13

Gestational Hyperglycemia, Excessive Pregnancy Weight Gain and Risk of Fetal Overgrowth

Xinhua Chen, Theresa O. Scholl,
Robert A. Steer and T. Peter Stein
University of Medicine and Dentistry of New Jersey – School of Osteopathic Medicine
USA

1. Introduction

Between 1989 and 2004 the prevalence of gestational diabetes mellitus (GDM) in the US increased from 1.9% to 4.2% in parallel with the well documented obesity epidemic (Getahun et al., 2008; Mokdad et al., 2001). However, an additional 9-20% of pregnant women, with a milder form of glucose intolerance which does not meet the diagnostic criteria for GDM, may also be at risk of type 2 diabetes, cardiovascular disease and problems while pregnant (Stamilio et al., 2004; Mello et al., 1997; Bo et al., 2004; Nordin et al., 2006).

Fetal overgrowth, defined as macrosomia (birth weight >4000g) or large-for-gestational-age birth (LGA, birth weight >90th percentile for a given gestational age) increases maternal morbidity from operative delivery and also causes serious consequences to the offspring including birth trauma, obesity during childhood and type 2 diabetes and metabolic syndrome in adult life (Boney et al., 2005; Zhang & Bowes, 1995; Langer, 2000).

GDM and excessive pregnancy weight gain, especially in obese women are known risk factors for fetal overgrowth (Ray et al., 2001; Hillier et al., 2008). Although previous research has suggested that metabolic abnormalities are also present in pregnant women with less severe hyperglycemia, the clinical implications of milder maternal hyperglycemia are poorly described (Chen et al., 2010; Cheng et al., 2006; Nordin et al., 2006).

The primary objective of this chapter is to use prospective data from a population of low income and minority women to examine (i) the influence of maternal hyperglycemia including GDM and less severe maternal hyperglycemia on risk of fetal overgrowth; (ii) the association of longitudinally measured excessive pregnancy weight gain with risk of fetal overgrowth (IOM, 2009); (iii) the independent contribution of gestational hyperglycemia and excessive pregnancy weight gain to fetal overgrowth.

Because gestational hyperglycemia and excess weight gain during pregnancy are preventable risk factors, early detection and treatment of mild hyperglycemia and monitoring pregnancy weight gain may be important for reducing the risk of LGA, for reducing childhood and later obesity and for improving the long term risk for metabolic disease.

2. Maternal hyperglycemia and fetal overgrowth

2.1 Fetal overgrowth

Fetal growth is dependent on the capacity of mother to supply nutrients and also on the capacity of the placenta to transfer these nutrients to the fetus (Oken & Gillman., 2003; Ehrenberg et al., 2004). Maternal factors including parity, length of gestation, mother's adult size, and mother's own birth weight are strongly related to fetal growth and development (Langer, 2000). The prevalence of fetal overgrowth was reported as 8-16% from women without GDM and 15-40% from women with gestational hyperglycemia (Mello et al., 1997; Ostlund et al., 2003; Bo et al., 2004; Gruendhammer et al., 2003).

2.2 GDM and fetal overgrowth

Despite different diagnostic criteria, many studies confirmed that GDM increases the risk of macrosomia or LGA birth (Ricart et al., 2005; Ray et al., 2001; Ehrenberg et al., 2004). Maternal hyperglycemia increases fetal growth via delivery of excess maternal plasma glucose to the fetus, which results in fetal hyperinsulinemia and promotes fetal overgrowth (HAPO, 2008; Oken & Gillman., 2003). GDM women undergoing intensive diabetic care had similar neonatal birth weights and macrosomia rates compared to non-GDM women (Ogonowski et al., 2008) and a clinical trial of continuous glucose monitoring in GDM resulted in a significant improvement in infant birth weight with a reduced risk of macrosomia (Murphy et al., 2008).

2.3 Significance of mild gestational hyperglycemia and LGA birth

2.3.1 Prevalence of mild gestational hyperglycemia

Recent studies have paid more attention to pregnancy outcomes of women with gestational hyperglycemia less severe than overt GDM. The prevalence of mild hyperglycemia (defined as abnormal plasma glucose concentration during glucose challenge test with a diagnostic oral glucose tolerance test (OGTT) that did not meet the criteria of GDM) in women screened for GDM was 32% in Caucasian women (Mello et al, 1997), 25% in Mexican-Americans (Yogev et al, 2004) and 9% in multiethnic US population where 70% were African American (Stamilio et al., 2004). The relatively high prevalence of less severe maternal hyperglycemia raises important questions about effects on the fetus since these women are not provided the usual diabetic care for GDM.

2.3.2 The impact of mild gestational hyperglycemia on fetal overgrowth is inconsistent

Studies suggest that an impaired maternal OGTT is associated with adverse maternal-fetal outcomes especially risk of macrosomia and LGA birth (Vambergue et al., 2000; Ostlund et al., 2003). The degree of maternal glucose intolerance was associated with a graded increase in the incidence of fetal macrosomia (Sermer et al., 1995). Moreover, the recent hyperglycemia and adverse pregnancy outcome study (HAPO) found a strong association of maternal glucose concentrations below levels diagnostic of diabetes with increased infant birth weight (HAPO, 2008), but others found no significant increase in the risk of LGA in mildly hyperglycemic women (Nordin et al., 2006; Gruendhammer et al., 2003). Bo et al suggested that metabolic syndrome in mid-pregnancy might be an independent predictor of macrosomia in women with some degree of gestational hyperglycemia, including GDM and mild hyperglycemia without GDM (Bo et al., 2004).

Conflicting data on mild hyperglycemia and fetal overgrowth can be, at least in part, due to the different population studied and the criteria used for mild hyperglycemia. Although the HAPO study included multiple countries and populations and had a large sample size, it was focused on developing an international consensus for the diagnosis and treatment of carbohydrate intolerance during pregnancy, and was not designed to compare the difference in LGA between GDM and less severe hyperglycemic pregnancies (HAPO, 2008). Thus, to establish the risk of adverse fetal outcomes in relation to milder degrees of maternal hyperglycemia is clinically important, particularly in high risk US populations.

2.4 The Camden study

Camden Study is a prospective cohort study of pregnancy outcome and complications in young, generally healthy women residing in one of the poorest cities in the continental United States (Webster & Bishaw, 2006). Women with serious non-obstetric problems (e.g., Lupus, type 1 or 2 diabetes, seizure disorders, malignancies, acute or chronic liver disease, drug or alcohol abuse and psychiatric problems) were excluded from participation. The sample for this analysis totaled 2,373 pregnant women with live births who enrolled between 1996-2006.

2.4.1 Definition of GDM and mild hyperglycemia non-GDM in Camden study

The diagnosis of GDM was made using a two-step approach. All participants were initially screened by measuring the plasma glucose concentration 1h after a 50-g oral glucose challenge test (GCT) at 28±0.1 (mean±SE) weeks' gestation. A diagnostic OGTT was performed on that subset of women exceeding the glucose threshold value (>140 mg/dl). The diagnostic criteria for GDM was the Carpenter/Coustan conversion as recommended by the American Diabetes Association (ADA) which defines GDM by two or more glucose values over the cut points of 95,180,155,140 mg/dl at fasting, 1, 2, and 3 hours during a 100g OGTT (American Diabetes Association, 2000). Women with a positive GCT and fewer than two abnormal glucose values were identified as having an impaired GCT without GDM (impaired GCT non-GDM). All of patients diagnosed with GDM obtained dietary counseling and/or insulin treatment for their glycemic control; patients with impaired CGT non-GDM were untreated.

We identified 2,092 women (88.1%) with normal GCT, 182 women (7.7%) with impaired GCT non-GDM and 99 women (4.2%) with GDM (table 1). Ethnic composition of the cohort was 46% Hispanic, 37.6% African American and 16.6% Caucasian plus others. When the maternal characteristics were rank ordered with respect to glucose tolerance status, older maternal age, higher pre-pregnant body mass index (BMI), obesity and prior history of GDM, all were found to be positively associated with maternal glycemic status (normal GCT, impaired GCT non-GDM or GDM) and represented a linear increasing trend in terms of severity (p for trend <0.001 for each).

2.4.2 Maternal hyperglycemia and LGA birth

LGA is defined as a neonatal birth weight greater than the 90th percentile for gestational age that has been adjusted for ethnicity, parity and infant sex (Zhang & Bowes, 1995). Women with GDM or impaired GCT without GDM had a ~2-fold increased risk for bearing an LGA infant as compared to women with normal GCT (table 2, model 1) after controlling for maternal confounding variables and using a standard which adjusted LGA for maternal ethnicity, parity and fetal gender. This increased risk persisted after additional adjustments

Characteristics	All patients	Normal GCT	Impaired GCT non-GDM	GDM
N (%)	2373 (100)	2092 (88.1)	182 (7.7)	99 (4.2)
Age (yr)[1]	22.1±0.1	21.7±0.1	24.4±0.4	26.3±0.6
Pre-pregnant BMI (kg/m^2)[1]	25.7±0.1	25.4±0.1	26.6±0.5	29.8±0.8
BMI categories[1]				
<18.5	146 (6.2)	141 (6.7)	5 (2.8)	0
18.5-24.9	1157 (48.8)	1050 (50.2)	82 (45.1)	25 (25.3)
25-29.9	587 (24.7)	503 (24.0)	50 (27.5)	34 (34.3)
≥30	483 (20.4)	398 (19.0)	45 (24.7)	40 (40.0)
Cigarette smoking	440 (18.5)	381(18.2)	39 (21.4)	20 (20.2)
Ethnicity[2]				
Hispanic	1089 (45.9)	949 (45.4)	82 (45.0)	58 (58.6)
African American	891(37.6)	803 (38.4)	67 (36.8)	21 (21.2)
Caucasian & other	393 (16.6)	340 (16.3)	33 (18.1)	20 (20.2)
Medicaid	2323 (97.9)	2047 (97.9)	178 (97.8)	98 (99.0)
Prior GDM in multiparas[1]	33 (1.4)	15 (0.7)	8 (4.4)	10 (10.0)
Primiparas[2]	923 (38.9)	833 (39.8)	60 (33.0)	30 (30.3)

Data are mean ± SE or n (%).
Normal GCT, during a glucose challenge test, glucose ≤140mg/dl; Impaired GCT non-GDM, glucose >140mg/dl during a glucose challenge test and non-GDM; GDM, gestational diabetes mellitus (same in tables 2,4,5).
1. p for linear contrasts among groups <0.001 from ANOVA, or Mantel-Haenszel chi-square test;
2. p for linear contrasts among groups <0.05 from Mantel-Haenszel chi-square test.

Table 1. Characteristics of Study Participants

for pre-pregnant BMI and net maternal weight gain (net weight gain=total weight gain-infant birth weight) in women with impaired GCT non-GDM (Table 2, model 2), but it was non-significant in women with GDM.

		LGA	AOR (95% CI)[1]	
	N	Unadjusted %	Model 1[2]	Model 2[3]
GDM	99	10.1	2.05 (1.03, 4.10)	1.52 (0.74, 3.13)
Impaired GCT non-GDM	182	12.1	2.48 (1.50, 4.09)	2.50 (1.50, 4.14)
Normal GCT	2092	5.3	Reference	Reference

LGA, large-for-gestational age infant; AOR, adjusted odds ratio; 95% CI, 95% confidence interval (same as in tables 4-5).
[1] p for linear trend <0.01.
[2] Model 1 was adjusted for age and cigarette smoking in addition to using a standard which adjusted LGA for maternal ethnicity, parity and fetal gender.
[3] Model 2 was adjusted for all variables in model 1 with additional adjustment for pre-pregnant BMI and net of weight gain (kg) during pregnancy.

Table 2. Maternal Hyperglycemia and LGA birth

2.4.3 What do we learn from the Camden study?

Complicating the interpretation of previous studies has been the inability to adjust the observations for important factors related to fetal growth such as pre-pregnant obesity or gestational weight gain, often because the data were not available (Hillier et al., 2008; Rosenberg et al., 2005; Aberg et al., 2001). Our study in Camden also differs because of the inclusion of several ethnic groups (Vambergue et al., 2000; Bo et al., 2004; Mello et al., 1997). With our large cohort, we had the power to control for known potential confounders that influence the fetal overgrowth, including pre-pregnant BMI and net gestational weight gain. We confirmed that untreated maternal mild hyperglycemia (impaired GCT with one abnormal or no abnormal glucose value at OGTT) in otherwise young and healthy women in the US was associated with a 2-3 fold increased risk of delivering an LGA infant (table 2). These observations are consistent with previous findings from populations studied worldwide by the HAPO group and other studies (HAPO, 2008; Stamilio et al 2004). In addition, increased risk of LGA birth in GDM women (all of whom were treated by diet or with insulin) was associated with high maternal pre-pregnant BMI.

3. Pregnancy weight gain and LGA birth

3.1 Significance of optimal pregnancy weight gain and fetal growth

To optimize gestational weight gain for both mother and fetus is critical and remains controversial. A large number of studies have found that excess gestational weight gain is associated with decreased risk of small-for-gestational age birth and with increased risk for LGA birth (Oken et al., 2009; Jensen et al., 2005; Hinkle et a., 2010), regardless the definition or the scales used for excess pregnancy weight gain (Kiel et al., 2007; Jain et al., 2007).

3.2 Weight gain and maternal obesity

The independent contribution of excess gestational weight gain and maternal obesity on the risk of LGA or macrosomia has been extensively investigated (Jensen et al., 2005; Jain et al., 2007), because obesity is a common problem during pregnancy (Chu et al., 2007; Sebire et al., 2001; Rosenberg et al., 2005). Even in women with a normal pre-pregnant BMI, a higher pregnancy weight gain was associated with an increased risk of LGA, while a normal weight gain by the 1990 The Institute of Medicine (IOM) guidelines was associated with a decreased risk of LGA (DeVader et al., 2007). The definition of an optimal gestational weight gain in obese pregnancy remains controversial (Nohr et al., 2008). Jain et al observed that overweight/obese women who gain weight within the IOM recommendation achieve better fetal outcomes (Jain et al., 2007), while others found weight gain within IOM ranges did not reduce the risk of LGA among the obese (Dietz et al., 2009). It was suggested that limited or no weight gain in more severely obese pregnant women may increase favorable neonatal outcomes (Kiel et al., 2007; Jensen et al., 2005). Thus, an optimal gestational weight gain may need to be further defined by obesity severity (Hinkle et al., 2010; Oken et al., 2009).

3.3 What are problems in the research of weight gain during pregnancy?

There are limited data that link excess pregnancy weight gain measured prior to screening for GDM and /or longitudinal gestational weight gain measures through out the pregnancy to adverse pregnancy outcomes. In 2009, the IOM published revised gestational weight gain guidelines for how much weight a woman should gain during pregnancy to optimize both maternal and child outcomes. The report highlighted the importance of intervention in pregnancy to prevent obesity in the post-partum for mother and child (IOM, 2009).

3.4 The US Institute of medicine new guidelines for gestational weight gain

The new 2009 IOM guidelines are based on the WHO BMI (kg/m^2) categories (WHO, 1998) and include the recommended total pregnancy weight gain (kg) or rates of weight gain during the 2nd and 3rd trimester (kg/week). Weight gain below or above the recommended range is defined as inadequate or excessive gain, respectively.

Prepregnancy BMI	BMI (kg/m^2) (WHO)	Total weight gain range		Rate of weight gain 2nd and 3rd trimester (mean, range)[2]	
		(lbs)	(kg)	(lbs/wk)	(kg/wk)
Under weight	<18.5	28-40	12.5-18.0	1.0 (1.0-1.3)	0.51 (0.44-0.58)
Normal weight	18.5-24.9	25-35	11.5-16.0	1.0 (0.8-1.0)	0.42 (0.35-0.50)
Overweight	25.0-29.9	15-25	7.0-11.5	0.6 (0.5-0.7)	0.28 (0.23-0.33)
Obese (includes all classes)	≥30.0	11-20	5.0-9.0	0.5 (0.4-0.6)	0.22 (0.17-0.27)

[1] IOM, Institute of Medicine in US.

[2] Calculations assume a 0.5-2kg (1.1-4.4 lbs) weight gain in the first trimester (based on Siega-Riz et. al., 1994; Abrams et al 1995, Carmichael et al 1997).

Table 3. New recommendations for total and rate of weight gain during pregnancy, by prepregnancy BMI (IOM, 2009)[1]

3.5 Assessment of pregnancy weight gain

We explored the associations between gestational weight gain assessed throughout pregnancy with LGA using the 2009 IOM guidelines for weight gain during pregnancy. Inadequate, adequate and excessive pregnancy weight gain at weeks 24, 28, 32 and at delivery was categorized according to IOM recommendations (table 3). Maternal obesity was defined as BMI ≥30 (WHO, 1998); height was measured with a stadiometer at entry. Gestational duration was based upon gestation from participants' last normal menstrual period confirmed or modified by ultrasound. Pregnancy weight was measured at week 12, 24, 28, 32 and at delivery. Total gestational weight gain was computed as the difference between weight at delivery and recalled pre-pregnant weight. Gestational weight gain during the 2nd and 3rd trimester was computed as the difference between weights measured at each visit minuses the weight measured at week 12. The rate of weight gain was the weight gain (kg) divided by gestational age (weeks).

3.6 Excess pregnancy weight gain measured mid to late gestations and LGA birth

The proportion of women with excess pregnancy weight gain at weeks 24, 28, and 32 was similar to delivery (48.5%, 52%, 54% and 50% respectively). Depending on the gestation, 21-27% had an adequate weight gain and 22-30% had an inadequate gain throughout the four time points.

Compared to women with adequate weight gain, excessive weight gain was associated with a 1.58-2.66 fold increased risk of LGA birth (table 4) after controlling for all the confounding

variables with the exception of pre-pregnant BMI (p for trend <0.0001 for each model). Similar results were obtained when additional adjustment for pre-pregnant BMI. In addition, women with inadequate weight gain had a reduced risk of LGA birth at week 28 and 32 (p<0.05).

3.7 Contribution of Camden data

These data confirmed that excess pregnancy weight gain throughout the 2nd and 3rd trimesters and at delivery significantly increased risk of LGA, whereas inadequate pregnancy weight gain reduced LGA risk. The current study has several important strengths. Firstly, we used the most recent IOM recommendations (2009) for the estimation of excess weight gain by BMI categories and the analysis models were fully adjusted for potential confounding, including pre-pregnant BMI. In contrast, more arbitrary criteria were used to define excess weight gain in previous studies (Herring et al., 2009; Rosenberg et al., 2005), and pre-pregnant BMI either was not available or was not adjusted for in the analysis (Hillier et al., 2008; Rosenberg et al., 2005). Secondly, there are limited data on longitudinal measures of pregnancy weight gain (Herring et al., 2009; Saldana et al., 2006). We used multiple measures of pregnancy weight gain starting prior to the screen for GDM. The relationship between excess pregnancy weight gain assessed relatively early in pregnancy and risk of LGA could be important for preventive strategies. Total weight gain is not an ideal measure to evaluate in relation to fetal growth in GDM patients, because most of patients are treated and their weight gain is monitored after the diagnosis.

	Week 24		Week 28		Week 32		At delivery	
Weight gain	LGA (%)	AOR (95% CI)	LGA (%)	AOR (95% CI)	LGA (%)	AOR (95% CI)	LGA (%)	AOR (95% CI)
Adequate	3.5	Reference	5.1	Reference	6.1	Reference	3.6	Reference
Inadequate	3.2	0.90 (0.47,1.71)	2.6	0.50 (0.27, 0.95)	2.3	0.49 (0.24, 0.98)	2.3	0.62 (0.31, 1.25)
Excessive	8.7	2.62 (1.55, 4.43)	8.0	1.65 (1.05, 2.61)	7.6	1.58 (1.00, 2.50)	9.1	2.66 (1.69, 4.19)

[1] Models were adjusted for age and cigarette smoking in addition to using a standard which adjusted LGA for parity, ethnicity and infant gender.
[2] p for trend <0.0001 for week 24, 28, 32 and delivery respectively.

Table 4. Excess pregnancy weight gain and LGA birth[1,2]

4. Association of various degree of gestational hyperglycemia, excess pregnancy weight gain with LGA birth

4.1 Does excess gestational weight gain prior to screening GDM predict risk of GDM?

High gestational weight gain between early and mid pregnancy was positively associated with risk of GDM or impaired glucose tolerance (Hedderson et al., 2010; Herring et al., 2009). In the Camden study, we found a positive association between excess weight gain prior to or at the time of screening for GDM (weeks 24 and 28) with increased risk for GDM (AOR 1.57, 95% CI 1.01, 2.44 for week 24, AOR 1.94, 95% CI 1.28, 2.95 for week 28). This association was not significant at week 32 or at delivery which may suggest an effect of treatment and weight monitoring after the diagnosis of GDM. We did not observe a

significant association between excess weight gain and impaired GCT non-GDM (p>0.05 for all time points).

4.2 The association of gestational hyperglycemia and excess weight gain with LGA

Combined association of gestational hyperglycemia and excess weight gain on the risk of LGA has not been examined extensively. Hillier et al observed at GDM screening that macrosomia risk was increased across the spectrum of maternal glucose levels and that this relationship was further modified by excessive maternal weight gain (Hillier et al., 2008). A weight gain of 40lbs or more nearly doubled the risk of fetal macrosomia among glucose intolerant women including those with GDM. However, results were not adjusted for pre-pregnancy BMI which can complicate the relationship between maternal hyperglycemia and pregnancy weight gain. Thus, our next goal was to examine the independent and combined contributions of hyperglycemia and excess weight gain on risk of LGA. An analysis stratified by excessive weight gain was used to index the influence of various degrees of maternal glycemic status on LGA risk, using women with non-excess pregnancy weight gain (adequate and inadequate gain combined) and a normal GCT as the reference group. Our results showed that excess weight gain (at week 24, 28, 32 or at delivery) was positively associated with a 2-6 fold increased risks for delivering an LGA infant (table 5) regardless of whether the women were diagnosed with GDM, impaired GCT non-GDM or normal GCT. Furthermore, women with non-excess weight gain and an impaired GCT non-GDM also had a 2-3 fold increased risk of LGA birth during all of four time points, whereas risk of LGA was not increased in the GDM group with non-excess weight gain.

	Weight gain at week 24		Weight gain at week 28		Weight gain at week 32		Weight gain at delivery	
	LGA (%)	AOR (95% CI)[3]	LGA (%)	AOR (95% CI)[3]	LGA (%)	AOR (95% CI)[3]	LGA (%)	AOR (95% CI)[3]
Excess weight gain								
GDM	11.5	4.03 (1.67, 9.73)	10.5	3.31 (1.39, 7.90)	11.3	3.20 (1.34, 7.63)	14.3	6.07 (2.58, 14.70)
Impaired GCT non-GDM	16.0	6.14 (3.16, 11.90)	14.6	4.97 (2.53, 9.71)	14.1	4.62 (2.18, 8.31)	14.9	6.42 (3.20, 12.88)
Normal GCT	7.8	2.91 (1.88, 4.48)	7.2	2.43 (1.58, 3.73)	6.8	2.02 (1.33, 3.10)	8.2	3.58 (2.29, 5.60)
Non-excess weight gain[2]								
GDM	5.6	1.64 (0.37, 7.21)	6.7	1.69 (0.38, 7.50)	5.9	1.31 (0.30, 5.71)	4.7	1.62 (0.37, 7.11)
Impaired GCT non-GDM	8.1	2.78 (1.17, 6.59)	9.5	2.98 (1.31, 6.77)	9.9	2.69 (1.19, 6.08)	9.1	3.79 (1.65, 8.68)
Normal GCT	2.8	Reference	3.1	Reference	3.6	Reference	2.5	Reference

[1] Model was adjusted for age, pre-pregnant BMI and cigarette smoking in addition to using a standard which adjusted LGA for maternal ethnicity, parity and fetal gender.
[2] Adequate and inadequate weight gain is combined.
[3] p for trend <0.0001.

Table 5. Maternal hyperglycemia and LGA infant: Stratified by excess weight gain[1]

4.3 What do we learn?

These data confirmed that hyperglycemia and excess weight gain are independently associated with risk of fetal overgrowth. Women with excess weight gain at any of four times in gestation and hyperglycemia, even a mild hyperglycemia, had a substantially increased risk of LGA. Risk of LGA was not increased among gestational diabetics without an excessive weight gain but only among the group with impaired GCT non-GDM. Thus, excess pregnancy weight gain and hyperglycemia are independent risk factors for LGA.

5. Conclusion

By using the most updated IOM guidelines (2009) on pregnancy weight gain, we found that healthy, young women with mild but untreated hyperglycemia were at increased risk for fetal overgrowth (LGA). The risk of LGA birth in women with GDM, who are treated by diet or with insulin after diagnosis, was dependent on maternal pre-pregnant weight. Excess pregnancy weight gain assessed longitudinally through out mid to late gestation consistently showed strong associations with LGA risk. In addition, excess pregnancy weight gain and hyperglycemia appeared to be independent risk factors for LGA. The risk for LGA was increased still further in women with excess weight gain, even in those with mild hyperglycemia. Because prepregnancy obesity, mild gestational hyperglycemia, and excess weight gain during pregnancy are preventable risk factors, these findings suggest that early detection and treatment of mild hyperglycemia and monitoring pregnancy weight gain during early gestation are both important for reducing the risk of LGA, for reducing childhood and later obesity and for improving the long term risk for metabolic disease in the offspring.

6. Acknowledgements

This work was supported by grants from the National Institute of Child Health and Human Development (HD18269 and HD38329 to T.O.S.) and National Institute of Diabetes and Digestive and Kidney Diseases (1R21DK078865-01 and 5R21DK078865-02 to X.C.).

7. References

Aberg, A., Rydhstroem H., & Frid, A. (2001). Impaired glucose tolerance associated with adverse pregnancy outcome: A population-based study in southern Sweden. *Amer J Obstet Gynecol V*ol.184, No.2, (January 2001), pp.77-83, ISSN 1097-6868.

Abrams, B., Carmichael, S., & Selvin, S. (1995). Factors associated with the pattern of maternal weight gain during pregnancy. *Obstet Gynecol* Vol.86, No.2, (August 1995), pp.170-6, ISSN 0029-7844.

American Diabetes Association. (2000). Gestational diabetes mellitus. *Diabetes Care* Vol.23, No. 1, (January 2000), pp. S77-9, ISSN 0149-5992.

Bo, S., Menato, G., Gallo, M., Bardelli, C., Lezo, A., Signorile, A. Gambino, R., Cassader, M., Massobrio, M., & Pagano, G. (2004). Mild gestational hyperglycemia, the metabolic syndrome and adverse neonatal outcomes. *Acta Obstet Gynecol Scand* Vol.83, No.4, (March 2004), pp.335-40, ISSN 0001-6349.

Boney, C., Verma, A., Tucker, R., & Vohr, B. (2005). Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* Vol.115, No.3, (March 2005), pp.e290-6, ISSN 1098-4275.

Carmichael, S., Abrams, B. & Selvin S. (1997). The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Public Health* Vol. 87, No.12, (December 1997), pp.1984-88, ISSN 1938-3207.

Chen X, Scholl TO, Leskiw M, Savaille J, Stein TP. (2010). Differences in maternal circulating fatty acids composition and dietary fat intake in women with gestational diabetes or mild gestational hyperglycemia. *Diabetes Care* Vol.33, No.9, (September), pp.2049-54, ISSN 0149-5992.

Cheng, Y., Esakoff, T., Block-Kurbisch, I., Ustinov, A., Shafer, S., & Caughey, A. (2006). Screening or diagnostic: markedly elevated glucose loading test and perinatal outcomes. *J Matern Fetal Neonatal Med* Vol. 19, No. 11, (November 2006), pp.729-34, ISSN 1476-7058.

Chu, S., Callaghan W., Kim S., Schmid C., Lau, J., England, L., & Dietz, P. (2007). Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care* Vol. 30, No.8, (August 2007), pp.2070-76, ISSN 0149-5992.

DeVader, S., Neeley, H., Myles, T., & Leet, T. (2007). Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. *Obstet Gynecol* Vol.110, No.4, (October 2007), pp.745-51, ISSN 0029-7844.

Dietz, P., Callaghan, W., & Sharma, A. (2009). High pregnancy weight gain and risk of excessive fetal growth. *Amer J Obstet Gynecol V*ol.201, No.1, (July 2009), pp.51.e1-6, ISSN 0002-9378.

Ehrenberg, H., Mercer, B., & Catalano, P. (2004). The influence of obesity and diabetes on the prevalence of macrosomia. *Amer J Obstet Gynecol V*ol.191, No.3, (September 2004), pp.964-8, ISSN 0002-9378.

Getahun, D., Nath, C., Ananth, C., Chavez, M., & Smulian, J. (2008). Gestational diabetes in the United States: temporal trends 1989 through 2004. *Amer J Obstet Gynecol V*ol.198, No.5, (May 2008), pp.525.e1-5, ISSN 0002-9378.

Gruendhammer, M., Brezinka, C., & Lechleitner, M. (2003). The number of abnormal plasma glucose values in the oral glucose tolerance test and the feto-maternal outcome of pregnancy. *Eur J Obstet Gynecol Reprod Biol* Vol.108, No.2, (June 2003), pp.131-6, ISSN 0301-2115.

Hedderson, M., Gunderson, E., & Ferrara, A. (2010). Gestational weight gain and risk of gestational diabetes mellitus. *Obstet Gynecol* Vol.115, No.3, (March 2010), pp.597-604, ISSN 0029-7844.

Herring, S., Oken, E., Rifas-Shiman, S., Rich-Edwards, J., Stuebe, A., Kleinman, K., & Gillman, M. (2009). Weight gain in pregnancy and risk of maternal hyperglycemia. *Amer J Obstet Gynecol V*ol.201, No.1, (July 2009), pp.61.e1-7, ISSN 0002-9378.

Hillier, T., Pedula, K., Vesco, K., Schmidt, M., Mullen, J., LeBlanc, E., & Pettitt, D. (2008). Excess gestational weight gain: modifying fetal macrosomia risk associated with maternal glucose. *Obstet Gynecol* Vol.112, No.5, (November 2008), pp.1007-14, ISSN 0029-7844.

Hinkle, S., Sharma, A., & Dietz, P. (2010). Gestational weight gain in obese mothers and associations with fetal growth. *Am J Clin Nutr* Vol.92, No.3, (September 2010), pp.644-51, ISSN 0002-9165.

IOM (Institute of Medicine). Weight gain during pregnancy: reexamining the guidelines. (April 2009). The National Academies Press, Washington DC. Available from: <http://www.nap.edu/catalog/12584.html>

Jain, N., Denk, C., Kruse, L., & Dandolu, V. (2007). Maternal obesity: can pregnancy weight gain modify risk of selected adverse pregnancy outcomes? *Am J Perinatol* Vol.24, No.5, pp. 291-8, ISSN 0735-1631.

Jensen, D., Ovesen, P., Beck-Nielsen, H., Mølsted-Pedersen, L., Sørensen, B., Vinter, C., & Damm, P. (2005). Gestational weight gain and pregnancy outcomes in 481 obese glucose-tolerant women. *Diabetes Care* Vol. 28, No.9, (September 2005), pp.2118-22, ISSN 0149-5992.

Kiel, D., Dodson, E., Artal, R., Boehmer, T., & Leet, T. (2007). Gestational weight gain and pregnancy outcomes in obese women. *Obstet Gynecol* Vol.110, No.4, (October 2007), pp.752-8, ISSN 0029-7844.

Langer, O. (2000). Fetal macrosomia: Etiologic factors. *Clinical Obstetrics Gynecology* Vol.43, No.2, (June 2000), pp.283-97, ISSN 0100-7203.

Mello, G., Parretti, E., Mecacci, F., Lucchetti, R., Lagazio, C., Pratesi, M., & Scarselli, G. (1997). Risk factors for fetal macrosomia: the importance of a positive oral glucose challenge test. *Eur J Endocrinol* Vol.137, No.1, (July1997), pp.27-33, ISSN 0804-4643.

Mokdad, A., Bowman B., Ford E., Vinicor, F., Marks, J., & Koplan, J. (2001). The Continuing Epidemics of Obesity and Diabetes in the United States. *JAMA* Vol.286, No.10, (September 2001), pp.1195-1200, ISSN 0098-7484.

Murphy, H., Rayman, G., Lewis, K., Kelly, S., Johal, B., Duffield, K., Fowler, D., Campbell, P., & Temple R. (2008). Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. *BMJ* Vol.337, a1680. Published online 2008 September. doi: 10.1136/bmj.a1680, ISSN 0959-8146.

Nohr, E., Vaeth, M., Baker, J., Sørensen, T., Olsen, J., & Rasmussen K. (2008). Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *Am J Clin Nutr* Vol. 87, No.6, (June 2008), pp.1750-9, ISSN 0002-9165.

Nordin, N., Wei, J., Naing, N., & Symonds, E. (2006). Comparison of maternal-fetal outcomes in gestational diabetes and lesser degrees of glucose intolerance. *J Obstet Gynaecol Res* Vol.32, No.1, (February 2006), pp.107-14, ISSN 1341-8076.

Ogonowski, J., Miazgowski, T., Czeszyńska, M., Jaskot, B., Kuczyńska, M., & Celewicz, Z. (2008). Factors influencing risk of macrosomia in women with gestational diabetes mellitus undergoing intensive diabetic care. *Diabetes Res Clin Pract* Vol.80, No.3, (June 2008), pp. 405-10, ISSN 0168-8227.

Oken, E., & Gillman, M. (2003). Fetal origins of obesity. *Obesity Research* Vol.11, No.4, (April 2003), pp.496-506, ISSN 1930-7381.

Oken, E., Kleinman, K., Belfort, M., Hammitt J., & Gillman, M. (2009). Associations of Gestational Weight Gain With Short- and Longer-term Maternal and Child Health Outcomes. *Am J Epidemiol* Vol.170, No.2, (July 2009), pp.173-80, ISSN 0002-9262.

Östlund, I., Hanson, U., Björklund, A., Hjertberg, R., Eva, N., Nordlander E., Marja-Liisa, S., & Wager J. (2003). Maternal and fetal outcomes if gestational impaired glucose tolerance is not treated. *Diabetes Care* Vol.26, No.7, (July 2003), pp.2107-11, ISSN 0149-5992.

Ray, J., Vermeulen, M., Shapiro, J., & Kenshole, A. (2001). Maternal and neonatal outcomes in pregestational and gestational diabetes mellitus, and the influence of maternal obesity and weight gain: the Deposit study. *QJM* Vol.94, No.7, (July 2001), pp.347-56, ISSN 1460-2725.

Ricart, W., López, J., Mozas, J., Pericot, A., Sancho, M., González, N., Balsells, M., Luna, R., Cortázar, A., Navarro, P., Ramírez, O., Flández, B., Pallardo, L., Hernández, A.,

Ampudia, J., Fernández-Real, J., & Corcoy, R. (2005). Potential impact of American Diabetes Association (2000) criteria for diagnosis of gestational diabetes mellitus in Spain. *Diabetologia* Vol.48, No.6, (June 2005), pp.1135-41, ISSN 0012-186X.

Rosenberg, T., Garbers, S., Lipkind, H., & Chiasson, M. (2005). Maternal obesity and diabetes as risk factors for adverse pregnancy outcomes: differences among 4 racial/ethnic groups. *Am J Publ Hlth* Vol.95, No.9, (September 2005), pp.1544-51, ISSN 0090-0036.

Saldana, T., Siega-Riz, A., Adair, L., & Suchindran, C. (2006). The relationship between pregnancy weight gain and glucose tolerance status among black and white women in central North Carolina. *Am J Obstet Gynecol* Vol.195, No.6, (December 2006), pp. 1629-35, ISSN 0002-9378.

Sebire, N., Jolly, M., Harris, J., Wadsworth, J., Joffe, M., & Beard, R., Regan, L. & Robinson, S. (2001). Maternal obesity and pregnancy outcome: a study of 287 213 pregnancies in London. *International Journal of Obesity* Vol.25, No.8, (August 2001), pp.1175-82, ISSN 0307-0565.

Sermer, M., Naylor, D., Gare, D., Kenshole, A., Ritchie, J., Farine, D., Cohen, H., McArthur, K., Holzapfel, S., Biringer, A., & Chen, E. (1995). Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes: the Toronto tri-hospital gestational diabetes project. *Am J Obstet Gynecol* Vol.173, No.1, (July 1995), pp. 146-56, ISSN 0002-9378.

Siega-Riz, A., Adair, L., & Hobel, C. (1994). Institute of Medicine maternal weight gain recommendations and pregnancy outcome in a predominantly Hispanic population. *Obstetrics Gynecology* Vol.84, No.4, (October 1994), pp.565-73, ISSN 0029-7844.

Stamilio, D., Olsen, T., Ratcliffe, S., Sehdev, H., & Macones, G. (2004). False-positive 1-hour glucose challenge test and adverse perinatal outcomes. *Obstet Gynecol* Vol.103, No.1, (January 2004), pp. 148-56, ISSN 0029-7844.

The HAPO Study Cooperative Research Group. (2008). Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* Vol.358, No.19, (May 2008), pp. 1991-2002, ISSN 1533-4406.

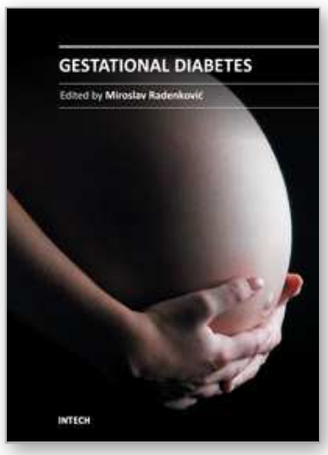
Vambergue, A., Nuttens, M., Verier-Mine, O., Dognin, C., & Cappoen, J., & Fontaine P. (2000). Is mild gestational hyperglycaemia associated with maternal and neonatal complications? The Diagest Study. *Diabet Med* Vol.17, No. 3, (March 2000), pp. 203-8, ISSN 1464-5491.

Webster, B., & Bishaw, A. (2006). Income, earnings, and poverty data from the 2005 American community survey. (August 2006). US Government Printing Office, Washington, DC. Available from: <https://www.census.gov/prod/2007pubs/acs-08.pdf>

World Health Organization (WHO). (1998). Obesity: preventing and managing the global epidemic. WHO Consultation on Obesity Report, Geneva. Geneva, June, 1997.

Yogev, Y., Langer, O., Xenakis, E., & Rosenn, B. (2004). Glucose screening in Mexican-American women. *Obstet Gynecol* Vol 103, No.6, (June 2004), pp. 1241-5, ISSN 0029-7844.

Zhang, J. & Bowes, W. (1995). Birth-weight-for-gestational-age patterns by race, sex, and parity in the United States population. *Obstet Gynecol* Vol.86, No.2, (August 1995), pp. 200-8, ISSN 0029-7844.



Gestational Diabetes

Edited by Prof. Miroslav Radenkovic

ISBN 978-953-307-581-5
Hard cover, 382 pages
Publisher InTech
Published online 02, November, 2011
Published in print edition November, 2011

Gestational diabetes mellitus is defined as hyperglycemia with onset or first recognition during pregnancy. The incidence of gestational diabetes is still increasing and this pathological condition has strong association with adverse pregnancy outcomes. Since gestational diabetes can have long-term pathological consequences for both mother and the child, it is important that it is promptly recognized and adequately managed. Treatment of gestational diabetes is aimed to maintain euglycemia and it should involve regular glucose monitoring, dietary modifications, life style changes, appropriate physical activity, and when necessary, pharmacotherapy. Adequate glycemic control throughout the pregnancy can notably reduce the occurrence of specific adverse perinatal and maternal outcomes. In a long-term prospect, in order to prevent development of diabetes later in life, as well to avoid associated complications, an adequate education on lifestyle modifications should start in pregnancy and continue postpartum.

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen