SICKLE CELL DISEASE AND PREGNANCY

Kate Ryan
Central Manchester University Hospitals NHS Foundation Trust
Content

• Overview of Sickle Cell Disease and pregnancy
  • Outcomes
• Preconceptual management
• Antenatal management
• Postnatal management
• The role of transfusion in pregnancy

With thanks to Dr Jo Howard for sharing slides
Pregnancy in sickle cell disease

SCD is associated with high maternal and fetal adverse outcomes

- HbSS worse outcomes compared to HbSC
- Higher in economically disadvantaged countries
**Sickle cell specific complications**

- Sickle cell crises
- Acute chest syndrome

**Pregnancy-specific complications**

- Thromboembolism
- Urinary tract infection
- Spontaneous abortion
- Proteinuric hypertension

**Increased incidence of:**

- Antepartum hospitalisations
- Postpartum infection
- Caesarean section
- Low birth weight
- Preterm birth
- Prematurity
- IUGR
Increased maternal mortality

- Range from 0% to 9.2% in studies of centres across the world
- UK national data: approx 1 death per year

- US Co-operative study (1980’s, 1990’s)
  - 0.4% mortality

- US In-patient sample 2000-2003
  - 72.4 deaths per 100,000 in SCD (0.07%)
  - 12.7 deaths per 100,000 overall (0.01%)
Maternal morbidity

- Increased risk of
  - Hypertension and pre-eclampsia
  - Acute painful crisis: 20-56%
  - Anaemia
  - Infections (especially UTI: 16-23%)
  - Acute chest syndrome (11-17%)
  - VTE (Increase in DVT not PE – US cohort)
  - Caesarean section: 30-62%
Fetal complications

• Increased perinatal mortality and stillbirth rate
  
• Fetal growth restriction
  • 10-44%
  
• Increased preterm delivery
  • 16-33%
  
• Increased fetal distress in labour
Pre-pregnancy care

- Discuss pregnancy and contraception at each sickle clinic
- Vaccination and medication advice
  - Ensure on folic acid and penicillin V
  - Stop hydroxycarbamide at least 3 months prior to conception
  - Stop ACE inhibitors
- Partner screening and genetic counselling
- Assessment for chronic disease complications
  - Pulmonary hypertension screening
  - BP and urinalysis (record baseline proteinuria)
  - Retinal screening
  - Screen for iron overload
  - Red cell antibodies
Pre-pregnancy care

- Precipitating factors
- Risks of anaemia, crises and infection
- Risks of fetal complications
- Chance of baby being affected – discussion of reproductive options
Antenatal care

• Multidisciplinary team approach (Obs and Haem, midwife)
• Screen for chronic complications
• Avoid precipitating factors
• Advice about persistent vomiting
• Influenza vaccine

• Partner testing (ideally done pre-conceptually)
  • NHS screening programme target PND offered by 12/40)
Medications during pregnancy

• Folic acid 5mg od
• Penicillin V 250mg bd
• Iron supplementation ONLY if evidence of iron deficiency
• Aspirin 75mg od from 12/40
  • Applying evidence from pre-eclampsia data
• STOP hydroxycarbamide, ACE inhibitors
Pre-eclampsia and aspirin

- Early trials showed benefit of low dose aspirin, but not replicated in large trials
- Cochrane review (2007)
  - >32,000 women in trials
  - Small- moderate benefits (15% decrease)
  - May be of benefit in subgroups
- NICE (2010)
  - Women at high risk of pre-eclampsia should take low dose aspirin from 13/40
Thromboprophylaxis

- Anecdotal evidence of increased VTE

- Advice based on RCOG green top guidelines:
  - Antenatal prophylaxis: Intermediate risk
    - Consider antenatal prophylaxis if admitted

- Consider other risk factors
  - Obesity, age >35 years, systemic infection, prolonged immobilisation, multiparity, multiple pregnancy
USS Schedule

- 7-9 weeks: viability scan
- 11-14 weeks: routine first-trimester scan
- 20 weeks: detailed anomaly scan
- Serial growth scans every 4 weeks from 24 weeks
Painful crisis during pregnancy

- Women who become unwell should have sickle cell crisis excluded as a matter of urgency

- Multidisciplinary management
- Analgesia
  - AVOID pethidine
- Fluids and oxygen if required
- Thromboprophylaxis if admitted to hospital

- Manage as per Sickle Cell Protocol (avoid NSAIDS)
The role of transfusion during pregnancy
Transfusion in pregnancy

• Early retrospective studies showed decrease in maternal and perinatal mortality in transfused patients when compared with historical controls.

• BUT high risk of adverse effects
  • Alloimmunisation
    • Haemolytic disease of the newborn
Evidence base for prophylactic transfusion in pregnancy

Cochrane systematic review 2013

- 2 trials (98 women HbSS)
- No clear benefit of prophylactic transfusion over selective (emergency) approach
- Data and quality of evidence insufficient to advocate change in existing policies

Systematic review (Malinowski: Blood 2015) . 7 studies

Prophylactic transfusions associated with reduced:

- Maternal mortality
- Vaso-occlusive pain episodes
- Pulmonary complications
- Neonatal mortality and preterm birth
<table>
<thead>
<tr>
<th>Group</th>
<th>Outcomes</th>
<th>Studies, n</th>
<th>Study subject, n</th>
<th>OR (95% CI)</th>
<th>Significance (heterogeneity), $P$ ($I^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal</td>
<td>Mortality</td>
<td>7,14,15,18,20-29</td>
<td>955</td>
<td>0.23 (0.06-0.91)</td>
<td>.04 (20%)</td>
</tr>
<tr>
<td></td>
<td>Vaso-occlusive pain episodes</td>
<td>5,10,13,17-19,26-30</td>
<td>1219</td>
<td>0.26 (0.09-0.76)</td>
<td>.01 (90%)</td>
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<td>Pulmonary complications*</td>
<td>9,10,15,17-19,26-30</td>
<td>1019</td>
<td>0.25 (0.09-0.72)</td>
<td>.01 (77%)</td>
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<tr>
<td></td>
<td>Pulmonary infection</td>
<td>5,16,19,26-28</td>
<td>792</td>
<td>0.26 (0.05-1.27)</td>
<td>.10 (83%)</td>
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<td>Pulmonary embolism</td>
<td>3,19,26-28</td>
<td>237</td>
<td>0.07 (0.01-0.41)</td>
<td>&lt;.01 (1%)</td>
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<tr>
<td></td>
<td>Acute chest syndrome</td>
<td>2,15,17</td>
<td>102</td>
<td>0.28 (0.06-1.26)</td>
<td>.10 (0%)</td>
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<tr>
<td></td>
<td>Urinary tract infection</td>
<td>3,16,20-30</td>
<td>149</td>
<td>1.09 (0.22-5.42)</td>
<td>.92 (61%)</td>
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<tr>
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<td>Pyelonephritis</td>
<td>3,16,10,26-29</td>
<td>455</td>
<td>0.19 (0.07-0.51)</td>
<td>&lt;.01 (34%)</td>
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<td>Endometritis</td>
<td>2,26-29</td>
<td>80</td>
<td>0.76 (0.17-3.44)</td>
<td>.72 (40%)</td>
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<td>Preeclampsia</td>
<td>6,15,16,17,26-29</td>
<td>282</td>
<td>1.01 (0.49-2.08)</td>
<td>.98 (0%)</td>
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<tr>
<td>Fetal</td>
<td>Perinatal mortality</td>
<td>8,10,15,18,26-28</td>
<td>1140</td>
<td>0.43 (0.19-0.99)</td>
<td>&lt;.05 (58%)</td>
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<tr>
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<td>Intrauterine fetal demise</td>
<td>8,14,15,17,19,26-30</td>
<td>458</td>
<td>0.47 (0.17-1.33)</td>
<td>.15 (32%)</td>
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<tr>
<td></td>
<td>Neonatal death</td>
<td>5,15,19,26-30</td>
<td>374</td>
<td>0.26 (0.07-0.93)</td>
<td>.04 (0%)</td>
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<td>Small for gestational age/low birth weight</td>
<td>10,15,17-19,26-30</td>
<td>1187</td>
<td>0.71 (0.44-1.16)</td>
<td>.17 (35%)</td>
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<td></td>
<td>Preterm delivery</td>
<td>3,10,16,17,27-30</td>
<td>1123</td>
<td>0.59 (0.37-0.96)</td>
<td>.03 (38%)</td>
</tr>
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</table>

*Pulmonary complications (infections, infarctions, and/or embolism).
UK Obstetric Surveillance Survey

- 26 women (24%) required antenatal transfusion (45% of SS women, 5% of SC)
- 15 women had top up
- 11 women had exchange transfusion
  - 5 had one exchange only
  - 6 had repeated exchanges
Standard approach in UK

Standards for the clinical care of adults with sickle cell disease in the UK

In the absence of clear evidence to guide practice
  - Empirical blood transfusion is not necessary in pregnancy

Current indications for transfusion in pregnancy
  - Chronic transfusion programme
  - Anaemia with cardiorespiratory compromise
  - Hb <60g/L
  - Twin pregnancies
  - History of severe SCD related complications
RCOG Guidelines

• Routine prophylactic transfusion is not recommended during pregnancy for women with Sickle Cell Disease

• If acute exchange transfusion is required for the treatment of sickle complications it may be appropriate to continue the transfusion regimen for the remainder of the pregnancy

• Blood should be matched by extended phenotyping including full Rh (C, D and E) and Kell typing.
Alloimmunisation in SCD

Alloimmunisation: development of antibodies against allogeneic red cell antigens

- haemolytic transfusion reactions
- difficulties in cross-matching blood
- may produce HDN

Frequency of red cell antigens varies between different populations

- Antibodies usually anti- C, E and K
- Some patients have multiple alloantibodies
  - Need frozen blood or directed donors
National comparative SCD audit 2014

n=1227 sickle cell patients

Blood groups
• 60% C and E neg (R_0) (~2% donors)
• 1.2% K pos (~9% donors)
• 70% recorded genotype/phenotype

27/1267(2.1%), history of hyperhaemolysis
Intrapartum and postpartum care
Delivery

- Consider induction at 38-40 weeks
- Vaginal delivery as recommended mode of delivery
- Cross match blood if atypical abs are present

- Unit able to manage high risk pregnancies
- Multidisciplinary team
- Keep warm and encourage fluids
- Close fetal monitoring
Postpartum care

• Increased risk of SCD crisis (25%)
• Maintain maternal oxygen sats and hydration

• Offer early testing of baby in high risk couple
Post-natal thromboprophylaxis

- Review RCOG green top guidelines

- SCD = Intermediate risk
  - 7 days LMWH prophylaxis

- If additional risk factors, give 6/52 treatment
  - Caesarean, obesity, multiparity, pre-eclampsia, increased age
CMFT study

Aims

• To observe using standard care approach which patients required transfusions
• If on-demand transfusion affected outcome
• Can we predict women more likely to require transfusions?

Method

• Data collection of pregnancy episodes in all women with SCD between 2003-2014
• All patients managed according to local protocol
• Patients on chronic transfusion programmes excluded
• Patient details and pregnancy outcomes recorded
Results

* 38 pregnancies included
  * Mean age at booking 29 (16-43)
Transfusion episodes

* 23 (61%) pregnancies required at least one transfusion
Transfusion episodes

- 23 (61%) pregnancies required at least one transfusion
Indications for transfusion

- Symptomatic anaemia: 25
- Acute chest syndrome: 3
- Post partum haemorrhage: 5
- Caesarean section: 1
- Other: 2
Gestation at time of transfusion

- 1st trimester: 5
- 2nd trimester: 2
- 3rd trimester: 15
- Post partum: 14
Characteristics of patients requiring transfusion vs. those not transfused

<table>
<thead>
<tr>
<th></th>
<th>Required on demand transfusion (n=23)</th>
<th>Not transfused (n=15)</th>
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</thead>
<tbody>
<tr>
<td>Received Hydroxycarbamide in previous year</td>
<td>22%</td>
<td>20%</td>
</tr>
<tr>
<td>Previous acute chest syndrome</td>
<td>9%</td>
<td>13%</td>
</tr>
<tr>
<td>Mean number of hospital admissions in previous year*</td>
<td>1.11</td>
<td>0.15</td>
</tr>
<tr>
<td>Mean steady state haemoglobin**</td>
<td>85.0 g/L</td>
<td>99.6 g/L</td>
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</tbody>
</table>

*Not quite statistically significant p=0.057

** Significant difference p=0.003
Summary

- Sickle cell pregnancy is a high risk time for mother and fetus
- Multidisciplinary expert care needed
- Follow protocol based on national guidelines
- The role of prophylactic transfusion is unclear but the majority of Hb SS women need transfusion at some point
- Each women should be assessed individually.