# The Effect of Short Term Maternal Fasting on Fetal Biophysical and Neonatal Biochemical Profile – A Pilot Study and a Short Critical Review of the Literature

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**Abstract:** *Aim:* To determine the net effect of strict maternal short term fasting on fetal biophysical parameters.

*Study Design:* Prospective observational study among healthy women with a single term fetus, delivered by scheduled cesarean who had strict preoperative fast. Each subject serves as its ***own control***. The Biophysical Profile Score was recorded. Statistics used paired t , non parametric Wilcoxon , McNemar tests (as appropriate) and correlations.

*Results:* Twenty one women were recruited. We found no difference when the separate scoring entities were analyzed in the two maternal states. No correlation was found between maternal - fetal biochemical and hormonal status. All neonates were healthy.

*Conclusion:* Short term fasting in healthy mothers is well tolerated by both the mother and the neonate. Standards need not to be adapted in the assessment of the low risk fetus and glucose containing drinks should not be offered in order to decrease the false positive rate of the biophysical profile.

**Keywords:** Maternal fasting, fetal assessment.

## INTRODUCTION

Traditional assessment of the fetal well being and especially the non stress test (NST) recommends glucose intake before assessment or as a "facilitator" for decreased fetal movements or/and non reassuring antenatal NST [1] . This concept draws mainly from reports of increased fetal movements following a non physiological maternal intravenous glucose administration [2, 3], as well as oral carbohydrate intake [4]. Nevertheless others using the glucose clamp technique and sustained maternal hyperglycemia reported a transient decrease in fetal movements and recovery to baseline within an hour without any overshooting in the fetal activity [5]. Studies focused directly towards the fasting effect on the fetal activity at term are scarce and mainly based on hypoglycemia of diabetic mothers [6]. Extensive reports accumulated on the fetal and neonatal consequences of prolonged maternal nutrition deprivation states [7]. The effect of physiological short term intermittent fasting on the fetal behavior at term is controversial and differential in report to the fetal activities: fetal breathing movements increase after carbohydrate intake (oral glucose tolerance test or standard meal) whether the fetal body movements were reported higher in the fasting state [8-10]. The principal metabolic fuels in the fetus are glucose and amino acids. Glucose serves as the min substrate for the maintenance energy production and energy storage in glycogen and adipose tissue. Placental metabolism and nutrient transfer to the fetus and placenta-fetal metabolic interactions are key regulatory aspects of fetal fuel metabolism. Uterine, placental and fetal glucose uptake rates are directly related to maternal glucose concentration, whereas the partition of uterine glucose uptake into fetal and uteroplacental glucose uptake independently regulated by fetal glucose concentration [11]. To provide for the increasing glucose requirements of the growing fetus over gestation, fetal glucose concentration decreases relative to that of the mother by progressive development of fetal insulin secretion and insulin sensitive tissue and increased transplacental glucose concentration gradient. The fetal glucose utilization is about 5-7 mg/ml/kg fetal weight near term. In the human fetus glucose and insulin are oriented towards glucose storage (fat and glycogen) rather than oxidation. Fetal insulin secretion also increases and is subject to modification. Variability in maternal and thus fetal glucose concentration is a principal cause of enhanced fetal insulin secretion. The pathologic maternal chronic hyperglycemic/ hypoglycemic on fetal hormonal and behavior states were extensively studied [12, 13]. However human data on the effect of the acute maternal fasting on fetal behavior is extremely scarce. Even more, maternal fasting in healthy women does not imply any hypoglycemic state as in diabetic women.

The fetal well being assessment can be conducted under either set of maternal conditions; knowledge of the effect of transitory fasting states in healthy mothers may lead to different normal standards for biologic variations and fetal biophysical parameters. The short term maternal fasting is the closest simulation to the relative non satiety state that may draw a recommendation of additional food intake in cases of antenatal fetal well being assessment.

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**Table 1. Biophysical Profile Score Determinants**

| Component | Score 2 | Score 0 |
|---|---|---|
| **Nonstress test** | ≥ 2 accelerations of ≥15 bpm for ≥ 15 sec in 20-40 min | 0 or 1 accelerations in 20-40 min |
| **Fetal Breathing** | ≥ 1 episode of rhythmic breathing lasting for ≥ 30 sec within 30 min | < 30 sec of breathing in 30 min |
| **Fetal movement** | ≥ 3 discrete body or limb movements within 30 min | ≤ 2 movements in 30 min |
| **Fetal Tone** | ≥ 1 episode of extension of a fetal extremity with return to flexion, or opening or closing of hand | No movements or no extension \ flexion |
| **Aminotic Fluid Volume** | Single vertical pocket > 2 cm | Largest single vertical pocket ≤ 2 cm |

The aim of the study was to determine the effect of strict maternal short term fasting on the fetal biophysical and adequate neonatal biochemical parameters in healthy term non complicated pregnancies.

## STUDY DESIGN

A prospective observational study was carried out at the university affiliated hospital, Shaare Zedek Medical Center, Jerusalem, between June 2006 and December 2006 . Healthy women who intended to deliver by scheduled cesarean and were consented to a strict over-night preoperative fast of 8 hours were recruited. The pregnancies were uncomplicated; all had an one hour glucose c tolerance (GCT) screening test at 24-28 weeks gestation lower than 140 mg%, single fetus, 38-40 weeks gestation. Concomitant maternal complication of pregnancy (gestational diabetes, hypertension, antenatal bleeding, other current maternal diseases) and fetal complications (intrauterine fetal growth restriction, estimated fetal weight above 4000 grams, fetal/ neonatal anemia, fetal malformations) were excluded.

Each subject will be referred as its ***own control***: non fasting (satiety) at the routine admission and fasting prior to cesarean. Our departmental protocol requires medical admission notes, biophysical profile score (BPS) and routine blood sampling 24 hours prior to the cesarean. The women are admitted to the obstetrical ward the next day after 8 hours of fast and an intravenous line established. A load of 1000 ml of normal saline is routinely infused to prepare for regional anesthesia. The maternal blood samples before and after fasting were obtained from the routine samples required from the preoperative preparatory process; umbilical blood samples were collected at delivery.

The maternal and the umbilical blood samples were analyzed for hemoglobin, electrolytes, cortisol, insulin and acid base balance. Glucose and electrolytes were measured using the Vitros 5.1 analyzer Othro-Clinical Diagnostics. Glucose is a colorimetric assay with an intra assay (CV)s less than 1.8%. Sodium and potassium are potentiometric assays with inter assay CVs less than 1.0%. Serum/plasma insulin levels were measured using the Abbott Axsym System. The assay is a Microparticle Enzyme Immunoassay (MEIA) with inter and intra assay CVs less than 10%. Serum/plasma cortisol levels were measured using the Beckman Coulter Access Immunoassay System. The assay is a paramagnetic particle, chemiluminescent immunoassay with an inter and intra assay CV of less than 8%. Maternal urinalysis for ketones presence was performed with a Multistix -8 SG reagent strip (Bayer Corporation Diagnostics Division, Philadelphia, PA) and results recorded. The Biophysical profile score (BPS) employed was composed of five fetal biophysical variables as following : NST, fetal breathing , fetal movement, fetal tone, amniotic fluid volume and scored according to Manning [14] (Table), as well as maternal perception of fetal movements recorded.

The computerized department perinatal database was used for the demographic characteristics.

Sample size estimate was based on the mean of each of the BPS variables and the expected difference in the mean between the fasting and non fasting state for each patient in the study. Assuming that the differences between the states will be of a medium effect, alpha =5% (two tailed) and a power of 75 % we calculated a sample size of 24 women.

### Statistical Analysis

Quantitative variables were analyzed by paired t test and non parametric Wilcoxon test. Qualitative variables were compared by McNemar test. Correlations are reported as Pearson's coefficient ®.

## RESULTS

Twenty five women of Jewish origin were recruited during the study period. Four women were not included due to an incomplete set of data that impaired the statistical analysis: one woman declined the study after fasting; one decided after the inclusion into the study not to deliver by a non medical indicated cesarean, two cases the maternal blood samples and were unfit for biochemical analysis. Twenty one women were included in the study analyses. All women had antenatal care, first trimester sonographic assessment of the gestational age and recorded multivitamin preparation intake. None smoked during the pregnancy. The maternal and neonatal characteristics are depicted in Table **2**. All deliveries were scheduled cesarean and not in labor. The indications for cesarean sections were: repeated cesarean section 10(47.6%), breech presentation 8 (38%), maternal request 3 (14.2%). The neonates were healthy and none required NICU admission due to metabolic reasons. Two were admitted for 48 hours evaluation: one due to transient tachypnea of the newborn and distended abdomen; another was suspected to suffer from a previously unknown aneuploidy, confirmed later as trisomy 21. Both had normal dextrose evaluations of 43 and 76 respectively. Eleven (47.6%) of the neonates were males.

**Table 2. Maternal and Neonatal Characteristics**

| Characteristic | Mean ± SD | Range: Min-Max |
|---|---|---|
| **Age (years)** | 32.75±4.6 | 24-39 |
| **Parity (N)** | 1.5±1.1 | 0-4 |
| **Previous C/S (N)** | 1.1± 0.9 | 0-3 |
| **Maternal BMI** | 27.8±3.3 | 22.6-35 |
| **Neonatal weight (grams)** | 3227.5±324.9 | 2660-3690 |
| **Placental weight (grams)** | 674.5 ±52.5 | 580-770 |

The 21 recruited patients with complete data had a BPP score and maternal perception of the fetal movements recorded in parallel to the NST. A score of 8 and more was obtained in all women either before or after fasting. We found no difference when the separate scoring entities were analyzed in the two maternal states; i.e. fetal breathing movements, movement and tone scored did not chang. Maternal fetal movements perceptions recorded parallel to the NST remained unchanged after the fast period, mean of 5.3 ± 1.5 versus 4.9 ± 1.9 respectively (p=0.3) ; the time to the record of the first movement was less than 15 minutes in 18 (85%) of the patients, in a state of satiety as well as after fasting.

Analyses of the biochemical maternal data before and after fasting are depicted in Table **3**. The women had a hemoglobin level above 10gr/dL (mean 11.8± 1.08) with a minimum of 10gr/dL and a maximum of 13.6 gr /dL. All women had none or small ketones load in the urines (0 to +1).

Analyses of the umbilical blood at delivery are depicted in Table **4**.

We found a significant correlation, i.e. ® = 0.65 only between the maternal glucose (in satiety and after fasting) and maternal BMI. The maternal satiety glucose and insulin levels were strongly correlated ®=0.7, while the fasting values were poorly correlated ®=0.1. No correlation was found between the other components of the maternal profile during satiety and fasting. No correlation was found between maternal - fetal biochemical and hormonal status; i.e. ®glucose 0.3, ® insulin 0.2 and ® cortisol 0.1.

## DISCUSSION

Reports on the effect of maternal fasting on fetal assessment have been mainly based on insulin induced hypoglycemia in animal studies and diabetic mothers. Data on glucose ingestion and fetal heart tracing are contradictory and based on obsolete definitions in order to exclude gestational diabetes ( for examples GCT cutoff criteria of 150 mg/dL ) and absence of neonatal data to base the selection of the population included in the study [15]. Others evaluated the fetal heart rate reaction after a non physiological oral or intravenous glucose load and found an increase in the baseline fetal heart rate in both diabetic and non diabetic mothers [2, 16-19], however uncorrelated to the outcome and other biophysical profile parameters. This present study, despite its limited number of subjects evaluates the effect of maternal fasting on all fetal biophysical profile parameters. The inclusion criteria were strict, eliminated any matching bias in a homogenous ethnic population and the results incorporate detailed neonatal outcomes. Essentially, a fasting period of eight hours had no significant effect on the biophysical profile and the time required to achieve it compared to physiological satiety. The results also correlated to a normal maternal perception of fetal movements. We found no differential outcomes regarding the effect of maternal fasting on fetal breathing and body movements as reported by others [8, 10, 20]. Nevertheless these reports focused on fine sonographic parameters and computerized fetal heart tracing and did not use the well accepted biophysical scoring system to be used in the daily practice. Even more, our study points the physiological maternal biochemical and hormonal response to short term fasting performs as a "stability glycemic mechanism", despite the mild "stress" effect observed on the cortisol levels changes. Albeit the wide variability in the hormonal levels reported in the literature and the diurnal rhytms the ma-

**Table 3. Maternal Biochemical and Hormonal Data in Satiety and Fasting State**

| Characteristic | Satiety state (mean±SD) | Fasting state (mean±SD) | P value |
|---|---|---|---|
| Glucose (mg%) | 84.5±15.9 | 78.5±4.5 | 0.1 |
| Insulin (mU/L) | 30.9±27.1 | 9.8±4 | 0.002 |
| Cortisol * (mcg%) | 18.3±2.5 | 20.6±4.6 | 0.021 |
| $Na^+$ (mEq/L) | 137.2±1.6 | 136.8±1.9 | 0.2 |
| $K^+$ (mEq/L) | 3.8±0.3 | 3.9±0.2 | 0.4 |
| pH ( venous) | 7.4±0.03 | 7.4±0.02 | 0.05 |

*Blood samples were collected between 8-10 AM.

**Table 4. Umbilical Cord Blood Sample Biochemical and Hormonal Data**

| Characteristic | Mean±SD | Range Min-Max |
|---|---|---|
| **Glucose (mg/dL)** | 63.6±7.2 | 51-75 |
| **Insulin (mU/L)** | 4.1±4.2 | 1.5-6.6 |
| **Cortisol (mcg/dL)** | 5.3±1.8 | 2.5-9.3 |
| **pH** | 7.3±0.04 | 7.2-7.4 |

ternal and umbilical blood levels in our study were comparable with the literature and unaffected by the mode of delivery [21]. Maternal fasting did not result in any hypoglycemic state and was characterized by significantly lower insulin levels. This adaptation had no influence the immediate fetal and neonatal status. Accentuated changes in the fasting glucose levels were observed in pregnancies after extended fasting of 10-12 hours, and especially in obese patients [22]. The relative short fasting period employed in our study and the normal BMI range of the women participants may have alleviate this changes. Maternal and not fetal cortisol levels were significantly increased by the fasting. Interestingly, our results at term concord with previous animal and human reports indicating that id pregnancy short term food deprivation induces rapid expression of corticotropin releasing hormone (CRH) in several brain regions, parallel increased plasma concentrations and risk of preterm birth, without any direct fetal effect [23]. Since no mother received an intravenous glucose load or labored, the results are a reflection of the short term starvation effect [24, 25]. This may point to the fact that the effect of food deprivation occurs physiologically at any time in pregnancy and its effect on the occurrence of preterm birth may be additive to other factors. Our study shows also that the effect is not transmitted to the fetus and has no influence on the neonatal status. However this aspect requests additional detailed studies and even the creation of gradients in the prolonged food deprivation periods.

Short term fasting in healthy mothers is well tolerated by both the mother and the neonate. The outcomes recorded in our study further suspend any comparison between maternal induced hypoglycemia in diabetes and physiological status. Further studies, in our opinion difficult to design and standardize, are required to evaluate directly the value of glucose ingestion in cases of unsatisfactory fetal assessment. Therefore, standards need not to be adapted in order to perform the practical accepted scoring for the assessment of the low risk fetus. Glucose containing drinks should not be offered in order to decrease the false positive rate of the biophysical profile; even more this unsupported practice may unnecessarily delay action decisions and be detrimental to the neonatal status.

## SYNOPSIS

Short term maternal fasting is well tolerated by the fetus and the practice of glucose containing drinks in order to decrease the false positive rate of the biophysical profile is unwarranted.

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