than before. There is accumulating evidence that the type of work and environmental
exposures in the working environment may have adverse effects on foetal development, (Burdorf A 2006, Figa`-Talamanca I 2006). A large number of physical, chemical and psychosocial factors as well as physical load occurring in the workplace have been found or suggested to increase the risk of adverse pregnancy outcomes including spontaneous abortion, pre-term delivery (PD), low birth weight (LBW), birth defects and still birth (Burdorf A 2006, Thulstrup AM 2006). There is also evidence that occupational stress may harm foetal development (Fenster L 1995).


However, some studies showed no effect (Klebanoff MA 1990, Savitz DA 1996, Rabkin CS 1990, Saurel-Cubizolles MJ 1982, Hanke W 1999) in a number of studies, limitations related to the measurement of exposure may have led to underestimation of the true effect. These limitations include having a reference group that includes