

# A lower carbohydrate diet is best

HELEN ROBINSON

OBSTETRIC PHYSICIAN

# The Effects of Carbohydrate Restriction in Patients With Diet-Controlled Gestational Diabetes

CAROL A. MAJOR, MD, M. JOANN HENRY, RNC, MSHS, CDE,  
MARGARITA DE VECIANA, MD, AND MARK A. MORGAN, MD

**Objective:** To determine the effect of carbohydrate restriction on perinatal outcome in patients with diet-controlled gestational diabetes mellitus (GDM).

**Methods:** Women with diet-controlled GDM were divided non-randomly into two groups based on their dietary carbohydrate content: those with low dietary carbohydrate content (below 42%) and those with high dietary carbohydrate content (exceeding 45%). Subjects kept dietary accounts and were followed with daily fasting and postprandial glucose assessments. Subjects also were tested daily for urinary ketones. Glycosylated hemoglobin, mean fasting and postprandial glucose values, incidence of macrosomia and large

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance during pregnancy,<sup>1</sup> complicates approximately 3–8% of all pregnancies and is associated with adverse perinatal outcomes including macrosomia, birth trauma, shoulder dystocia, and cesarean delivery.<sup>2–5</sup> Investigators<sup>6</sup> have suggested that maternal hyperglycemia, leading to excess fetal glucose, affects growth and development in utero. The increased adiposity that we see frequently in the neonates of women with poorly controlled diabetes seems to be, in part, related to persistent fetal hyperglycemia resulting in excessive insulin production. Although the degree of

# Methods

- ▶ University of California Irvine Medical Centre
- ▶ June 1993 – June 1994
- ▶ 42 women with diet controlled gestational diabetes

# Non-randomised groups

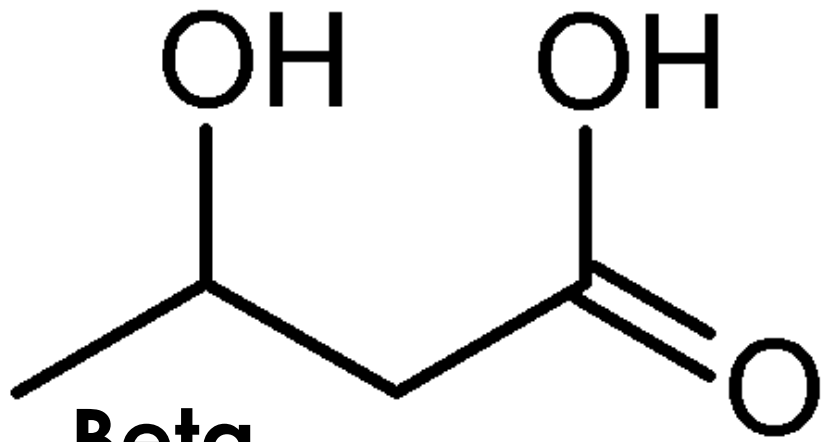
- ▶ Patients seen in Tuesday diabetes clinic: low-carbohydrate diet < 42% carbohydrate (21)
- ▶ Patients seen in other diabetes clinic: high-carbohydrate diet 45 – 50% carbohydrate (21)
- ▶ Clinic staff were the same on both days

# Key findings

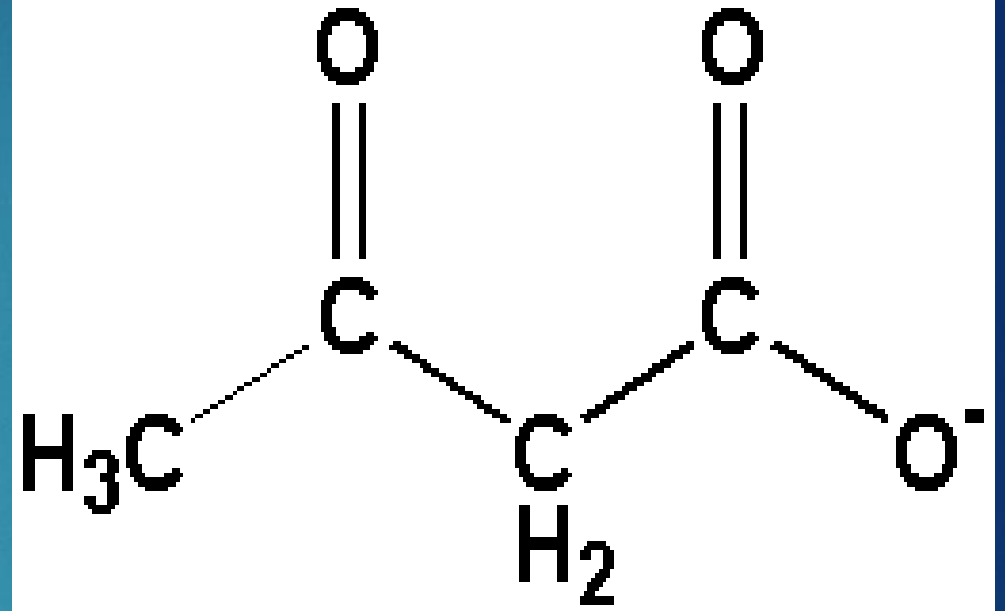
- ▶ Large for gestational age infants:
  - ▶ Low carb 9%
  - ▶ High carb 42%
  - ▶ **P < 0.035 RR 0.22**
  
- ▶ C-section for cephalopelvic disproportion or macrosomia:
  - ▶ Low carb 3%
  - ▶ High carb 48%
  - ▶ **P < 0.037, RR=0.15**



What are we so  
scared of?



**Beta-  
hydroxybutyrate**

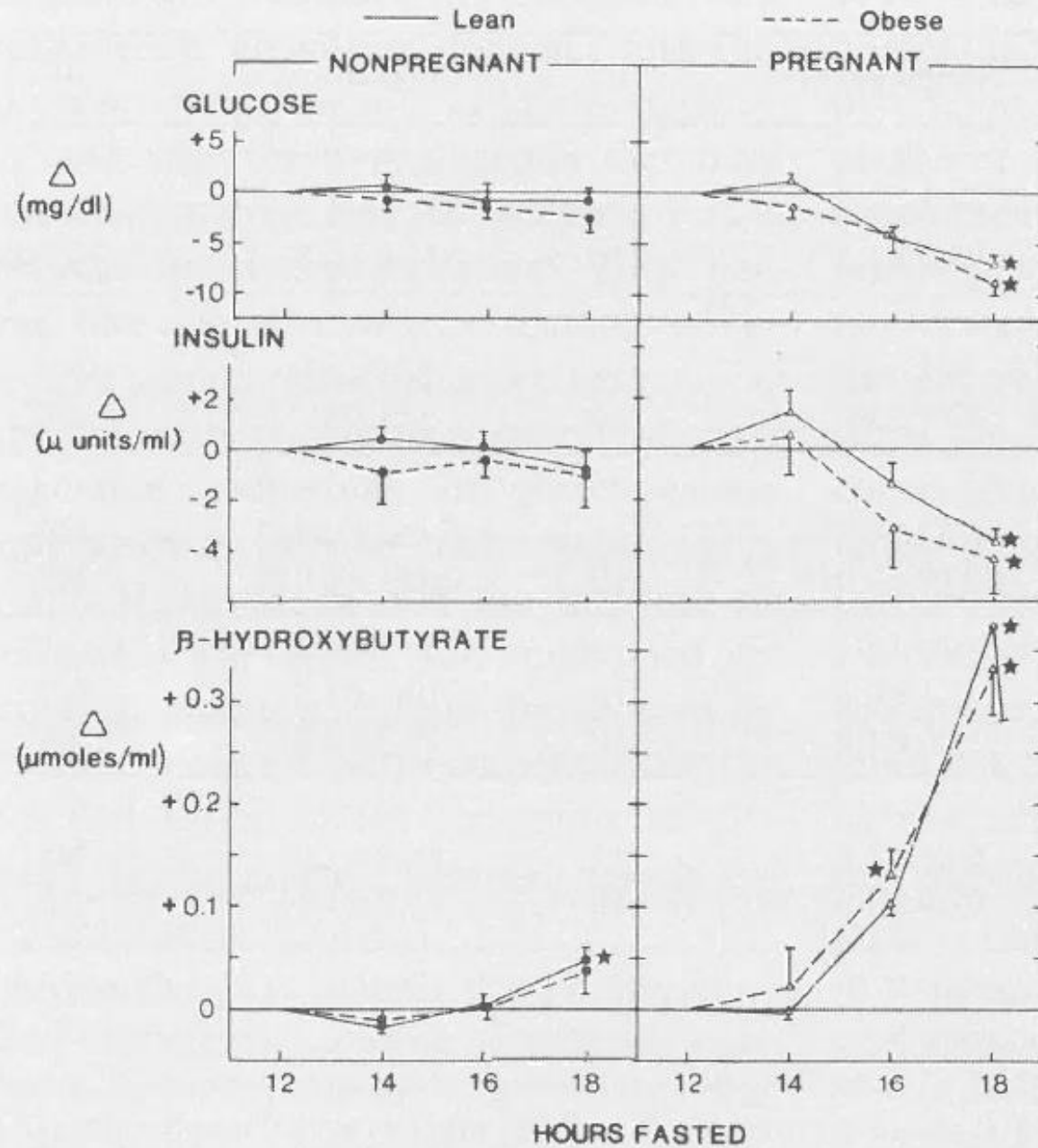


**Acetoacetate**

# Dietary advice in GDM

- ▶ No clear evidence for optimal amount of carbohydrate in GDM diet
- ▶ American Diabetes Association 2002:
  - ▶ *'Nutrition therapy for GDM promotes nutrition for maternal and fetal health with adequate energy levels for appropriate gestational weight gain, achievement and maintenance of normoglycemia, and **absence of ketones**'*





27 non-pregnant  
21 pregnant

# What is so bad about ketones in pregnancy?

- ▶ Studies linking maternal ketones with:
  - ▶ **Low intelligence quotient in the offspring**
  - ▶ Oligohydramnios at term
  - ▶ Fetal heart decelerations at term
  - ▶ Non-reactive non-stress tests at term (reactivity of heart rate to movement)
- ▶ Small number of studies
- ▶ Conflicting results – 7 found an association, 5 found no association
- ▶ Causality not demonstrated

# IQ: Initial studies – Churchill 1969

- ▶ Two retrospective studies looking at **random** urinary ketones
- ▶ Association between urinary ketones and IQ at 4 years
- ▶ Multiple confounders not accounted for
- ▶ Data later reviewed by Naeye and accounted for confounders - no association found

Churchill. Am J Obst & Gynecol 1969

Churchill. Perinatal factors affecting human development 1969

# All studies of ketones and IQ in pregnancy

## ▶ Urine Ketones

- ▶ Association – Three (including 2 from Churchill)
- ▶ No association – Four

## ▶ Serum Ketones

- ▶ Association – Two
  - ▶ (1991, 1998 – patients from 1977-1983)
  - ▶ Both from Northwestern University in Chicago
- ▶ No association - None

**Table 4. Partial Correlations between Indexes of the Mothers' Antepartum Lipid Metabolism and Children's Intelligence at Two and Three to Five Years.\***

METABOLIC INDEX	SECOND TRIMESTER		THIRD TRIMESTER	
	NO. OF WOMEN	r	NO. OF WOMEN	r
<b>Mental-development index</b>				
Plasma $\beta$ -hydroxybutyrate	112	NS	157	-0.21† (-0.06, -0.35)
Plasma free fatty acids	111	NS	146	NS
Acetonuria‡	81	NS	130	NS
<b>Stanford-Binet test</b>				
Plasma $\beta$ -hydroxybutyrate	109	NS	156	-0.20§ (-0.04, -0.35)
Plasma free fatty acids	114	NS	148	-0.27¶ (-0.11, -0.41)
Acetonuria‡	82	NS	140	NS

\*Results were corrected for socioeconomic status, race or ethnic origin, and patient group (pregestational diabetes mellitus, gestational diabetes mellitus, or no diabetes). Values in parentheses are 95 percent confidence limits. NS denotes not significant.

†P<0.01.

‡Assessed only in women with diabetes.

§P<0.02.

¶P<0.002.

# Serum studies adjusted for:

- ▶ Mother's IQ
- ▶ Parental education
- ▶ Family income

# Factors that affect IQ

- ▶ Genetics – increases with age (not as important in infants)
- ▶ Family environment (more important in childhood)
- ▶ Parental education
- ▶ Socioeconomic status
- ▶ Prenatal and early nutrition
- ▶ Pregnancy exposure to alcohol, smoking and illicit drugs
- ▶ Head injuries
- ▶ Mental illness
- ▶ ?Musical training
- ▶ Physical activity
- ▶ Father's job

Makharia A Ind Pyschiatry Jul – Dec 2016

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# Adverse fetal markers at term

- ▶ Two studies found an association between maternal ketonuria at term at one **random** time point:
  - ▶ Fetal heart rate decelerations
  - ▶ Oligohydramnios
  - ▶ Nonreactive non-stress tests.
- ▶ One study found no association between **random** maternal ketonuria in 2<sup>nd</sup> and 3<sup>rd</sup> trimester:
  - ▶ Fetal distress
  - ▶ Asphyxia neonatorum
  - ▶ 5-minute Apgars



# Correlation between serum and urine ketones

- ▶ 180 women with GDM in the third trimester – 378 simultaneous fasting urine and serum samples performed at consecutive clinic visits

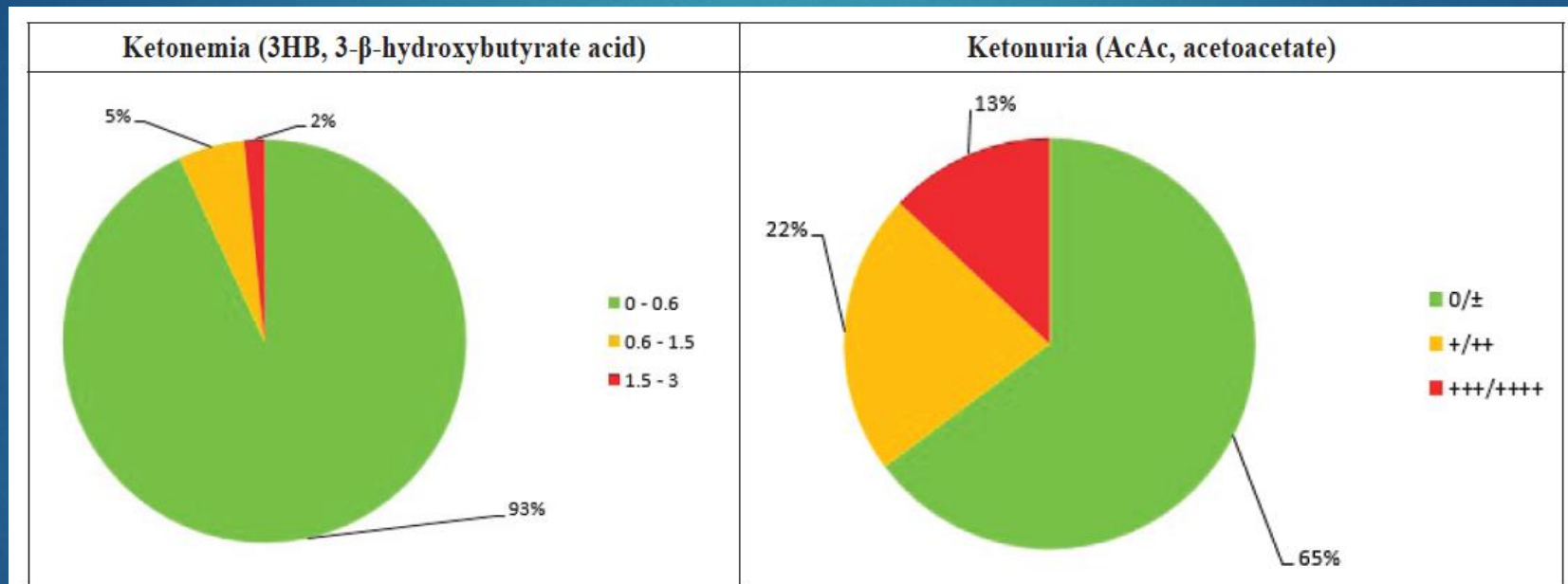


Figure 2. Percentage of ketonemia and ketonuria in the study population.

# Prevalence of maternal urinary ketones

- ▶ Only one study to date directly evaluates prevalence:
  - ▶ Nine women tested urine for ketones every 3-4 days from end of first trimester.
  - ▶ 89% had ketones present at least once in the pregnancy

# Maybe ketones make us more intelligent

- ▶ Ketones cross the placenta – taken up by the fetal brain and used to make lipids
- ▶ Pregnancy is a state of ketogenesis
- ▶ Breast milk is ketogenic

# Summary

- ▶ Lack of evidence of harm for maternal ketones
- ▶ Maybe ketones are good for the developing brain
- ▶ Lack of evidence to recommend avoiding ketones and thereby arguing that carbohydrate restriction in pregnancy is 'dangerous'