2012 International Conference on
Diabetes and Metabolism
Korea Diabetes Pregnancy Study Group

8 November, 2012
Grand Hilton Seoul Hotel, Seoul

Gestational diabetes mellitus in Korea: Now and Future

서울의대
분당서울대학교병원
내과 장학철

Gestational Diabetes Mellitus

- Gestational diabetes mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy.
- Associated with adverse pregnancy outcome
- Women with GDM are at increased risk to develop type 2 diabetes later in life.
- Long-term complications in offspring of mother with GDM

Third International Workshop-Conference on GDM

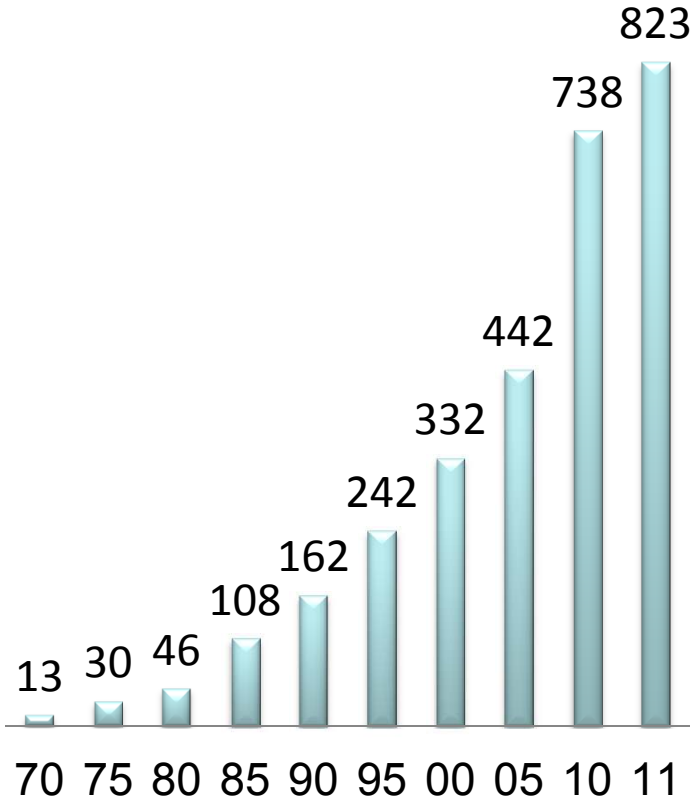
Contents

- Korea Med Search – GDM study in Korea
- Adverse pregnancy outcome
- Incidence of GDM
- Long-term follow-up studies
- Detection and Diagnosis of GDM in Korea

임신성 당뇨병 관련 논문 수

Pub Med Search: GDM

논문 수: 10,262

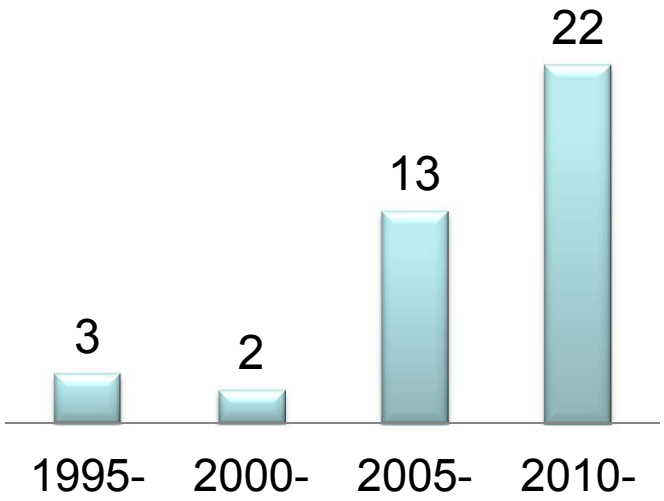


2012. 10.15

Pub Med Search: GDM AND Korea

논문 수: 56

GDM-42



International Journal of Gynecology & Obstetrics 51 (1995) 115–122

International Journal of GYNECOLOGY & OBSTETRICS

Article

Screening for gestational diabetes mellitus in Korea

H.C. Jang*[a,e], N.H. Cho[c,e], K.B. Jung[b], K.S. Oh[b], S.L. Dooley[d], B.E. Metzger[c,e]

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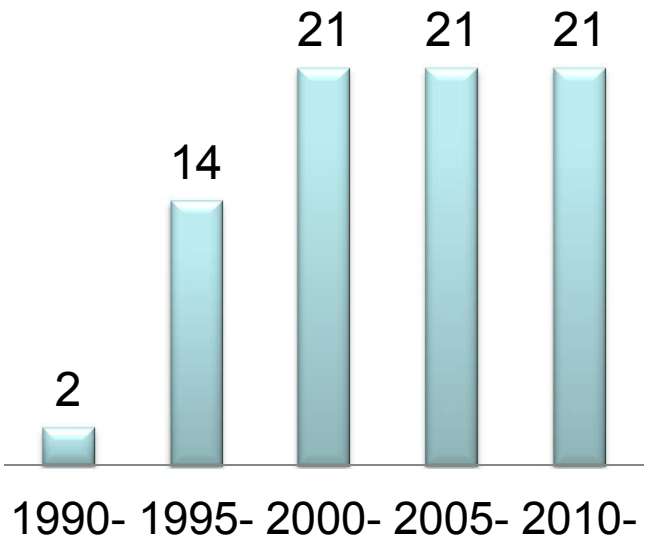
Received 15 May 1995; revision received 1 July 1995; accepted 7 July 1995

- Prevalence of GDM: 2.2%
- Screening strategy: Universal screening using 135 mg/dl
- Early screening for GDM: ≥2 risk factors

임신성 당뇨병 관련 논문 수

Korea Med Search: GDM

논문 수: 79



2012. 10.15

대한내과학회잡지 : 제43권 제6호 1992

한국인 임신성 당뇨병의 임상적 특성

차병원 내과, *차병원 산부인과, **연세대학교 의과대학 내과학교실

김유리 · 안명옥* · 확인평* · 김문종* · 차경섭*
정춘희** · 안광진** · 정윤석** · 이현철** · 허갑범**

거대아 발생빈도: 26.8% vs 6.5%
분만 후 당뇨병 빈도: 17.1%

대한주산회지 제3권 제1호 1992
Kor J Perinatol pp 63~68
Vol. 3, No. 1, Mar. 1992

임신성 당뇨병에 대한 산전 진찰

서울 을지병원 산부인과

이 진 · 박근영 · 배현미 · 홍서유

임신성 당뇨병 빈도: 3.1%

Korea Med 검색: 국내 임신성 당뇨병 연구

Adverse pregnancy outcome in GDM (29)

- J Korean Pediatr Soc. 1997;40:809: *perinatal complications in newborn of GDM mother (case control study)*
- Korean J Obstet Gynecol. 1998;41:593: *higher A1C and poor pregnancy outcome (C-section, macrosomia, neonatal hypoglycemia*
- J Korean Pediatr Soc. 1999;42:339: *fetal hyperinsulinemia-Birth weight, neonatal AC*
- J Korean Diabetes Assoc. 1999;23:506: *USG- fetal disproportionate growth*
- Korean J Obstet Gynecol. 1999;42:2712: *Diabetic preganancy-CM*
- Korean J Obstet Gynecol. 2001;44:1033: *OAV-poor neonatal outcome*

Korea Med 검색: 국내 임신성 당뇨병 연구

Screening Strategy for GDM (23)

- Korean J Obstet Gynecol. 1998;41:2126: *selective screening with GCT*
- Korean J Obstet Gynecol. 1998;41:2588: *Carpenter-Coustan vs NDDG criteria for diagnosis of GDM*
- Korean J Obstet Gynecol. 1999;42:1055: *women with risk factors of GDM (4.7% vs. 0.8%)*
- Korean J Obstet Gynecol. 1999;42:1403: *duration of fasting and 50 g GCT*
- Korean J Obstet Gynecol. 1999;42:1987: *univeral screening is preferred*
- Korean J Obstet Gynecol. 2001;44:2212: *75 g OGTT vs. 100 g OGTT*
- J Korean Diabetes Assoc. 2002;26:221: *C-C criteria > NDDG criteria for GDM*

Korea Med 검색: 국내 임신성 당뇨병 연구

Treatment or Education (8)

- J Korean Diabetes Assoc. 1999;23:326: *USG for LGA*
- J Korean Diabetes Assoc. 2001;25:93: *SMBG*
- Korean J Obstet Gynecol. 2001;44:780: *weight gain and birth weight*

Epidemiology or Genetics (19)

- Korean J Med. 1999;57:916: **glucokinase promoter**
- J Korean Diabetes Assoc. 2000;24:46: **postpartum diabetes -9.5%**
- J Korean Diabetes Assoc. 2000;24:267: **postpartum testing**
- J Korean Diabetes Assoc. 2002;26:319: **insulin sensitivity & secretion in previous GDM**
- Korean J Obstet Gynecol. 2005;48:978: **mitochondrial DNA**
- J Korean Diabetes Assoc. 2006;30:398: **GAD antibody +**
- Korean J Nutr. 2008;41:41: **Diet intake and GDM**
- Korean Diabetes J. 2008;32:38: **MODY3**
- Korean Diabetes J. 2009;33:279: **adipokine (resistin)**

대한산부회지 제44권 제4호 2001
Vol. 44 No. 4 April 2001

정상 및 임신성 당뇨병 임신부의 임신 중 체중 증가량와 신생아 체중

성균관의대 삼성제일병원 산부인과, 내과*, 소아과†
김문영 · 양재혁 · 장학철* 박정은* 임창훈* 정호연* 한기옥* 윤현구*
한인권* 김미정† · 한혜경†

Table 2. Rate of maternal weight gain during pregnancy

	Normal (n=130)	GDM (n=46)
Total weight gain (kg)	14.9±3.9	11.5±5.5†
RWG prepregnancy to 13 weeks (kg/wk)	0.09±0.10	0.18±0.23†
RWG 14 to 27 weeks (kg/wk)	0.52±0.14	0.45±0.23
RWG 28 to 33 weeks (kg/wk)	0.52±0.22	0.23±0.29†
RWG 34 weeks to delivery (kg/wk)	0.46±0.26	0.33±0.24†

RWG: Rate of weight gain

Table 5. Correlation coefficients ‖ between birth weight and maternal weight gain during pregnancy

	Birthweight	
	Normal	GDM
Total weight gain	0.22†	0.55†
RWG§ prepregnancy to 13 weeks	0.05	0.40*
RWG 14 to 27 weeks	0.17*	0.55†
RWG 28 to 33 weeks	0.16*	0.04
RWG 34 weeks to delivery	0.06	0.22

* P<0.05, † P<0.01
§ RWG: Rate of weight gain; ‖ Correlation coefficients were calculated after adjusting for maternal age, prepregnancy weight, parity and gestational age at delivery.

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RCT: Treatment of Mild GDM Reduces Adverse Outcome

Study subjects: 24-30 weeks of gestation; GCT 135-200 mg/dL
Mild GDM: FPG < 95 mg/dL and 2 or 3 glucose values exceeded established thresholds (1-hour, 180; 2-hour, 155; and 3-hour, 140 mg/dL)

Outcome	NICHD RCT		P
	Not treated	Treated	
BW >90th percentile	14.5	7.1	<0.001
C-peptide >95th percentile	22.8	17.7	0.07
NICU admission	11.6	9.0	0.19
Shoulder Dystocia	4.0	1.5	0.02
Preeclampsia	5.5	2.5	0.02

Landon MB et al. NEJM 361:1339-48, 2009

Increased Macrosomia and Perinatal Morbidity Independent of Maternal Obesity and Advanced Age in Korean Women With GDM

Table 2—*Obstetric outcome in the study subjects*

	GDM group	Normal control group	*P*
n	65	153	
Gestational age at delivery (weeks)	38.8 ± 1.2	39.6 ± 1.2	<0.001
Preterm delivery (<37 weeks)	4 (6.2)	4 (2.6)	NS
Preeclampsia	7 (10.8)	2 (1.3)	<0.01
Polyhydramnios	3 (4.6)	2 (1.3)	NS
Total cesarean section	36 (55.4)	69 (45.1)	NS
Primary cesarean section	26 (40.0)	35 (22.9)	<0.05
Perineal laceration (3° and 4°)	2 (3.1)	7 (4.6)	NS

Data are means ± SD or *n* (%).

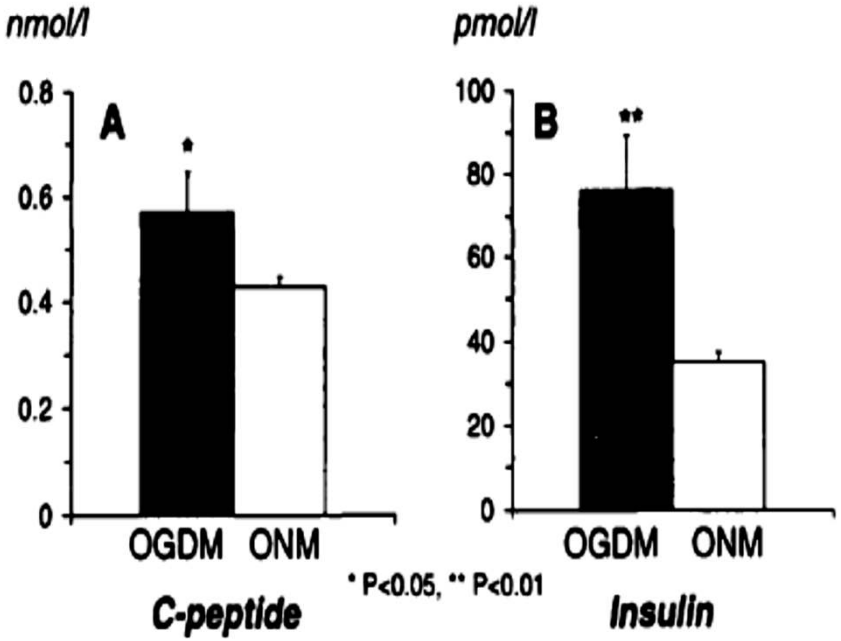
Table 3—*Neonatal outcomes and anthropometric measurements in offspring of the study subjects*

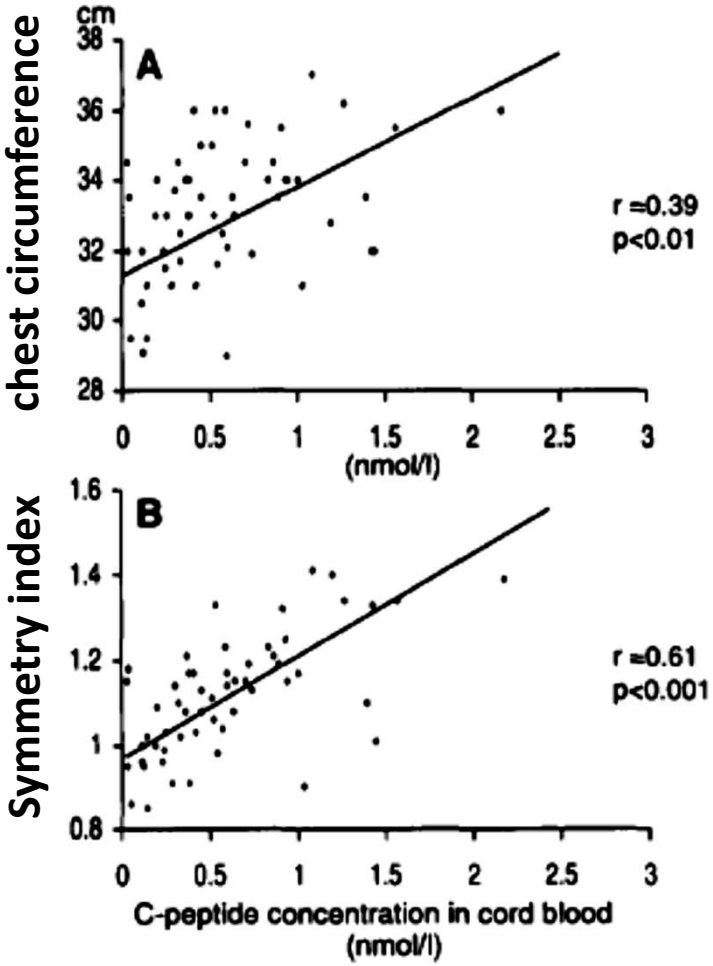
	GDM group	Normal control group	*P*
n	65	153	
Birth weight (g)	3,514 ± 519	3,376 ± 358	<0.05
LGA infant	26 (40.4)	20 (13.1)	<0.001
Birth weight >4,000 g	9 (13.8)	5 (3.3)	<0.01
Phototherapy	15 (23.1)	6 (3.9)	<0.001*
Length (cm)	50.1 ± 2.1	50.1 ± 1.9	NS
Head circumference (cm)	34.3 ± 1.5	34.4 ± 1.2	NS
Chest circumference (cm)	33.2 ± 1.8	32.6 ± 1.3	<0.01
Symmetry index	1.11 ± 0.13	1.05 ± 0.06	<0.001

Data are means ± SD or *n* (%). *Ajusted for effect of gestational weeks at delivery.

Jang HC et al. Diabetes Care 20:1582-8, 1997

Increased Macrosomia and Perinatal Morbidity Independent of Maternal Obesity and Advanced Age in Korean Women With GDM





Jang HC et al. Diabetes Care 20:1582-8, 1997

Pregnancy outcome in Korean women stratified by GCT and OGTT

	Screen negative (n=2120)	Screen positive, Normal OGTT (n=545)	GDM by C-C criteria† (n=37)	GDM by NDDG criteria (n=74)	P-value
Preterm delivery (<37wk)	71(3.3%)	20(3.7%)	3(8.1%)	7(9.5%)*	<0.05
Total C-section	**642(30.3%)**	**201(36.9%)***	**18(48.6%)***	**41(55.4%)***	**<0.001**
Preeclampsia	**9 (0.4%)**	**11 (2.0%)***	**2 (5.4%)***	**6 (8.1%)***	**<0.001**
Gestational age at delivery (week)	39.5±1.5	39.4±1.4*	39.0±1.5*	38.8±1.4*	<0.01
Apgar score (1 min)	8.5±1.0	8.5±1.0	8.4±0.9	8.4±0.9	0.42
Apgar score (5 min)	9.7±0.7	9.7±0.7	9.6±0.7	9.6±0.7	0.73
Birth weight (g)	3301±450	3360±435*	3379±461	3464±532*	<0.001
LGA infant	**287(13.5%)**	**88(16.1%)**	**10(27.0%)***	**25(33.8%)***	**<0.0001**
Macrosomia (>4,000 g)	106(5.0%)	29(5.3%)	2(5.4%)	10(13.5%)*	.<0.05

* P<0.05 compared with women with screen negative
†C-C criteria: Carpenter-Coustan Criteria

(당뇨병28:122,2004)

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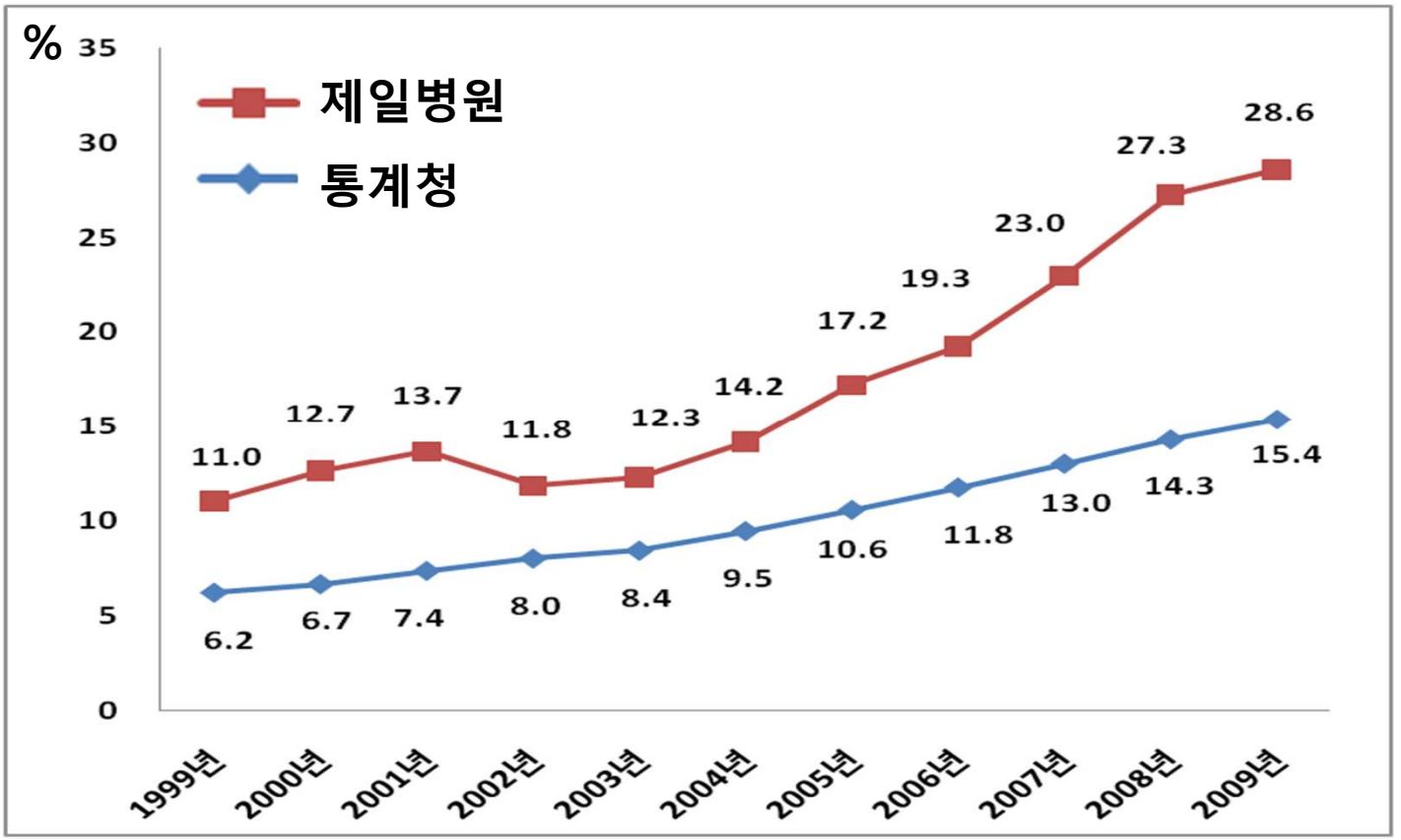
The incidence of GDM is increasing in Korea

Year	Delivery(n)	GDM(n)	Incidence(%)
2002	8,627	344	**4.0**
2003	9,464	338	**3.6**
2004	8,972	250	**2.8**
2005	8,112	172	**2.1**
2006	7,725	222	**2.9**
2007	7,730	325	**4.2**
2008	7,112	329	**4.6**
2009	6,352	333	**5.2**
2010	6,694	303	**4.5**
2011	6,542	356	**5.4**
Total	77,330	2,972	**3.8**

김문영, 제일병원

연도별 고령 산모 비율(%)



김문영, 제일병원

고령 산모가 늘어나면서 임신 중 당뇨병으로 병원을 찾는 사람이 매년 27%씩 증가 (국민건강보험공단 , 2012.10.9)

임산부의 날, MBN News

고령 산모가 늘어나면서 임신 중 당뇨병으로 병원을 찾는 사람이 매년 27%씩 증가 (국민건강보험공단 , 2012.10.9)

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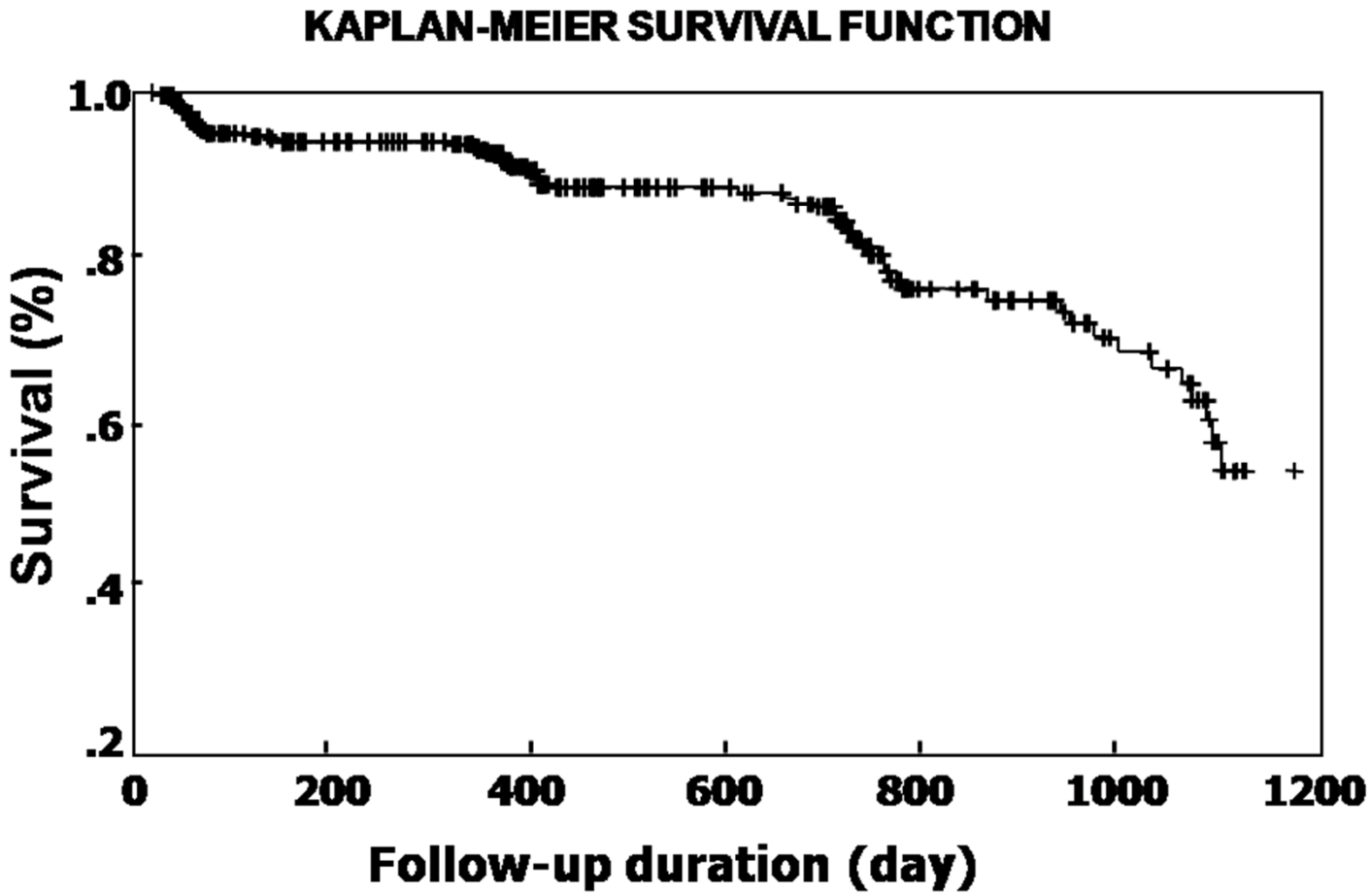
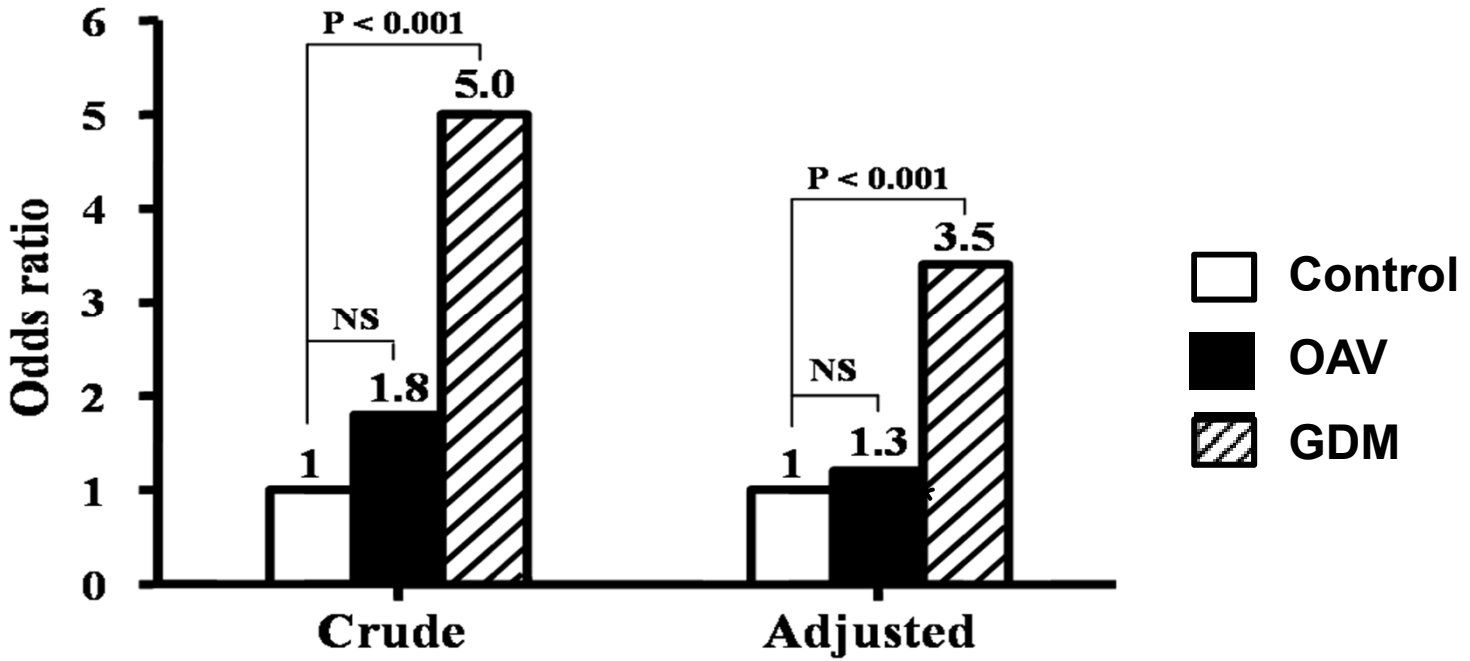
Cumulative Incidence of Type 2 Diabetes in 909 Korean Women with Previous GDM



Cho et al. Diabetes Res Clin Pract. 2006;71:177-83

Odds Ratio for T2 DM in Korean Women with GDM compared with General Population

- Case-Control Design
- 620 women with GDM and 248 women with OAV follow up: 2.1 years
- 868 controls: age- and sex-matched from the 2001 KNHNS*



Adjustment for confounding factors such as age, family history of diabetes, educational level, income level, smoking habit, drinking status, waist circ., systolic BP, lipid profile
*KNHNS: Korea National Health Nutrition Survey

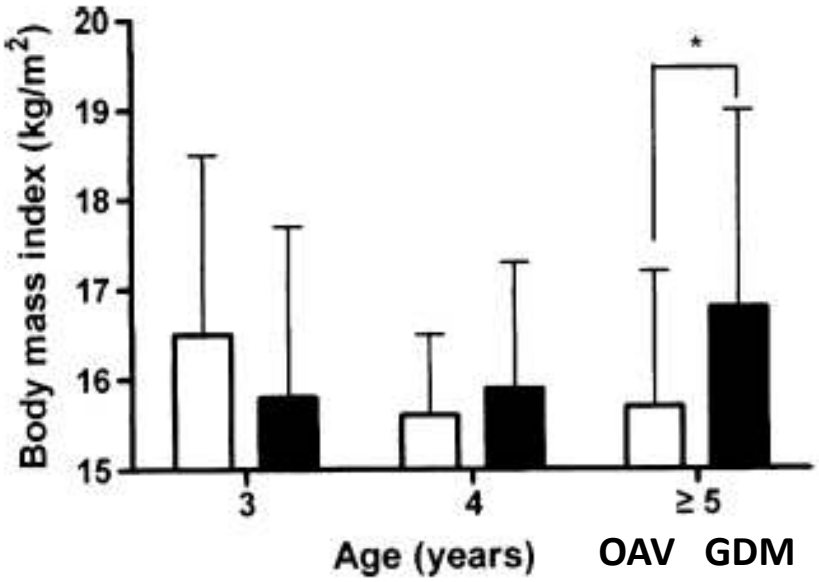
Lee et al. Diabetes Res Clin Pract. 2008;81:124-29

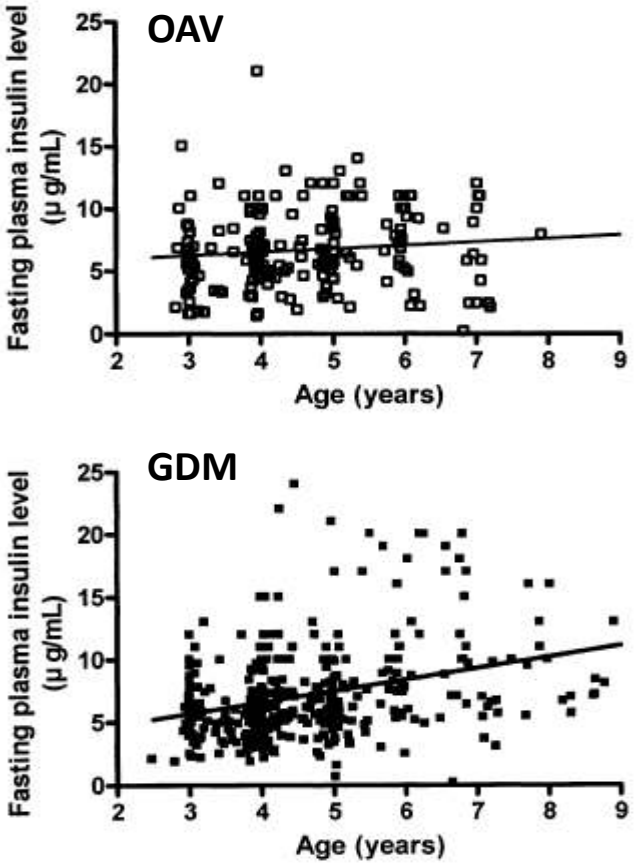
Available online at www.sciencedirect.com
ScienceDirect
Diabetes Research and Clinical Practice 78 (2007) 238–245
DIABETES RESEARCH AND CLINICAL PRACTICE
www.elsevier.com/locate/diabres

Early manifestation of cardiovascular disease risk factors in offspring of mothers with previous history of gestational diabetes mellitus

Hoon Lee [a], Hak C. Jang [b], Hae K. Park [c], Nam H. Cho [a,*]

- 202 offspring of GDM mothers and 96 offspring of OAV mothers





Comparison between Prepubertal ODMs and Sibling controls (1)

	ODM (n=45)	Sibling (n=18)
Age at study (yr)	5.5±1.2	9.5±2.1
Male/Female	23/22	10/8
Maternal age at delivery (yr)	34.0±3.6	30.9±2.6
Birthweight (kg)	3.30±0.43	3.27±0.54
Macrosomia (Birthweight ≥4 kg)	4 (8.9%)	1 (5.6%)
Prediabetes	7 (16%)	1 (3%)
Fasting insulin	11.9±4.1	16.1±8.1
HOMA-IR	2.3±0.96	3.3±1.8
Insulinogenic Index	0.63±0.51	0.85±0.44

* Prediabetes: fasting glucose ≥100 mg/dL or postprandial 2hr glucose ≥140 mg/dL or HbA1c ≥ 5.7%

분당서울대병원 소아과 정혜림

Comparison between Prepubertal ODMs and Sibling controls (2)

	ODM (n=45)	Sibling (n=18)
Cholesterol ≥200mg /dL	4 (8.9%)	1 (5.6%)
LDL–Chol ≥130 mg/dL	1 (2.2%)	1 (6%)
HDL-Chol <40 mg/dL	4 (8.9%)	2 (12%)
Triglyceride ≥ 110 mg/dL	4 (8.9%)	3 (18%)
BMI-z	0.33±0.82	0.47±0.85
BMI ≥ 1SD	6 (13%)	3 (17%)
Waist to height ratio >0.5	5 (11%)	3 (17%)
% Fat for age ≥ 1SD* ≥ 2SD*	 37 (83%) 20 (45%)	 14 (78%) 8 (45%)

*Based on *Journal of Clinical Densitometry 2009;12:e229*

분당서울대병원 소아과 정혜림

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Detection and Diagnosis of GDM

Organization	*Screening*	*Diagnosis*
American College of Obstetricians and Gynecologists (ACOG) (2001[12])	Conduct risk assessment (timing not discussed) or practice universal screening at 24–28 weeks. Low risk[a]: may exclude from screen Moderate risk: 24–28 weeks High risk[b]: can screen early in pregnancy Screen test 50-g 1-h GT: if > 130 (or 140)[c] perform 100-g 3-h GTT	Using 100 g 3-h GTT, two abnormal values from either of the following criteria: Carpenter/Coustan Fasting ≥ 95 1 h ≥ 180 2 h ≥ 155 3 h ≥ 140 National Diabetes Data Group Conversion Fasting ≥ 105 1 h ≥ 190 2 h ≥ 165 3 h ≥ 145
ADA (2007)[23,24]	Risk assessment at first prenatal visit. Low risk[e]: may exclude from screen Moderate risk: 24–28 weeks gestation High risk[f]: screen at first prenatal visit; if at first visit not GDM, screen again at 24–28 weeks using GTT (1-step approach) or 50-g oral glucose load and then 100-g GTT (2-step method) Screen test 50-g GTT: ≥ 140 or ≥ 130	Fasting > 126 or casual glucose >200 meets criteria if confirmed on subsequent day Two abnormal values from 100-g GTT 100-g GTT Fasting ≥95 1 h ≥ 180 2 h ≥ 155 3 h ≥ 140 75-g GTT can be used but not as well validated

Diagnosis of GDM in Pregnancy: Threshold Values

Diagnosis of GDM & Proportion of HAPO Cohort with values ≥ Threshold*			
Glucose Measure	mmol/l	mg/dl	≥threshold (%)
FPG	5.1	92	8.3
1-hr OGTT-PG	10.0	180	14.0
2-hr OGTT-PG	8.5	153	16.1

*GDM = 1 or more values ≥ threshold

Plasma Glucose Concentrations at Specified OR

Glucose	Odds Ratio		
mg/dl*	1.5	1.75	2.0
FPG	90	92	95
1-Hr PG	167	180	191
2-Hr PG	142	153	162

*Mean of threshold values for ↑: birthweight, cord serum C-peptide, % body fat >90th percentile

Frequencies of Outcomes: Glucose Values < or ≥ Threshold

Outcome	% All Values < Threshold	% Any ≥ 92/180/153 (5.1/10.0/8.5)
Birthweight >90th percentile	8.3	16.2
Cord C-peptide >90th percentile	6.7	17.5
% Body fat >90th percentile	8.5	16.6
Preeclampsia	4.5	9.1
Preterm birth (<37 weeks)	6.4	9.4
Shoulder dystocia/birth injury	1.3	1.8
Primary Cesarean section	16.8	24.4

Gestational diabetes—Staying with old or marrying new guidelines

- **Staying with old guidelines** (Sean C. Blackwell, MD)
  - The HAPO Study was an observational study, not a treatment trial.
  - There is insufficient evidence to determine whether nutritional modification would have a clinically significant impact at this glycemic level.
  - There is still the potential for increased harm because of the designation of a woman as having GDM. (visit, test, labor induction, cesarean delivery, etc.)

Gestational diabetes—Staying with old or marrying new guidelines

- **Marry old and new guidelines** (Dwight J. Rouse, MD)
- A simplified diagnostic approach..
- The diagnostic thresholds are based explicitly on the relationship to pregnancy outcomes .
- The data from which the thresholds are derived, are robust and generalizeable.
- The pregnancy outcomes that were chosen to inform the diagnostic thresholds are specific to the pathophysiologic condition of hyperglycemia in pregnancy:
- A rigid but pragmatic statistical framework was used to choose the thresholds.
- Randomized trial evidence from 2 well-done trials is now available to show that diagnosis and treatment of mild gestational diabetes mellitus.

KDA 임신성 당뇨병 진료지침

- **진단기준**

1. 첫 번째 산전 방문 검사 시 다음 중 하나 이상을 만족하면 기왕의 당뇨병이 있는 것으로 진단한다. [E]
1-1. 공복 혈장 혈당 ≥ 126 mg/dL
1-2. 무작위 혈장 혈당 ≥ 200 mg/dL
1-3. 당화혈색소 ≥ 6.5%

2. 임신 24-28주 사이에 시행한 2시간 75 g 경구당부하검사 결과 다음 중 하나 이상을 만족하는 경우 임신성 당뇨병으로 진단할 수 있다. [E]
2-1. 공복 혈장 혈당 ≥ 92 mg/dL
2-2. 당부하 1시간 후 혈장 혈당 ≥ 180 mg/dL
2-3. 당부하 2시간 후 혈장 혈당 ≥ 153 mg/dL

3. 기존의 2단계 접근법으로 100 g 경구당부하검사를 시행한 경우는 다음 기준 중 두 가지 이상을 만족하는 경우 임신성 당뇨병으로 진단한다. [E]
3-1. 공복 혈장 혈당 ≥ 95 mg/dL
3-2. 당부하 1시간 후 혈장 혈당 ≥ 180 mg/dL
3-3. 당부하 2시간 후 혈장 혈당 ≥ 155 mg/dL
3-4. 당부하 3시간 후 혈장 혈당 ≥ 140 mg/dL

요 약

- 국내 임신성 당뇨병 연구가 더 활성화가 되어야 하겠다.
- 임신성 당뇨병 등록사업으로 임신성 당뇨병 발생률 및 임신성적에 관한 연구가 시급하겠다.
- 100 g OGTT를 이용하는 경우, 임신성 당뇨병 진단기준은 Carpenter-Coustan Criteria를 이용하여야 하겠다.
- 자녀들에 대한 장기간 추적연구가 필요하겠다.
- 임신성 당뇨병 진단기준을 검증하기 위한 국내연구가 필요하다.

감사합니다.