Pregnancy outcomes in Korean women with diabetes

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Conflict of interest disclosure

None

Committee of Scientific Affairs

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Contents

- Epidemiology of diabetes in pregnancy

- Hyperglycemia and adverse outcome of pregnancy

- Pregnancy outcomes in Korean women with PGDM and GDM

- Summary and Conclusions

Classification of diabetes in pregnancy

- Type 1 diabetes (results from β-cell destruction, usually leading to absolute insulin deficiency)

- Type 2 diabetes (results from a progressive insulin secretory defect on the background of insulin resistance)

- Other specific types of diabetes due to other causes, e.g., genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced (such as in the treatment of HIV/AIDS or after organ transplantation)

- Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly overt diabetes)

Rates of deliveries by GDM and pre-existing diabetes in Korea

	2010			2011			2012		
Age	Deliveries, n	Gestational diabetes, n (%)	Pre-existing diabetes, n (%)	Deliveries, n	Gestational diabetes, n (%)	Pre-existing diabetes, n (%)	Deliveries, n	Gestational diabetes, n (%)	Pre-existing diabetes, n (%)
15–20 years	3339	23 (0.7)	19 (0.6)	3448	21 (0.6)	18 (0.5)	2871	38 (1.3)	24 (0.8)
21–30 years	166 342	4255 (2.6)	2,371 (1.4)	149 122	5044 (3.4)	2221 (1.5)	119 389	5335 (4.5)	1894 (1.6)
31–40 years	281 279	15 974 (5.7)	8,625 (3.1)	279 671	21 188 (7.6)	7682 (2.8)	248 033	23 787 (9.6)	7482 (3.0)
41–49 years	8882	733 (8.3)	599 (6.7)	9984	1037 (10.4)	600 (6.0)	10 138	1281 (12.6)	672 (6.6)
≥ 35 years	78 591	5554 (7.1)	3,596 (4.6)	80 615	7410 (9.2)	3327 (4.1)	74 448	8393 (11.3)	3481 (4.7)
Total	459 842	20 985 (4.6)	11,614 (2.5)	442 225	27 290 (6.2)	10 521 (2.4)	380 431	30 441 (8.0)	10 072 (2.7)

Son KH et al. Diabet Med 2015; 32:477-486
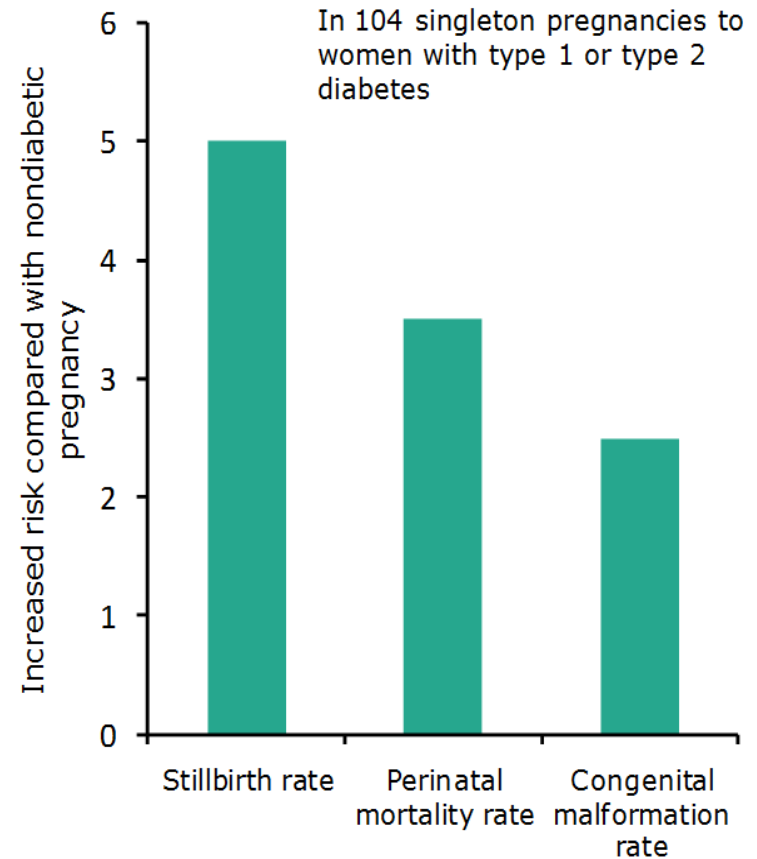
700,000 /yr in England and Wales

- Up to 5% PGDM or GDM
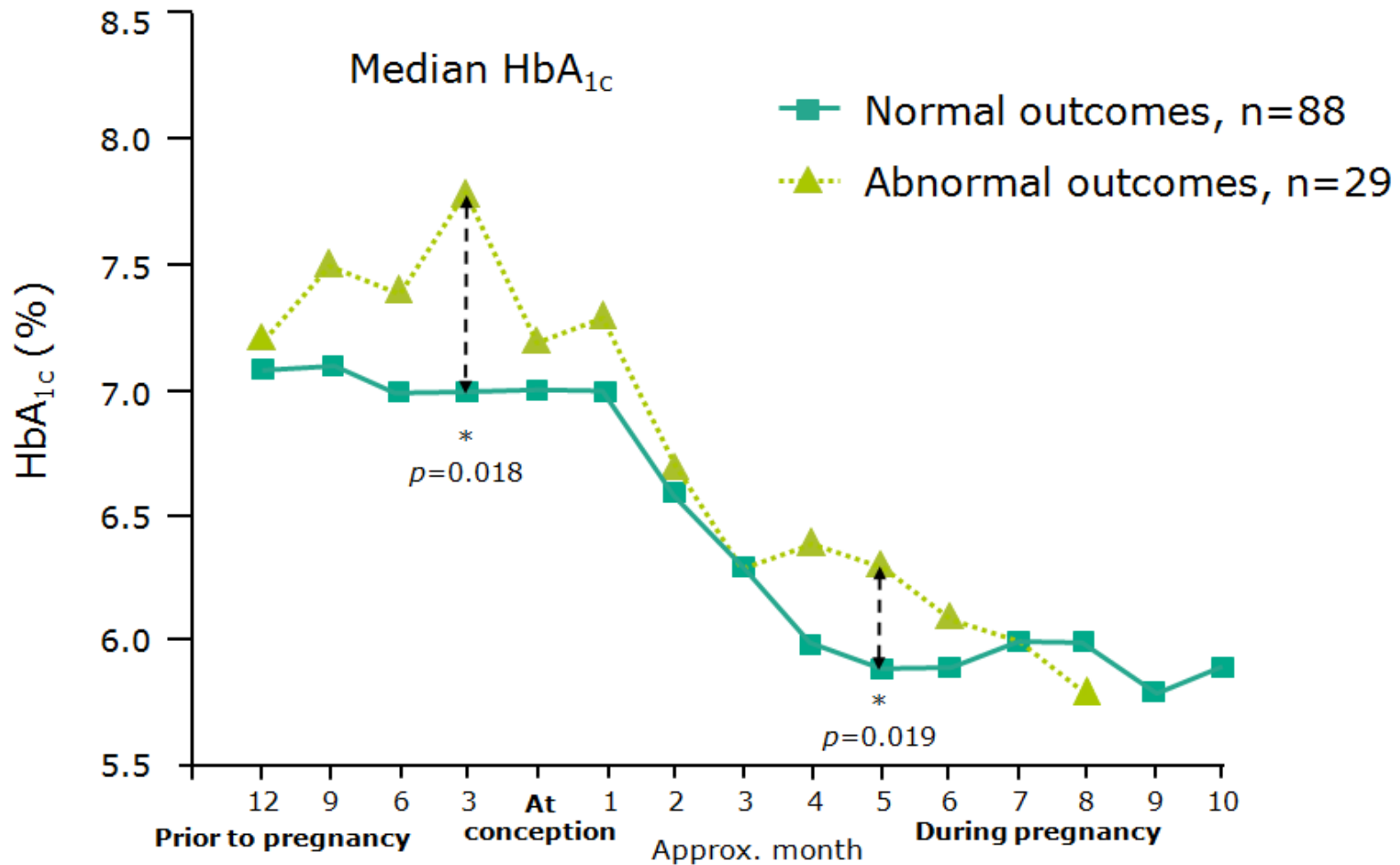- 87.5% GDM
- 7.5%   T1DM
- 5%   T2DM

- NICE guileline 2015 -

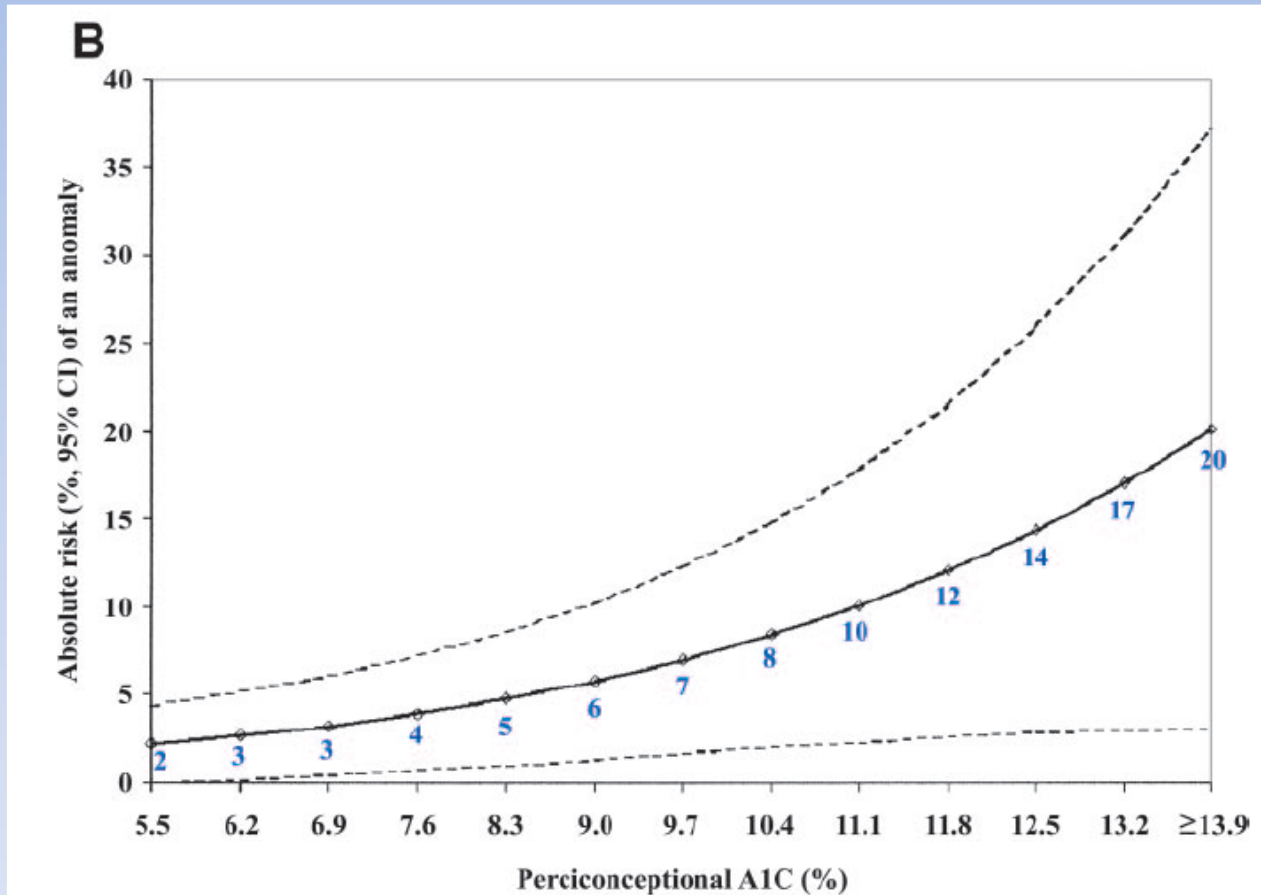# Diabetes in pregnancy and risk of complications

- Pre-existing diabetes in pregnancy is associated with high rates of complications:
  - Fetal/neonatal
    - Congenital malformations
    - Perinatal mortality
    - Excess fetal growth
    - Traumatic delivery
    - Neonatal hypoglycaemia
    - Hyperbilirubinaemia
    - Diabetic fetopathy
  - Maternal
    - Pregnancy-induced hypertension/ pre-eclampsia
    - Polyhydramnios
    - Operative delivery

In 104 singleton pregnancies to women with type 1 or type 2 diabetes

Dunne *et al. Diabetes Care* 2009;32:1205–6

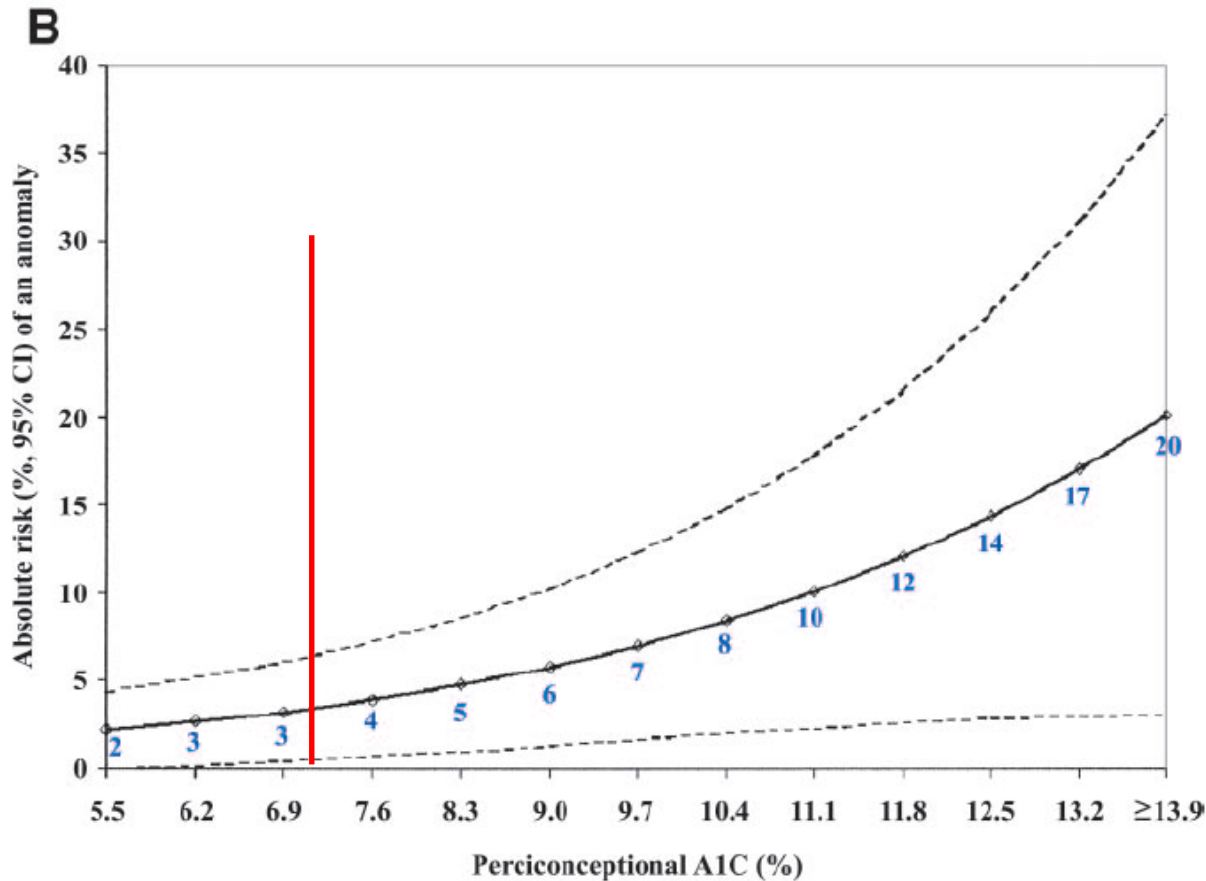# Blood glucose control is linked with outcomes in diabetic pregnancy

Glucose control and risk of malformation

Guerin A. Diabetes Care 30:1920, 2007

Glucose control and risk of malformation

For every 1% decrease in A1c, there is approximately 50% relative risk reduction for a congenital anomaly

Guerin A. Diabetes Care 30:1920, 2007

Diabetes in pregnancy and risk of complications

Outcome	Pregnant women with type 1 or type 2 diabetes	National data (background population)	Rate ratio
Pre-term delivery	37%	7.3%	5
Birth weight ≥90th percentile	52%	10%	5.2
Shoulder dystocia	7.9%	3%	2.6
Erb's palsy	4.5/1000	0.42/1000	11
Neonatal unit admission	56%	10%	5.6
Term admission for special care	33%	10%	3.3

Confidential Enquiry into Maternal and Child Health (CEMACH): Pregnancy in Women with Type 1 and Type 2 Diabetes in 2002–03, England, Wales and Northern Ireland. London: CEMACH; 2005

Maternal and fetal outcome in Type 1 vs type 2 DM: metaanalysis

Women type 2 DM

↑ Perinatal mortality OR 1.50 (1.15-1.96)

↓ Ketoacidosis   OR 0.09 (0.02-0.34)

↓ C-section   OR 0.80 (0.59-0.94)

No significant differences:

Major congenital malformation

Stillbirth

 Neonatal mortality

Spontaneous abortion

SGA/LGA/Macrosomia

Hypoglycemia

RDS

Balsells M. JCEM 2009

Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nationwide study

Helen R. Murphy[1,2] · Ruth Bell[3] · Cher Cartwright[4] · Paula Curnow[4] ·
Michael Maresh[5] · Margery Morgan[6] · Catherine Sylvester[4] · Bob Young[4] ·
Nick Lewis-Barned[7]

- Population-based cohort of 3036 pregnant women with diabetes from 155 maternity clinics in England and Wales in 2015 and changes since 2002/2003

- Stillbirth rates among women with type 1 and type 2 diabetes have decreased since 2002/2003.

- Rates of preterm delivery and LGA infants are lower in women with type 2 compared with type 1 diabetes.

- In women with type 1 diabetes, suboptimal glucose control and high rates of perinatal morbidity persist with substantial variations between clinics.

Original Article

DIABETES & METABOLISM JOURNAL

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Maternal and Neonatal Outcomes in Korean Women with Type 1 and Type 2 Diabetes

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[2]Department of Clinical Trials for Medical Devices, Severance Hospital, Yonsei University Health System, Seoul,
Departments of [3]Ambulatory Nursing Team, [4]Obstetrics and Gynecology, [5]Pediatrics, [6]Medicine, Cheil General Hospital & Women's Healthcare Center,
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Maternal outcomes

Subjects: 163 women with PGDM during 2003-2010 at CGH

	Type 1 diabetes	Type 2 diabetes	P value
Number	13	150	
Miscarriage	0	6 (4.0)	0.602[a]
Termination of pregnancy	0	2 (1.4)	0.846[a]
Method of delivery			0.188
Vaginal delivery	6 (46.2)	38 (26.8)	0.124
Induction	0	1 (0.7)	0.916[a]
Repeated C/S	1 (7.7)	51 (35.9)	0.032[a]
Primary C/S	6 (46.2)	52 (36.6)	0.497
Pre-eclampsia[b]	5 (38.5)	12 (8.2)	0.006[a]
Preterm delivery (n=144)			
Preterm delivery <37 wk	3 (23.1)	12 (13.7)	0.088[a]
Early preterm delivery <34 wk	0	2 (1.4)	0.667[a]

Neonatal outcomes

Characteristic	Type 1 diabetes	Type 2 diabetes	P value
Number	13	142	
Neonatal weight, g	3,501.5±689.6	3,366.3±531.4	0.394
Neonatal birth weight centiles			
LGA ≥90th centile	6 (46.2)	29 (20.4)	0.044
SGA ≤10th centile	2 (15.4)	12 (8.5)	0.332[a]
Macrosomia	5 (38.5)	19 (13.4)	0.032[a]
Neonatal complication			
Asphyxia, TTN, RDS, MAS	6 (46.2)	59 (41.8)	0.492
Hyper bilirubinemia, jaundice	3 (23.1)	46 (32.6)	0.357[a]
Hypocalcaemia	1 (7.7)	3 (2.1)	0.300[a]
Hypoglycemia	0	8 (5.7)	0.485[a]
Polycythemia[b]	0/10	1/109 (0.9)	0.916[a]
Cardiac hypertrophy, heart failure[b]	0/13	1/141 (0.7)	0.916[a]
Malformation	1 (7.7)	8 (5.6)	0.515[a]
Birth injury	0	4 (2.8)	0.702[a]
Admission of neonatal care	5 (41.7)	19 (14.8)	0.030[a]

Preconception planning is important

- Pregnancy planning is key
- Meta-analysis of preconception care and major congenital malformations in recipients and non-recipients (Ray *et al*, 2001)
    - Recipients: 2.1% vs. non-recipients: 6.5%
    - Relative risk 0.36 (95% CI ;0.22–0.59)

- Preconception care is recommended
    - "Women with diabetes and childbearing potential should be educated about the need for good glucose control before pregnancy and should participate in effective family planning" (Kitzmiller *et al*, 2008)

UK CEMACH report: pre-pregnancy preparation is still suboptimal

Pre-pregnancy	Type 1 (n=2767)	Type 2 (n=1041)
Counselling documented	1056 (38.2%)	258 (24.8%)
Glycaemic test recorded	1108 (40.0%)	306 (29.4%)
Folic acid	1187 (42.9%)	306 (29.4%)

Confidential Enquiry into Maternal and Child Health (CEMACH): Pregnancy in Women with Type 1 and Type 2 Diabetes in 2002–03, England, Wales and Northern Ireland. London: CEMACH; 2005

Pregnancy outcomes of GDM

Diagnosis of GDM

Pregnancy Outcomes in Korean Women with Gestational Diabetes Diagnosed by the IADPSG Criteria: A Prospective Cohort Study

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77th Scientific Sessions of ADA

IADPSG vs 2003 ADA Criteria

	IADPSG criteria	2003 ADA criteria
	(2-h 75-g Oral Glucose Tolerance Test)	
Fasting (mg/dl)	≥ 92	≥ 95
1-h (mg/dl)	≥ 180	≥ 180
2-h (mg/dl)	≥ 153	≥ 155
	Any of the cut-off values above	At least two of the cut-off values above

- **Prevalence of GDM**
  - 2.1% by 2003 ADA, 6.2% by IADPSG criteria

- pregnancy outcomes:

  LGA   OR; IADPSG 2.39 (1.50-3.81), ADA 2.07 (1.08-3.94)
  macrosomia OR; IADPSG 2.53 (1.26-5.10), ADA 3.34 (1.39-8.00)
  neonatal hypoglycemia OR; IADPSG 3.84 (1.00-14.74), ADA 4.98 (1.17-21.31)
  preeclampsia OR; IADPSG 6.90 (1.84-25.87), ADA 2.47 (0.28-22.11)
  neonatal hyperbilirubinemia OR; IADPSG 1.57 (1.07-2.31), ADA 0.63 (0.36-1.13)

- No significant differences:
  primary cesarean section
  shoulder dystocia or birth injury
  neonatal intensive care

Conclusion

- The prevalence of GDM by IADPSG criteria was relatively low compared with other countries.

- However, GDM by IAPDSG criteria was significantly associated with risk of adverse maternal and neonatal outcomes.

Maternal gestational weight gain

Goals for weight gain

Prepregnancy BMI	Total wt.gain (kg)	Rate of wt.gain(2&3Tri.)kg/wk
Underweight (<18.5)	12.5 - 18	0.51 (0.44-0.58)
Normal weight (18.5-24.9)	11.5 - 16	0.42 (0.35-0.50)
Overweight (25-29.9)	7 - 11.5	0.28 (0.23-0.33)
Obese (≥30)	5 - 9	0.22 (0.17-0.27)

Calculations assume a 0.5–2 kg (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)

Institute of Medicine, 2009

Low Gestational Weight Gain Improves Infant and Maternal Pregnancy Outcomes in Overweight and Obese Korean Women with GDM

Research Design

- Subjects : 215 women with obese GDM (BMI≥25kg/m^2)

- Modified Institute of Medicine (IOM) guidelines :
  - Inadequate weight gain: < 5.0 kg for obese (BMI≥30) and < 6.8 kg for overweight (25≤BMI<30)
  - Normal weight gain: 5.0-9.1 kg for obese and 6.8-11.3 kg for overweight
  - Excessive weight gain: > 9.1 kg for obese and > 11.3 kg for overweight)

- The subjects were divided into three groups according to modified IOM guidelines for weight gain during pregnancy:
  - Inadequate (n=42)
 - Normal (n=96)
  - Excessive (n=77)

Table II. Changes in body weight and insulin treatment of subjects during pregnancy.

	Gestational weight gain			
	Inadequate ($n=42$)	Normal ($n=96$)	Excessive ($n=77$)	p value
BMI at diagnostics	29.1 ± 2.6^b	29.8 ± 2.8^b	31.9 ± 3.4^a	<0.0001
BMI at delivery	29.2 ± 2.5^c	30.7 ± 2.6^b	33.6 ± 3.0^a	<0.0001
Total weight gain during pregnancy (kg)	2.4 ± 2.1^c	7.2 ± 1.8^b	13.8 ± 3.2^a	<0.0001
Total weight gain from prepregnancy to diagnosis (kg)	2.2 ± 3.0^c	5.0 ± 2.4^b	9.5 ± 3.7^a	<0.001
Total weight gain from diagnosis to delivery (kg)	0.2 ± 2.0^c	2.2 ± 2.4^b	4.3 ± 2.7^a	<0.001
Insulin treatment, n (%)	11 (26.2)	42 (43.8)	36 (48.0)	0.032
Insulin dosage (U/day)	6.2 ± 13.7^b	13.5 ± 21.0^a	13.7 ± 19.7^a	0.030

Data are mean $\pm$ standard deviation or n (%). Trends across the weight-gain groups were evaluated by logistic regression analysis with covariates of plasma glucose levels of 2-h OGTT, prepregnancy BMI, maternal age, gestational age, and parity. BMI, body mass index.
[a,b,c]Means with different superscript letters are significantly different at $p < 0.05$.

Fetal outcomes
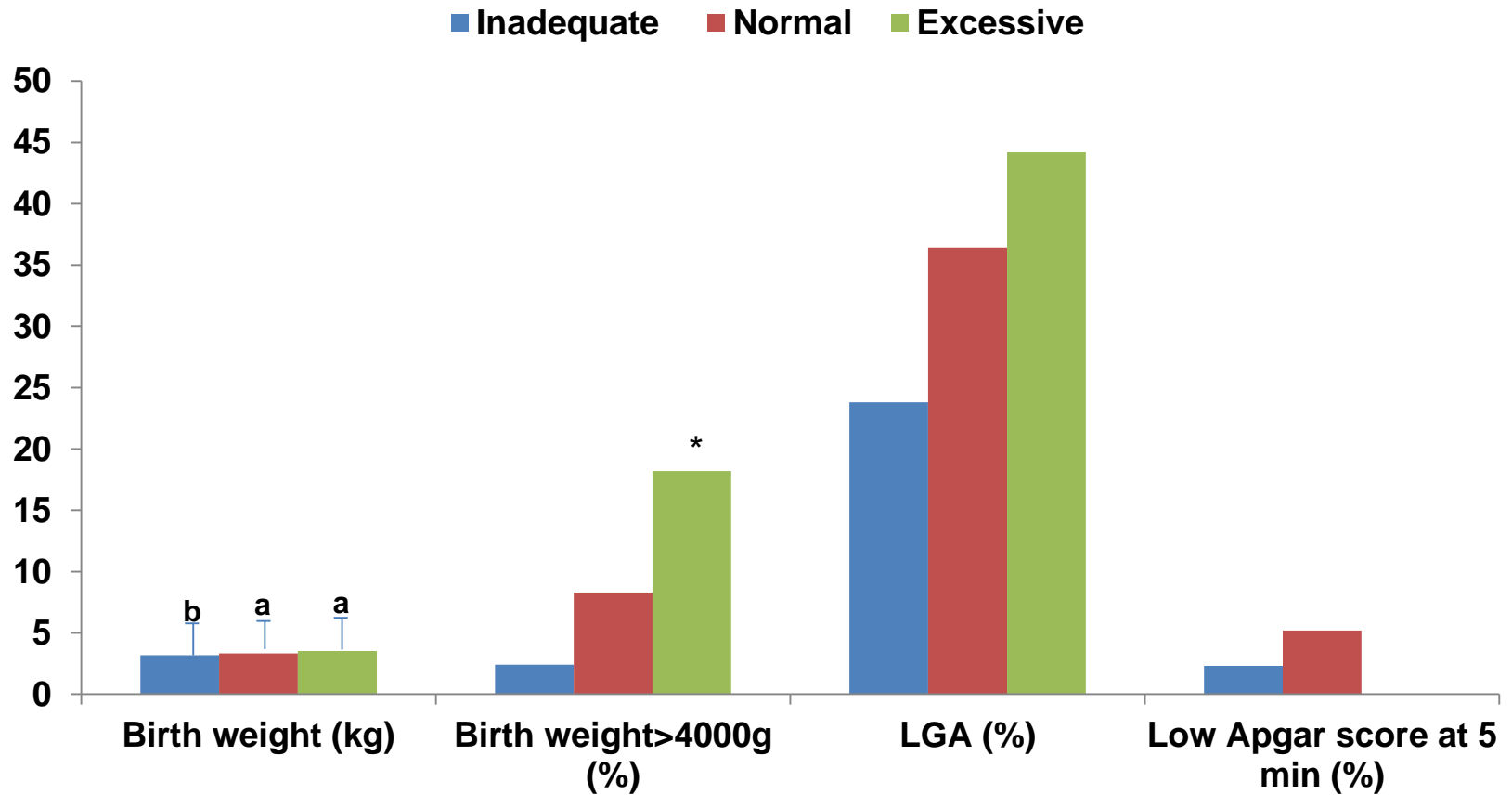
* **Significantly different among the groups at p<0.05**
a,b,c**Means with different superscript letters are significantly different at p<0.05.**

Summary

- Currently used weight gain targets and treatment for overweight and obese Asian women with GDM were not completely successful.

- The best results were found in women who were not only treated for GDM but also gained the minimal weight gain, well below IOM recommendations, and those women had an incidence of LGA infants similar to the normal population, with no adverse effects.

- Therefore, Asian overweight and obese women with GDM might need to gain much less weight than the IOM guidelines.

RESEARCH ARTICLE

Early gestational weight gains within current recommendations result in increased risk of gestational diabetes mellitus among Korean women

Baseline characteristics of the subjects

	(14.8%)	(22.6%)	(62.7%)	
	Inadequate ($n = 108$)	Normal ($n = 165$)	Excessive ($n = 458$)	p value
Maternal age (years)	33.4 ± 3.6	32.8 ± 4.5	32.9 ± 3.6	0.2984
Maternal height (cm)	160.9 ± 5.3	161.0 ± 4.5	161.5 ± 4.6	0.3562
Pre-gestational BMI (kg/m^2)	21.6 ± 3.4	21.2 ± 3.2	21.4 ± 3.2	0.6128
Family history of diabetes, n (%)	31 (28.7)	30 (18.2)	118 (25.8)	0.0825
Gestational diabetes mellitus, n (%)	22 (20.0)	49 (29.7)	127 (27.7)	0.0495
Gestational hypertension, n (%)	12 (11.1)	19 (11.5)	79 (17.3)	0.0448
Parity = 0, n (%)	65 (60.2)	98 (59.4)	276 (60.3)	0.9807
Smokers, n (%)	10 (9.3)	17 (10.3)	49 (10.5)	0.9458

Data are mean $\pm$ standard deviation or n (%).
BMI, body mass index.

Weight gain during pregnancy

	Inadequate ($n = 108$)	Normal ($n = 165$)	Excessive ($n = 458$)	p value
Gestational age at GDM screening (weeks)	24.7 ± 0.86	24.9 ± 0.93	25.0 ± 1.1	0.1202
Gestational age at delivery (weeks)	38.8 ± 2.0	39.1 ± 1.1	38.9 ± 1.8	0.3164
Body weight at GDM screening (kg)	58.0 ± 8.8^{b}	60.1 ± 7.9^{b}	65.1 ± 9.0^{a}	<0.0001
Weight gain until GDM screening (kg)	2.1 ± 3.0^{c}	5.1 ± 0.9^{b}	9.1 ± 2.7^{a}	<0.0001
Weight gain from GDM screening to delivery (kg)	6.1 ± 4.3	5.1 ± 2.6	5.7 ± 3.1	0.0637
Total weight gain during pregnancy (kg)	8.2 ± 3.5^{c}	10.2 ± 2.9^{b}	14.8 ± 4.4^{a}	<0.0001

OR for GDM development and pregnancy outcome according to weight gain at 24–28 weeks of gestation

	Crude odds ratio	p value	Adjusted odds ratio[a]	p value
Model 1: GDM development		0.0448		<0.001
Inadequate	0.565 (0.325–0.978)	0.0475	0.437 (0.239–0.800)	0.0085
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	0.854 (0.584~1.249)	0.4155	0.779 (0.522–1.162)	0.2209
Model 2: GH development		0.0740		0.0446
Inadequate	0.946 (0.446–2.010)	0.8861	0.924 (0.431–1.980)	0.8501
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	1.593 (1.002~2.672)	0.0521	1.611 (1.007–2.714)	0.0502
Model 3: LGA		0.0995		0.0514
Inadequate	0.552 (0.057~5.386)	0.3874	0.516 (0.052–5.075)	0.5702
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	2.751 (0.802~9.438)	0.1076	2.776 (0.804–9.591)	0.1065
Model 4: SGA		0.4237		0.2165
Inadequate	2.089 (0.619~7.052)	0.2351	2.069 (0.608–7.037)	0.2445
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	1.726 (0.636~7.052)	0.2842	1.782 (0.653–4.863)	0.2592
Model 5: preterm delivery		0.0079		0.0280
Inadequate	8.231 (1.737~38.99)	0.0079	8.681 (1.824–41.31)	0.0066
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	5.325 (1.243~22.82)	0.0243	5.508 (1.282–23.66)	0.0218
Model 6: Caesarian section		0.4477		0.5711
Inadequate	1.396 (0.810–2.407)	0.2297	1.320 (0.757–2.300)	0.3281
Normal	1.00 (Ref)		1.00 (Ref)	
Excessive	1.223 (0.815–1.836)	0.3317	1.214 (0.802–1.837)	0.3591

GDM, gestational diabetes mellitus; GH, gestational hypertension; LGA, large for gestational age; SGA, small for gestational age.
[a]Adjusted for maternal age, family history of diabetes, smoking and gestational weeks.

Conclusion

- Both target weight gain and energy intake recommendations for early pregnancy may not be optimal for Korean women.

- Race-specific recommendations are needed to decrease the risk of GDM without increasing adverse pregnancy outcomes.

Long-term outcome
for mother and offspring

- Development of T2DM in women with GDM-

Applied nutritional investigation

Nutritional risk factors of early development of postpartum prediabetes and diabetes in women with gestational diabetes mellitus

Sung-Hoon Kim M.D., Ph.D. [a], Moon-Young Kim M.D. [b], Jae-Hyug Yang M.D. [b], So-Young Park M.D. [a], Chang Hoon Yim M.D. [a], Ki Ok Han M.D. [a], Hyun Koo Yoon M.D. [a], Sunmin Park Ph.D. [c,*]

Kim SH, Nutrition 2011;782

Antepartum factors predicting postpartum dysglycemia using dependent variable of log AUC of glucose at 6-12 wks after delivery

Independent variables (R^2=0.14)	Beta	P value
BMI	0.054	0.03
Family history of diabetes	0.38	0.05
HOMA-B at late pregnancy	-0.003	0.004
Insulin dosage during late pregnancy	1.1	<0.0001

AUC : area under the curve of glucose during oral glucose tolerance test at 6-12 wks after delivery

Postpartum factors predicting postpartum dysglycemia using dependent variable of log AUC of glucose at 6-12 wks after delivery

Independent variables (R^2=0.43)	Beta	P value
BMI at postpartum	0.059	0.04
HbA$_{1c}$ at postpartum	1.2	<0.0001
Plasma triglyceride at postpartum	0.003	0.0083
HOMA-B at postpartum	-0.007	0.0001
Energy intake as the percent of estimated energy requirement	0.009	0.05
Breast feeding	-0.016	0.25

Postpartum dietary fat intake
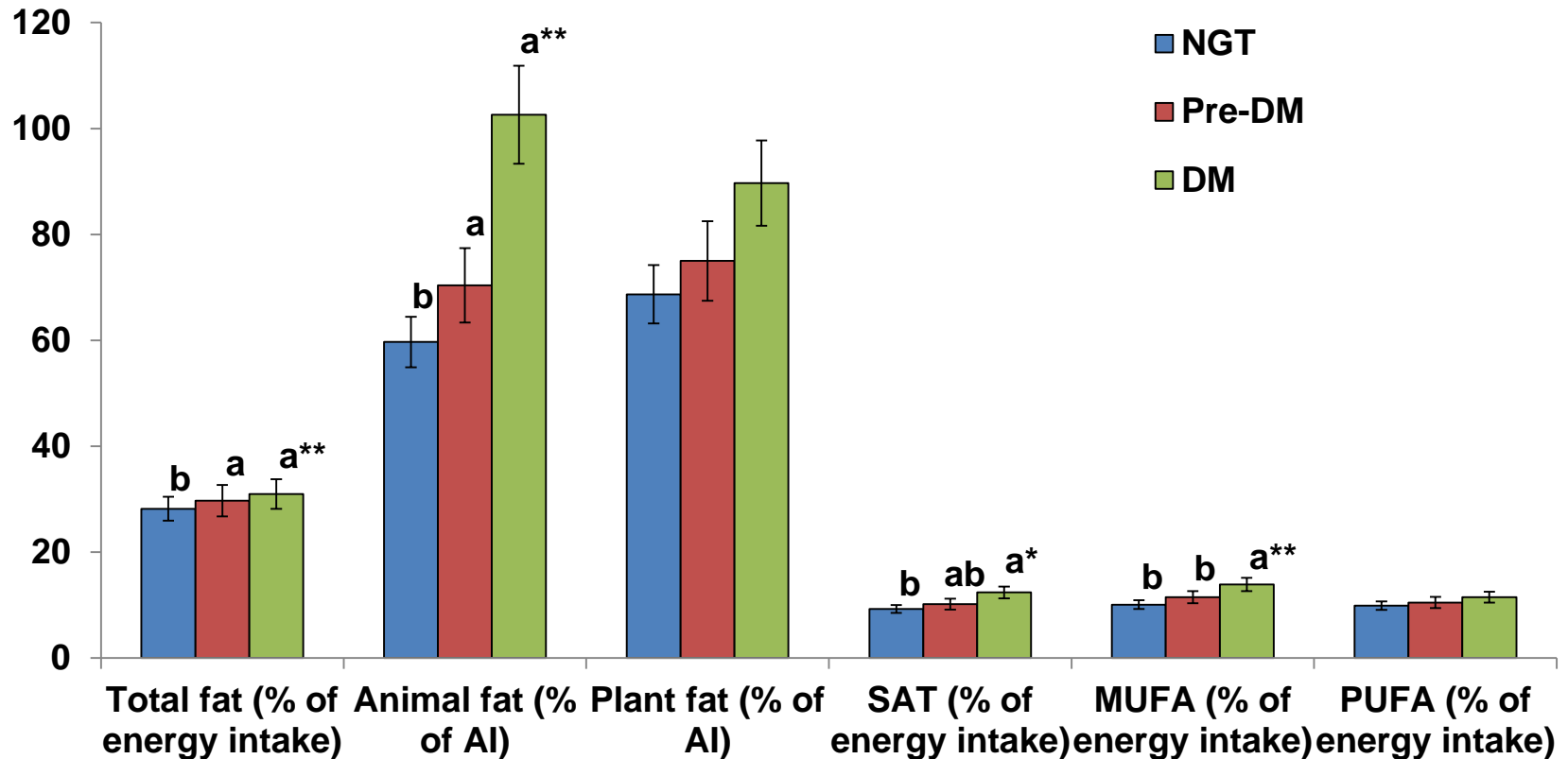
AI, Adequate intake

* Significantly different among three groups at P<0.05. ** P<0.01.
a,bMeans in the same row with different superscripts were significantly different by Tukey test at P<0.05.

Conclusion

- Simple dietary and lifestyle modifications such as maintaining ideal body weight and avoiding excessive consumption of animal foods, energy and fat might prevent or delay the onset of type 2 diabetes in women with a history of gestational diabetes mellitus

Take home messages

1. The key to improving outcome of pregnancy in women with diabetes is strict glycemic control

2. Preconception counseling and prepregnancy care before pregnancy are important

3. Not only meticulous glucose control bus also appropriate gestational weight gain are essential

4. More research about long-term follow up and intervention for mothers and their offspring are needed

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Thank you for your attention !