

GESTATIONAL DIABETES
for GP Obstetric Shared Care
Accreditation Seminar

Simon Kane

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Objectives

- History and definitions
- Definition and Australian data
- Pathophysiology and prevalence
- Rationale for management
- Learning Objective – the SA PPG
- Management
- Metformin

Historical background

- First description of diabetes approx. 1500BC
- First description diabetes in pregnancy 1824
- In 1882 maternal mortality reported as 60%, and perinatal mortality 47%
- Insulin discovered 1922. Use in pregnancy led to reduction in maternal mortality
- 1949 'White's Classification' and subsequent acceptance of the term 'Gestational Diabetes'

White's Classification (abridged)

- Class A: diet alone, onset any age
 - A1: gestational diabetes; diet controlled
 - A2: gestational diabetes; medication controlled
- Class B: onset age 20 + or duration <10 years
- Class C: onset age 10-19 or duration 10–19 years
- Class D: onset before age 10 or duration greater than 20 years
- etc

Diabetes

- Type 1 diabetes
 - Pregnancy very hazardous prior to insulin therapy
 - Fetal & neo-natal mortality >50%
 - Incidence approximately 0.5% of obstetric population
- Type 2 diabetes
 - Carries risks at least equal to type 1
 - May be *first detected* in pregnancy
- Gestational diabetes
 - Carbohydrate intolerance of variable severity with onset or first recognition in pregnancy(ADIPS)
- Maturity Onset Diabetes of the Young (MODY)
 - Onset at <25yrs, genetic mutation, familial
 - Not usually insulin dependent

Historical background 2

- 1954 first description of obstetric risk associated with GDM
- 1957 O'Sullivan proposed 3 hour 100gm OGTT for patients with risk factors, and use of 1 hour 50g glucose load for those without
- Confusion and controversy begins
- 1979 First International Workshop on GDM
- 1998 International Association of Diabetes and Pregnancy Study Groups

Screening for GDM

- 2003 NICE (UK): “Evidence does not support routine screening for gestational diabetes and therefore it should not be offered”
- USPSTF Assessment (2008): The USPSTF concludes that the current evidence is insufficient to assess the balance between the benefits and harms of screening women for GDM either before or after 24 weeks gestation.
- “Opinions re GDM as a clinical entity have been more prolific than research-generated data”
 - Langer 2005

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GDM Definition

- “Carbohydrate intolerance of variable severity recognised for the first time in pregnancy”
- “Carbohydrate intolerance of variable severity with onset or first recognition in pregnancy” (ADIPS)
-and *resolving* post-partum

Definition

- Heterogeneous group
 - “true” GDM
 - Pre-existing type 2 diabetes
 - MODY

Gestational diabetes mellitus in Australia, 2005–06

- First national report on the incidence of (GDM) among Australian women of child-bearing age who give birth in hospital.
- Incidence is increasing. In 2005–06, GDM was diagnosed in 4.6% of confinements among women aged 15–49 years.
- The incidence of confinements with GDM among women aged 15–49 years increased by over 20% between 2000–01 and 2005–06.

Gestational diabetes mellitus in Australia, 2005–06

- The risk of GDM increases with age. In 2005–06, from 1% among 15–19 year old women to 13% among women aged 44–49 years.
- Women aged 30–34 years accounted for more than one-third of GDM cases in 2005–06.

Gestational diabetes mellitus in Australia, 2005–06

- Age-adjusted incidence rate of GDM among Indigenous Australian women was 1.5 times that of Other Australian women across all age groups.
- Women born overseas had twice the incidence rate of GDM compared with women born in Australia.
- Women born in Southern Asia had the greatest incidence at 3.4 times the rate of women born in Australia.

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Pathophysiology

- ↑ Insulin resistance and hyperinsulinaemia
 - Placental hormones
 - ↑ adiposity
 - ↓ exercise

Prevalence

- 2% - 14%
- Population
- Testing methods
- Diagnostic criteria
- Increasing
 - Obesity
 - Maternal age increasing

Impact of new criteria

Diabetologia (2011) 54:1670-1675

Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria

E. P. O'Sullivan · G. Avalos · M. O'Reilly ·
M. C. Denney · G. Gaffney · F. Dunne ·
on behalf of the Atlantic DIP collaborators

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Abstract

Aims/hypothesis New diagnostic criteria for gestational diabetes mellitus (GDM) have recently been published. We wished to evaluate what impact these new criteria would have on GDM prevalence and outcomes in a predominantly European population.

Methods The Atlantic Diabetes In Pregnancy (DIP) programme performed screening for GDM in 5,500 women with an oral glucose tolerance test at 24–28 weeks. GDM was defined according to the new International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria and compared with previous WHO criteria; maternal and neonatal adverse outcomes were prospectively recorded.

Results Of the participants, 12.4% and 9.4% were diagnosed with GDM using IADPSG and WHO criteria, respectively. IADPSG GDM pregnancies were associated with a statisti-

cally significant increased incidence of adverse maternal outcomes (gestational hypertension, polyhydramnios and Caesarean section) and neonatal outcomes (prematurity, large for gestational age, neonatal unit admission, neonatal hypoglycaemia and respiratory distress). The odds ratio for the development of these adverse outcomes remained significant after adjustment for maternal age, body mass index and non-European ethnicity. Those women who were classified as having normal glucose tolerance by WHO criteria but as having GDM by IADPSG criteria also had significant adverse pregnancy outcomes.

Conclusions/interpretation GDM prevalence is higher when using newer IADPSG, compared with WHO, criteria, and these women and their offspring experience significant adverse pregnancy outcomes. Higher rates of GDM pose a challenge to healthcare systems, but improved screening provides an opportunity to attempt to reduce the associated morbidity for mother and child.

LMH Data

- 2011 – 9% pregnancies complicated by diabetes, predominantly GDM, and 50% required treatment
- New guidelines introduced in October 2015.
- New GDM monthly average
 - 2015/2016 33.3
 - since October 58.3
- GDM commencing insulin
 - 2015/2016= monthly average 16
 - from October = 35

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Rationale for Management

- Adverse perinatal effects
- Long-term effects of intra-uterine hyperinsulinaemia
- Risk of subsequent diabetes
- Public Health
 - Increased awareness of diabetes
 - Dietary and lifestyle modifications

Rationale for Management

- Adverse perinatal effects
 - ACHOIS(2005)
 - Dodd(2007)
 - HAPO (2008)

ACHOIS nejm 2005

- Multicentre trial, 1000 women with GDM randomised to diabetic or routine management
- Serious perinatal outcomes (death, bone fracture, nerve palsy, shoulder dystocia) 1% vs 4%
- Macrosomia 10% vs 21%
- More IOL's, no difference in LSCS rate
- Same rate neo-natal metabolic complications
- Higher post-partum measures of well-being in intervention group

Screening for gestational
diabetes: The effect of varying
blood glucose definitions in the
prediction of adverse
maternal and infant health
outcomes

Dodd et al ANZJOG 2007

Dodd et al ANZJOG 2007

- 17,000 women screened with OGCT
- 1800 positive screen
- With increasing plasma glucose values, there was a significant increase in pre-eclampsia, Caesarean section, shoulder dystocia and neonatal hypoglycaemia

HAPO 2008

- 25,000 women, 15 centres, 9 countries
- Continuum of risk across the spectrum of glucose levels *below those diagnostic of diabetes*
- Macrosomia
- Primary Caesarean section
- Neo-natal hyperinsulinaemia and hypoglycaemia

HAPO

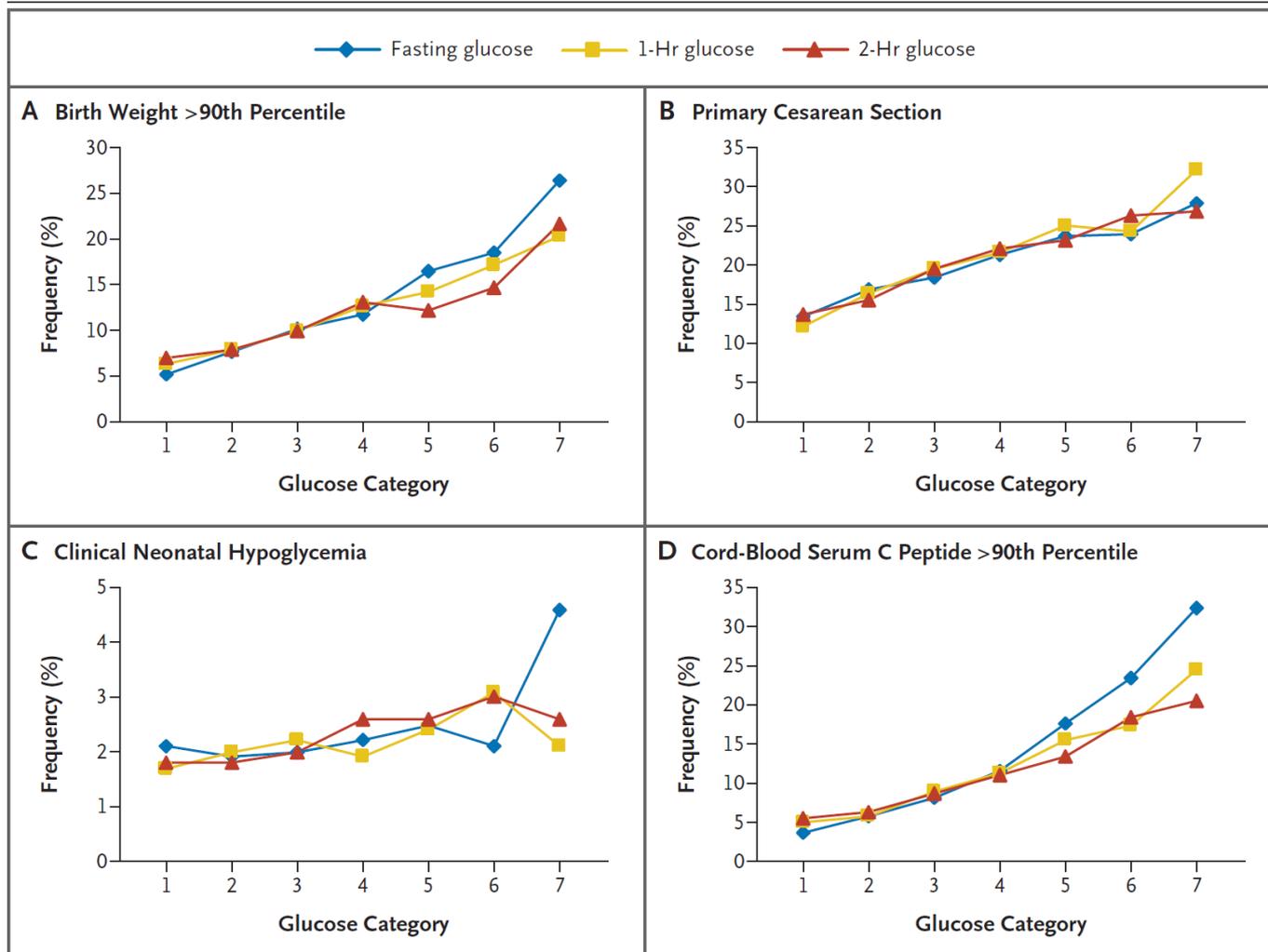


Figure 1. Frequency of Primary Outcomes across the Glucose Categories.

Is treatment beneficial?

BMJ 2010;340:c1395
doi:10.1136/bmj.c1395

BMJ

RESEARCH

Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis

Karl Horvath, project manager EBM review center,¹ head of outpatient facility diabetes and metabolism,² Klaus Koch, project manager,³ Klaus Jeitler, scientific assistant,¹ Eva Matyas, scientific assistant,¹ Ralf Bender, head of department of medical biometry,³ Hilda Bastian, head of department of health information,³ Stefan Lange, deputy director,³ Andrea Siebenhofer, professor for chronic care and health services research,⁴ project manager¹

¹EBM Review Center, Medical University of Graz, Auenbruggerplatz 15, 8036 Graz, Austria

²Division of Endocrinology and Nuclear Medicine, Department of Internal Medicine, Medical

ABSTRACT

Objective To summarise the benefits and harms of treatments for women with gestational diabetes mellitus.

Design Systematic review and meta-analysis of randomised controlled trials.

Data sources Embase, Medline, AMED, BIOSIS, Cochrane

INTRODUCTION

Gestational diabetes mellitus, defined as “carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy,”¹ is associated with an increased risk of complications for mother and child during pregnancy and birth.²

Is treatment beneficial?

BMJ 2010;340:c1395

doi:10.1136/bmj.c1395

- Five RCTs of specific vs. usual treatment
- 13 RCTs of different intensities of specific treatments
- Treatment for GDM, consisting of treatment to lower blood glucose concentration alone or with special obstetric care, seems to lower the risk of some perinatal complications

Rationale for Management

- Adverse perinatal effects
- Long-term effects of intra-uterine hyperinsulinaemia
- **Risk of subsequent diabetes**

Lactation and Progression to Type 2 Diabetes Mellitus After Gestational Diabetes Mellitus

A Prospective Cohort Study

Erica P. Gunderson, PhD, MPH, MS, RD; Shanta R. Hurston, MPA; Xian Ning, MS; Joan C. Lo, MD; Yvonne Crites, MD; David Walton, MD; Kathryn G. Dewey, PhD; Robert A. Azevedo, MD; Stephen Young, MD; Gary Fox, MD; Cathie C. Elmasian, MD; Nora Salvador, MD; Michael Lum, MD; Barbara Sternfeld, PhD; and Charles P. Quesenberry Jr., PhD, for the Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy Investigators*

Background: Lactation improves glucose metabolism, but its role in preventing type 2 diabetes mellitus (DM) after gestational diabetes mellitus (GDM) remains uncertain.

Objective: To evaluate lactation and the 2-year incidence of DM after GDM pregnancy.

Design: Prospective, observational cohort of women with recent GDM. (ClinicalTrials.gov: NCT01967030)

Setting: Integrated health care system.

Participants: 1035 women diagnosed with GDM who delivered singletons at 35 weeks' gestation or later and enrolled in the Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy from 2008 to 2011.

Measurements: Three in-person research examinations from 6 to 9 weeks after delivery (baseline) and annual follow-up for 2 years that included 2-hour, 75-g oral glucose tolerance testing; anthropometry; and interviews. Multivariable Weibull regression models evaluated independent associations of lactation measures with incident DM adjusted for potential confounders.

Results: Of 1010 women without diabetes at baseline, 959 (95%) were evaluated up to 2 years later; 113 (11.8%) developed incident DM. There were graded inverse associations for lactation intensity at baseline with incident DM and adjusted hazard

ratios of 0.64, 0.54, and 0.46 for mostly formula or mixed/inconsistent, mostly lactation, and exclusive lactation versus exclusive formula feeding, respectively (P trend = 0.016). Time-dependent lactation duration showed graded inverse associations with incident DM and adjusted hazard ratios of 0.55, 0.50, and 0.43 for greater than 2 to 5 months, greater than 5 to 10 months, and greater than 10 months, respectively, versus 0 to 2 months (P trend = 0.007). Weight change slightly attenuated hazard ratios.

Limitation: Randomized design is not feasible or desirable for clinical studies of lactation.

Conclusion: Higher lactation intensity and longer duration were independently associated with lower 2-year incidences of DM after GDM pregnancy. Lactation may prevent DM after GDM delivery.

Primary Funding Source: National Institute of Child Health and Human Development.

Ann Intern Med. 2015;163:889-898. doi:10.7326/M15-0807 www.annals.org
For author affiliations, see end of text.

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* For a list of the Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy investigators, see the **Appendix** (available at www.annals.org).

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Learning Objectives

- Describe the current antenatal management in accordance with the Statewide Obstetric Shared Care Protocols
- SA PPG (Policy) (Clinical Guideline) Diabetes Mellitus and Gestational Diabetes

Screening And Diagnosis

- Based on booking-in history
- Early OGTT if risk factors
 - 26-28 week OGTT if early test negative
- 26-28 week OGTT for all others
- OGTT can be done later if clinical concern

- GCT no longer utilised in South Australia (ADIPS and WHO Guidelines 2014)

High Risk factors at screening

- Previous GDM
- Maternal age 40+
- Family history of DM
- BMI > 35 kg/m²
- Previous macrosomia (>4.5kg or >90th centile)
- Polycystic ovarian syndrome
- Medication: corticosteroids, antipsychotics

Moderate Risk factors at screening

- Ethnicity
 - Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African
- BMI 25 – 35 kg/m²
- One major or two minor risk factors is an indication for an early OGTT (12-16 weeks)

Screening and Diagnosis

- **Diagnostic if:**

fasting level ≥ 5.1 mmol/l

or

1 hour level ≥ 10.0 mmol/l

or

2 hour level ≥ 8.5 mmol/l

OGTT Alternatives

- Random blood glucose ≥ 7 mmol/L
- Fasting blood glucose ≥ 5.1 mmol/L
- HbA1c
- 1-2 weeks of QID BGL testing
- Declined – dietary advice and document risks discussion
- Women on Metformin should have BGL testing, NOT OGTT

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Management 1

- Screen positive women referred to Diabetes Education Service
- Group Education session
 - Dietician for dietary advice
 - Diabetes Educator, glucometer, NDSS forms
- BGL monitoring and phone clinic
- Antenatal care continues as routine
- Individual sessions possible (eg. interpreter)

Management 2

- More than 2-3 readings per week out of range is indication for treatment
- Pattern of abnormal readings helps to dictate treatment
- Insulin
 - Usually Lantus nocte
 - And/or NovoRapid with meals
- Oral hypoglycaemics - Metformin

Obstetric Management

- Routine antenatal review
 - As per standard schedule
 - Use of GROW chart (if BMI <40)
- Fetal US growth surveillance may be indicated
 - Suspected macrosomia
 - Large dose insulin
 - Poor control
 - BMI >40

Management 3

- NALHN DANCE CLINIC CARE
 - Type 1 and most Type 2
 - GDM Poor control
 - GDM Poor compliance
 - GDM > 20 units total dose insulin/day

Management 4

- DANCE – Diabetes AnteNatal Care and Education
 - Endocrinologist
 - Obstetrician
 - Midwife
 - Diabetic Educator
 - Dietician

 - (Expression of breast milk from 36 weeks)

Management 5

- Diet and exercise
- Weight gain targets (IOM)
 - Obese women 5-9kg
- Blood glucose monitoring
 - Fasting < 5.1 mmol/l, 2hr post-prandial < 6.7
- If well controlled on diet-alone continue routine care and management. IOL <41weeks
- If on treatment IOL before 40 weeks
- Some evidence to support IOL for macrosomia

Delivery Decision

- Delivery before full term not indicated unless:
 - Macrosomia
 - Polyhydramnios
 - Poor metabolic control
 - Other indications
- LSCS
 - Steroid loading may be required
 - Insulin cover

Neonatal management

- Awareness of maternal GDM
- Hypoglycaemia
- Respiratory distress syndrome
- Jaundice

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Metformin

- MIG trial published NEJM 2008
 - 751 women with GDM at 20-33 weeks gestation
 - 363 women assigned metformin, 92.6% continued until delivery and 46.3% received supplemental insulin.
 - The rate of the primary composite outcome (neonatal hypoglycemia, respiratory distress, need for phototherapy, birth trauma, 5-minute Apgar score less than 7, or prematurity) was 32.0% in the group assigned to metformin and 32.2% in the insulin group (relative risk, 0.99; 95% confidence interval, 0.80 to 1.23)

Metformin

Review Article

Metformin for the management of gestational diabetes mellitus

Kamal P. SINGH,¹ Farhad RAHIMPANAH² and Margot BARCLAY²

¹*School of Public Health and Community Medicine, University of New South Wales, Sydney, Australia and* ²*Liverpool Hospital, Sydney, New South Wales, Australia*

Introduction: Glycaemic control in women with gestational diabetes mellitus (GDM) has typically been achieved with diet, exercise and insulin therapy. Controversy exists in the literature about a potential role for metformin.

Methods: A literature review was completed aiming to compare the glycaemic control, maternal and fetal outcomes of metformin therapy with insulin. Searches were completed on databases, including Medline, PubMed and ScienceDirect. Seven randomised control trials (RCTs) fit the inclusion criteria, with a total sample size of 1514 women.

Results: The majority of studies found no difference in glycaemic control between metformin and insulin groups. When comparing maternal outcomes, those receiving metformin therapy recorded less maternal weight gain in four studies. A number of studies reported lower rates of neonatal hypoglycaemia, and one reported higher rates of preterm birth in the metformin group. There were no other differences in the recorded maternal and fetal outcomes.

Discussion: The Jadad score for assessing risk of bias for most included studies was either 3 or 4. The criteria for diagnosis of GDM, maternal and neonatal complications varied between studies. Only one study has published follow-up data, and most are single-centre trials with relatively small sample sizes.

Conclusion: Though there is a growing body of evidence to suggest a role for metformin in GDM management, further large-scale, multicentre RCTs are needed before guidelines can be altered.

Key words: gestational diabetes mellitus, literature review, metformin, pregnancy.

Post-partum follow-up

- > 90% normoglycaemia post-partum
- OGTT after 6-8 weeks, then 2 yearly

Summary

- GDM and pregestational diabetes are different, but overlap
- New IADPSG and SA PPG criteria remain controversial and drive increased prevalence with
- Obesity, increasing maternal age and new migrants
- Obstetric management is individualised
- Ongoing follow-up required after birth