SICKLE CELL DISEASE AND PREGNANCY

Kate Ryan

Central Manchester University Hospitals NHS Foundation Trust

Content

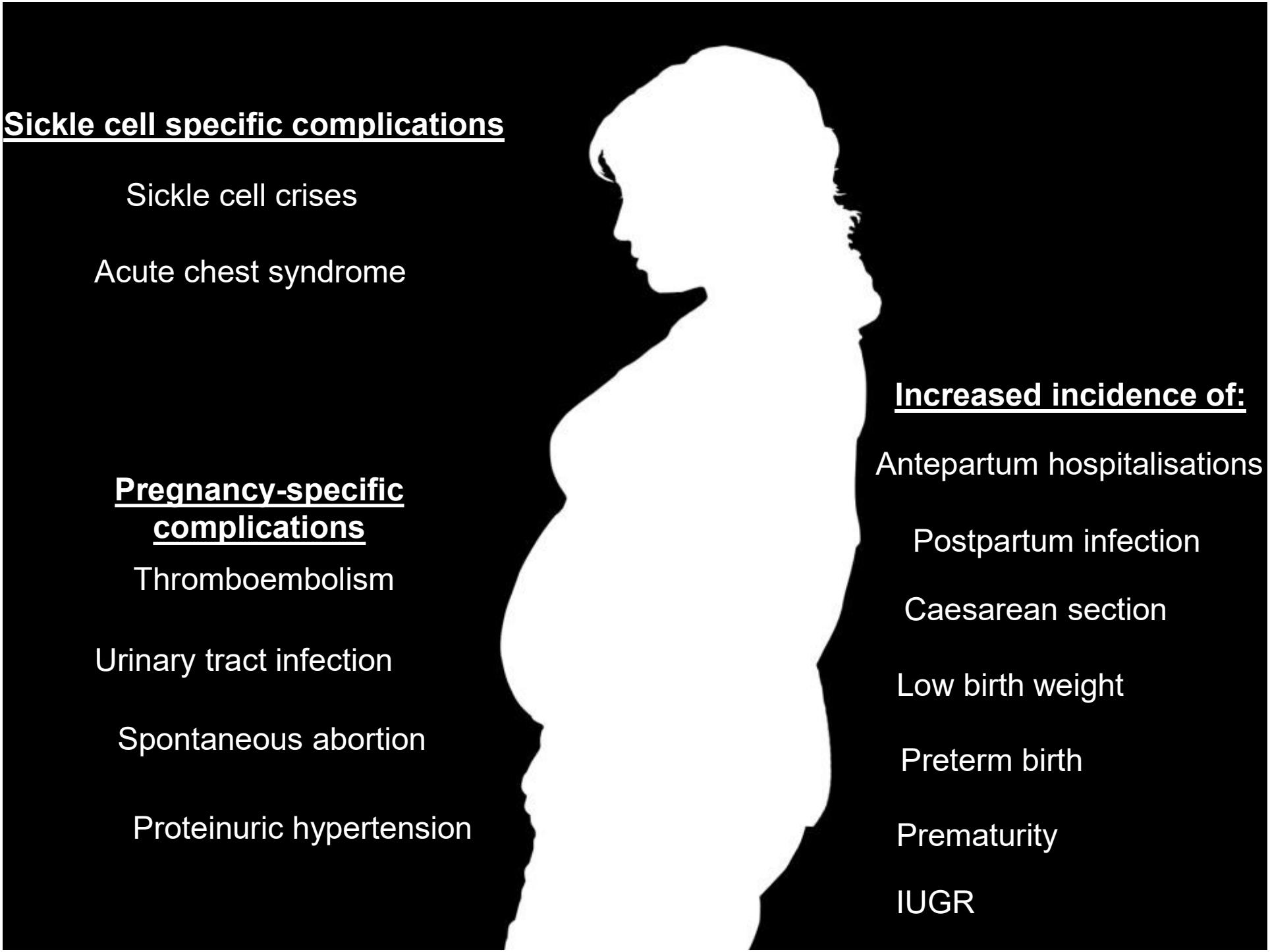
- Overview of Sickle Cell Disease and pregnancy
  - Outcomes
- Preconceptual management
- Antenatal management
- Postnatal management
- The role of transfusion in pregnancy

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 4. Outcomes in cohort studies of prophylactic transfusion compared with on-demand transfusion in pregnant women with SCD (cohort studies)

Group	Outcomes	Studies, n	Study subject, n	OR (95% CI)	Significance (heterogeneity), P (I^2)
Maternal	Mortality	7[14,15,18,26-29]	955	0.23 (0.06-0.91)	.04 (20%)
	Vaso-occlusive pain episodes	11[10,15,17-19,26-30]	1219	0.26 (0.09-0.76)	.01 (90%)
	Pulmonary complications*	9[10,15,17-19,26-28,30]	1019	0.25 (0.09-0.72)	.01 (77%)
	Pulmonary infection	5[18,19,26-28]	792	0.26 (0.05-1.27)	.10 (83%)
	Pulmonary embolism	3[19,26,28]	237	0.07 (0.01-0.41)	<.01 (1%)
	Acute chest syndrome	2[15,17]	102	0.28 (0.06-1.26)	.10 (0%)
	Urinary tract infection	3[15,29,30]	149	1.09 (0.22-5.42)	.92 (61%)
	Pyelonephritis	6[15,19,26-29]	455	0.19 (0.07-0.51)	<.01 (34%)
	Endometritis	2[26,29]	80	0.76 (0.17-3.44)	.72 (40%)
	Preeclampsia	6[10,14,15,17,26,29]	282	1.01 (0.49-2.08)	.98 (0%)
Fetal	Perinatal mortality	8[10,15,18,19,26-28,30]	1140	0.43 (0.19-0.99)	<.05 (58%)
	Intrauterine fetal demise	8[14,15,17,19,26,28-30]	458	0.47 (0.17-1.33)	.15 (32%)
	Neonatal death	5[15,19,26,28,30]	374	0.26 (0.07-0.93)	.04 (0%)
	Small for gestational age/low birth weight	10[10,15,17-19,26-30]	1187	0.71 (0.44-1.16)	.17 (35%)
	Preterm delivery	9[10,15,17-19,27-30]	1123	0.59 (0.37-0.96)	.03 (38%)

*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

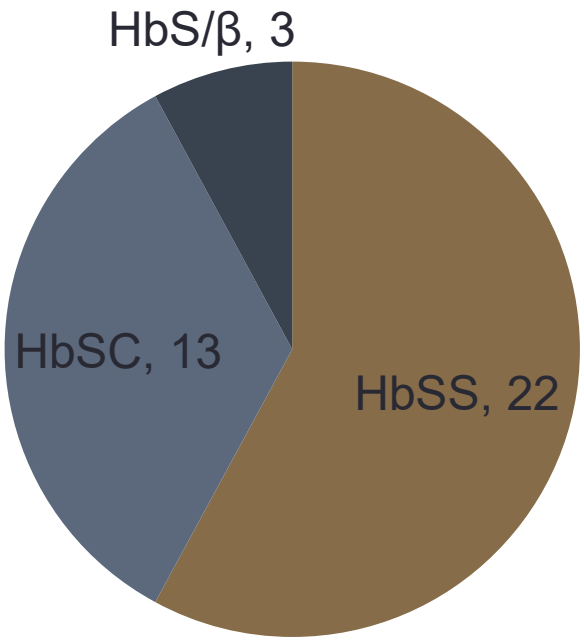
- To observe using standard care approach which patients required transfusions
- If on-demand transfusion affected outcome
- Can we predict women more likely to require transfusions?

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

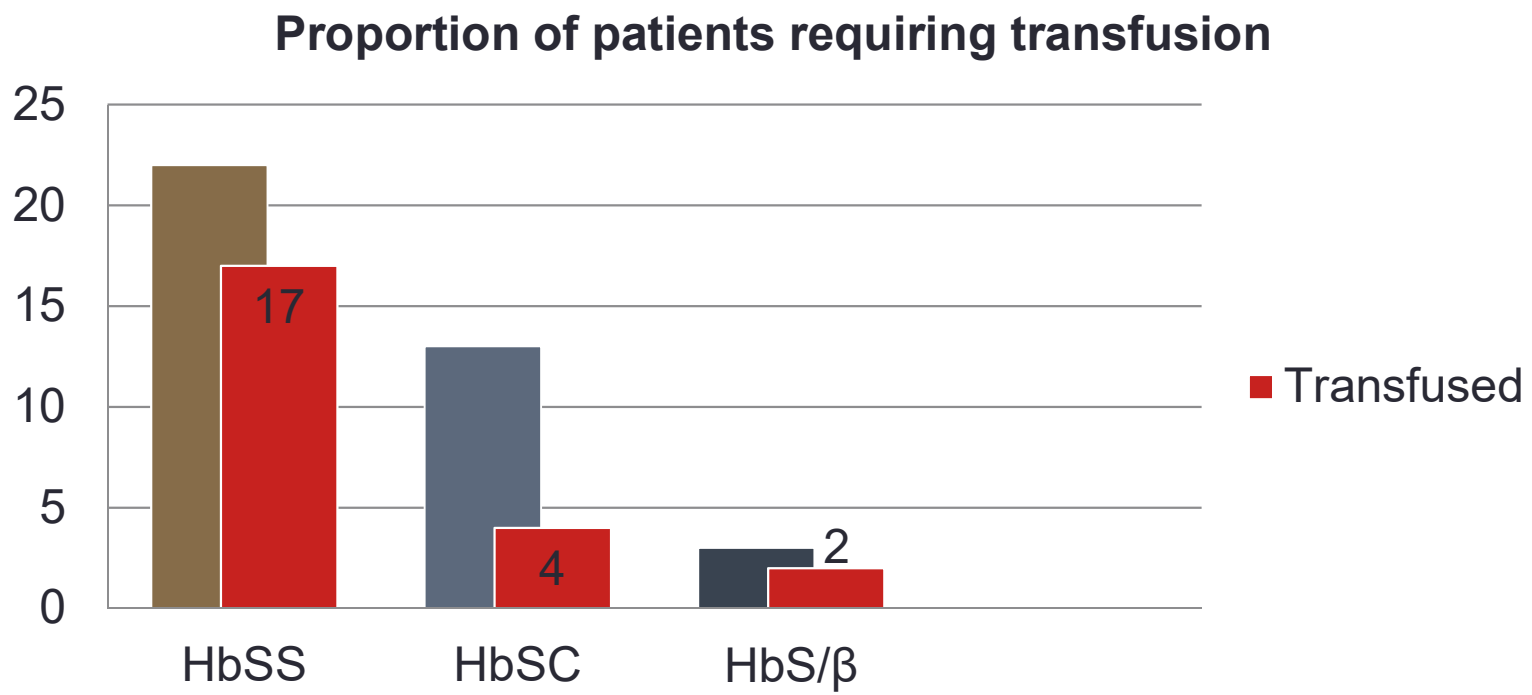
Results

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



Transfusion episodes

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



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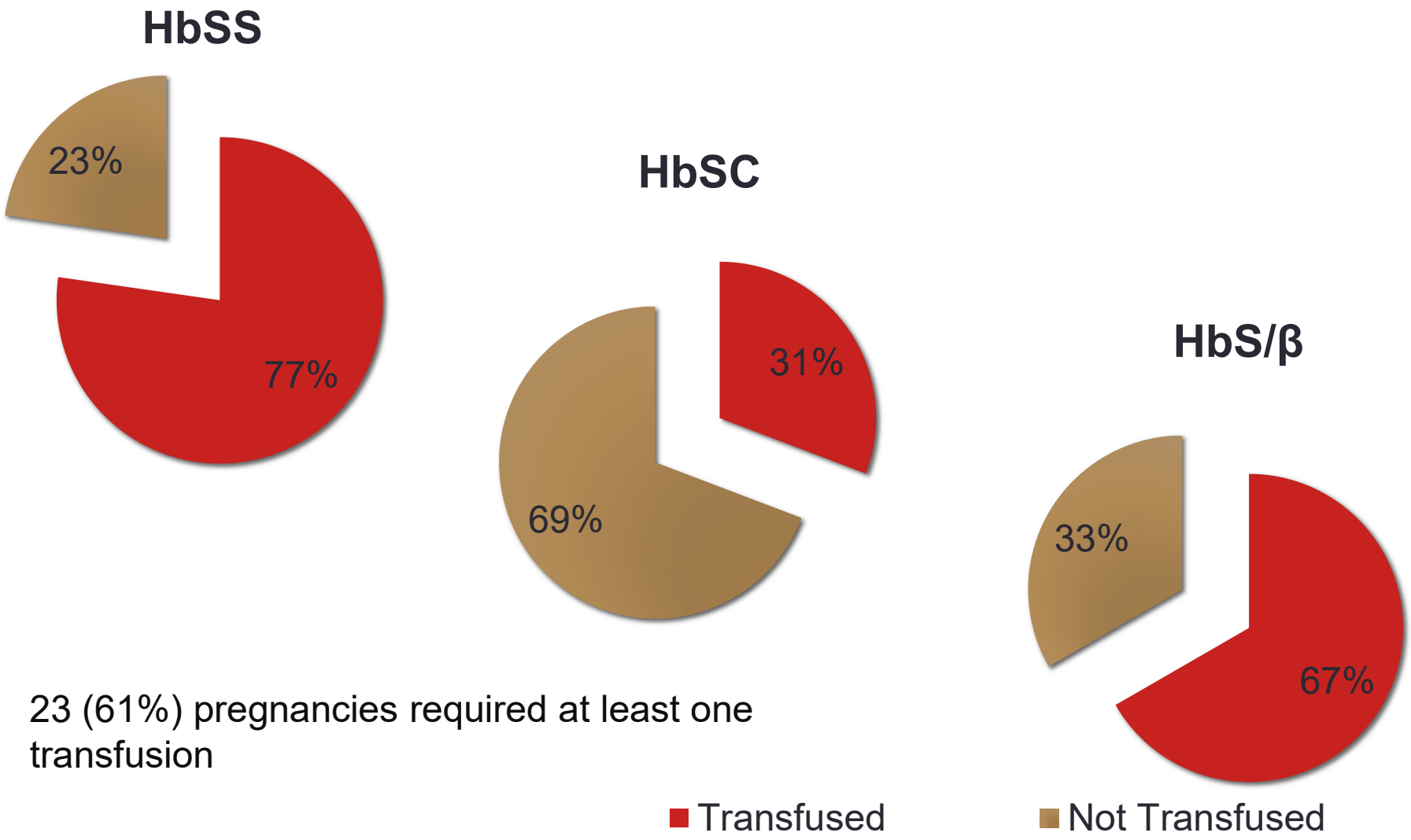

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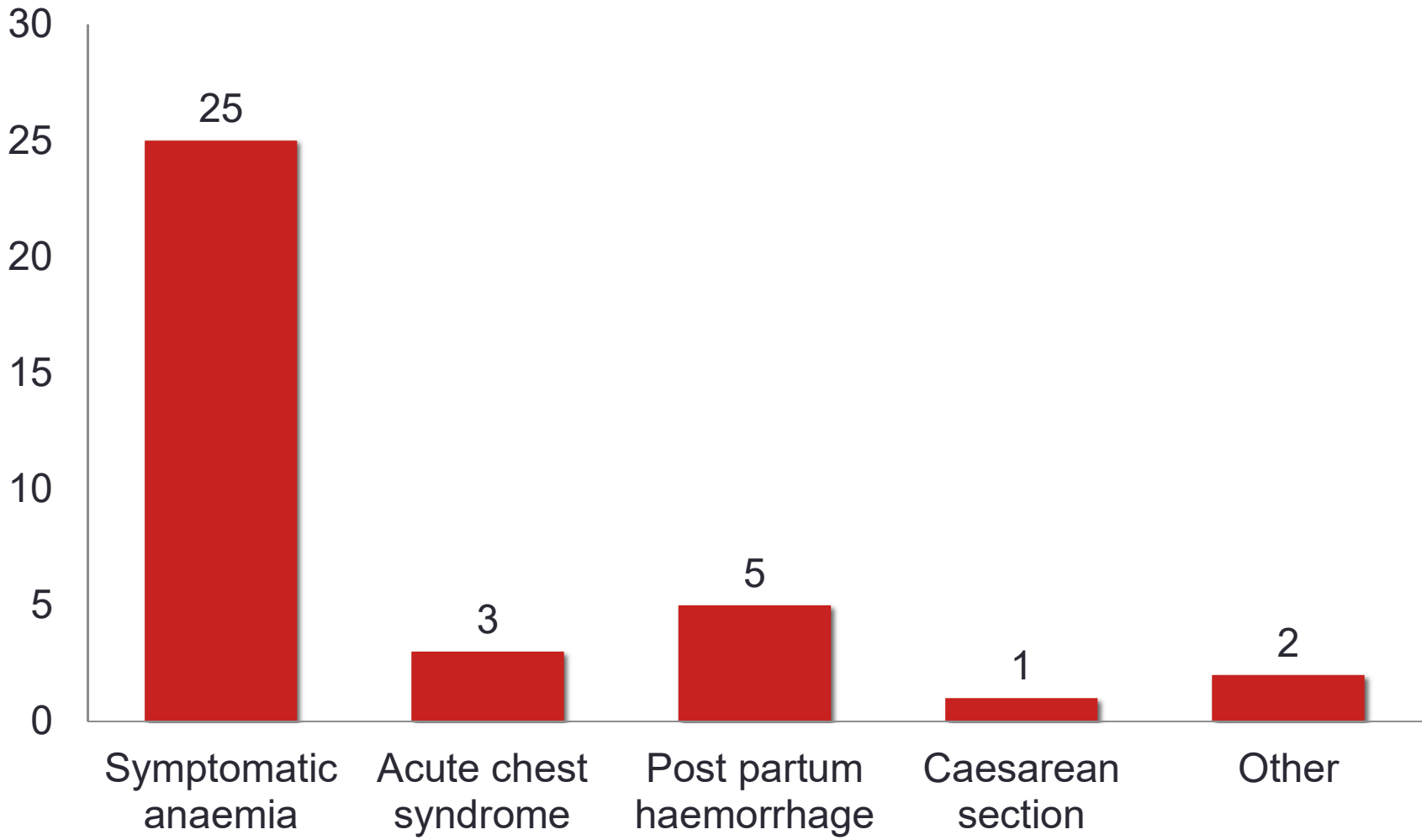
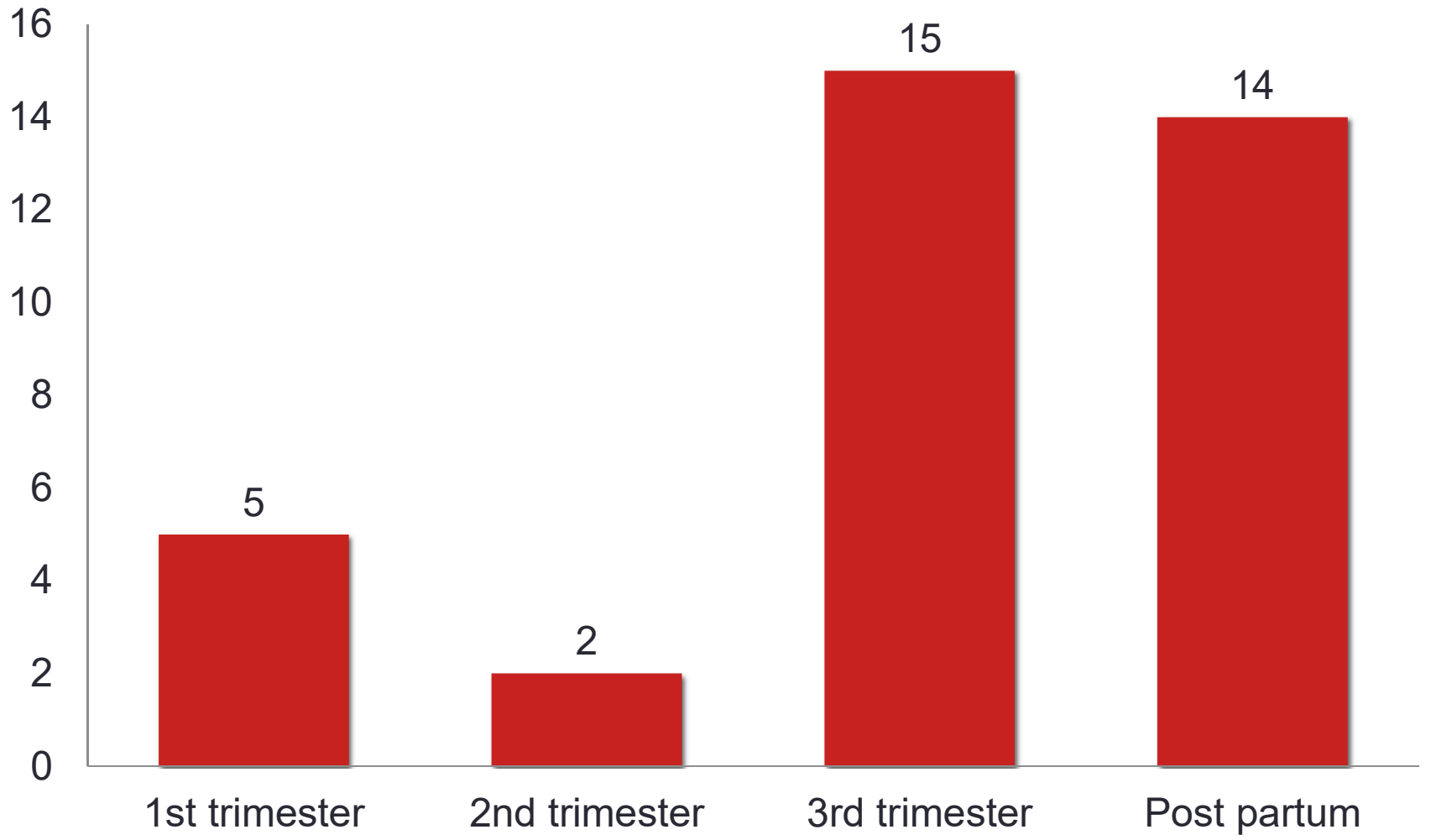
Indications for transfusion



Gestation at time of transfusion



Characteristics of patients requiring transfusion vs. those not transfused

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

*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.