Diabetes

Acute Medical Problems in Pregnancy

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Society for Acute Medicine
7th International Conference
3-4 October 2013, SECC,
Diabetes In Pregnancy
What every Acute Physician Needs to Know

- How to manage DKA in pregnancy
  - how and why it differs in pregnancy
  - How to prevent it

- Will highlight how common hypoglycaemia in diabetic pregnancies are
Diabetes and Pregnancy

≈ 52 cases of DKA / year in England, Wales & NI

Risk of Hyperglycaemia

≈ 750 cases of ≥1 episode severe hypo/ year in England, Wales & NI

CEMACH 2002 - February 2003
The Basics: Diabetic Ketoacidosis

- ↓ insulin
- ↑ Glycaemia
- ↑ Lipolysis
- ↑ Ketoneogenesis
The Basics: Diabetic Ketoacidosis

**Fat**

- Fatty Acids and Glycerol

**Liver**

Acetyl-CoA

- + Oxaloacetate
- TCA Cycle for energy
- Hydroxybutyric acid (\(\beta\)-OHB)
- Acetoacetic acid (AcAc)
- Acetone
In Non Diabetic Pregnancies

Metabolic Changes in Pregnancy Predispose to ketosis

- **↑ Lipolysis**
  - accelerated starvation 2nd & 3rd trimesters
- **↓ caloric intake 2nd,**
  - nausea or hyperemesis gravidarum)
- **↓ buffering capacity**
  - compensated respiratory alkalosis
  - increased renal excretion of bicarbonate
- **↑ insulin antagonists**
  - human placental lactogen, prolactin, and cortisol
Four cases of women with vomiting in the third trimester of pregnancy associated with a severe metabolic acidosis

Review

Starvation ketoacidosis in pregnancy

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In non-diabetic pregnancy
Metabolic compensation for the pregnancy related respiratory alkalosis (i.e. less HCO3- buffer).

<table>
<thead>
<tr>
<th>ABGs</th>
<th>Non-pregnant</th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaCO2</td>
<td>40</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>PaO2</td>
<td>100</td>
<td>107</td>
<td>105</td>
<td>103</td>
</tr>
<tr>
<td>pH</td>
<td>7.40</td>
<td>7.44</td>
<td>7.44</td>
<td>7.44</td>
</tr>
<tr>
<td>HCO3-</td>
<td>24</td>
<td>21</td>
<td>20</td>
<td>18</td>
</tr>
</tbody>
</table>
Who Gets Diabetic Ketoacidosis (DKA)?

- Uncommon <3% of pre-gestational women with type 1 DM
  - The incidence of DKA among 635 pregnant patients who had pregestational type 1 diabetes mellitus was 1.73%*
  - Previous DKA a risk factor

- New presentation of type 1 DM 3-fold higher in late pregnancy

- Can rarely occur in type 2 DM and GDM (sub-clinical type 1DM)

Who Gets Diabetic Ketoacidosis (DKA)?

• The incidence of DKA among 635 pregnant patients who had pregestational type 1 diabetes mellitus was 1.73%*

• Relates to Approx. 52 cases a year in England, Wales and NI

Hypoglycaemia during pregnancy in women with pre-existing diabetes

Women with type 1 diabetes
• Recurrent episodes of hypoglycaemia 61%
• ≥1 episode of hypoglycaemia requiring help 25%

Women with type 2 diabetes
• Recurrent episodes of hypoglycaemia 21%
• ≥1 or more episode of hypoglycaemia requiring help 4%

CEMACH Type 1 and Type 2 diabetes pregnancies 3808 in England, Wales and Northern Ireland March 2002 - February 2003
Hypoglycaemia during pregnancy

- 80% of events occur in the first 20 weeks
- Also a period of increased frequency postpartum

Hypoglycaemia is not however dangerous to the fetus

Fetal Loss in Diabetic Ketoacidosis

- Fetal loss is ≈ 9 % for a single episode of DKA*
  - despite substantial improvements in neonatal care
- Ketoacids and glucose readily cross the placental barrier
- Maternal dehydration reduced utero-placental perfusion and compromise fetal outcomes
- Fetal hyperinsulinaemia increases fetal oxygen demand and predisposes to hypoxia

# Fetal Loss in Diabetic Ketoacidosis

Table 1  Incidence and fetal mortality rates in diabetic pregnancies complicated by diabetic ketoacidosis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Period</th>
<th>Incidence</th>
<th>Fetal mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lufkin et al⁵</td>
<td>1950–79</td>
<td>18/277 (7.9%)</td>
<td>5/18 (27.7%)</td>
</tr>
<tr>
<td>Kilvert et al⁵</td>
<td>1971–90</td>
<td>11/635 (1.73%)</td>
<td>22%</td>
</tr>
<tr>
<td>Chauhan et al⁶</td>
<td>1976–81</td>
<td>51/227 (22%)</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>1986–91</td>
<td>9/301 (3%)</td>
<td>10%</td>
</tr>
<tr>
<td>Cullen et al⁷</td>
<td>1985–95</td>
<td>11/520 (2%)</td>
<td>1/11 (9%)</td>
</tr>
</tbody>
</table>

Causes of Diabetes ketoacidosis in pregnancy:

- The usual:
  - Infections
  - failure to take insulin
    » Teenages
- Pump failure
  - No depot insulin
  - ↓Time to DKA
- Emesis
- Medications
  - Betamethasone
  - Dexamethasone
  - beta-2-adrenergic agonist

Diagnosing Early Diabetic Ketoacidosis

Urine ketone DO NOT measure β-OHB but Acetoacetate

- Neither acetone nor B-OHB reacts as strongly with nitroprusside, used in the urine strips as acetoacetate

- Urine ketone DO NOT reflect real time ketosis

- Blood Ketone testing tests B-Hydroxybutyrate

- Insulin needed for ketone body utilization and excretion

![Chemical Reaction Diagram](attachment:image.png)
Testing for Ketoacidosis

Normal blood ketones < 0.6 mmol/l

<table>
<thead>
<tr>
<th>Blood (mmol/L)</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.6</td>
<td>negative</td>
</tr>
<tr>
<td>0.6 to 1.5</td>
<td>small to</td>
</tr>
<tr>
<td>moderate</td>
<td></td>
</tr>
<tr>
<td>1.6 to 3.0</td>
<td>usually large</td>
</tr>
<tr>
<td>≥ 3.0</td>
<td>Very large</td>
</tr>
</tbody>
</table>

Proactive self management required

All pregnant women with Type 1 DM need to be able to detect early DKA and proactively treat this with increased administration of insulin.
Diagnosing Diabetic Ketoacidosis in Pregnancy

- Think about it!
- ↑ ventilation; emesis can be attributed to pregnancy
- Likely to present at lower blood glucose values (rarely <10 mmol/l) than in a non-pregnant women
- DKA in pregnant patients develops more rapidly
  - pumps
- pH <7.3
- ↓ serum bicarbonate level
- ↑ anion gap
- Blood ketones ≥ 3.0 mmol/l
Managing Diabetes Ketoacidosis in Pregnancy

Pregnancy itself does not alter the management of DKA

- Involve the diabetic obstetric team early
- Two patients not one
- Fetal monitoring for gestational ages >24 weeks
- Avoid beta-2-adrenergic agonist
  - magnesium sulfate recommended tocolysis of preterm labor
  - DKA can precipitate preterm labour
- Emergency caesarean section not before adequately resuscitated and treatment
Managing Diabetes Ketoacidosis in Pregnancy

- Initiation of insulin
- Volume resuscitation
- Search for the precipitating cause, and
  - Signs of infection can be masked by hypothermia 2\textsuperscript{nd} to acidosis
- Laboratory monitoring blood ketones and electrolytes
- Maximize oxygenation

![Graph showing changes in plasma ketone body concentrations over time following initiation of therapy.](image.png)

*Fig. 7. Rise in acetoacetate concentration during the treatment of diabetic ketoacidosis. Since the nitroprusside reacts primarily with acetoacetate, a more positive reaction (purple color) occurs as the total ketone body concentration is decreasing (ie, with factitious ketosis).*
Diabetic Ketoacidosis

Urine ketone are unreliable

- With insulin initiation B-OHB fall as converted back to acetoacetate

- Hence the urine ketone testing (nitroprusside reaction) may paradoxically worsen as the DKA is resolving

\[
\text{Acetyl CoA} 
\quad \rightarrow 
\text{Acetoacetyl CoA} 
\quad \rightarrow 
\text{3-hydroxy-3-methylglutaryl CoA} 
\quad \uparrow 
\text{Acetoacetate} 
\quad \rightarrow 
\text{Acetone} + \text{CO}_2 \quad \text{B-Hydroxybutyrate}
\]
Managing Diabetes Ketoacidosis in Pregnancy

(1) Fluid replacement
- 1–2 litres of isotonic saline in the first hour.
- 300–500 ml/hour of 0.9% or 0.45% saline thereafter.
- Add 5% dextrose when serum glucose approaches 12 mmol/l.

(2) Insulin therapy
- Loading dose 0.4 U/kg regular insulin.
- Continuous infusion at 6–10 U/hour
- Double infusion rate if no response in 1 hour.
- Decrease infusion to 1–2 U/hour as serum glucose drops to 12 mmol/l.
- Continue infusion 12–24 hours after resolution of ketosis.

But only once Ketones cleared, cover with dextrose if need be

Managing Diabetes Ketoacidosis in Pregnancy

(3) Electrolyte replacement
- Potassium replacement.
- Check phosphorus, magnesium.

(4) Search and treat precipitating factor like infection

(5) Others
- Admit to high dependency unit.
- Supplemental oxygen.
- Place in left lateral position to avoid aortocaval compression.
- Monitor fetal heart rate.
- Monitor urine output.
Management of Diabetic Ketoacidosis

PREVENTION IS BETTER THAN CURE
All Type 1 Women who are Pregnant need to be able to test for Ketones and Know how to Respond Proactively to Ketosis
All Pregnant women should be performing Blood ketone testing

NICE 63 2008

• Women with type 1 DM who are pregnant should be offered ketone testing strips and advised to test for ketonuria or ketonaemia if they become hyperglycaemic or unwell

ADA Clinical Practice Recommendations: Jan, 2003

• Blood Ketone testing methods that quantify ß-HBA, are preferred over urine ketone testing for diagnosing and monitoring ketoacidosis
Diabetes In Pregnancy
What every Acute Physician ALSO Needs to Know

• Today’s type 1 diabetic pregnant diabetic women may well be wearing >£5000 of Gadgets and Gizmos
  – please look for them
  – please look after them
Familiarize Yourselves with the Gadgets and Gizmos of Diabetes

Elements of the Paradigm Veo:
- MiniLink™ Transmitter
- Paradigm Veo
- Sensor
- Infusion Set
In Summary

• DKA in type 1 DM in pregnancy is uncommon
• All type 1 DM in pregnancy need to be able to test blood ketones and know what to do with the results
• Use blood ketones strips to monitor DKA management
• Involve the diabetic obstetric team early
• Have your own DKA protocols in place
• Do not rush into a Caesarean section
• Do not throw away the attached accessories
Thank you

Risk of Hyperglycaemia

Risk of Hypoglycaemia
References

Questions