Infection & sepsis in obstetrics

Nuala Lucas
Declarations

– UKOSS obstetric sepsis co-investigator
– HIQA Enquiry – sepsis maternal death
Role of the anaesthetist

Challenges of management

Context & clinical picture

Role of the anaesthetist
Obs sepsis in under-resourced world
http://www.who.int/topics/millennium_development_goals/en/
WHO analysis of causes of maternal death: a systematic review,

Khan et al
Lancet 2006
Obs sepsis in developing world

- **2008 - 342 900 maternal deaths worldwide**
  - HIV disease accounted for 60 000 of these deaths

- **HIV infection**
  - Increased susceptibility to infection
  - More aggressive course e.g. Pneumocystis jirovecii
  - Most significant associated infection TB

- **Without HIV**
  - MMR 580/100 000 (640)
Context

Sepsis

- Resourced world
- Under-resourced world
Obstetric sepsis, 1846
After the introduction of hand washing...
Background history

- **1928**
  - Maternal mortality report to ministry of health
  - Sepsis leading cause of death 37%
- **1930’s- advent of penicillin & sulphonamides**
- **1952-54 1st Confidential Enquiry Report**
  - Sepsis
The first patient was admitted with a temperature of 104°F. She was given Prontosil in the evening and the team was in and out of the ward all night in the oddest assortment of nightwear. The next morning the patient’s temperature was normal and she recovered rapidly.

Changing patterns – deaths from sepsis
Direct causes of maternal death 1985-2008

- Thromboembolic
- Haemorrhage
- Sepsis
Death rates from genital tract sepsis

- USA
  - Bauer et al 2011
- Netherlands
  - Kramer et al 2009
- Denmark
  - Bødker et al 2009
Sepsis *mortality vs morbidity*

- Mortality has been used as measure of quality of maternal services
- The Continuum of adverse pregnancy events
  healthy pregnancy $\rightarrow$ morbidity $\rightarrow$ severe morbidity $\rightarrow$ Death

SAVING MOTHERS’ LIVES 2006-08: Briefing on genital tract sepsis

During the 2006 – 2008 triennium, sepsis was the leading cause of direct maternal deaths, accounting for 26 direct deaths and a further 3 deaths classified as ‘Late Direct’. Whilst maternal mortality is declining overall, maternal deaths due to sepsis have risen in recent triennia, particularly those associated with Group A streptococcal infection (GAS).

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate / 100,000 maternities</th>
<th>Numbers* (all organisms)</th>
<th>Numbers* (GAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2002</td>
<td>0.65</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>2003-2005</td>
<td>0.85</td>
<td>21</td>
<td>8</td>
</tr>
<tr>
<td>2006-2008</td>
<td>1.13</td>
<td>29</td>
<td>13</td>
</tr>
</tbody>
</table>

* Direct and indirect maternal deaths together

This alert is being published in advance of the full Saving Mothers Lives (SML) report because of the significance of the facts and findings relating to deaths due to genital tract infection.
Causes & risk factors

- Caesarean
- Amniocentesis
- Cervical suture
- Prolonged SROM
- Vaginal trauma

Patient factors

- Obesity
- Anaemia
- Impaired glucose tolerance
- HB SS/SC/trait

CMACE, 2011
# Progression to ‘severe sepsis’

<table>
<thead>
<tr>
<th></th>
<th>aOdds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;25 years</td>
<td>10.17</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.71</td>
</tr>
<tr>
<td>Anaemia</td>
<td>21.5</td>
</tr>
<tr>
<td>Operative vaginal delivery</td>
<td>2.89</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>8.74</td>
</tr>
<tr>
<td>&gt;500 ml blood loss</td>
<td>7.96</td>
</tr>
<tr>
<td>Severe PET</td>
<td>3.35</td>
</tr>
</tbody>
</table>

*Acosta et al, BJOG, 2012*
Timing

Gestation

- 29 deaths
- >24/40: 21
- <24/40: 8

Onset of sepsis

- Before delivery: 9
- After delivery: 20

CMACE 2006-8
Clinical features

- Fever
- D&V
- Anxious
- Vaginal discharge
- Abdominal/ perineal pain
- Temp
  - high/normal/low
- Tachycardia
- Tachypnoea
- Hypotension/poor perfusion
# The pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>β haemolytic streptococcus Lancefield group A</td>
<td>25</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>25</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>17</td>
</tr>
<tr>
<td>HIV</td>
<td>11</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10</td>
</tr>
<tr>
<td>Streptococcus unspecified</td>
<td>8</td>
</tr>
<tr>
<td>Clostridium species</td>
<td>5</td>
</tr>
<tr>
<td>β haemolytic streptococcus Lancefield group B</td>
<td>5</td>
</tr>
<tr>
<td>TB</td>
<td>6</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>4</td>
</tr>
<tr>
<td>Proteus species</td>
<td>4</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>3</td>
</tr>
</tbody>
</table>

Microbiological causes of sepsis identified in UK Confidential Enquiries 1991-93 to 2006-08, Lucas IJOA 2012
Contribution of deaths from GAS

<table>
<thead>
<tr>
<th>Year</th>
<th>Non GAS</th>
<th>GAS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006-2008</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Non GAS
- GAS
- Total

Group A Strep – worrying trends

- Evidence suggests
  - frequency of severe, invasive GAS infections is increasing
  - strains of streptococci with increased pathogenic potential are appearing

  *Schleiss, 2010*

- 1995 – WHO working group GAS
- 2002 Eurosurveillance programme established
Maternal sepsis deaths – improving care

Learning points
Maternal sepsis deaths – improving care

Missed opportunities
Missed opportunities

1. Failure to recognise/respond to the sick woman
2. Antibiotic failings
3. Fluid balance in the septic parturient
4. Removing the source of the sepsis
Missed opportunities

1. Failure to **recognise**/ respond to the sick woman
   - Clinical skills
   - Early warning scores
Recognition of the sick woman

Clinical skills

– Improvements in training BUT increasing earlier subspecialisation
– Impact on medical/skills knowledge outside immediate area of expertise
How can we improve this?

- Undergraduate education?
- Raise awareness of specific problems?
- CRISP/ALERT/PROMPT courses mandatory?
Most patients who suffer adverse outcomes have documented deterioration
Most patients who suffer adverse outcomes have documented deterioration

“development of a national obstetric early warning chart ... which will help in the more timely recognition, treatment and referral of women who have, or are developing, a critical illness.”

CEMACH 2003-5
Detecting critical illness – is MEWS the answer?

Original Article

A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS)*

S. Singh,¹ A. McGlenan,² A. England² and R. Simons²
• Prospective review 676 admissions
• 200 patients ‘triggered’
• 86 met defied ‘morbidity’ criteria
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>89%</td>
<td>81–95%</td>
</tr>
<tr>
<td>Specificity</td>
<td>79%</td>
<td>76–82%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>39%</td>
<td>32–46%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>98%</td>
<td>96–99%</td>
</tr>
</tbody>
</table>
4P study - *Pregnancy Physiology Pattern Prediction*

Aims to establish

- normal distributions of blood pressure, temperature, respiratory rate, heart rate and oxygen saturation
- 14/40 – 2 weeks post partum

Watkinson/Makillop

*Oxford Biomedical Research Centre*
Other difficulties with diagnosis?

- Fever
- D&V
- Anxious
- Vaginal discharge
- Abdominal/perineal pain
- Temp
  - high/normal/low
- Tachycardia
- Tachypnoea
- Hypotension/poor perfusion
Improving diagnostic accuracy?

White cell count
- Rises in pregnancy and at delivery
- Declines to pre-pregnancy levels by one week

Serum biomarkers
Lactate
Procalcitonin
1. Failure to recognise/ respond to the sick woman

“Detection of life threatening illness alone is of little value...it is the subsequent management that will alter the outcome.”

CEMACH 2003-05
WELCOME TO THE SURVIVING SEPSIS CAMPAIGN WEBSITE

Introduction

The Surviving Sepsis Campaign (SSC), an initiative of the European Society of Intensive Care Medicine (ESICM), the International Sepsis Forum (ISF), and the Society of Critical Care Medicine, was developed to improve the management, diagnosis, and treatment of sepsis. The agreement among the three societies and funding for the campaign came to a conclusion on December 31, 2008 (view final newsletter). ISF has officially withdrawn from the SSC however, ESICM and SCCM continue to collaborate maintaining this website and the database so that all associated materials remain as resources. This unprecedented global effort to reduce death from sepsis was accomplished through the guidance and support of the three collaborating societies and their members. The Institute for Healthcare Improvement worked with campaign leadership to lend expertise in reinforcing the campaign as a quality improvement initiative.
Clinical care ‘bundles’

“A bundle is a group of evidence-based care components for a given disease that, when executed together, may result in better outcomes than if implemented individually”
The sepsis six

1. Give high flow oxygen \textit{via non-rebreath bag}
2. Take blood cultures
3. Give IV antibiotics
4. Start IV fluid resuscitation \textit{Hartmann's or equivalent}
5. Check haemoglobin and lactate
6. Monitor accurate hourly urine output \textit{may require catheter}

\textit{Daniels et al}
\textit{Emergency Medicine Journal, 2010}
Antibiotic timing - *does it really matter?*

- Importance of rapid antibiotic administration in sepsis long been recognised
- ‘A recurring feature ....is a delay in starting intravenous antibiotics’

*CEMACH 2003-5*
Timing of antibiotics – does it matter?

‘Every additional hour without effective antibiotic therapy can increase risk of death in patients with hypotensive sepsis by 7.6% during the first 6 hours’

Kumar et al
Crit Care Med, 2006
### Antibiotics

**Strategy**
- Start Urgently
- Adequate doses, IV NOT oral
- Senior micro input
- Daily review
- Don’t wait for micro results
- Don’t stop too soon

**Which drug(s)**
- **Difficult!**
- Lamont et al, BJOG, 2011
- CMACE
  - Augmentin + metronidazole
  - Severe sepsis
    - Piperacillin–tazobactam plus gentamicin
Missed opportunities

1. Failure to recognise/respond to the sick woman
2. Antibiotic failings
3. Fluid balance in the septic parturient
Fluid balance in obstetrics

Arterial hypotension in septic shock may be refractory to fluid resus

- Fluid overload → pulmonary / cerebral oedema

2 questions

1) Which fluid?
2) How to resuscitate?
Fluid balance in obstetrics

Which fluid?
Fluid balance in obstetrics

Additional challenges in the parturient

– Physiology
– Pathology – co-existing disease
– Pharmacology- syntocinon, prostaglandins
– Monitoring - ‘or lack of’
Fluid balance in obstetrics

Additional challenges in the parturient

- Physiology
- Pathology – co-existing disease
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Missed opportunities

1. Failure to recognise/respond to the sick woman
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3. Fluid balance in the septic parturient
4. Removing the source of the sepsis
   - Radiology – CT
   - Surgery
Defining a new role for the anaesthetist?

1) Caring for septic obstetric patients
2) Training the team
Obstetricians’ knowledge of physiological parameters

Sabir et al, IJOA, 2009
1) Caring for septic (sick) obstetric patients

<table>
<thead>
<tr>
<th></th>
<th>Obstetrician</th>
<th>Obstetric physician</th>
<th>Obstetric anaesthetist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstetric physiology</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Critical care skills</td>
<td>X</td>
<td>?</td>
<td>✓</td>
</tr>
</tbody>
</table>
Workload

• 5400 deliveries pa
• 40 epidural rate
• 24% CS rate
• Obs antenatal clinic
• Comprehensive CG structure
• 1 obs fellow
The obstetric intensivist?

Significant impact on workload

Future training
Defining a new role for the anaesthetist?

1) Caring for septic obstetric patients
2) Training the team

Skills Drills for Sepsis?
## Sepsis vs other emergencies

<table>
<thead>
<tr>
<th></th>
<th>Occult Haemorrhage</th>
<th>Preeclampsia</th>
<th>“Fetal Distress”</th>
<th>Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Signs</td>
<td>Observations</td>
<td>Observations</td>
<td>Observations</td>
<td>Observations</td>
</tr>
<tr>
<td>Early Symptoms</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Urgency to Treat</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Protocols Exist?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Auditable/Testable</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Suitable for Team Training</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
• Mandatory rigorous annual training programme
• Computerised guidelines
Effect of training on adherence to sepsis guidelines

Fig. 5  Hours until first dose of antibiotics (in light color, the improvement for the 2007 cohort).

Jos et al
Am J Em Med 2009
The future....

Studies to watch

- PROCESS (North America) - *Protocolized Care for Early Septic Shock*
- Australasian Resuscitation of Sepsis Evaluation
- ProMISE study (UK) – *Protocolised Management in Sepsis*
Take home messages

- Impact of morbidity
- Difficulties of diagnosis
- Timing of antibiotics
Major cause of morbidity
The continuum of maternal morbidity

Impact of morbidity
Difficulties of diagnosis
Timing of antibiotics
EWS, watch out for the 4P study results
Role of biomarkers

- Impact of morbidity
- Difficulties of diagnosis
- Timing of antibiotics
Early antibiotics

The sepsis 6

- Impact of morbidity
- Difficulties of diagnosis
- Timing of antibiotics