EFFECT OF MATERNAL NUTRITIONAL INTAKE ON BABY’S BODY COMPOSITION AT BIRTH IN OBESE WOMEN: A RETROSPECTIVE OBSERVATIONAL COHORT STUDY

By

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for any proprietary material contained therein.
Dedicated to my beloved Kabakka, Bujji mama and Sindhu.

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LIST OF ABBREVIATIONS

4 C model = 4 compartment model

95% CI = 95% confidence intervals

%BF = percent body fat

BMI = body mass index

DHA = Docosahexaenoic acid

EPA = Eicosapentaenoic acid

FFQ = Food Frequency Questionnaire

FWH questionnaire = Four Week Physical Activity History Questionnaire

GA = gestational age

LTPA = Leisure Time Physical Activity

MHMC = MetroHealth Medical Center

MLTPA = Minnesota Leisure - Time Physical Activity

N = total number of subjects / sample size

PA record = Physical Activity record

PUFA = Polyunsaturated fatty acid

SD = standard deviation

V_O2 peak = peak maximal oxygen consumption

WHO = World Health Organization
Effect of Maternal Nutritional Intake on Baby’s Body Composition at Birth in Obese Women: A Retrospective Study

Abstract

By

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**Purpose:** This study was to determine the relationship of maternal nutrition in obese women on infant body composition.

**Methods:** Healthy, obese (BMI ≥ 25 kg/m²) pregnant women between the ages of 18 and 40 years and GA of 8 to 16 weeks were recruited at MHMC. Exclusion criteria were any major maternal or infant illnesses. During the first and third trimesters, all mothers underwent a detailed nutritional assessment, body composition and BMI. Infant body composition was measured during the first week of life.

**Results:** In a stepwise multiple regression analysis, carbohydrate intake, Omega 3:6 ratio and physical activity in early pregnancy were independently associated with the infant’s %BF (adjusted r squared 0.245, P = 0.006).

**Conclusions:** Increased maternal carbohydrate intake, decreased omega 3:6 ratio and physical activity during early pregnancy are significantly associated with increased infant %BF. This implies that the critical window for affecting adiposity is early in pregnancy and not later.
BACKGROUND AND SIGNIFICANCE

Obesity, defined in adults as a BMI of 30 kg/m$^2$ or greater is a growing global epidemic with the prevalence being 38% in adult population in 2013$^1$. In the United States, more than one-third of adults and 17% (or 12.7 million) of children between 2 - 19 years of age are obese$^2$. The obesity prevalence rate in the state of Ohio is 30 – 35 %. Despite interventional programs aimed at reducing obesity, there have been no significant changes in obesity prevalence in either children or adults between 2003-2004 and 2011-2012$^2$.

Obesity is associated with a multitude of morbidities and mortality. It is well documented on how obesity could affect the overall quality of life, resulting in disability$^7$-$^{14}$. It is implicated in many conditions like cancer, metabolic syndrome and cardiovascular disease$^4$. In spite of the growing body of evidence regarding obesity, there are still many areas which are unexplored. The true cause of obesity still eludes us. Due to the multifactorial etiology of obesity, the management strategy has to be multifaceted. There is no single approach to tackle the epidemic. Since the treatment options (weight loss pills, dieting regimens or physical exercise) have been observed to be not very promising, we need to focus on prevention as the prime technique to curb obesity. It is hence very important to understand the implications of obesity in disease process to be able to develop effective interventions.

One of the likely reasons for adult obesity is childhood obesity$^3$. Childhood obesity has many factors associated to it and is a complex process. Obesity has certain profound physical and psychological effects in childhood such as musculoskeletal,
respiratory, autoimmune problems, depression and low self-esteem impacting the overall quality of life\textsuperscript{5,6} and can also result in long term morbidities in adults.

Several theories have been proposed to suggest the fetal origin of adult diseases. David Barker’s hypothesis states that specific intrauterine events have the capability to produce different phenotypes from a single genotype.

To better understand the fetal origins of obesity, it is essential to investigate external and internal factors impacting in utero development. In addition to the genetic make-up and hormonal milieu, the prime determinants of fetal growth are the nutrient and oxygen supply\textsuperscript{15,16}. Experiments in sheep and humans showed that maternal nutrition in early pregnancy can exercise major effects on placental growth and therefore alter fetal development\textsuperscript{17,18}. The Dutch hunger winter story is a classic example. In a study done by Heijmans BT in 2008\textsuperscript{57}, it was shown that individuals who were prenatally exposed to famine during the Dutch Hunger Winter in 1944 - 1945 had, 6 decades later, less DNA methylation of the imprinted Insulin like Growth Factor 2 (IGF2) gene compared with their unexposed, same-sex siblings. The association was specific for periconceptional exposure, reinforcing that very early mammalian development is a crucial period for establishing and maintaining epigenetic marks. It was proved that periconceptional diet may persistently influence DNA methylation levels with phenotypic consequences.

It has been documented that a woman’s birth weight influences the birth weight of her offspring\textsuperscript{19,20}. Women who were themselves small for gestational age (SGA) at birth were at increased risk of giving birth to a SGA infant (odds ratio = 2.21, 95% confidence interval = 1.41, 3.48)\textsuperscript{19}. Although there are studies on maternal obesity and nutrition during pregnancy affecting baby’s birth weight, there is a paucity of studies
on these factors influencing baby’s body composition especially the % body fat. It has been suggested by Barker’s hypothesis that adult diseases can be associated with the fetal environment. This leads us to the assumption that factors during fetal environment might be linked to neonatal adiposity and therefore adult obesity. This is of paramount importance because a strong association has been established between adult diseases like coronary heart disease and type 2 diabetes with altered birth proportions, rather than with birth weight\textsuperscript{21,22}.

Based on the above, we designed this study to observe the influence of fetal environment on neonatal adiposity. The purpose of this study was to determine the differential influence of maternal nutrient intake during early and late pregnancy on the baby’s body composition at birth (percent body fat %BF).

**METHODS**

**OVERVIEW OF STUDY DESIGN:**

This is a retrospective observational cohort study using data from a prospective randomized controlled trial determining whether fish oil supplementation in pregnancy decreased maternal insulin resistance and neonatal adiposity. The primary study showed no effect of fish oil on maternal insulin resistance and neonatal adiposity. Overweight and obese but otherwise healthy pregnant women were recruited in the antenatal clinic of MetroHealth Medical Center (MHMC) from 2009 to 2011. Data were collected in the first trimester and early third trimester. During these visits, all mothers underwent a detailed nutritional assessment via the Food Frequency Questionnaire (FFQ) (Harvard Food Frequency Questionnaire, 2007, Harvard University, Cambridge, MA) and body
composition by air displacement plethysmography using the Bod Pod (COSMED, Rome, Italy). In addition at these visits, the mothers underwent determination of their BMI (BMI = wt/ht\(^2\)) (weight on a calibrated scale and height using stadiometer) coupled with an evaluation of physical activity, using the Minnesota Leisure Time Physical Activity Questionnaire in order to determine the effect of these variables on neonate’s body composition. Babies had their body composition measured during the first 72 hours of life by the Pea Pod (COSMED, Rome, Italy). The details of these techniques are described in the study variables and measures section.

**INCLUSION CRITERIA:**

We included obese pregnant women between the ages of 18 to 40 years, with a body mass index or BMI (wt/ht\(^2\)) of ≥ 25 at the first antenatal visit (first trimester). Gestational age was between 8 weeks and 16 weeks based on clinical information and/or ultrasound prior to 20 weeks gestation. All women were confirmed singleton pregnancies, non-smokers and took no medications which might affect glucose or lipid metabolism.

**EXCLUSION CRITERIA:**

Women with the following medical problems were excluded from the study.

- Metabolic syndromes: Any component of metabolic syndrome such as hyperlipidemia, pregestational diabetes which poses a risk for excess fetal growth (women who developed GDM during pregnancy were not excluded), hypertension or use of antihypertensive medications due to increased risk of adverse pregnancy outcome.
• Blood dyscrasias such as hemophilias, Von Willebrand's disease, moderate or high titer IgG anticardiolipin antibodies, prolonged activated PTT, presence of lupus anticoagulant, homozygous for prothrombin gene (G20210A) mutation, antithrombin III deficiency, protein S (low levels outside of pregnancy) or Protein C deficiency, heparin use or known thrombophilia (thrombophilias include homozygous for Factor V Leiden). Platelet or red blood cell disorder including idiopathic thrombocytopenia purpura, alloimmune thrombocytopenia, iron deficiency anemia with hemoglobin ≤ 8 gm/dl and significant anemia due to hemoglobinopathy but not sickle cell trait.

• Other medical problems: Known maternal medical complications: cancer (including melanoma but excluding other skin cancers), known seropositive HIV studies with viral load greater than 1,000 copies/ml or CD4 count less than 350/mm³, hyperhomocysteinemia, hyperthyroidism, renal disease with altered renal function (serum creatinine > 1.5 mg/dL), epilepsy, systemic lupus (not discoid lupus), scleroderma, polymyalgia rheumatic, active liver disease (acute hepatitis, chronic active hepatitis, persistently abnormal liver enzymes), chronic pulmonary disease (asthma of any degree of severity is not an exclusion) and structural, functional or ischemic heart disease. Neither mitral valve prolapse nor paroxysmal supraventricular tachycardia are considered exclusions.

• Drug usage: Tobacco, illicit drug or alcohol abuse during current pregnancy (excluding marijuana use) and daily use of non-steroidal anti-inflammatory agents.
Obstetric complications: Other exclusion criteria were history of spontaneous preterm delivery less than 36 weeks or 2 kg in previous pregnancy, cerclage which might have interfered with the natural course of delivery and participation in another intervention study that influenced maternal and fetal morbidity and mortality. Medically indicated preterm births were not an exclusion.

Infants with any problems that excluded them from having estimation of body composition such as respiratory distress syndrome or those on mechanical ventilators. Major fetal anomalies, known chromosomal abnormality with the exception of balanced translocations are also criteria for exclusion.

**STUDY VARIABLES AND MEASURES:**

The procedures or methodologies used in the assessment of maternal anthropometric, nutritional and body composition parameters are as described:

1. Maternal nutritional intake was measured using the food frequency questionnaire (Harvard Food Frequency Questionnaire, developed at Harvard University, Cambridge, MA by Walter Willett, M.D., and his colleagues). It is a nineteen page, pen and paper checklist of foods and beverages with a frequency response section for subjects to report how often each item was consumed over a specified period of time. It takes approximately 20 minutes for an individual to complete the questionnaire. The FFQ at the baseline visit considered the amounts over the past year. Whereas when the pregnant women returned for the 34-36 month visit, we asked them to think about their average amounts since the baseline visit which
essentially reflected their dietary intake during the second trimester of pregnancy. A research nurse from the clinical research unit (CRU) went over the FFQ when the women came in for their study visits. Computerized software programs were used to calculate the nutritional intake. In deciding among options for dietary assessment, we would add that the ability to assess intakes of foods as well as nutrients is highly desirable for a full understanding of disease relationships, and diet records do relatively less well than food frequency questionnaires for foods because of greater day to day variability\textsuperscript{23,25}. In addition, the ability to collect repeated measurements over time is important because the food supply and diets of individuals are constantly evolving; in this case, the FFQ has major advantages because of the low burden on participants and cost\textsuperscript{24,25}. Using the criteria for validity espoused by Kristal et al., FFQs seem to do well and comparably with 4 to 7 days of diet records for intakes of most energy-adjusted nutrients, which are the most relevant intakes for epidemiologic studies\textsuperscript{25}. In a study which reported on the validity and reproducibility of dietary intake by level of cognition, the FFQ appeared to have good 1-year reproducibility. The intraclass correlations ranged from 0.70 for folate to 0.50 for vitamin B\textsubscript{12}, with an average of 0.59 over all 15 dietary components including protein, carbohydrate, saturated fat, polyunsaturated fat and cholesterol\textsuperscript{29}. Another study done in men, resulted in the correlations of the dietary patterns between FFQ and the diet records ranging from 0.45 to 0.74, suggesting the usefulness of an FFQ in assessing dietary patterns relative to diet records (ie, the gold standard) and went on to indicate reasonable reproducibility.
and validity of the major dietary patterns defined by factor analysis using data from the FFQs\textsuperscript{30}.

2. Maternal and neonatal body composition was measured using the technique of air displacement plethysmography. It is a whole body densitometry to measure the body composition in individuals. The commercially available system in adults is Bod Pod and the one used to evaluate infants is Pea Pod. They determine the body density and from there derive body fat and lean body mass. The technique of Bod Pod is reliable and valid in that it offers a quick, comfortable, automated, noninvasive, and safe measurement process and accommodation of various subject types\textsuperscript{11}. Reliability was high for percentage body fat and body density in adults\textsuperscript{31}. In a trial to examine the reliability of this air displacement plethysmography device (BodPod), subjects aged 18 – 38 years had percentage body fat of 7.9 – 43.1 %. Over trials performed on 3 different days, paired t-tests revealed no significant within-day differences. BF estimates within a day had high correlations of $r = 0.98$\textsuperscript{32}.

Primary outcome of our study was baby’s percent body fat measured using the Pea Pod. In validation studies, where reference values for percentage body fat (%BF) were obtained from a 4-compartment (4-C) body-composition model (commonly called the multi compartment model is the reference or criterion method for body composition assessment), the Pea Pod was found to have high reliability and accuracy for determining percentage body fat in infants and therefore this method is used for monitoring changes in body composition during infant growth in both research and clinical settings. Reproducibility of %BF
values obtained with the PEA POD system was 0.4 +/- 1.3%. Mean %BF obtained with the PEA POD system (16.9 +/- 6.5%) did not differ significantly from that obtained with the 4-C model (16.3 +/- 7.2%), and the regression between %BF for the 4-C model and that for the PEA POD system (R2 = 0.73, SEE = 3.7%BF) did not deviate significantly from the line of identity (y = x)\textsuperscript{12}. The PEA POD was administered by trained clinical personnel at least twice for each infant; if the percentage of body fat differed by 0.2%, the test was repeated a third time. For each outcome, the average of the 2 closest measures was used.

3. Minnesota Leisure - Time Physical Activity Questionnaire: Subjects were presented with a range of activities (like walking, biking, jogging, etc) and they had to answer with a ‘yes’ or ‘no’ depending on whether they did or did not perform any of these activities in the past 12 months. The questionnaire lists 63 activities broadly grouped into 8 general categories. The MLTPA questionnaire is acceptably valid as shown in a study which comprehensively evaluated it by correlating the questionnaire results directly with data from the 48 hour PA record, 48 hour Caltrac accelerometer and FWH Questionnaire and indirectly with VO\textsubscript{2} peak and percent body fat\textsuperscript{34}. The LPTA questionnaire demonstrated a moderate association with % BF (r = - 0.24, p < 0.05) and with VO\textsubscript{2} peak (r = 0.47, p < 0.01)\textsuperscript{34}. The sample questionnaire is provided in the appendix as Figure 1 (appendix).
DATA ANALYSIS

Data were analyzed via SPSS v.22 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). The data were described using the following: mean +/- standard deviation for interval data (parametric); median with the interquartile range (ordinal data and non-parametric interval data) and percentages with the 95% confidence intervals (rates). A normal distribution for interval level data was defined as having both skewness and kurtosis between – 3 and + 3.

For the bivariate correlations, a Pearson correlation was computed for parametric (normally distributed) data. Spearman correlation was used for interval level, non-parametric data. The independent variables which were significantly correlated with the baby’s percent body fat (see Table 3, p < 0.1) were selected as potential independent variables for the multivariate analysis. In addition the goal was to represent the major groups of nutrients which contribute to the baby’s body fat (i.e., carbohydrates, fats and total calories). Since physical activity was also associated with % BF, it was selected as a potential independent variable.

A stepwise, multiple linear regression was done. A multiple regression was used to determine the association of dependent variable (infant percent body fat) with two or more independent variables (Calories, carbohydrates, sucrose, linoleic acid, ratio of omega 3 and omega 6, maternal gestational age, maternal physical activity and baby’s gender). Stepwise multiple regression is a semi-automated process of building a model by successively adding or removing variables based on the F values of their estimated coefficients. The advantage of stepwise model building over other regression techniques is that it is the most sophisticated of these statistical methods. This method results in a
model with the smallest possible set of predictor variables. One advantage of the Stepwise method is that it should always result in the most parsimonious model. This could be important if you wanted to know the minimum number of variables you would need to measure to predict the criterion variable\textsuperscript{56}.

The infant’s percent body fat is the dependent variable. The independent variables for the multivariate analysis were: carbohydrates, total calories, ratio omega 3: omega 6, linoleic acid, sucrose, maternal BMI, baby gender and maternal physical activity.

For all multivariate analyses, there were no issues with collinearity among the independent variables. In addition, upon examining the residuals, the assumptions of a linear model and homogeneity of variance were met in all of the multiple linear regressions.

**RESULTS**

Of the 49 mothers recruited, 38 mother infant pairs completed the study. Of the 49 who did not complete the study, 9 mother infant pairs were excluded secondary to missing infant body composition (PeaPod data) measurements with the remaining being secondary to lack of second visit maternal nutritional data. The maternal and infant characteristics of the 38 pairs who completed the study are reported in tables 1 and 2 respectively (refer Appendix).

Of the 38 mothers enrolled, the following first trimester maternal characteristics were significantly \( (p \leq 0.1) \) associated with their infant’s percent body fat (%BF): carbohydrate intake (Pearson \( r = + 0.35, p = 0.034 \) two-tail); linoleic acid \( (r = + 0.33, p = 0.040) \); omega 3:6 ratio \( (r = - 0.28, p = 0.090) \); along with maternal BMI \( (r = + 0.28, p = \)
0.084) and physical activity (r = - 0.33, p = 0.044). Other variables that predicted infant %BF included the maternal total caloric intake (r = 0.29), linoleic acid (r = 0.33), sucrose (r = 0.33), total sugars (r = 0.33) and omega 6 (r = 0.33) with P value of < 0.05. The list of all significant correlations during the first visit is given in table 3.

There was found to be no significant correlation between the second visit/late trimester nutritional intake with baby’s percent body fat as illustrated in table 4. None of the maternal nutritional variables (calories, carbohydrates, linoleic acid, alpha linolenic acid, sucrose, glucose, total sugars, omega 6, omega 3, ratio omega 3 : omega 6) along with maternal BMI, physical activity and baby gender significantly predict the infant %BF.

The statistically significant first trimester stepwise multiple regression associations with baby’s % body fat are carbohydrates ( r = + 0.35, P = 0.017 ), ratio omega 3 : omega 6 ( r = - 0.28, P = 0.022 ) and physical activity ( r = - 0.33, P = 0.045). The adjusted R squared and P values for the model are 0.245 and 0.006 respectively (refer to appendix, table 5). When a similar analysis was run for third trimester data, no significant variables were found.

Even though an association was noted between insulin resistance and %BF in early (r = - 0.305, p = 0.06) and late pregnancy (r = - 0.227, p = 0.17), the results did not reach statistical significant. In addition, no association was noted between insulin resistance and Omega 3:6 (early: r = - 0.116, p = 0.48; late: r = - 0.125, p = 0.45).
DISCUSSION

The key findings of our study is that in the first trimester, increased maternal carbohydrate intake leads to an increase in infant body fat but decreased physical activity and a higher omega 3 : 6 ratio is associated with a decrease in the percentage of infant body fat. All three variables are independently associated with the percentage of infant body fat and explained almost a quarter of the variance in infant’s body fat (adjusted $R^2 = 0.245$). Whereas during the third trimester, these 3 conditions were not associated with infant percent body fat. This implies that the critical window for affecting adiposity is early in pregnancy and not later.

Long term rather than short-term maternal nutrition in overweight or obese women is more likely to influence baby's body composition. This conclusion can be arrived at as evidenced by how the FFQ at the baseline visit takes into account food intake over the past year. Whereas when the pregnant women returned for the 34-36 week visit, we asked them to think about their average amounts since early pregnancy, indicating the pre pregnancy dietary influence is predominant. These data supports the theory that late pregnancy maternal nutrition is not associated with infant percent body fat, though infant body fat accumulation occurs more in later part of pregnancy. Early pregnancy maternal nutrition and physical activity are associated with baby body fat probably indicating influence of pre-pregnancy factors. Suggestions to alter maternal nutrition can only be contemplated after showing its effect at least on body composition and weight at birth.
• Our observations are showing possibility of effect of pre pregnancy maternal nutrition on baby body composition, % body fat, probably independent of maternal obesity.

• Pre and early pregnancy maternal nutrition is showing an effect on baby body composition (adiposity). This can be explained by “programming” effect as suggested by David Barker.

According to Barker’s hypothesis intrauterine growth restriction, low birth weight and prematurity have a causal relationship to origins of adult diseases like hypertension, diabetes mellitus and coronary heart disease. This is a very important observation of twentieth century. His findings state that birth weight is inversely related to increased early death secondary to coronary heart disease. It is well know that birth weight is determined by prenatal environment. Adaptations to complex prenatal and postnatal environments through various genetic interactions allow the offsprings to survive early natal period but would have adverse consequences much later.58

It is axiomatic that preparation for pregnancy should begin with good nutrition and health care in childhood so that women enter motherhood having achieved optimal growth and health. Unfortunately, the available data on the influence of maternal macronutrient (carbohydrates, protein, etc) consumption and physical activity on infant body composition is very limited. However, our results are consistent with those from some prior studies.

In the past, it has been shown that eating primarily high-glycemic carbohydrates by pregnant women results in feto–placental overgrowth while intake of low-glycemic carbohydrates are associated with infants whose birth weights fall between
the 25th and the 50th percentile\textsuperscript{36}. In previous studies, a western diet\textsuperscript{35} and wheat based diet\textsuperscript{36} during pregnancy were shown to be associated with a lower birth weight, which in turn could alter body composition later\textsuperscript{37,38}. In a study from Pune, India, over 400 children whose birth weights were available from the labor room records were tested for their plasma glucose and insulin concentrations 30 minutes after the glucose load at 4 years of age. The results showed an inverse relation to birth weight\textsuperscript{60}. The findings were solidified when the association was confirmed at 8 years of age. However, soon it was clear that the association was U shaped, and that the increased risk in large babies was driven by maternal obesity and diabetes\textsuperscript{61}. These findings could have an implication on the growing epidemic of obesity and metabolic syndromes.

There have been many types of maternal non-weight-bearing and weight bearing exercises studied during pregnancy and none appear to increase the risk of an abnormal short-term outcome\textsuperscript{41}. Further, there are also studies such as the Danish National Birth Cohort which closely examined 80,000 pregnant women and found that exercise at any level had protective effects on the risk of SGA and LGA births relative to no exercise\textsuperscript{43}. In one study of carefully matched rural populace from northern Vermont, at age 5, the 20 offsprings from the exercising women are 2 kg lighter and have less subcutaneous fat compared to 20 matched controls\textsuperscript{42}. A study by Clapp et al.\textsuperscript{44} randomized 46 pregnant women to weight-bearing activities or no exercise and found that maternal physical activity improves fetal growth, without increasing infant adiposity. In a different study by the same team, Clapp et al. randomized 75 non obese pregnant women to one of three varying weight-bearing physical activity regimens. Mothers who were active during late pregnancy compared to those who were not had offspring with reduced neonatal fat
mass\textsuperscript{45}. Our finding of early pregnancy increased physical activity/exercise resulting in decreased infant percent body fat in healthy obese pregnant women is novel and supportive of the existing literature suggesting potential mechanisms by which maternal physical activity may result in reduced offspring adiposity.

There is rising evidence from infants and adults that the distribution of fat depots is a stronger predictor for the metabolic and cardiovascular risk than the total amount of fat\textsuperscript{48,49}. Moreover, it has been established that acquisition of fat cells early in life appears to be an irreversible process\textsuperscript{50}. However, we do not have data on fat depots in our study.

In this context, our finding of increased ratio of omega 3 and 6 negatively associated with decreased neonatal body fat is stimulating for future researchers. Previous studies have shown that neonatal central adiposity (determined using waist: length ratio) is negatively associated with percentage energy from saturated fat in late pregnancy\textsuperscript{46}. In a randomized control trial done on 208 healthy pregnant women which investigated the maternal and fetal leptin in relation to the infant body composition after reducing the omega 6 : omega 3, it was concluded that cord leptin was positively related to weight, body fat, and lean body mass (LBM) at birth, and inversely associated with weight, BMI, fat mass, and LBM at 2 years and weight gain up to 2 years\textsuperscript{47}. In this study the intervention to reduce the omega 6/omega 3 clearly did not show any effect on infant adiposity for up to 2 years. There is some evidence that not only the amount of ingested fat but also the qualitative composition of fatty acids in the diet during pregnancy and lactation may play an independent role in determining the risk of becoming overweight or obese in the offspring\textsuperscript{51}. Indirect evidence can be drawn from epidemiologic data for a role of fatty acid composition for human adipose tissue development, which show that the
omega 6:omega3 fatty acid ratio in the diet of populations in industrialized countries has changed considerably toward an increasing dominance of omega 6 fatty acids over recent decades. It is further interesting to observe an increasing trend in rates of childhood obesity over the same time period. It is of important to note that arachidonic acid (AA), an omega 6 fatty acid, inhibits cell proliferation and promotes differentiation to adipocytes in the preadipocyte stage mediated through action of its metabolite prostacyclin, whereas the omega 3 long chain PUFAs DHA and EPA seem to counteract this process. Furthermore, omega 3 fatty acids were also shown to act on mature adipocytes in the process of lipid storage and accumulation. Project Viva study in 302 American children, a higher ratio of cord blood omega 6: omega 3 fatty acid was associated with a greater fat mass and odds of obesity in the children, which indicates that enhanced maternal-fetal omega 3 long chain PUFA status is associated with a lower risk of childhood obesity.

There is currently little evidence to support the hypothesis that dietary intervention to modify fat composition during pregnancy would be a promising strategy to prevent childhood obesity in humans. More research is clearly needed to address the question if and how the risk of developing obesity can be modified by dietary intervention early in life.

It is evident from fuel mediated teratogenesis that nutrition in early pregnancy may affect placental gene expression and later function. But it is not until the third trimester that fetal growth has reached a stage where nutrients are required in appreciable quantities. Studies in healthy and undernourished women show that, up to the last trimester, there is very little difference in fetal weight between the two groups. We by
now know the importance of late pregnancy (third trimester) maternal nutrition and its effect on fetal growth. Most of the fetal body fat is deposited between the twenty eighth and fortieth weeks of pregnancy. In the early stages of gestation there is no fat laid down apart from essential lipids and phospholipids. All of the studies on fetal growth and maternal nutrition indicate that most of the growth in the fetal size occurs in the latter part of pregnancy emphasizing the nutritional interventions towards the later half of pregnancy.

After a thorough literature search, we found only one article which studied the association between maternal pregnancy diet and childhood body composition. This study used diet scores and carbohydrate quality to evaluate maternal dietary patterns during the third trimester and eventually could not find any association between third trimester maternal diet and infant weight at 4 to 6 months of age. However, the diet scores reflect predominantly healthy diet (dietary patterns were evaluated by a priori diet scores i.e., alternative healthy eating index) during pregnancy rather than unhealthy eating habits which are more likely to cause unfavorable birth outcomes in terms of birth weight and body fat.

Our study has several strengths which includes information on many confounders such as maternal pre pregnancy BMI, gestational age, folic acid consumption, physical activity, etc. We also have data on various aspects of body composition owing to our comprehensive body composition measures in infants and use of FFQ to assess dietary patterns in mothers which is a very valid approach as stated earlier.
However, our study population has a selection towards overweight/obese otherwise healthy pregnant women and the results of other similar nutritional studies might not be comparable.

Nevertheless, our novel findings suggest that prevention of obesity in young infants should not focus solely on maternal diet during pregnancy but should focus on healthy dietary interventions beginning much earlier in the reproductive age period. Obesity is difficult to alter in a short time especially during a phase like pregnancy where dietary restrictions are not prudent and as shown by some studies (Barker) such restrictions may have negative health influences at birth as well as adult life.

Our study also highlights the importance for future additional longitudinal studies for infant body composition.

**Implications for practice and research**

The importance of the knowledge gained from this study is the potential of obtaining a better understanding of the mechanisms involved in the development of increased fetal growth and adiposity which has occurred over the last 25 years in infants of obese women. The increase of obesity in all segments of the population is a grave public health concern. If we can better understand the mechanisms of fetal growth and adiposity then studies like ours may provide the data necessary to plan for future specific diagnostic and treatment modalities during gestation in order to improve both short and long term outcomes. It will also better serve in establishing evidence so that changes can be made to dietary recommendations before and during early pregnancy. Along with this uncertainty about relationship between fetal growth or birth weight and adult obesity and diseases,
there is another interrelated ambiguity about relationship between maternal nutrition or obesity and birth weight and body composition.

We also are of the opinion from our study conclusions that there is cause for concern about the later health consequences of compromised or excessive nutrient supply during early fetal and infant life and there definitely is a need for future research in this area, particularly emphasizing the need for data which better characterize dietary patterns and patterns of pre and postnatal growth. Hence the need to observe influence of maternal nutrition on baby birth weight and body composition. If such influences are found then there will be justification to think about altering maternal nutrition during pregnancy.

**Limitations**

FFQ could introduce recall bias and also result in data skewing since foods specific to certain ethnic groups are not included which might comprise the major intake. Like any structured self-administered questionnaire with prespecified response options, the FFQ provides the option for nonresponse. Missing values can affect the calculation of nutrient intake. In dietary analyses it is assumed that a blank on the questionnaire really means that the food was not consumed, hence intake is considered to be zero\(^\text{27}\). Although the common practice of setting missing foods to zero intake does not attempt to attribute the best estimate of true intake, it does represent a reasonably good estimate\(^\text{28}\).

As physical activity questionnaires are subjective methods; the results are highly dependent on the respondent’s cognition. As benefits of physical activity are becoming more published, social desirability of reporting “healthy” behaviors may have increased over the last two decades. This may result in over-reporting of physical activity\(^\text{13}\). In
infants as young as the first week of life, crying and movements might have been associated with Pea Pod non-compliance to some extent. According to Fields and Allison\textsuperscript{33}, subject non-compliance might result in a 7.2\% fat unit difference as compared with the four-compartment model.

Early adiposity may be directly proportional to adult life as it is positively correlated with childhood obesity. Future studies ranging from pre conception, pregnancy and immediate post pregnancy period are required to extend our understanding of influences of maternal nutrition on neonates and infants.

**Conclusions**

- Early pregnancy or pre-pregnancy maternal increased carbohydrate intake, decreased omega 3:6 ratio and decreased physical activity are independently associated with baby body fat and explain about 25\% of the infants percent body fat.

- Increased carbohydrate intake, decreased omega 3: 6 ratio and decreased physical activity during late pregnancy were not associated with infants percent body fat.

- Further study is needed to find if adiposity at birth leads to adult obesity. If it is associated it will provide another possible intervention to prevent obesity by way of modifying maternal nutrition before conception and during early pregnancy.
Appendix

Figure 1: Minnesota LTPA questionnaire

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>Did you perform this activity?</th>
<th>Month of activity</th>
<th>Average number of times per month</th>
<th>Time per occasion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>YES</td>
<td>J</td>
<td>F</td>
</tr>
</tbody>
</table>

Section A: Walking and Miscellaneous

- Walking for pleasure
- Walking to work
- Walking during work breaks
- Using stairs when elevator is available

Section B: Conditioning exercise

- Jog/Walk combination
Table 1: Maternal baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean +/- S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>26.7 +/- 5.0 (years)</td>
</tr>
<tr>
<td>Gestational age (visit 1)</td>
<td>14.4 +/- 17 (weeks)</td>
</tr>
<tr>
<td>BMI (visit 1)</td>
<td>32.4 +/- 6.4 (Kg/m²)</td>
</tr>
<tr>
<td>Gestational age (visit 2)</td>
<td>35.2 +/- 0.8 (weeks)</td>
</tr>
<tr>
<td>BMI (visit 2)</td>
<td>36.0 +/- 5.7 (Kg/m²)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>% African american</td>
<td>34.2% (95% C.I 19.6 - 51.4)</td>
</tr>
<tr>
<td>% Caucasian</td>
<td>52.6% (95% C.I 35.8 - 69)</td>
</tr>
<tr>
<td>% Others</td>
<td>13.2% (95% C.I 4.4 - 28.1)</td>
</tr>
</tbody>
</table>
### Table 2: Infant baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean +/- S.D</th>
<th>95% C.I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baby EGA (weeks)</td>
<td>39.1 +/- 1.1</td>
<td>38.7 to 39.4</td>
</tr>
<tr>
<td>Baby birth weight (Kgs)</td>
<td>3.2 (3.0 to 3.4)*</td>
<td></td>
</tr>
<tr>
<td>Baby BF PP (%)</td>
<td>13.3 (12.2 to 16.5)*</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>52.6%</td>
</tr>
</tbody>
</table>

*Median (interquartile range)

EGA = expected gestational age; PP = peapod
Table 3: Univariate Correlations of First Trimester Nutrients with Percent Infant Body Fat

<table>
<thead>
<tr>
<th>Variable</th>
<th>Daily Intake (N = 38)</th>
<th>Pearson R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean +/- S.D</td>
<td></td>
</tr>
<tr>
<td>Total Calories (kcal)</td>
<td>2400 +/- 1446</td>
<td>0.29*</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>331 +/- 208</td>
<td>0.34***</td>
</tr>
<tr>
<td>Linoleic acid (g)</td>
<td>14.7 +/- 10.2</td>
<td>0.33***</td>
</tr>
<tr>
<td>Alpha linolenic acid (g)</td>
<td>1.46 +/- 1.0</td>
<td>0.31*</td>
</tr>
<tr>
<td>Sucrose (g)</td>
<td>70.8 +/- 55.7</td>
<td>0.33***</td>
</tr>
<tr>
<td>Glucose (g)</td>
<td>36.6 +/- 29.8</td>
<td>0.32*</td>
</tr>
<tr>
<td>Total sugars (g)</td>
<td>175.5 +/- 127.7</td>
<td>0.33***</td>
</tr>
<tr>
<td>Omega 6 (g)</td>
<td>14.5 +/- 9.5</td>
<td>0.33***</td>
</tr>
<tr>
<td>Total Omega 3 (g)</td>
<td>1.6 +/- 1.2</td>
<td>0.29*</td>
</tr>
<tr>
<td>Omega 3: Omega 6</td>
<td>0.013 +/- 0.021</td>
<td>-0.34***</td>
</tr>
</tbody>
</table>

*p < 0.1, two-tailed

*** p < 0.05, two-tailed
Table 4: Univariate Correlations of Third Trimester Nutrients with Percent Body Fat

<table>
<thead>
<tr>
<th>Variable</th>
<th>Daily Intake (N = 38)</th>
<th>Pearson R*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean +/- S.D</td>
<td></td>
</tr>
<tr>
<td>Total Calories (kcal)</td>
<td>2317 +/- 1332.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>317.3 +/- 198.2</td>
<td>0.112</td>
</tr>
<tr>
<td>Linoleic acid (g)</td>
<td>30.5 +/- 115.1</td>
<td>-0.183</td>
</tr>
<tr>
<td>Alpha linolenic acid (g)</td>
<td>1.4 +/- 0.8</td>
<td>0.113</td>
</tr>
<tr>
<td>Sucrose (g)</td>
<td>62.4 +/- 51.0</td>
<td>0.036</td>
</tr>
<tr>
<td>Glucose (g)</td>
<td>33 +/- 28.6</td>
<td>0.264</td>
</tr>
<tr>
<td>Total sugars (g)</td>
<td>163 +/- 117.2</td>
<td>0.173</td>
</tr>
<tr>
<td>Omega 6 (g)</td>
<td>13.8 +/- 8.3</td>
<td>0.092</td>
</tr>
<tr>
<td>Total Omega 3 (g)</td>
<td>1.5 +/- 0.8</td>
<td>0.07</td>
</tr>
<tr>
<td>Omega 3: Omega 6</td>
<td>0.01 +/- 0.01</td>
<td>-0.214</td>
</tr>
</tbody>
</table>

*All “p values” are > 0.1 (two tail)
**Table 5: Stepwise Multiple Linear Regression (Infant's Percent Body Fat)**

**First trimester**

In the multiple regression analysis, carbohydrates, physical activity and omega 3 : omega 6 were independently associated with baby’s percent body fat (\( p = 0.006, R^2 = 0.245 \)).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson r</th>
<th>Adjusted ( R^2 ) change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>0.346</td>
<td>0.096</td>
<td>0.017</td>
</tr>
<tr>
<td>Physical activity</td>
<td>-0.329</td>
<td>0.045</td>
<td>0.022</td>
</tr>
<tr>
<td>Ratio omega 3 : omega 6</td>
<td>-0.28</td>
<td>0.104</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Adjusted \( r \) squared = 0.245; \( p = 0.006 \)

**Third trimester**

When a similar analysis was run for third trimester data, no significant variables were found. No model is generated in SPSS if stepwise multiple regression cannot pull in any significant variables.
Bibliography


49. Liu KH, Chan YL, Chan WB, Kong WL, Kong MO, Chan JC. Sonographic measurement of mesenteric fat thickness is a good correlate with cardiovascular risk factors: comparison with subcutaneous and preperitoneal fat thickness, magnetic resonance imaging and anthropometric indexes. *Int J Obes Relat Metab Disord.* Oct 2003;27(10):1267-1273.


